

## Supplementary Online Material

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This supplementary material has been provided by the authors to give readers additional information about their work.

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## 2. Inclusion and Exclusion criteria

The inclusion and exclusion criteria was based on a strategy (Table 1) that identified the population and disease condition, interventions, comparators, outcomes, and study types of interest (also known as the PICOS criteria). The criteria listed in Table 1 were used after the initial, broad searches were completed and after the top-level list of articles (titles and abstracts) was identified.

However, due to the large number of studies included at the level 1 screen, the studies identified as being relevant for the review were re-screened using the more stringent criteria presented in Table 2 (Protocol Amendment). The criteria listed in Table 3 were used at the level 2 screening the full-text articles.

**Table S1** List of criteria for the inclusion and exclusion of studies during the initial screening process (Level 1)

| Criteria      | Included                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Excluded                                                                                                                                                                                                                                                                                                                             |
|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Population    | <ul style="list-style-type: none"> <li>Adult (<math>\geq 18</math> years) patients with moderately to severely active RA (including patients with early and established RA)</li> <li>Treatment-naïve patients</li> <li>Patients who had intolerance or inadequate response to prior conventional DMARDs</li> <li>Patients who had intolerance or inadequate response to previous bDMARDs</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>Juvenile idiopathic arthritis</li> <li>Studies that include only juveniles</li> <li>Patients with mild RA<sup>a</sup>; if the study population is mixed (i.e., mild to severe), exclude those studies in which data are not reported separately for moderate or severely active RA</li> </ul> |
| Interventions | <ul style="list-style-type: none"> <li>Baricitinib (Olumiant)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <ul style="list-style-type: none"> <li>Studies that do not have an intervention of interest in at least 1 arm</li> </ul>                                                                                                                                                                                                             |
| Comparators   | <ul style="list-style-type: none"> <li>Methotrexate (Trexall, Rheumatrex, amethopterin, Rasuvo, Otrexup)</li> <li>Sulfasalazine (Azulfidine, Salazopyrin, Sulazine, sulfazine)</li> <li>Leflunomide (Arabloc, Arava, Lunava, Respo)</li> <li>Hydroxychloroquine (Plaquenil, Axemal, Dolquine, Quensyl, Quineprox)</li> <li>Azathioprine (Azasan, Imuran, Azamun, Imurel)</li> <li>Infliximab (Remicade, Inflectra)</li> <li>Adalimumab (Humira, Trudexa, ABP 501, BI695501, CHS-1420, GP2017, M923, PF-06410293)</li> <li>Certolizumab pegol (Cimzia)</li> <li>Golimumab (Simponi)</li> <li>Etanercept (Enbrel, Avent, BX2922, CHS-0214, ENIA11, Etacept, Etanar, GP2013, GP2015, HD203, LBEC0101, M923, PRX-106, SB4, TuNEX, Yisaipu)</li> <li>Abatacept (Orencia)</li> <li>Anakinra (Kineret)</li> <li>Rituximab (Rituxan, MabThera, Zytux, Reditux)</li> <li>Tocilizumab (Actemra, RoActemra, atlizumab)</li> <li>Sarilumab (Kevzara)</li> <li>Sirukumab (proposed brand name: Plivensia)</li> <li>Tofacitinib (Xeljanz, Jakvinus, tasocitinib)</li> </ul> | <ul style="list-style-type: none"> <li>Studies that do not have a comparator of interest in at least 1 arm</li> <li>Non-pharmacological studies, e.g., exercise, Chinese medicine, etc.</li> </ul>                                                                                                                                   |



| Criteria     | Included                                                                                                                                                                                                                                                                                                                                                                                                   | Excluded                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              | At the level 1 screening, all therapy versions (i.e., any dose or combination) of the interventions listed above will be included                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Study design | <ul style="list-style-type: none"> <li>Randomised, controlled, prospective clinical trials</li> <li>Randomised clinical trials that compare interventions in clinical settings</li> <li>Long-term follow-up studies (e.g., open-label follow-up studies with continuation of treatments in their respective randomised group)</li> <li>Systematic reviews (including meta-analyses)<sup>b</sup></li> </ul> | <ul style="list-style-type: none"> <li>Non-randomised clinical trials</li> <li>Preclinical studies</li> <li>Phase 1 studies</li> <li>Prognostic studies</li> <li>Retrospective studies</li> <li>Prospective observational studies</li> <li>Case reports</li> <li>Commentaries and letters (publication type)</li> <li>Consensus reports</li> <li>Non-systematic reviews</li> <li>Secondary analyses</li> <li>Animal models</li> </ul> |
| Language     | <ul style="list-style-type: none"> <li>All languages</li> </ul>                                                                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>None</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                |
| Date         | <ul style="list-style-type: none"> <li>1999 to present</li> </ul>                                                                                                                                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>None</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                |

bDMARD = biologic disease-modifying antirheumatic drug; DAS-28 = Disease Activity Score in 28 Joints; DMARD = disease-modifying antirheumatic drug; RA = rheumatoid arthritis.

<sup>a</sup> If the disease severity of included patients was not clearly stated in the article, the following approach was used and validated by Lilly: if DAS-28 scores were reported, then DAS-28 scores of > 3.2 were considered to be moderate RA; DAS-28 scores of > 5.1 were considered to be severe RA. If DAS-28 scores were not reported, then swollen and tender joint counts both > 6 was considered to be a good proxy for moderate to severe RA.

<sup>b</sup> Systematic reviews and meta-analyses will be used only for identification of primary studies that may have been missed in the electronic searches.

**Table S2** List of criteria for the inclusion and exclusion of studies during the Level 1b Screening process

| Criteria   | Included                                                                                                                                                                                                                                                                                                                                                                                            | Excluded                                                                                                                                                                                                                                                                                                                                                                         |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Population | <ul style="list-style-type: none"> <li>Adult (<math>\geq 18</math> years) patients with moderately to severely active RA (including patients with early and established RA)</li> <li>Treatment-naïve patients</li> <li>Patients who had intolerance or inadequate response to prior conventional DMARDs</li> <li>Patients who had intolerance or inadequate response to previous bDMARDs</li> </ul> | <ul style="list-style-type: none"> <li>Juvenile idiopathic arthritis</li> <li>Studies that include only juveniles</li> <li>Patients with mild RA<sup>a</sup>; if the study population is mixed (i.e., mild to severe), exclude those studies in which data are not reported separately for moderate or severely active RA</li> <li>Patients with low disease activity</li> </ul> |

| Criteria                      | Included                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Excluded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Interventions and comparators | <ul style="list-style-type: none"> <li>Baricitinib (Olumiant)</li> <li>Methotrexate (Trexall)</li> <li>Sulfasalazine (Azulfidine)</li> <li>Leflunomide (Arabloc)</li> <li>Hydroxychloroquine (Plaquenil)</li> <li>Infliximab (Remicade, Inflectra)</li> <li>Adalimumab (Humira, Trudexa)</li> <li>Certolizumab (Cimzia)</li> <li>Golimumab (Simponi)</li> <li>Etanercept (Enbrel)</li> <li>Abatacept (Orencia)</li> <li>Anakinra (Kineret)</li> <li>Rituximab (Rituxan)</li> <li>Tocilizumab (Actemra, RoActemra)</li> <li>Sarilumab (Kevzara)</li> <li>Sirukumab (proposed brand name: Plivensia)</li> <li>Tofacitinib (Xeljanz, Jakvinus)</li> <li>Placebo</li> </ul> <p>At the level 1 screening, all therapy versions (i.e., any dose or combination) of the interventions listed above will be included</p> | <ul style="list-style-type: none"> <li>Studies that do not have an intervention or comparator of interest in at least 2 of the study arms</li> <li>Non-pharmacological studies, e.g., exercise, Chinese medicine, etc.</li> <li><b>Protocol Amendment:</b> Biosimilars</li> <li><b>Protocol Amendment:</b> Azathioprine (Azasan, Imuran)</li> <li>Studies comparing conventional DMARDs to NSAIDs, glucocorticoids, Diclofenac, etc.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                  |
| Study design                  | <ul style="list-style-type: none"> <li>Phase 3, randomised, controlled, prospective clinical trials</li> <li>Randomised clinical trials that compare interventions in clinical settings</li> <li>Long-term follow-up or extension studies of RCTs where patients remain in their respective randomised group</li> <li>Systematic reviews (including meta-analyses) published in 2014 or 2015<sup>b</sup></li> </ul>                                                                                                                                                                                                                                                                                                                                                                                              | <ul style="list-style-type: none"> <li><b>Protocol Amendment:</b> Phase 2, randomised, controlled, prospective clinical trials</li> <li>Non-randomised clinical trials</li> <li>Single-arm studies</li> <li><b>Protocol Amendment:</b> Long-term follow-up or extension studies of RCTs in which patients do not remain in their respective randomised group</li> <li><b>Protocol Amendment:</b> Maintenance studies and step-down treatment studies</li> <li>Preclinical studies</li> <li>Phase 1 studies</li> <li>Prognostic studies</li> <li>Retrospective studies</li> <li>Prospective observational studies</li> <li>Case reports</li> <li>Commentaries and letters (publication type)</li> <li>Consensus reports</li> <li>Pooled analyses</li> <li><b>Protocol Amendment:</b> Post hoc analyses</li> <li>Non-systematic reviews</li> </ul> |

| Criteria | Included                                                                                                                                                                                                                                         | Excluded                                                                                                                                                                                                                                                                                                                                                                                                |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|          |                                                                                                                                                                                                                                                  | <ul style="list-style-type: none"> <li>▪ <b>Protocol Amendment:</b> Systematic reviews (including meta-analyses) published prior to 2014 <ul style="list-style-type: none"> <li>– Secondary analyses</li> <li>– Animal models</li> </ul> </li> </ul>                                                                                                                                                    |
| Outcomes | <ul style="list-style-type: none"> <li>▪ Studies reporting efficacy and safety data, HRQoL, WPAI-RA, or health care resource utilisation</li> <li>▪ MRI studies that specifically mention the Sharp/Van der Heijde bone erosion score</li> </ul> | <ul style="list-style-type: none"> <li>▪ <b>Protocol Amendment:</b> Studies that report only MRI outcomes and do not specifically mention the Sharp/Van der Heijde bone erosion score</li> <li>▪ <b>Protocol Amendment:</b> Studies that report only bone mineral density</li> <li>▪ <b>Protocol Amendment:</b> Studies that investigate ultrasound and radiography in assessing bone damage</li> </ul> |
| Language | <ul style="list-style-type: none"> <li>▪ English-language publications</li> </ul>                                                                                                                                                                | <ul style="list-style-type: none"> <li>▪ Non-English-language publications</li> </ul>                                                                                                                                                                                                                                                                                                                   |
| Date     | <ul style="list-style-type: none"> <li>▪ 1999 to present</li> </ul>                                                                                                                                                                              | <ul style="list-style-type: none"> <li>▪ None</li> </ul>                                                                                                                                                                                                                                                                                                                                                |

bDMARD = biologic disease-modifying antirheumatic drug; DAS-28 = Disease Activity Score in 28 Joints; DMARD = disease-modifying antirheumatic drug; HRQoL = health-related quality of life; MRI = magnetic resonance imaging; NSAID = non-steroidal anti-inflammatory drug; RA = rheumatoid arthritis; RCT = randomised, controlled trial; WPAI-RA = Work Productivity and Activity Impairment Questionnaire–Rheumatoid Arthritis.

<sup>a</sup> If the disease severity of included patients was not clearly stated in the article, the following approach was used and validated by Lilly: if DAS-28 scores were reported, then DAS-28 scores of > 3.2 were considered to be moderate RA; DAS-28 scores of > 5.1 were considered to be severe RA. If DAS-28 scores were not reported, then swollen and tender joint counts both > 6 was considered to be a good proxy for moderate to severe RA.

<sup>b</sup> Systematic reviews and meta-analyses will be used only for identification of primary studies that may have been missed in the electronic searches.

**Table S3** List of criteria for the inclusion and exclusion of studies during the Full-Text Review Process (Level 2)

| Criteria              | Included                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Excluded                                                          |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| Population            | <ul style="list-style-type: none"> <li>Same as Table 2</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Same as Table 2</li> </ul> |
| Interventions         | <ul style="list-style-type: none"> <li>Interventions listed in Table 2 that meet the following criteria: <ul style="list-style-type: none"> <li>Licensed treatments at the labelled doses</li> <li>Treatments not yet licensed in any form or dose</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>Same as Table 2</li> </ul> |
| Comparators           | <ul style="list-style-type: none"> <li>Same as Table 2</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Same as Table 2</li> </ul> |
| Outcomes <sup>a</sup> | <p>To be included in the review, a study must report at least 1 of the outcomes of interest.</p> <ul style="list-style-type: none"> <li>Efficacy measurements: <ul style="list-style-type: none"> <li>ACR criteria</li> <li>ACR score</li> <li>Proportion of patients achieving an ACR 20 response</li> <li>Proportion of patients achieving an ACR 50 response</li> <li>Proportion of patients achieving an ACR 70 response</li> <li>ACR remission</li> <li>Proportion of patients achieving an ACR 50 response in the subgroup of patients who are TNF<math>\alpha</math> inhibitor naïve, have inadequate response to TNF<math>\alpha</math> or other biologics, or who are intolerant to TNF<math>\alpha</math> or other biologics (if reported)</li> <li>Proportion of patients achieving an ACR 20 response in the subgroup of patients who are TNF<math>\alpha</math> inhibitor naïve, have inadequate response to TNF<math>\alpha</math> or other biologics or who are intolerant to TNF<math>\alpha</math> or other biologics (if reported)</li> <li>Individual components of the ACR: <ul style="list-style-type: none"> <li>HAQ-DI</li> <li>Pain VAS</li> <li>Tender joint count</li> <li>Swollen joint count</li> <li>Physician global assessment</li> <li>Patient global assessment</li> <li>Modified Sharp score</li> <li>Erosion score</li> <li>Joint space narrowing score</li> <li>DAS-28 ESR for RA</li> <li>DAS-28 CRP for RA</li> <li>SDAI</li> <li>CDAI</li> <li>Physical function assessed by HAQ or HAQ-DI</li> </ul> </li> </ul> </li> <li>Endpoints measuring the following: <ul style="list-style-type: none"> <li>Morning joint stiffness and/or joint pain (severity and duration) (may be assessed by different instruments)</li> <li>Tiredness or fatigue (may be assessed by different instruments)</li> </ul> </li> <li>EULAR or ACR remission defined as: <ul style="list-style-type: none"> <li>CDAI score <math>\leq 2.8</math></li> <li>SDAI score <math>\leq 3.3</math></li> <li>DAS-28 <math>&lt; 2.6</math></li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>None</li> </ul>            |

| Criteria     | Included                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Excluded                                                                                                            |
|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
|              | <ul style="list-style-type: none"> <li>• RAPID3 <math>\leq 1</math></li> <li>• DAS-44 <math>&lt; 1.6</math></li> <li>• Boolean definition of remission (EULAR or ACR where all measures must be <math>&lt; 1</math>)</li> <li>• WPAI-RA</li> <li>• Health care resource utilisation</li> </ul> <ul style="list-style-type: none"> <li>▪ HRQoL outcomes from the following: <ul style="list-style-type: none"> <li>– EQ-5D</li> <li>– SF-36</li> </ul> </li> </ul> <p>Safety outcomes reported at study endpoint:</p> <ul style="list-style-type: none"> <li>▪ Overall rate of AEs</li> <li>▪ Overall rate of serious AEs</li> <li>▪ Discontinuations due to <ul style="list-style-type: none"> <li>– Lack of efficacy</li> <li>– AEs</li> </ul> </li> <li>▪ Individual AEs, such as the following: <ul style="list-style-type: none"> <li>– Specific myelosuppressive events, e.g., anaemia, leukopaenia, neutropaenia, or thrombocytopaenia or lymphopaenia or lymphocytopenia</li> <li>– Thrombocytosis</li> <li>– Serious infections</li> <li>– Opportunistic infections</li> <li>– Malignancies</li> <li>– Cardiovascular events</li> <li>– Elevations in ALT or AST (<math>&gt; 3</math> times upper limit of normal) with total bilirubin (<math>&gt; 2</math> times upper limit of normal)</li> <li>– Injection-related combinations</li> <li>– Intravenous reactions</li> </ul> </li> <li>▪ Death</li> <li>▪ Initial or prolonged inpatient hospitalisation</li> </ul> |                                                                                                                     |
| Study design | <ul style="list-style-type: none"> <li>▪ Randomised, controlled, prospective clinical trials</li> <li>▪ Randomised clinical trials that compare interventions in clinical settings</li> <li>▪ Long-term follow-up studies (e.g., open-label follow-up studies if patients continued in the group to which they were randomised)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>▪ Same as Table 2</li> <li>▪ Systematic reviews and meta-analyses</li> </ul> |
| Language     | <ul style="list-style-type: none"> <li>▪ English-language and German-language publications</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>▪ Other non-English-language publications</li> </ul>                         |
| Date         | <ul style="list-style-type: none"> <li>▪ 1999 to present</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>▪ None</li> </ul>                                                            |

ACR = American College of Rheumatology; AE = adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CDAI = Clinical Disease Activity Index; CRP = C-reactive protein; DAS-28 = Disease Activity Score in 28 Joints; DAS-44 = Disease Activity Score in 44 Joints; ESR = erythrocyte sedimentation rate; EULAR = European League Against Rheumatism; HAQ = Health Assessment Questionnaire; HAQ-DI = Health Assessment Questionnaire–Disability Index; HRQoL = health-related quality of life; RA = rheumatoid arthritis; RAPID3 = Routine Assessment of Patient Index Data 3; SDAI = Simplified Disease Activity Index; SF-36 = SF-36 Health Survey; TNF $\alpha$  = tumour necrosis factor alpha; VAS = visual analogue scale; WPAI-RA = Work Productivity and Activity Impairment Questionnaire–Rheumatoid Arthritis.

<sup>a</sup> Time points of interest include 12, 24, and 52 weeks. If any of these specific time points are not available, we will collect data at the following time points: 12 weeks  $\pm$  2 weeks, 24 weeks  $\pm$  4 weeks, and 52 weeks  $\pm$  8 weeks.

### 3. Search Terms

**Table S4** Embase search strategy (Search Conducted on 11 December 2017)

| Search No.                        | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Results |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| <b>Population and/or patients</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |
| #1                                | 'rheumatoid arthritis'/exp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 187,860 |
| #2                                | (rheumatoid:ti,ab,de OR reumatoid:ti,ab,de) AND (arthrit*:ti,ab,de OR disease*:ti,ab,de)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 209,600 |
| #3                                | #1 OR #2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 211,674 |
| <b>Intervention</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |
| #4                                | 'baricitinib'/exp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 410     |
| #5                                | baricitinib:ti,ab,de,tn OR olumiant:ti,ab,de,tn                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 413     |
| #6                                | #4 OR #5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 413     |
| <b>Comparator: cDMARDs</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |
| #7                                | 'methotrexate'/exp OR 'salazosulapyridine'/exp OR 'leflunomide'/exp OR 'hydroxychloroquine'/exp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 184,376 |
| #8                                | Methotrexate:ti,ab,de,tn OR MTX:ti,ab,de,tn OR rheumatrex:ti,ab,de,tn OR amethopterin:ti,ab,de,tn OR 'methotrexate sodium':ti,ab,de,tn OR rasuvo:ti,ab,de,tn OR trexall:ti,ab,de,tn OR otrexup:ti,ab,de,tn OR sulfasalazine:ti,ab,de,tn OR azulfidine:ti,ab,de,tn OR salazopyrin:ti,ab,de,tn OR sulazine:ti,ab,de,tn OR sulfazine:ti,ab,de,tn OR leflunomide:ti,ab,de,tn OR arabloc:ti,ab,de,tn OR arava:ti,ab,de,tn OR lunava:ti,ab,de,tn OR repso:ti,ab,de,tn OR hydroxychloroquine:ti,ab,de,tn OR plaquenil:ti,ab,de,tn OR axemal:ti,ab,de,tn OR dolquine:ti,ab,de,tn OR quensyl:ti,ab,de,tn OR quineprox:ti,ab,de,tn | 183,171 |
| #9                                | #7 OR #8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 191,491 |
| <b>Comparator: bDMARDs</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |
| #10                               | 'infliximab'/exp OR 'adalimumab'/exp OR 'certolizumab pegol'/exp OR 'golimumab'/exp OR 'etanercept'/exp OR 'abatacept'/exp OR 'recombinant interleukin 1 receptor blocking agent'/exp OR 'rituximab'/exp OR 'tocilizumab'/exp OR 'sarilumab'/exp OR 'sirukumab'/exp OR 'tofacitinib'/exp                                                                                                                                                                                                                                                                                                                                 | 124,151 |

| Search No.                                | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Results   |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| #11                                       | infliximab:ti,ab,de,tn OR remicade:ti,ab,de,tn OR 'monoclonal antibody cA2':ti,ab,de,tn OR 'MAb cA2':ti,ab,de,tn OR 'CT-P13':ti,ab,de,tn OR Remsima:ti,ab,de,tn OR Inflectra:ti,ab,de,tn OR adalimumab:ti,ab,de,tn OR humira:ti,ab,de,tn OR trudexa:ti,ab,de,tn OR '331731-18-1':ti,ab,de,tn,rn OR 'D2E7 antibody':ti,ab,de,tn OR LU200134:ti,ab,de,tn OR 'ABP 501':ti,ab,de,tn OR BI695501:ti,ab,de,tn OR M923:ti,ab,de,tn OR 'PF-06410293':ti,ab,de,tn OR GP2017:ti,ab,de,tn OR 'CHS-1420':ti,ab,de,tn OR certolizumab:ti,ab,de,tn OR 'certolizumab pegol':ti,ab,de,tn OR cimzia:ti,ab,de,tn OR golimumab:ti,ab,de,tn OR simponi:ti,ab,de,tn OR 'TNFR-Fc fusion protein':ti,ab,de,tn OR etanercept:ti,ab,de,tn OR enbrel:ti,ab,de,tn OR Avent:ti,ab,de,tn OR BX2922:ti,ab,de,tn OR 'CHS-0214':ti,ab,de,tn OR ENIA11:ti,ab,de,tn OR Etacept:ti,ab,de,tn OR Etanar:ti,ab,de,tn OR GP2013:ti,ab,de,tn OR GP2015:ti,ab,de,tn OR HD203:ti,ab,de,tn OR LBEC0101:ti,ab,de,tn OR M923:ti,ab,de,tn OR 'PRX-106':ti,ab,de,tn OR SB4:ti,ab,de,tn OR TuNEX:ti,ab,de,tn OR Yisaipu:ti,ab,de,tn OR abatacept:ti,ab,de,tn OR orenicia:ti,ab,de,tn OR anakinra:ti,ab,de,tn OR kineret:ti,ab,de,tn OR rituximab:ti,ab,de,tn OR rituxan:ti,ab,de,tn OR mabthera:ti,ab,de,tn OR zytux:ti,ab,de,tn OR rexitux:ti,ab,de,tn OR tocilizumab:ti,ab,de,tn OR atlizumab:ti,ab,de,tn OR actemra:ti,ab,de,tn OR roactemra:ti,ab,de,tn OR sarilumab:ti,ab,de,tn OR sirukumab:ti,ab,de,tn OR tofacitinib:ti,ab,de,tn OR tasocitinib:ti,ab,de,tn OR xeljanz:ti,ab,de,tn OR jakvinus:ti,ab,de,tn OR kevzara:ti,ab,de,tn OR plivensia:ti,ab,de,tn | 127,327   |
| #12                                       | #10 OR #11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 127,327   |
| <b>All interventions and comparators</b>  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |
| #13                                       | #6 OR #9 OR #12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 283,407   |
| <b>Study type (RCTs)</b>                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |
| #14                                       | 'randomized controlled trial (topic)'/exp OR 'phase 3 clinical trial (topic)'/exp OR 'phase 2 clinical trial (topic)'/exp OR 'controlled clinical trial (topic)'/exp OR 'randomization'/exp OR 'clinical trial (topic)'/de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 311,082   |
| #15                                       | 'randomized controlled trial'/exp OR 'controlled clinical trial'/exp OR 'phase 2 clinical trial'/exp OR 'phase 3 clinical trial'/exp OR 'phase 4 clinical trial'/exp OR 'multicenter study'/exp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 762,802   |
| #16                                       | Randomized:ti,ab OR randomised:ti,ab OR randomly:ti,ab                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1,000,302 |
| #17                                       | ('randomized controlled' NEXT/1 trial*):ti,ab,de OR ('randomised controlled' NEXT/1 trial*):ti,ab,de OR ('randomized clinical' NEXT/1 trial*):ti,ab,de OR ('randomised clinical' NEXT/1 trial*):ti,ab,de OR (randomized NEXT/1 trial*):ti,ab,de OR (randomised NEXT/1 trial*):ti,ab,de OR 'random allocation':ti,ab,de OR 'double blind method':ti,ab,de OR 'single blind method':ti,ab,de OR ((singl*:ti,ab,de OR doubl*:ti,ab,de OR treb*:ti,ab,de OR tripl*:ti,ab,de) AND (blind*:ti,ab,de OR mask*:ti,ab,de)) OR (allocated NEXT/1 random*):ti,ab,de OR (random NEXT/1 assignment*):ti,ab,de OR (open-label NEXT/1 trial*):ti,ab,de OR (open-label NEXT/1 stud*):ti,ab,de OR 'open label trial':ti,ab,de OR ('non-blinded' NEXT/1 stud*):ti,ab,de                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 871,158   |
| #18                                       | #14 OR #15 OR #16 OR #17                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 1,630,752 |
| <b>Exclusion terms, excluding animals</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |
| #19                                       | 'animal'/exp NOT 'human'/exp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 4,953,190 |
| <b>Exclusion terms, by study type</b>     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |

| Search No.                         | Terms                                                                                                                     | Results   |
|------------------------------------|---------------------------------------------------------------------------------------------------------------------------|-----------|
| #20                                | Comment*:ti OR Letter:it OR Editorial:it OR 'case report'/exp OR 'phase 1 clinical trial'/exp                             | 3,732,046 |
| #21                                | 'case study':ti OR 'case studies':ti OR 'case report':ti OR 'case reports':ti OR 'case series':ti                         | 334,134   |
| #22                                | #20 OR #21                                                                                                                | 3,804,477 |
| <b>Exclusion terms, population</b> |                                                                                                                           |           |
| #23                                | 'juvenile rheumatoid arthritis'/exp                                                                                       | 18,670    |
| #24                                | 'juvenile idiopathic arthritis':ti,ab,de OR (juvenile:ti,ab,de AND arthritis:ti,ab,de)                                    | 21,044    |
| #25                                | #23 OR #24                                                                                                                | 21,044    |
| <b>All relevant studies</b>        |                                                                                                                           |           |
| #26                                | #3 AND #13 AND #18                                                                                                        | 9,180     |
| #27                                | #26 NOT (#19 OR #22 OR #25)                                                                                               | 7,676     |
| <b>Limits</b>                      |                                                                                                                           |           |
| #28                                | #27 AND [1-5-2016]/sd NOT [11-12-2017]/sd AND [2016-2017]/py Filters applied:<br>Dates limited from 2015/03/01 to present | 1,387     |

bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug;

RCT = randomised, controlled trial.



**Table S5** Cochrane search strategy (Search Conducted on 11 December 2017)

| Search No.                               | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Results |
|------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| <b>Population and/or patients</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |
| #1                                       | #1 MeSH descriptor: [Arthritis, Rheumatoid] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 4,811   |
| #2                                       | #2 (rheumatoid or reumatoid) and (arthrit* or disease*) (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 10,547  |
| #3                                       | #1 OR #2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 10,724  |
| <b>Intervention</b>                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |
| #4                                       | baricitinib:kw (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 108     |
| #5                                       | Baricitinib OR olumiant (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 115     |
| #6                                       | #4 OR #5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 115     |
| <b>Comparator: cDMARDs</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |
| #7                                       | methotrexate OR sulfasalazine OR leflunomide OR hydroxychloroquine:kw (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 7,468   |
| #8                                       | methotrexate OR MTX OR rheumatrex OR amethopterin OR "methotrexate sodium" OR rasuvo OR trexall OR otrexup OR sulfasalazine OR azulfidine OR salazopyrin OR sulazine OR sulfazine OR leflunomide OR arabloc OR arava OR lunava OR repso OR hydroxychloroquine OR plaquenil OR axemal OR dolquine OR quensyl OR quineprox (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 9,745   |
| #9                                       | #7 OR #8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 9,745   |
| <b>Comparator: bDMARDs</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |
| #10                                      | infliximab OR adalimumab OR "certolizumab pegol" OR golimumab OR "TNFR-Fc fusion protein" OR abatacept OR anakinra OR rituximab OR tocilizumab OR atlizumab OR sarilumab OR sirukumab OR tofacitinib OR tasocitinib:kw (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 5,461   |
| #11                                      | infliximab OR remicade OR "monoclonal antibody cA2" OR "MAb cA2" OR "CT-P13" OR Remsima OR Inflectra OR adalimumab OR humira OR trudexa OR "331731-18-1" OR "D2E7 antibody" OR LU200134 OR "ABP 501" OR BI695501 OR M923 OR "PF-06410293" OR GP2017 OR "CHS-1420" OR certolizumab OR "certolizumab pegol" OR cimzia OR golimumab OR simponi OR "TNFR-Fc fusion protein" OR etanercept OR enbrel OR Avent OR BX2922 OR "CHS-0214" OR ENIA11 OR Etacept OR Etanar OR GP2013 OR GP2015 OR HD203 OR LBEC0101 OR M923 OR "PRX-106" OR SB4 OR TuNEX OR Yisaipu OR abatacept OR orenicia OR anakinra OR kineret OR rituximab OR rituxan OR mabthera OR zytux OR reditux OR tocilizumab OR atlizumab OR actemra OR roactemra OR sarilumab OR sirukumab OR tofacitinib OR tasocitinib OR xeljanz OR jakvinus OR kevozara OR plivensia (Word variations have been searched) | 8,062   |
| #12                                      | #10 OR #11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 8,062   |
| <b>All interventions and comparators</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |
| #13                                      | #6 OR #9 OR #12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 15,525  |
| <b>Study type (RCTs)</b>                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |
| #14                                      | MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 22,828  |
| #15                                      | MeSH descriptor: [Clinical Trials, Phase III as Topic] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 311     |
| #16                                      | MeSH descriptor: [Clinical Trials, Phase II as Topic] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 178     |

| Search No.                                | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Results |
|-------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| #17                                       | MeSH descriptor: [Controlled Clinical Trials as Topic] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 23,205  |
| #18                                       | MeSH descriptor: [Random Allocation] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 20,636  |
| #19                                       | MeSH descriptor: [Clinical Trials as Topic] this term only                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 57,778  |
| #20                                       | #14 or #15 or #16 or #17 or #18 or #19                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 67,695  |
| #21                                       | "Randomized Controlled Trial" OR "Controlled Clinical Trial" OR "Clinical Trial Phase II" OR "Clinical Trial Phase III" OR "Clinical Trial Phase IV" OR "Multicenter Study":pt (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                   | 521,085 |
| #22                                       | randomized or randomised or randomly:ti,ab,kw (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 624,981 |
| #23                                       | "randomized controlled" NEXT trial* OR "randomised controlled" NEXT trial* OR "randomized clinical" NEXT trial* OR "randomised clinical" NEXT trial* OR randomized NEXT trial* OR randomised NEXT trial* OR "random allocation" OR "double blind method" OR "single blind method" OR ((singl* OR doubl* OR treb* OR tripl*) AND (blind* OR mask*)) OR allocated NEXT random* OR random NEXT assignment* OR "open-label" NEXT trial* OR "open-label" NEXT stud* OR "open label trial" OR "non-blinded" NEXT stud* (Word variations have been searched) | 723,579 |
| #24                                       | #20 OR #21 OR #22 OR #23                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 855,024 |
| <b>Exclusion terms, excluding animals</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |
| #25                                       | MeSH descriptor: [Animals] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 8,407   |
| #26                                       | MeSH descriptor: [Humans] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 1,621   |
| #27                                       | #25 not #26                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 6,786   |
| <b>Exclusion terms, by study type</b>     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |
| #28                                       | Comment OR Letter OR Editorial OR "Case Reports" OR "Clinical Trial Phase I":pt (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                  | 14,382  |
| #29                                       | "case study" OR "case studies" OR "case report" OR "case reports" OR "case series":ti (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                            | 1,284   |
| #30                                       | #28 OR #29                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 15,573  |
| <b>Exclusion terms, population</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |
| #31                                       | MeSH descriptor: [Arthritis, Juvenile] explode all trees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 219     |
| #32                                       | "juvenile idiopathic arthritis" OR (juvenile AND arthritis) (Word variations have been searched)                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 687     |
| #33                                       | #31 OR #32                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 687     |
| <b>All relevant studies</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |
| #34                                       | #3 AND #13 AND #24                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 3,508   |
| #35                                       | #34 NOT (#27 OR #30 OR #33)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 3,266   |
| <b>Limits</b>                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |
| #36                                       | #35 AND Publication date from 2016/05/01 Filters applied: Dates limited from 2016/05/01 to present                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 528     |

bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug;

MeSH = Medical Subject Heading; RCT = randomized, controlled trial.

**Table S6** Biosis search strategy (Search Conducted on 11 December 2017)

| Search No.                               | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Results |
|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| <b>Population and/or patients</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |
| #1                                       | su("Arthritis Rheumatoid" OR "Rheumatoid Arthritis")                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 66,744  |
| #2                                       | ti,ab,su(rheumatoid OR reumatoid) AND ti,ab,su(arthrit* OR disease*)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 112,321 |
| #3                                       | #1 OR #2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 112,321 |
| <b>Intervention</b>                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |
| #4                                       | subst(baricitinib)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 41      |
| #5                                       | ti,ab,su,subst(baricitinib OR Olumiant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 92      |
| #6                                       | #4 OR #5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 92      |
| <b>Comparator: cDMARDs</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |
| #7                                       | subst(methotrexate OR sulfasalazine OR leflunomide OR hydroxychloroquine)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 52,703  |
| #8                                       | ti,ab,su,subst(methotrexate OR MTX OR rheumatrex OR amethopterin OR "methotrexate sodium" OR rasuvo OR trexall OR otrexup OR sulfasalazine OR azulfidine OR salazopyrin OR sulazine OR sulfazine OR leflunomide OR arabloc OR arava OR lunava OR repso OR hydroxychloroquine OR plaquenil OR axemal OR dolquine OR quensyl OR quineprox)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 60,760  |
| #9                                       | #7 OR #8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 60,760  |
| <b>Comparator: bDMARDs</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |
| #10                                      | subst(infliximab OR adalimumab OR "certolizumab pegol" OR golimumab OR "TNFR-Fc fusion protein" OR abatacept OR anakinra OR rituximab OR tocilizumab OR atlizumab OR sarilumab OR sirukumab OR tofacitinib OR tasocitinib)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 34,213  |
| #11                                      | ti,ab,su,subst(infliximab OR remicade OR "monoclonal antibody cA2" OR "MAb cA2" OR "CT-P13" OR Remsima OR Inflectra OR adalimumab OR humira OR trudexa OR "331731-18-1" OR "D2E7 antibody" OR LU200134 OR "ABP 501" OR BI695501 OR M923 OR "PF-06410293" OR GP2017 OR "CHS-1420" OR certolizumab OR "certolizumab pegol" OR cimzia OR golimumab OR simponi OR "TNFR-Fc fusion protein" OR etanercept OR enbrel OR Avent OR BX2922 OR "CHS-0214" OR ENIA11 OR Etacept OR Etanar OR GP2013 OR GP2015 OR HD203 OR LBEC0101 OR M923 OR "PRX-106" OR SB4 OR TuNEX OR Yisaipu OR abatacept OR orenicia OR anakinra OR kineret OR rituximab OR rituxan OR mabthera OR zytux OR reditux OR tocilizumab OR atlizumab OR actemra OR roactemra OR sarilumab OR Kevzara OR sirukumab OR Plivensia OR tofacitinib OR tasocitinib OR xeljanz OR jakvinus) OR rn("331731-18-1") | 41,237  |
| #12                                      | #10 OR #11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 41,237  |
| <b>All interventions and comparators</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |
| #13                                      | #6 OR #9 OR #12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 95,539  |
| <b>Study type (RCTs)</b>                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |
| #14                                      | su("Randomized Controlled Trials" OR "Randomized Controlled Trial" OR "Clinical Trials Phase III" OR "Clinical Trials Phase II" OR "Controlled Clinical Trials" OR "Controlled Clinical Trial" OR "Random Allocation" OR "Clinical Trials" OR "Clinical Trial") OR ti,su(randomized AND trial*) OR ti,su("phase 3" AND trial) OR ti,su("phase III" AND trial*) OR ti,su("phase 2" AND trial*) OR ti,su("phase II" AND trial*)                                                                                                                                                                                                                                                                                                                                                                                                                                    | 122,361 |

| Search No.                                | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Results   |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| #15                                       | dtype,su("Randomized Controlled Trial" OR "Controlled Clinical Trial" OR "Clinical Trial Phase II" OR "Clinical Trial Phase III" OR "Clinical Trial Phase IV" OR "Multicenter Study") OR ti,su("phase IV" AND trial*) OR ti,su("phase 4" AND trial*)                                                                                                                                                                                                                                                            | 6,035     |
| #16                                       | ti,ab(randomized OR randomised OR randomly)                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 463,144   |
| #17                                       | ti,ab,su("randomized controlled" P/0 trial* OR "randomised controlled" P/0 trial* OR "randomized clinical" P/0 trial* OR "randomised clinical" P/0 trial* OR randomized P/0 trial* OR randomised P/0 trial* OR "random allocation" OR "double blind method" OR "single blind method" OR ((singl* OR doubl* OR treb* OR tripl*) AND (blind* OR mask*)) OR allocated P/0 random* OR random P/0 assignment* OR "open-label" P/0 trial* OR "open-label" P/0 stud* OR "open label trial" OR "non-blinded" P/0 stud*) | 224,591   |
| #18                                       | #14 OR #15 OR #16 OR #17                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 553,952   |
| <b>Exclusion terms, excluding animals</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |           |
| #19                                       | su(animal) NOT su(human)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 8,620,434 |
| <b>Exclusion terms, by study type</b>     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |           |
| #20                                       | dtype(Comment* OR Letter OR Editorial) OR su("Case Report" OR "Case Reports" OR "Clinical Trial Phase I") OR ti,su("phase 1" AND trial*) OR ti,su("phase I" AND trial*)                                                                                                                                                                                                                                                                                                                                         | 209,404   |
| #21                                       | ti("case study" OR "case studies" OR "case report" OR "case reports" OR "case series")                                                                                                                                                                                                                                                                                                                                                                                                                          | 119,743   |
| #22                                       | #20 OR #21                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 327,949   |
| <b>Exclusion terms, population</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |           |
| #23                                       | su("Arthritis Juvenile" OR "Juvenile Arthritis")                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 4,822     |
| #24                                       | ti,ab,su("juvenile idiopathic arthritis") OR ti,ab,su(juvenile AND arthritis)                                                                                                                                                                                                                                                                                                                                                                                                                                   | 9,387     |
| #25                                       | #23 OR #24                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 9,387     |
| <b>All relevant studies</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |           |
| #26                                       | #3 AND #13 AND #18                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1,984     |
| #27                                       | #26 NOT (#19 OR #22 OR #25)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1,842     |
| #28                                       | #27 AND Filters applied: Dates limited from 1 May 2016 to present                                                                                                                                                                                                                                                                                                                                                                                                                                               | 180       |

bDMARD = biologic disease-modifying antirheumatic drug; BIOSIS = BioSciences Information Service of Biological Abstracts;

cDMARD = conventional disease-modifying antirheumatic drug; RCT = randomized, controlled trial.

**Table S7** Medline search strategy (Search Conducted on 11 December 2017)

| Search No.                        | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Results |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| <b>Population and/or patients</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |
| #1                                | "Arthritis, Rheumatoid"[MeSH]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 103,822 |
| #2                                | (rheumatoid OR reumatoid) AND (arthrit* OR disease*)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 127,239 |
| #3                                | #1 OR #2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 138,472 |
| <b>Intervention</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |
| #4                                | "baricitinib"[Supplementary Concept]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 29      |
| #5                                | "baricitinib"[All Fields] OR "Olumiant"[All Fields]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 73      |
| #6                                | #4 OR #5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 73      |
| <b>Comparator: cDMARDs</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |
| #7                                | "methotrexate"[Supplementary Concept] OR "sulfasalazine"[Supplementary Concept] OR "leflunomide"[Supplementary Concept] OR "hydroxychloroquine"[Supplementary Concept]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 41,680  |
| #8                                | "Methotrexate"[All Fields] OR "MTX"[All Fields] OR "rheumatrex"[All Fields] OR "amethopterin"[All Fields] OR "methotrexate sodium"[All Fields] OR "rasuvo"[All Fields] OR "trexall"[All Fields] OR "otrexup"[All Fields] OR "sulfasalazine"[All Fields] OR "azulfidine"[All Fields] OR "salazopyrin"[All Fields] OR "sulazine"[All Fields] OR "sulfazine"[All Fields] OR "leflunomide"[All Fields] OR "arabloc"[All Fields] OR "arava"[All Fields] OR "lunava"[All Fields] OR "repso"[All Fields] OR "hydroxychloroquine"[All Fields] OR "plaquenil"[All Fields] OR "axemal"[All Fields] OR "dolquine"[All Fields] OR "quensyl"[All Fields] OR "quineprox"[All Fields] | 59,542  |
| #9                                | #7 OR #8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 56,424  |
| <b>Comparator: bDMARDs</b>        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |
| #10                               | "infliximab"[Supplementary Concept] OR "adalimumab"[Supplementary Concept] OR "certolizumab pegol"[Supplementary Concept] OR "golimumab"[Supplementary Concept] OR "TNFR-Fc fusion protein"[Supplementary Concept] OR "abatacept"[Supplementary Concept] OR "anakinra"[Supplementary Concept] OR "rituximab"[Supplementary Concept] OR "tocilizumab"[Supplementary Concept] OR "atlizumab"[Supplementary Concept] OR "sarilumab"[Supplementary Concept] OR "sirukumab"[Supplementary Concept] OR "tofacitinib"[Supplementary Concept] OR "tasocitinib"[Supplementary Concept]                                                                                          | 25,980  |

| Search No.                               | Terms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Results   |
|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| #11                                      | "infliximab"[All Fields] OR "remicade"[All Fields] OR "monoclonal antibody cA2"[All Fields] OR "Mab cA2"[All Fields] OR "CT-P13"[All Fields] OR "Remsima"[All Fields] OR "Inflectra"[All Fields] OR "adalimumab"[All Fields] OR "humira"[All Fields] OR trudexa[All Fields] OR "331731-18-1"[All Fields] OR "D2E7 antibody"[All Fields] OR "LU200134"[All Fields] OR "ABP 501"[All Fields] OR "BI695501"[All Fields] OR "M923"[All Fields] OR "PF-06410293"[All Fields] OR "GP2017"[All Fields] OR "CHS-1420"[All Fields] OR "certolizumab"[All Fields] OR "certolizumab pegol"[All Fields] OR "cimzia"[All Fields] OR "golimumab"[All Fields] OR "simponi"[All Fields] OR "TNFR-Fc fusion protein"[All Fields] OR "etanercept"[All Fields] OR "enbrel"[All Fields] OR Avent[All Fields] OR "BX2922"[All Fields] OR "CHS-0214"[All Fields] OR "ENIA11"[All Fields] OR "Etacept"[All Fields] OR "Etanar"[All Fields] OR "GP2013"[All Fields] OR "GP2015"[All Fields] OR "HD203"[All Fields] OR "LBEC0101"[All Fields] OR "M923"[All Fields] OR "PRX-106"[All Fields] OR "SB4"[All Fields] OR "TuNEX"[All Fields] OR "Yisaipu"[All Fields] OR "abatacept"[All Fields] OR "orencia"[All Fields] OR "anakinra"[All Fields] OR "kineret"[All Fields] OR "rituximab"[All Fields] OR "rituxan"[All Fields] OR "mabthera"[All Fields] OR "zytux"[All Fields] OR "reditux"[All Fields] OR "tocilizumab"[All Fields] OR "atlizumab"[All Fields] OR "actemra"[All Fields] OR "roactemra"[All Fields] OR "sarilumab"[All Fields] OR "Kevzara"[All Fields] OR "sirukumab"[All Fields] OR "Plivensia"[All Fields] OR "tofacitinib"[All Fields] OR "tasocitinib"[All Fields] OR "xeljanz"[All Fields] OR "jakvinus"[All Fields] | 43,222    |
| #12                                      | #10 OR #11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 43,222    |
| <b>All interventions and comparators</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |           |
| #13                                      | #6 OR #9 OR #12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 97,786    |
| <b>Study type (RCTs)</b>                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |           |
| #14                                      | "Randomized Controlled Trials as Topic"[MeSH] OR "Clinical Trials, Phase III as Topic"[MeSH] OR "Clinical Trials, Phase II as Topic"[MeSH] OR "Controlled Clinical Trials as Topic"[MeSH] OR "Random Allocation"[MeSH] OR "Clinical Trials as Topic"[MeSH:NoExp]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 383,037   |
| #15                                      | "Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trial"[Publication Type] OR "Clinical Trial, Phase II"[Publication Type] OR "Clinical Trial, Phase III"[Publication Type] OR "Clinical Trial, Phase IV"[Publication Type] OR "Multicenter Study"[Publication Type]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 699,055   |
| #16                                      | "randomized"[Title/Abstract] OR "randomised"[Title/Abstract] OR "randomly"[Title/Abstract]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 735,279   |
| #17                                      | randomized controlled trial*[Text Word] OR randomised controlled trial*[Text Word] OR randomized clinical trial*[Text Word] OR randomised clinical trial*[Text Word] OR randomized trial*[Text Word] OR randomised trial*[Text Word] OR "random allocation"[Text Word] OR "double blind method"[Text Word] OR "single blind method"[Text Word] OR ((singl*[Text Word] OR doubl*[Text Word] OR treb*[Text Word] OR tripl*[Text Word]) AND (blind*[Text Word] OR mask*[Text Word])) OR allocated random*[Text Word] OR random assignment*[Text Word] OR open-label trial*[Text Word] OR open-label stud*[Text Word] OR "open label trial"[Text Word] OR non-blinded stud*[Text Word]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 735,401   |
| #18                                      | #14 OR #15 OR #16 OR #17                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 1,380,304 |

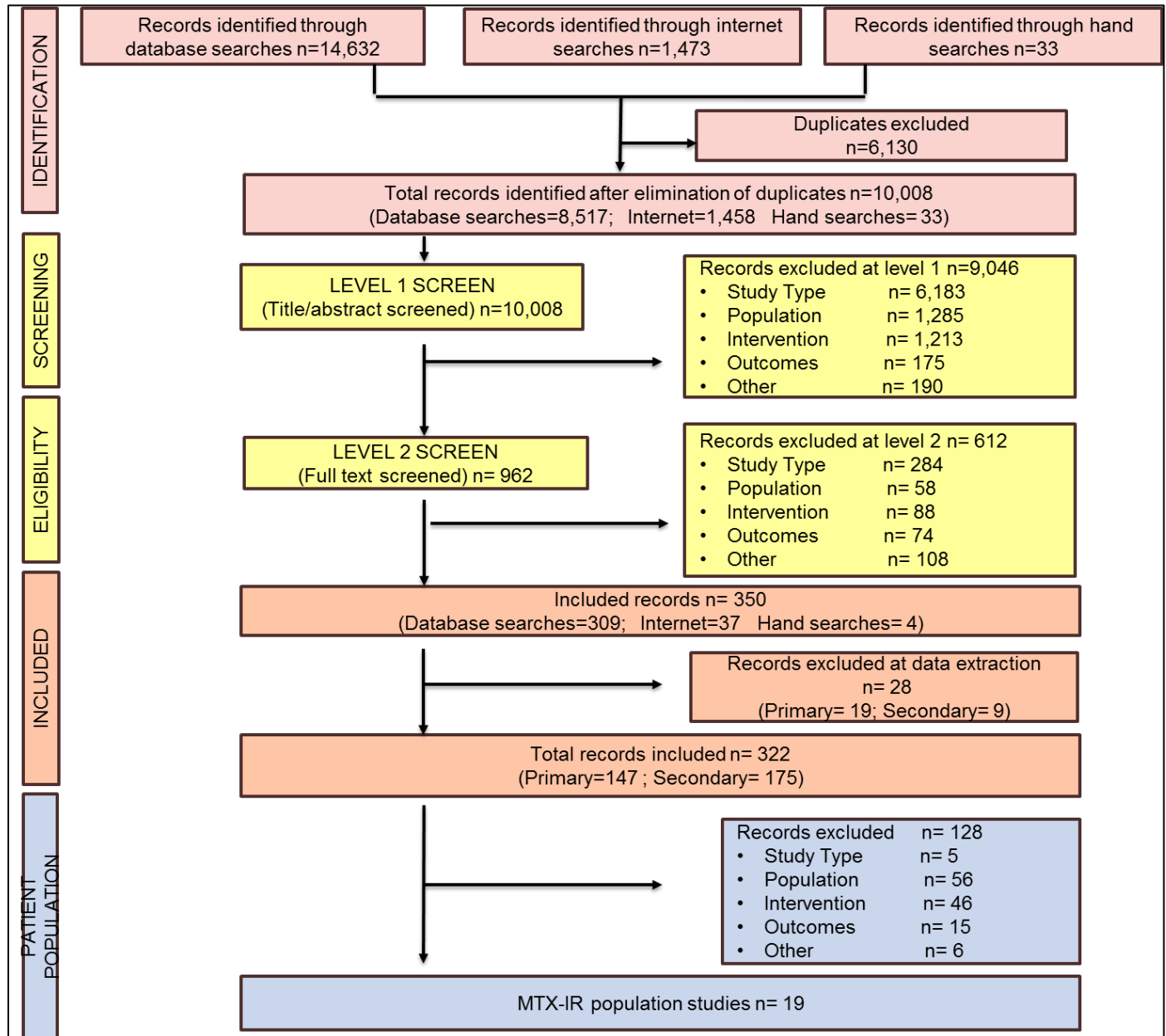
| Search No.                                | Terms                                                                                                                                                                         | Results    |
|-------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Exclusion terms, excluding animals</b> |                                                                                                                                                                               |            |
| #19                                       | "Animals"[MeSH] NOT "Humans"[MeSH]                                                                                                                                            | 4,401,377  |
| <b>Exclusion terms, by study type</b>     |                                                                                                                                                                               |            |
| #20                                       | "Comment"[Publication Type] OR "Letter"[Publication Type] OR "Editorial"[Publication Type] OR "Case Reports"[Publication Type] OR "Clinical Trial, Phase I"[Publication Type] | 3,268,852  |
| #21                                       | "case study"[Title] OR "case studies"[Title] OR "case report"[Title] OR "case reports"[Title] OR "case series"[Title]                                                         | 260,831    |
| #22                                       | #20 OR #21                                                                                                                                                                    | 3,355,740  |
| <b>Exclusion terms, population</b>        |                                                                                                                                                                               |            |
| #23                                       | "Arthritis, Juvenile"[MeSH]                                                                                                                                                   | 9,457      |
| #24                                       | "juvenile idiopathic arthritis"[Text word] OR (juvenile AND arthritis)                                                                                                        | 12,816     |
| #25                                       | #23 OR #24                                                                                                                                                                    | 12,816     |
| <b>All relevant studies</b>               |                                                                                                                                                                               |            |
| #26                                       | #3 AND #13 AND #18                                                                                                                                                            | 3,799      |
| #27                                       | #26 NOT (#19 OR #22 OR #25)                                                                                                                                                   | 3,423      |
| <b>Limits</b>                             |                                                                                                                                                                               |            |
| #28                                       | #27 AND Filters applied: Dates limited from 1 May 2016 to present                                                                                                             | <b>394</b> |

bDMARD = biologic disease-modifying antirheumatic drug; cDMARD = conventional disease-modifying antirheumatic drug;

MeSH = Medical Subject Heading; RCT = randomized, controlled trial.

## 4. PRISMA diagram

Figure S1 PRISMA Diagram



PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses



## 5. Quality assessment of the included trials

**Table S8** Summary of Quality Assessment of included Randomized Controlled Trials (primary analysis, N=19)

| Trial Name (Reference)              | Randomized Appropriately | Concealment of Allocation | Groups Similar for Prognostic Factors? | Were Care Providers, Participants, and Outcome Assessors Blind to Treatment Allocation? | Any Unexpected Imbalances in Drop-outs? | More Outcomes Measured Than Reported? | Did the Analysis Include an Intention-to-Treat Analysis? If so, Was This Appropriate, and Were Appropriate Methods Used to Account for Missing Data? |
|-------------------------------------|--------------------------|---------------------------|----------------------------------------|-----------------------------------------------------------------------------------------|-----------------------------------------|---------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| AIM <sup>1</sup>                    | Yes                      | Yes                       | Yes                                    | Yes                                                                                     | No                                      | No                                    | Yes                                                                                                                                                  |
| AMPLE <sup>2</sup>                  | Unclear                  | Unclear                   | Yes                                    | No                                                                                      | No                                      | No                                    | Yes                                                                                                                                                  |
| ARMADA <sup>3</sup>                 | Unclear                  | Yes                       | Yes                                    | Yes                                                                                     | Unclear                                 | No                                    | No                                                                                                                                                   |
| ATTEST <sup>4</sup>                 | Unclear                  | Unclear                   | Yes                                    | Yes                                                                                     | No                                      | No                                    | Yes                                                                                                                                                  |
| ATTRACT <sup>5</sup>                | Unclear                  | Yes                       | Yes                                    | Yes                                                                                     | Yes                                     | No                                    | Unclear                                                                                                                                              |
| Edwards et al. (2004) <sup>6</sup>  | Unclear                  | Unclear                   | Yes                                    | Yes                                                                                     | Yes                                     | No                                    | Yes                                                                                                                                                  |
| GO-FORTH <sup>7</sup>               | Unclear                  | Unclear                   | Yes                                    | Unclear                                                                                 | No                                      | No                                    | Yes                                                                                                                                                  |
| GO-FORWARD <sup>8</sup>             | Yes                      | Yes                       | Yes                                    | Unclear                                                                                 | Unclear                                 | No                                    | Yes                                                                                                                                                  |
| Keystone et al. (2004) <sup>9</sup> | Unclear                  | Unclear                   | Yes                                    | Unclear                                                                                 | No                                      | No                                    | Yes                                                                                                                                                  |
| Kim et al. (2007) <sup>10</sup>     | Unclear                  | Unclear                   | Yes                                    | Unclear                                                                                 | No                                      | No                                    | Yes                                                                                                                                                  |
| Li et al. (2013) <sup>11</sup>      | Unclear                  | Unclear                   | Yes                                    | Unclear                                                                                 | No                                      | No                                    | Yes                                                                                                                                                  |
| Machado et al. (2015) <sup>12</sup> | Unclear                  | No                        | Yes                                    | No                                                                                      | No                                      | No                                    | Yes                                                                                                                                                  |
| MOBILITY <sup>13</sup>              | Unclear                  | Yes                       | Yes                                    | Yes                                                                                     | No                                      | No                                    | Yes                                                                                                                                                  |
| RA-SCORE <sup>14</sup>              | Yes                      | Yes                       | Yes                                    | Yes                                                                                     | Yes                                     | No                                    | Yes                                                                                                                                                  |
| <b>RA-BEAM</b>                      | Unclear                  | Unclear                   | Unclear                                | Yes                                                                                     | No                                      | No                                    | Unclear                                                                                                                                              |

| Trial Name<br>(Reference)                | Randomized<br>Appropriately | Concealment of<br>Allocation | Groups<br>Similar for<br>Prognostic<br>Factors? | Were Care<br>Providers,<br>Participants, and<br>Outcome<br>Assessors Blind to<br>Treatment<br>Allocation? | Any Unexpected<br>Imbalances in<br>Drop-outs? | More Outcomes<br>Measured Than<br>Reported? | Did the Analysis Include an<br>Intention-to-Treat Analysis? If so,<br>Was This Appropriate, and Were<br>Appropriate Methods Used to<br>Account for Missing Data? |
|------------------------------------------|-----------------------------|------------------------------|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------|---------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RAPID-C <sup>15</sup>                    | Unclear                     | Unclear                      | Unclear                                         | Unclear                                                                                                   | Unclear                                       | No                                          | No                                                                                                                                                               |
| SERENE <sup>16</sup>                     | Unclear                     | Unclear                      | Yes                                             | unclear                                                                                                   | No                                            | No                                          | Yes                                                                                                                                                              |
| START <sup>17</sup>                      | Unclear                     | Unclear                      | Yes                                             | Yes                                                                                                       | No                                            | No                                          | Yes                                                                                                                                                              |
| Weinblatt et al.<br>(1999) <sup>18</sup> | Unclear                     | Yes                          | No                                              | Yes                                                                                                       | Unclear                                       | No                                          | Unclear                                                                                                                                                          |

## 6. List of trials included in the analysis

**Table S9** All trials included in the analysis in MTX-IR population (N=29) - Overview

| Trial name                                       | Trial No.   | Primary Analysis (Yes/No) | Sensitivity 1 <sup>a</sup> (Yes/NA) | Sensitivity 2 <sup>b</sup> (Yes/No) | Treatment 1                          | Treatments 2 / 3                            | Control           | ACR Endpoints 24 weeks |
|--------------------------------------------------|-------------|---------------------------|-------------------------------------|-------------------------------------|--------------------------------------|---------------------------------------------|-------------------|------------------------|
| AIM <sup>1</sup>                                 | NCT00048568 | Yes                       | NA                                  | Yes                                 | ABA 10mg + MTX (n=433)               | ---                                         | PBO + MTX (n=219) | ACR20/50/70            |
| AMPLE <sup>2</sup>                               | NCT00929864 | Yes                       | NA                                  | Yes                                 | ABA 125mg + MTX (n=318) <sup>c</sup> | ADA 40mg + MTX (n=328)                      | ---               | ACR20/50/70            |
| ARMADA <sup>3</sup>                              |             | Yes                       | NA                                  | Yes                                 | ADA 40mg + MTX (n=67)                | ---                                         | PBO + MTX (n=62)  | ACR20/50/70            |
| ATTEST <sup>4</sup>                              | NCT00095147 | Yes                       | NA                                  | Yes                                 | ABA 10mg + MTX (n=156)               | IFX 3mg + MTX (n=165)                       | PBO + MTX (n=110) | ACR20/50/70            |
| ATTRACT <sup>5</sup>                             |             | Yes                       | NA                                  | Yes                                 | IFX 3mg + MTX (n=86)                 | ---                                         | PBO + MTX (n=88)  | ACR20                  |
| <b>RA-BEAM<sup>19</sup></b>                      | NCT01710358 | Yes                       | NA                                  | Yes                                 | BARI 4mg + MTX (n=487)               | ADA 40mg + MTX (n=330)                      | PBO + MTX (n=488) | ACR20/50/70            |
| Edwards (2004) <sup>6</sup>                      |             | Yes                       | NA                                  | Yes                                 | <b>RTX 1000mg (n=40)<sup>d</sup></b> | RTX 1000mg + MTX (n=40)                     | PBO + MTX (n=40)  | ACR20/50/70            |
| GO-FORTH <sup>7</sup>                            | NCT00727987 | Yes                       | NA                                  | <b>No</b>                           | GOL 50mg + MTX (n=89)                | ---                                         | PBO + MTX (n=90)  | ACR20/50/70            |
| GO-FORWARD <sup>8</sup>                          | NCT00264550 | Yes                       | NA                                  | Yes                                 | GOL 50mg + MTX (n=89)                | ---                                         | PBO + MTX (n=133) | ACR20/50/70            |
| Keystone (2004) <sup>9</sup> [DE019]             |             | Yes                       | NA                                  | Yes                                 | ADA 40mg + MTX (n=207)               | ---                                         | PBO + MTX (n=200) | ACR20/50/70            |
| Kim (2007) <sup>10</sup>                         |             | Yes                       | NA                                  | <b>No</b>                           | ADA 40 mg + MTX (n=65)               | ---                                         | PBO + MTX (n=63)  | ACR20/50/70            |
| Li (2013) <sup>11</sup>                          | NCT01248780 | Yes                       | NA                                  | <b>No</b>                           | GOL 50mg + MTX (n=132)               | ---                                         | PBO + MTX (n=132) | ACR20/50/70            |
| Machado (2014) <sup>12</sup> [LARA] <sup>e</sup> | NCT00848354 | Yes                       | NA                                  | Yes                                 | ETN + MTX (n=284)                    | cDMARD + MTX (n=145)                        | ---               | ACR20/50/70            |
| MOBILITY <sup>13</sup>                           | NCT01061736 | Yes                       | NA                                  | Yes                                 | SARI 200mg + MTX (n=399)             | <b>SARI 150mg + MTX (n=400)<sup>d</sup></b> | PBO + MTX (n=398) | ACR20/50/70            |
| RA-SCORE <sup>14</sup>                           | NCT00578305 | Yes                       | NA                                  | Yes                                 | RTX 1000mg + MTX (n=63)              | ---                                         | PBO + MTX (n=60)  | ACR20/50/70            |
| RAPID-C <sup>15</sup>                            | NCT02151851 | Yes                       | NA                                  | <b>No</b>                           | CZP + MTX (n=312)                    | ---                                         | PBO + MTX (n=113) | ACR20/50/70            |

| Trial name                            | Trial No.   | Primary Analysis (Yes/No) | Sensitivity 1 <sup>a</sup> (Yes/NA) | Sensitivity 2 <sup>b</sup> (Yes/No) | Treatment 1                          | Treatments 2 / 3                     | Control           | ACR Endpoints 24 weeks |
|---------------------------------------|-------------|---------------------------|-------------------------------------|-------------------------------------|--------------------------------------|--------------------------------------|-------------------|------------------------|
| SERENE <sup>16</sup>                  |             | Yes                       | NA                                  | Yes                                 | RTX 500mg + MTX (n=168) <sup>d</sup> | RTX 1000mg + MTX (n=172)             | PBO + MTX (n=172) | ACR20/50/70            |
| START <sup>17</sup>                   |             | Yes                       | NA                                  | Yes                                 | IFX 3mg + MTX (n=360)                | ---                                  | PBO + MTX (n=363) | ACR20/50/70            |
| Weinblatt (1999) <sup>18</sup>        |             | Yes                       | NA                                  | Yes                                 | ETN + MTX (n=59)                     | ---                                  | PBO + MTX (n=30)  | ACR20/50/70            |
| J-RAPID <sup>20</sup> [Yamamoto 2011] | NCT00791999 | No                        | Yes                                 | No                                  | CZP + MTX (n=82)                     | ---                                  | PBO + MTX (n=77)  | ACR20/50/70            |
| Kang (2013) <sup>21</sup> [RA0025]    |             | No                        | Yes                                 | No                                  | CZP + MTX (n=81)                     | ---                                  | PBO + MTX (n=40)  | ACR20/50/70            |
| LITHE <sup>22</sup>                   | NCT00106535 | No                        | Yes                                 | No                                  | TCZ 8mg + MTX (n=398)                | ---                                  | PBO + MTX (n=393) | ACR20/50/70            |
| OPTION <sup>23</sup>                  | NCT00106548 | No                        | Yes                                 | No                                  | TCZ 8mg + MTX (N=205)                | ---                                  | PBO + MTX (N=204) | ACR20/50/70            |
| ORAL SCAN <sup>24</sup>               | NCT00847613 | No                        | Yes                                 | No                                  | TOFA 5mg + MTX (n=321)               | TOFA 10mg + MTX (n=316) <sup>d</sup> | PBO + MTX (n=160) | ACR20/50/70            |
| ORAL STANDARD <sup>25</sup>           | NCT00853385 | No                        | Yes                                 | No                                  | TOFA 5mg + MTX (n=204)               | TOFA 10mg + MTX (n=201) <sup>d</sup> | PBO + MTX (n=108) | ACR20/50/70            |
|                                       |             |                           |                                     |                                     |                                      | ADA 40mg + MTX (n=204)               |                   |                        |
| ORAL STRATEGY <sup>26</sup>           | NCT02187055 | No                        | Yes                                 | No                                  | TOFA 5mg + MTX (n=376)               | TOFA 5mg (n=384) <sup>d</sup>        | ---               | ACR20/50/70            |
|                                       |             |                           |                                     |                                     |                                      | ADA 40mg + MTX (n=386)               |                   |                        |
| RACAT <sup>27</sup>                   | NCT00405275 | No                        | Yes                                 | No                                  | ETN + MTX (n=175)                    | SSZ + HCQ + MTX (n=178) <sup>f</sup> | ---               | ACR20/50/70            |
| RAPID1 <sup>28</sup>                  | NCT00152386 | No                        | Yes                                 | No                                  | CZP + MTX (n=393)                    | ---                                  | PBO + MTX (n=199) | ACR20/50/70            |
| RAPID2 <sup>29</sup>                  | NCT00175877 | No                        | Yes                                 | No                                  | CZP + MTX (n=246)                    | ---                                  | PBO + MTX (n=127) | ACR20/50/70            |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; CZP certolizumab; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; TCZ tocilizumab; TOFA tofacitinib.

a- addition of trials that allowed for up to 20% of patients with prior bDMARD use (NA = not applicable as already part of primary analysis; Yes = added in analysis)

b- exclusion of trials solely conducted in Asia Pacific and/or low/unknown dose of MTX (<7.5 mg/week) (No = excluded from analysis; Yes = included in analysis)

c- labeled as "SUBCUT" (subcutaneous) in the analyses

d- treatment arms not included in the analysis, i.e. only presented for reasons of completeness

e- open-label trial, excluded via corresponding sensitivity analysis

f- labeled as "cDMARD + MTX" in the analyses

## 7. Methodology

### 7.1. Endpoints

The following endpoints were chosen for the analysis:

- ACR response (20%, 50%, and 70% improvement in criteria)<sup>30</sup>

Safety endpoints were not included as part of the NMA, as the majority of trials allowed the use of rescue therapy for the control arm if an ACR response of 20% was not observed. Hence, once patients on the control arm are allowed to be switched to the active treatment, there is no longer a common comparator for the network.

Therefore, only endpoints that are measured prior to rescue therapy (generally the 12-week outcomes) would have had a common comparator; however, in most of the publications, safety endpoints are only reported for the duration of the trial and not at intermediate endpoints.

Discontinuations were not included as part of the NMA for reasons that are also linked to rescue therapy. Discontinuation rates are included in many of the trials for ACR response, as most of the trials use an imputation method of no response for patients who have missing data. Therefore, discontinuations are already considered in the ACR response outcomes.

### 7.2. Overview of Analyses

NMA was conducted using Bayesian mixed treatment comparisons as described in the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) Technical Support Documents (TSDs)<sup>31</sup>.

Two classes of models were assessed:<sup>32</sup>

- i. separate models for baseline and treatment effect
- ii. simultaneous modelling of baseline and treatment effects

It was decided that the simultaneous model was to be used for several reasons: a) the data for both baseline and treatment effects come from the same sources, b) there were some networks that had zero cells and fitting this type of model increased the stability of the relevant models, and c) the evidence for several networks was sparse.

In addition, for sensitivity analysis, frequentist NMA using the Rücker method was conducted to assess the robustness of the results<sup>33</sup>. Note for cells with zero counts the following rule was implemented: if 1 arm in trial had 0 count then 0.5 was added to all arms for that trial.

The method based on Bayesian models was first proposed in 1996 by Higgins and Whitehead<sup>34</sup>. The results of the different interventions from the included trials were combined by means of a Bayesian NMA using a logistic-regression model with a binomial likelihood distribution for the categorical (ACR response) outcomes.<sup>35,36</sup>

As with any meta-analysis, NMA can be performed with a fixed-effects approach or a random-effects approach<sup>35,37</sup>. With a fixed-effects model, it is assumed that differences in true relative treatment effects (whether estimated directly or indirectly) are only caused by the difference in treatment and no other factors. There is no heterogeneity in true relative treatment effects beyond differences in treatment effect caused by the differences in type of interventions compared. With a random-effects assumption, differences in trial-specific response rates (beyond the differences attributable to the actual interventions compared) are exchangeable and the heterogeneity is constant between the different comparisons. The choice for a fixed or

random-effects model for the final analysis was evaluated on the basis of model fit (as measured by Deviance Information Criterion [DIC]), sensitivity of results, and assessment of residual deviance<sup>35,37</sup>.

For assessment of between-trial variance used in the random-effects model, NICE<sup>38,39</sup> recommend vague priors for the between trial variances [ $\sigma \sim \text{Uniform}(0, 2)$ ]. The Agency for Healthcare Research and Quality (AHRQ)<sup>40</sup> recommend a similar approach with an upper limit of 5. The upper limits reflect a between-trial variability that allows for a wide range of treatment effects. For the present analysis, for binary models, priors were tested at  $\sigma \sim \text{Uniform}(0, \sigma^2)$ , where  $\sigma=5$ . Appropriate priors for trial variance were assessed on a case-by-case basis. Baseline between trial  $\sigma$  was set at  $\text{Uniform}(0, 2)$ . It might be that the random-effects models were sensitive to the choice of vague priors resulting in unstable (i.e., wide) credible intervals (CrIs). This could be due to the combination of a low number of included trials, trials with small sample size, and a high degree of heterogeneity. In that case, informative priors [ $\text{Log normal}(-2.29, 1.58)$ ] were to be used instead.<sup>41</sup>

The initial model runs used 3 chains, with a burn-in of 10,000 simulations, and estimating the posterior probabilities from a sample of further 10,000 simulations. In order to address insufficient convergence and auto-correlation, this was increased to 4 chains, a burn-in of 60,000 and a sample of 120,000.

Bayesian NMA analyses were performed in JAGS via R version 3.4.2<sup>42</sup> using the R2JAGS package, and Frequentist NMA analysis was run using R version 3.4.2 using the netmeta package.<sup>33,43</sup>

### 7.3. Bayesian Mixed Treatment Comparisons

#### Binary Endpoint Model for Network Meta-Analysis:

For the primary analysis we modelled the proportion of patients who experienced an ACR response (20%, 50%, and 70%). This follows a binary endpoint model where the underlying model is that of a logistic regression. Observed data were included in the model using a binomial likelihood where the probability ( $p$ ) of response for study  $i$  and treatment  $k$  is as follows:

$$r_{i,k} \sim \text{Binomial}(p_{i,k}, n_{i,k})$$

Where  $r_{i,k}$  is the number of events in treatment arm  $k$  of study  $i$ , and  $n_{i,k}$  is the total number of subjects in treatment arm  $k$  of study  $i$ .

Treatments  $k$  included in the FE model were indexed as positive integers with the baseline treatment ( $b$ ) being the lowest index treatment in study  $i$ . A logit link function was used to map the probability of response to the linear model such that for treatment arm  $k$  of study:

$$\text{logit}(p_{i,k}) = \alpha_i + (\beta_{i,k} - \beta_{i,b})$$

Where  $\alpha_i$  is the study-specific baseline term, and  $\beta_{i,k} - \beta_{i,b}$  is the study-specific log odds ratio of treatment  $k$  compared to baseline  $b$ . For study arms receiving the baseline treatment (ie,  $k = b$ ), this simplifies to the study-specific baseline term  $\alpha_i$ . A vague prior  $\beta \sim N(0, 100^2)$  was used for the treatment effect coefficients.

The corresponding RE model replaces the constant treatment effect with the study-specific treatment effect  $\delta_{i,k}$ . This is normally distributed with mean  $mb_{i,k} = (\beta_{i,k} - \beta_{i,b})$  and variance



$\sigma^2$ , where  $\sigma^2$  is the RE variance and assumed to be constant across all treatment comparisons.

(Note that this model was be equivalent to a FE model when  $\sigma^2 = 0$ ). The following changes were made for the RE model:

$$\text{logit}(p_{i,k}) = \alpha_i + \delta_{i,k}$$

$$\delta_{i,k} \sim N(mb_{i,k}, \sigma^2)$$

$$mb_{i,k} = (\beta_{i,k} - \beta_{i,b})$$

The parameters of interest modelled were the log odds ratios ( $\beta$ ) which provide the relative treatment effect for each treatment compared to the reference treatment in the analyses.

Estimates of these parameters were iteratively sampled using Bayesian methods (as described in the heading below). The parameter value can be summarised by calculating the mean and standard error of these samples (i.e., mean log odds ratio and corresponding standard error which can be converted to odds ratios). In addition, the CrIs can be estimated from these samples. These are similar to confidence intervals (CIs) in a Frequentist analysis; however, the interpretation differs as described below for a 5% significance level:

*Frequentist 95% CIs: 95% probability that the true value lies within 95% of these intervals in the long run, if many samples were taken of the data*

*Bayesian 95% CrI: 95% probability that the true value of the parameter lies within the interval*

The 95% CrI in Bayesian analyses are the values corresponding to the lower 2.5 and upper 97.5 percentiles of samples taken for each parameter modelled.

Treatment effects are presented as odds ratios with associated 95% CrIs. If not noted otherwise, the reference treatment is placebo + methotrexate (PBO + MTX). For other estimates of interest, medians and associated 95% CrIs are reported.

## **Zero Cells**

Bayesian models with zero cells do not usually require special precautions (refer to <sup>39</sup>). However, in the case of the frequentist models (for the analysis of ACR70), we had to add the continuity correction of 0.5 to 0 cells for them to converge. This is known to generate biased estimates of effect size so these results should be interpreted with precaution.<sup>44,45</sup>

## **Choice of the treatment effect: random vs fixed effects**

As with any MA, NMA can be performed with a fixed effects approach or a random effects approach<sup>35,36</sup>. In Bayesian NMA, it is assumed that differences in trial-specific relative treatment effect (beyond the differences attributable to the actual interventions compared) are exchangeable and the heterogeneity is constant between the different comparisons. Initially, both fixed and random effects models were performed for each endpoint.

For Bayesian NMA the choice for a fixed or random effects model for the primary analysis was evaluated on:

- The model fit as measured by Deviance Information Criterion (DIC),
- Assessment of the residual deviance,
- Convergence of the models,
- Sensitivity of the results,

- Whether there is limited data to inform the random effects variance,
- Whether there is evidence of the random-effects prior dominating the posterior simulations indicating that there is not enough data in the analysis to inform this additional parameter.

### **Inconsistency, Model Fit, and Convergence**

It was pre-planned to explore the consistency assumption via the “node-splitting” approach as defined by Dias<sup>46</sup>. However, networks were primarily star-shaped, with only 2 closed loops. Both loops were informed by one trial, respectively. Therefore, this analysis was not performed.

Model fit was assessed with the DIC and the posterior mean of the total residual deviance.<sup>47</sup> Deviance measures the fit of the model to the data using the likelihood function. A good model fit is indicated by a total residual deviance approximately equal to the number of data points available. The DIC is a statistic that measures Bayesian model fit and penalizes the deviance by the model complexity. When comparing 2 DIC values, a difference of 5 or more is regarded as a meaningful difference.<sup>48</sup>

Convergence was verified by trace plots, monitoring the Monte Carlo error, and with Gelman-Rubin diagnostics.<sup>49</sup>

## **7.4. Sensitivity Analyses**

In addition to the analyses described above, the following sensitivity analyses were pre-planned and performed:

## Baseline-risk adjustment

In order to account for potential heterogeneity amongst ACR response rates in the PBO + MTX treatment arms, meta-regression models adjusting for baseline-risk were performed.<sup>38,50</sup>

## Inclusion / Removal of Trial Types

Additional sensitivity analyses were conducted, which included or removed specific trial types, to investigate the potential impact of treatment effect modifiers. These were:

- Inclusion of trials with prior bDMARD use in up to 20% of patients
- Removal of trials solely conducted in Asian-Pacific; or low (<7.5 mg/week) / unknown dose of methotrexate
- Removal of open-label trials.

**Table S10** provides an overview of all pre-planned sensitivity analyses.

**Table S10** Overview of pre-planned sensitivity analyses

| No.                                                                                            | Description                                                                                                                              | Comments                                                                                                                                                                                                                                                                                                                                             |
|------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 0                                                                                              | Primary model<br>(Simultaneous Fixed-effects / Random-effects models)                                                                    | <b>Fixed-effects</b> model chosen as main analysis approach<br>Random-effects model presented as supplementary information                                                                                                                                                                                                                           |
| 0a                                                                                             | <b>Baseline-risk</b> adjustment (for primary model)<br>(Simultaneous Fixed-effects / Random-effects models)                              | <b>Fixed-effects</b> model as main analysis approach                                                                                                                                                                                                                                                                                                 |
| 1                                                                                              | Inclusion of trials that allowed for up to 20% of patients with prior bDMARD use                                                         | List of trials included: J-RAPID, Kang (2013), RAPID1, RAPID2, LITHE, OPTION, ORAL SCAN, ORAL STANDARD, ORAL STRATEGY, RACAT<br>Note: this increased the number of CZP trials in the networks from 1 (primary model) to 5.<br>Note: These were the only networks that included TOFA and TCZ.<br><b>Fixed-effects</b> model as main analysis approach |
| 2                                                                                              | Removal of trials that were only conducted in Asian-Pacific countries and/or trials with previous low (<7.5 mg/week) or unknown dose MTX | List of trials excluded: Kim (2007), GO-FORTH, Li (2013), RAPID-C<br>Note: As a result, CZP was no longer part of the network.<br><b>Fixed-effects</b> model as main analysis approach                                                                                                                                                               |
| 3                                                                                              | Removal of open-label trials                                                                                                             | List of trials excluded: Machado (2014)<br><b>Fixed-effects</b> model as main analysis approach                                                                                                                                                                                                                                                      |
| Additional sensitivity analyses                                                                |                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                      |
| --                                                                                             | <b>Independent baseline</b> model (for primary model)<br>(Fixed-effects / Random-effects models)                                         | ---                                                                                                                                                                                                                                                                                                                                                  |
| --                                                                                             | <b>Frequentist NMA</b> (for primary model)<br>(Fixed-effects / Random-effects models)                                                    | ---                                                                                                                                                                                                                                                                                                                                                  |
| Sensitivity analyses that were pre-planned but not performed in the context of this manuscript |                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                      |

| No. | Description                                             | Comments                                                                                       |
|-----|---------------------------------------------------------|------------------------------------------------------------------------------------------------|
| 4   | Removal of trials due to inconsistency (node splitting) | Not performed as only 2 closed loops coming from single trials, respectively (RA-BEAM, ATTEST) |

## 8. ACR Response Data

**Table S11** Percentage of patients achieving ACR20/50/70 response per trial and treatment arm: MTX-IR population

| Trial                         | Treatment arm (as labelled in NMA) | Time-point (week) | Numbers analyzed | % achieving ACR20 response | % achieving ACR50 response | % achieving ACR70 response | Data used in primary model? | Exclusion reason |
|-------------------------------|------------------------------------|-------------------|------------------|----------------------------|----------------------------|----------------------------|-----------------------------|------------------|
| AIM <sup>1</sup>              | ABA 10mg + MTX                     | 24                | 424              | 67.9                       | 39.9                       | 19.8                       | Y                           |                  |
| AIM <sup>1</sup>              | PBO + MTX                          | 24                | 214              | 39.7                       | 16.8                       | 6.5                        | Y                           |                  |
| AMPLE <sup>2</sup>            | ABA SUBCUT + MTX                   | 24                | 318              | 65.7                       | 40.6                       | 21.7                       | Y                           |                  |
| AMPLE <sup>2</sup>            | ADA 40mg + MTX                     | 24                | 328              | 65.5                       | 40.5                       | 22.6                       | Y                           |                  |
| ARMADA <sup>3</sup>           | ADA 40mg + MTX                     | 24                | 67               | 67.2                       | 55.2                       | 26.9                       | Y                           |                  |
| ARMADA <sup>3</sup>           | PBO + MTX                          | 24                | 62               | 14.5                       | 8.1                        | 4.8                        | Y                           |                  |
| ATTEST <sup>4</sup>           | ABA 10mg + MTX                     | 28                | 156              | 66.7                       | 40.4                       | 20.5                       | Y                           |                  |
| ATTEST <sup>4</sup>           | IFX 3mg + MTX                      | 28                | 165              | 59.4                       | 37                         | 24.2                       | Y                           |                  |
| ATTEST <sup>4</sup>           | PBO + MTX                          | 28                | 110              | 41.8                       | 20                         | 9.1                        | Y                           |                  |
| ATTRACT <sup>5</sup>          | IFX 3mg + MTX                      | 26                | 86               | 48.8                       | -                          | -                          | Y                           |                  |
| ATTRACT <sup>5</sup>          | PBO + MTX                          | 26                | 88               | 20.5                       | -                          | -                          | Y                           |                  |
| RA-BEAM <sup>19</sup>         | ADA 40mg + MTX                     | 24                | 330              | 66.4                       | 45.5                       | 21.8                       | Y                           |                  |
| RA-BEAM <sup>19</sup>         | BARI 4mg + MTX                     | 24                | 487              | 73.9                       | 50.5                       | 29.8                       | Y                           |                  |
| RA-BEAM <sup>19</sup>         | PBO + MTX                          | 24                | 488              | 36.7                       | 19.3                       | 8                          | Y                           |                  |
| Edwards (2004) <sup>6</sup>   | RTX 1000mg + MTX                   | 24                | 40               | 72.5                       | 42.5                       | 22.5                       | Y                           |                  |
| Edwards (2004) <sup>6</sup>   | PBO + MTX                          | 24                | 40               | 37.5                       | 12.5                       | 5                          | Y                           |                  |
| GO-FORTH <sup>b7</sup>        | GOL 50mg + MTX                     | 24                | 86               | 70.9                       | 41.9                       | 26.7                       | Y                           |                  |
| GO-FORTH <sup>b7</sup>        | PBO + MTX                          | 24                | 88               | 33                         | 14.8                       | 5.7                        | Y                           |                  |
| GO-FORWARD <sup>8</sup>       | GOL 50mg + MTX                     | 24                | 89               | 59.6                       | 37.1                       | 20.2                       | Y                           |                  |
| GO-FORWARD <sup>8</sup>       | PBO + MTX                          | 24                | 133              | 27.8                       | 13.5                       | 5.3                        | Y                           |                  |
| Keystone (2004) <sup>9</sup>  | ADA 40mg + MTX                     | 24                | 207              | 63.3                       | 39.1                       | 20.8                       | Y                           |                  |
| Keystone (2004) <sup>9</sup>  | PBO + MTX                          | 24                | 200              | 29.5                       | 9.5                        | 2.5                        | Y                           |                  |
| Kim (2007) <sup>b10</sup>     | ADA 40mg + MTX                     | 24                | 65               | 61.5                       | 43.1                       | 21.5                       | Y                           |                  |
| Kim (2007) <sup>b10</sup>     | PBO + MTX                          | 24                | 63               | 36.5                       | 14.3                       | 7.9                        | Y                           |                  |
| Li (2013) <sup>b11</sup>      | GOL 50mg + MTX                     | 24                | 132              | 42.4                       | 18.9                       | 6.1                        | Y                           |                  |
| Li (2013) <sup>b11</sup>      | PBO + MTX                          | 24                | 132              | 15.9                       | 6.8                        | 1.5                        | Y                           |                  |
| Machado (2014) <sup>c12</sup> | ETN + MTX                          | 24                | 279              | 83.2                       | 62                         | 34.8                       | Y                           |                  |
| Machado (2014) <sup>c12</sup> | cDMARD + MTX                       | 24                | 142              | 50                         | 23.2                       | 11.3                       | Y                           |                  |
| MOBILITY (2015) <sup>13</sup> | SARI 200mg + MTX                   | 24                | 399              | 66.4                       | 46                         | 25                         | Y                           |                  |
| MOBILITY (2015) <sup>13</sup> | PBO + MTX                          | 24                | 398              | 33.4                       | 17                         | 7                          | Y                           |                  |
| RA-SCORE <sup>14</sup>        | RTX 1000mg + MTX                   | 24                | 60               | 51.7                       | 26.7                       | 8.3                        | Y                           |                  |
| RA-SCORE <sup>14</sup>        | PBO + MTX                          | 24                | 63               | 28.6                       | 11.1                       | 1.6                        | Y                           |                  |

| Trial                          | Treatment arm (as labelled in NMA) | Time-point (week) | Numbers analyzed | % achieving ACR20 response | % achieving ACR50 response | % achieving ACR70 response | Data used in primary model? | Exclusion reason              |
|--------------------------------|------------------------------------|-------------------|------------------|----------------------------|----------------------------|----------------------------|-----------------------------|-------------------------------|
| RAPID-C <sup>b15</sup>         | CZP 200 mg Q2W + MTX               | 24                | 312              | 54.8                       | 36.5                       | 16.7                       | Y                           |                               |
| RAPID-C <sup>b15</sup>         | PBO + MTX                          | 24                | 113              | 23.9                       | 7.1                        | 2.7                        | Y                           |                               |
| SERENE <sup>16</sup>           | RTX 1000mg + MTX                   | 24                | 170              | 50.6                       | 25.9                       | 10                         | Y                           |                               |
| SERENE <sup>16</sup>           | PBO + MTX                          | 24                | 172              | 23.3                       | 9.3                        | 5.2                        | Y                           |                               |
| START <sup>17</sup>            | IFX 3mg + MTX                      | 22                | 343              | 58                         | 32.1                       | 14                         | Y                           |                               |
| START <sup>17</sup>            | PBO + MTX                          | 22                | 340              | 25.6                       | 9.7                        | 4.7                        | Y                           |                               |
| Weinblatt (1999) <sup>18</sup> | ETN + MTX                          | 24                | 59               | 71.2                       | 39                         | 15.3                       | Y                           |                               |
| Weinblatt (1999) <sup>18</sup> | PBO + MTX                          | 24                | 30               | 26.7                       | 3.3                        | 0                          | Y                           |                               |
| J-RAPID <sup>20</sup>          | CZP + MTX                          | 24                | 82               | 73.2                       | 54.9                       | 29.3                       | N                           | Up to 20% of prior bDMARD use |
| J-RAPID <sup>20</sup>          | PBO + MTX                          | 24                | 77               | 24.7                       | 16.9                       | 1.3                        | N                           |                               |
| Kang (2013) <sup>21</sup>      | CZP + MTX                          | 24                | 81               | 66.7                       | 43.2                       | 17.3                       | N                           | Up to 20% of prior bDMARD use |
| Kang (2013) <sup>21</sup>      | PBO + MTX                          | 24                | 40               | 27.5                       | 20                         | 2.5                        | N                           |                               |
| LITHE <sup>22</sup>            | TCZ 8mg + MTX                      | 24                | 398              | 56.5                       | 32.2                       | 12.3                       | N                           | Up to 20% of prior bDMARD use |
| LITHE <sup>22</sup>            | PBO + MTX                          | 24                | 393              | 27.7                       | 10.2                       | 2                          | N                           |                               |
| OPTION <sup>23</sup>           | TCZ 8mg + MTX                      | 24                | 205              | 58.5                       | 43.9                       | 22                         | N                           | Up to 20% of prior bDMARD use |
| OPTION <sup>23</sup>           | PBO + MTX                          | 24                | 204              | 26.5                       | 10.8                       | 2                          | N                           |                               |
| ORAL SCAN <sup>24</sup>        | TOFA 5mg + MTX                     | 26                | 321              | 51.4                       | 32.4                       | 14.6                       | N                           | Up to 20% of prior bDMARD use |
| ORAL SCAN <sup>24</sup>        | PBO + MTX                          | 26                | 79               | 25.3                       | 8.9                        | 1.3                        | N                           |                               |
| ORAL STANDARD <sup>25</sup>    | TOFA 5mg + MTX                     | 24                | 204              | 51.5                       | 39.2                       | 19.6                       | N                           |                               |
| ORAL STANDARD <sup>25</sup>    | ADA 40mg + MTX                     | 24                | 204              | 47.1                       | 28.9                       | 8.8                        | N                           | Up to 20% of prior bDMARD use |
| ORAL STANDARD <sup>25</sup>    | PBO + MTX                          | 24                | 108              | 28.7                       | 12                         | 1.9                        | N                           |                               |
| ORAL STRATEGY <sup>26</sup>    | TOFA 5mg + MTX                     | 24                | 376              | 73.1                       | 46                         | 25                         | N                           | Up to 20% of prior bDMARD use |
| ORAL STRATEGY <sup>26</sup>    | ADA 40mg + MTX                     | 24                | 386              | 71                         | 43.8                       | 20.7                       | N                           |                               |
| RACAT <sup>27</sup>            | ETN + MTX                          | 24                | 163              | 55.2                       | 35.6                       | 16                         | N                           | Up to 20% of prior bDMARD use |
| RACAT <sup>27</sup>            | SSZ + HCQ + MTX <sup>d</sup>       | 24                | 159              | 56                         | 25.8                       | 5                          | N                           |                               |
| RAPID1 <sup>28</sup>           | CZP+ MTX                           | 24                | 393              | 58.8                       | 37.2                       | 21.4                       | N                           | Up to 20% of prior bDMARD use |
| RAPID1 <sup>28</sup>           | PBO + MTX                          | 24                | 199              | 13.6                       | 7.5                        | 3                          | N                           |                               |
| RAPID2 <sup>29</sup>           | CZP + MTX                          | 24                | 246              | 57.3                       | 32.5                       | 15.9                       | N                           | Up to 20% of prior bDMARD use |
| RAPID2 <sup>29</sup>           | PBO + MTX                          | 24                | 127              | 8.7                        | 3.1                        | 0.8                        | N                           |                               |

a- Percentages are based on reported patient numbers.

b- Trial solely in Asia Pacific and/or with low (<7.5 mg/week) or unknown MTX dose

c- Open-label trial

d- Re-labeled to “cDMARD+MTX” in the analysis

## 9. Results – Primary Analyses

### 9.1. Primary analyses (Simultaneous Fixed – effects)

#### 9.1.1. ACR20 Response

**Table S12** Primary Analysis: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% Crls) - ACR20 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% Crl Lower  | 95% Crl Upper  |
|-----------------------------------|-----------------------|----------------|----------------|----------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1              | 1              |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.31513</b> | <b>4.10118</b> | <b>6.88964</b> |
| ADA 40mg + MTX                    | PBO + MTX             | 3.99938        | 3.26199        | 4.89624        |
| ABA 10mg + MTX                    | PBO + MTX             | 3.64788        | 2.80663        | 4.74853        |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.10476        | 2.85834        | 5.90041        |
| IFX 3mg + MTX                     | PBO + MTX             | 3.25395        | 2.59896        | 4.10315        |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.25348        | 2.33861        | 4.5455         |
| GOL 50mg + MTX                    | PBO + MTX             | 3.72863        | 2.72952        | 5.12315        |
| cDMARD + MTX                      | PBO + MTX             | 1.93528        | 1.0355         | 3.52118        |
| ETN + MTX                         | PBO + MTX             | 9.05622        | 5.28742        | 15.20698       |
| SARI 200mg + MTX                  | PBO + MTX             | 4.13151        | 2.96458        | 5.7811         |
| CZP + MTX                         | PBO + MTX             | 3.4882         | 2.3303         | 5.32786        |
| PBO + MTX                         | BARI 4mg + MTX        | 0.18814        | 0.14515        | 0.24383        |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1              | 1              |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.75223        | 0.57099        | 0.99305        |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.68734        | 0.4771         | 0.98922        |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.77142        | 0.51096        | 1.1677         |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.61342        | 0.43467        | 0.86131        |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.61167        | 0.40606        | 0.93022        |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.70191        | 0.46766        | 1.05847        |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.36436        | 0.18805        | 0.6926         |
| ETN + MTX                         | BARI 4mg + MTX        | 1.69883        | 0.95195        | 3.01826        |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.77925        | 0.51198        | 1.18559        |
| CZP + MTX                         | BARI 4mg + MTX        | 0.6551         | 0.40724        | 1.08158        |
| PBO + MTX                         | ADA 40mg + MTX        | 0.25004        | 0.20424        | 0.30656        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ADA 40mg + MTX</b> | <b>1.32938</b> | <b>1.007</b>   | <b>1.75135</b> |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1              | 1              |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.91324        | 0.66109        | 1.26509        |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 1.02651        | 0.74847        | 1.40938        |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.81414        | 0.60565        | 1.10206        |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.81317        | 0.55808        | 1.19803        |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.93203        | 0.64804        | 1.357          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.48456        | 0.25382        | 0.90248        |
| ETN + MTX                         | ADA 40mg + MTX        | 2.25902        | 1.29139        | 3.90528        |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 1.03437        | 0.70072        | 1.52599        |
| CZP + MTX                         | ADA 40mg + MTX        | 0.87196        | 0.55973        | 1.39421        |
| PBO + MTX                         | ABA 10mg + MTX        | 0.27413        | 0.21059        | 0.3563         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.45488</b> | <b>1.0109</b>  | <b>2.09601</b> |



| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| ADA 40mg + MTX                    | ABA 10mg + MTX          | 1.095          | 0.79046        | 1.51266        |
| ABA 10mg + MTX                    | ABA 10mg + MTX          | 1              | 1              | 1              |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX          | 1.12305        | 0.72442        | 1.75091        |
| IFX 3mg + MTX                     | ABA 10mg + MTX          | 0.89207        | 0.6523         | 1.2205         |
| RTX 1000mg + MTX                  | ABA 10mg + MTX          | 0.88997        | 0.58999        | 1.36309        |
| GOL 50mg + MTX                    | ABA 10mg + MTX          | 1.01978        | 0.68122        | 1.54776        |
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.52904        | 0.27401        | 1.01391        |
| ETN + MTX                         | ABA 10mg + MTX          | 2.4704         | 1.38273        | 4.41892        |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.13008        | 0.74836        | 1.72845        |
| CZP + MTX                         | ABA 10mg + MTX          | 0.95498        | 0.59141        | 1.58038        |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.24362        | 0.16948        | 0.34985        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.29632</b> | <b>0.85638</b> | <b>1.95709</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 0.97417        | 0.70953        | 1.33605        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.89043        | 0.57113        | 1.38042        |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.79279        | 0.52366        | 1.21615        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.79219        | 0.4904         | 1.29134        |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 0.90915        | 0.56591        | 1.46675        |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.47172        | 0.233          | 0.92921        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 2.20036        | 1.17492        | 4.10811        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.00786        | 0.61651        | 1.64583        |
| CZP + MTX                         | ABA SUBCUT + MTX        | 0.85046        | 0.49833        | 1.48442        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.30732        | 0.24372        | 0.38477        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>IFX 3mg + MTX</b>    | <b>1.63021</b> | <b>1.16103</b> | <b>2.30061</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.22828        | 0.90739        | 1.65111        |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 1.12099        | 0.81934        | 1.53305        |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.26136        | 0.82227        | 1.90965        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.99887        | 0.67272        | 1.48745        |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.14381        | 0.78602        | 1.68279        |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.59304        | 0.30658        | 1.12125        |
| ETN + MTX                         | IFX 3mg + MTX           | 2.77433        | 1.55796        | 4.85694        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.26891        | 0.84668        | 1.90011        |
| CZP + MTX                         | IFX 3mg + MTX           | 1.07259        | 0.67345        | 1.724          |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.30736        | 0.22           | 0.4276         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>1.63486</b> | <b>1.07501</b> | <b>2.46269</b> |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.22976        | 0.8347         | 1.79186        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.12363        | 0.73363        | 1.69495        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.26232        | 0.77439        | 2.03915        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.00113        | 0.67229        | 1.48649        |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.14702        | 0.73332        | 1.7886         |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.59402        | 0.29507        | 1.16175        |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.78234        | 1.48963        | 5.08647        |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.27187        | 0.79162        | 2.03145        |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.07302        | 0.64179        | 1.81831        |
| PBO + MTX                         | GOL 50mg + MTX          | 0.26819        | 0.19519        | 0.36637        |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.42469</b> | <b>0.94476</b> | <b>2.1383</b>  |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.07293        | 0.73692        | 1.54312        |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 0.9806         | 0.64609        | 1.46796        |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 1.09993        | 0.68178        | 1.76706        |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 0.87427        | 0.59425        | 1.27224        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.87183        | 0.5591         | 1.36366        |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.52203        | 0.25771        | 1.00645        |
| ETN + MTX                         | GOL 50mg + MTX          | 2.433          | 1.30033        | 4.35891        |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 1.1101         | 0.69897        | 1.74907        |
| CZP + MTX                         | GOL 50mg + MTX          | 0.93724        | 0.56342        | 1.55329        |
| PBO + MTX                         | cDMARD + MTX            | 0.51672        | 0.284          | 0.96572        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>2.74452</b> | <b>1.44383</b> | <b>5.31782</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 2.06371        | 1.10805        | 3.93973        |
| ABA 10mg + MTX                    | cDMARD + MTX            | 1.89021        | 0.98628        | 3.64951        |
| ABA SUBCUT + MTX                  | cDMARD + MTX            | 2.1199         | 1.07618        | 4.29185        |
| IFX 3mg + MTX                     | cDMARD + MTX            | 1.68621        | 0.89186        | 3.26179        |
| RTX 1000mg + MTX                  | cDMARD + MTX            | 1.68345        | 0.86077        | 3.38899        |
| GOL 50mg + MTX                    | cDMARD + MTX            | 1.9156         | 0.99359        | 3.88032        |
| cDMARD + MTX                      | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX                         | cDMARD + MTX            | 4.66695        | 2.98845        | 7.30374        |
| SARI 200mg + MTX                  | cDMARD + MTX            | 2.13635        | 1.08364        | 4.30617        |
| CZP + MTX                         | cDMARD + MTX            | 1.80017        | 0.8896         | 3.86891        |
| PBO + MTX                         | ETN + MTX               | 0.11042        | 0.06576        | 0.18913        |
| <b>BARI 4mg + MTX</b>             | <b>ETN + MTX</b>        | <b>0.58864</b> | <b>0.33132</b> | <b>1.05047</b> |
| ADA 40mg + MTX                    | ETN + MTX               | 0.44267        | 0.25606        | 0.77436        |
| ABA 10mg + MTX                    | ETN + MTX               | 0.40479        | 0.2263         | 0.72321        |
| ABA SUBCUT + MTX                  | ETN + MTX               | 0.45447        | 0.24342        | 0.85112        |
| IFX 3mg + MTX                     | ETN + MTX               | 0.36045        | 0.20589        | 0.64186        |
| RTX 1000mg + MTX                  | ETN + MTX               | 0.35941        | 0.1966         | 0.67131        |
| GOL 50mg + MTX                    | ETN + MTX               | 0.41102        | 0.22942        | 0.76904        |
| cDMARD + MTX                      | ETN + MTX               | 0.21427        | 0.13692        | 0.33462        |
| ETN + MTX                         | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX                  | ETN + MTX               | 0.45792        | 0.24747        | 0.85566        |
| CZP + MTX                         | ETN + MTX               | 0.38631        | 0.20455        | 0.76456        |
| PBO + MTX                         | SARI 200mg + MTX        | 0.24204        | 0.17298        | 0.33732        |
| <b>BARI 4mg + MTX</b>             | <b>SARI 200mg + MTX</b> | <b>1.28328</b> | <b>0.84346</b> | <b>1.9532</b>  |
| ADA 40mg + MTX                    | SARI 200mg + MTX        | 0.96677        | 0.65531        | 1.4271         |
| ABA 10mg + MTX                    | SARI 200mg + MTX        | 0.88489        | 0.57855        | 1.33626        |
| ABA SUBCUT + MTX                  | SARI 200mg + MTX        | 0.9922         | 0.6076         | 1.62204        |
| IFX 3mg + MTX                     | SARI 200mg + MTX        | 0.78808        | 0.52628        | 1.18108        |
| RTX 1000mg + MTX                  | SARI 200mg + MTX        | 0.78624        | 0.49226        | 1.26323        |
| GOL 50mg + MTX                    | SARI 200mg + MTX        | 0.90082        | 0.57173        | 1.43067        |
| cDMARD + MTX                      | SARI 200mg + MTX        | 0.46809        | 0.23223        | 0.92282        |
| ETN + MTX                         | SARI 200mg + MTX        | 2.18378        | 1.16869        | 4.04082        |
| SARI 200mg + MTX                  | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX                         | SARI 200mg + MTX        | 0.84456        | 0.49834        | 1.45005        |
| PBO + MTX                         | CZP + MTX               | 0.28668        | 0.18769        | 0.42913        |
| <b>BARI 4mg + MTX</b>             | <b>CZP + MTX</b>        | <b>1.52648</b> | <b>0.92458</b> | <b>2.45553</b> |
| ADA 40mg + MTX                    | CZP + MTX               | 1.14684        | 0.71725        | 1.78657        |
| ABA 10mg + MTX                    | CZP + MTX               | 1.04715        | 0.63276        | 1.69087        |
| ABA SUBCUT + MTX                  | CZP + MTX               | 1.17583        | 0.67366        | 2.0067         |
| IFX 3mg + MTX                     | CZP + MTX               | 0.93232        | 0.58005        | 1.48488        |
| RTX 1000mg + MTX                  | CZP + MTX               | 0.93195        | 0.54996        | 1.55814        |
| GOL 50mg + MTX                    | CZP + MTX               | 1.06697        | 0.64379        | 1.77489        |
| cDMARD + MTX                      | CZP + MTX               | 0.5555         | 0.25847        | 1.12411        |
| ETN + MTX                         | CZP + MTX               | 2.5886         | 1.30794        | 4.88878        |
| SARI 200mg + MTX                  | CZP + MTX               | 1.18405        | 0.68963        | 2.00664        |
| CZP + MTX                         | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

## 9.1.2. ACR50 Response

**Table S13** Primary Analysis: Relative treatment effect of pairwise comparisons expressed as post. Median odds ratios (with 95% CrIs) - ACR50 response at week 2 - MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-----------------------|----------------|----------------|----------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1              | 1              |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>4.98588</b> | <b>3.82327</b> | <b>6.51445</b> |
| ADA 40mg + MTX                    | PBO + MTX             | 4.56728        | 3.6222         | 5.77669        |
| ABA 10mg + MTX                    | PBO + MTX             | 3.52577        | 2.62551        | 4.78608        |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.55585        | 3.10209        | 6.68819        |
| IFX 3mg + MTX                     | PBO + MTX             | 3.49819        | 2.60941        | 4.74666        |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.28002        | 2.17601        | 5.04489        |
| GOL 50mg + MTX                    | PBO + MTX             | 3.45909        | 2.36829        | 5.09424        |
| cDMARD + MTX                      | PBO + MTX             | 1.50771        | 0.69075        | 3.45121        |
| ETN + MTX                         | PBO + MTX             | 8.02507        | 4.10227        | 16.71772       |
| SARI 200mg + MTX                  | PBO + MTX             | 4.37452        | 3.0949         | 6.22084        |
| CZP + MTX                         | PBO + MTX             | 5.84551        | 3.34592        | 11.10324       |
| PBO + MTX                         | BARI 4mg + MTX        | 0.20057        | 0.1535         | 0.26156        |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1              | 1              |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.91622        | 0.70662        | 1.18552        |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.70865        | 0.47453        | 1.05679        |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.91438        | 0.61114        | 1.36788        |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.70185        | 0.47317        | 1.04883        |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.65871        | 0.4046         | 1.08651        |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.69426        | 0.44025        | 1.10781        |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.30259        | 0.13321        | 0.71691        |
| ETN + MTX                         | BARI 4mg + MTX        | 1.60929        | 0.79352        | 3.48598        |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.8764         | 0.56844        | 1.35781        |
| CZP + MTX                         | BARI 4mg + MTX        | 1.17438        | 0.63505        | 2.35272        |
| PBO + MTX                         | ADA 40mg + MTX        | 0.21895        | 0.17311        | 0.27608        |
| <b>BARI 4mg + MTX</b>             | <b>ADA 40mg + MTX</b> | <b>1.09144</b> | <b>0.84351</b> | <b>1.41519</b> |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1              | 1              |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.77398        | 0.53107        | 1.12283        |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.99869        | 0.72952        | 1.36212        |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.76627        | 0.52942        | 1.11585        |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.71845        | 0.45229        | 1.15659        |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.75677        | 0.49116        | 1.17391        |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.33053        | 0.14804        | 0.77261        |
| ETN + MTX                         | ADA 40mg + MTX        | 1.75643        | 0.88746        | 3.74289        |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 0.95709        | 0.63289        | 1.45234        |
| CZP + MTX                         | ADA 40mg + MTX        | 1.28005        | 0.70451        | 2.51899        |
| PBO + MTX                         | ABA 10mg + MTX        | 0.28363        | 0.20894        | 0.38088        |
| <b>BARI 4mg + MTX</b>             | <b>ABA 10mg + MTX</b> | <b>1.41113</b> | <b>0.94626</b> | <b>2.10735</b> |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.29202        | 0.89061        | 1.88299        |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1              | 1              |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.29027        | 0.79544        | 2.09266        |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 0.99104        | 0.70279        | 1.40793        |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.92952        | 0.56075        | 1.55871        |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| GOL 50mg + MTX        | ABA 10mg + MTX          | 0.97973        | 0.60562        | 1.59262        |
| cDMARD + MTX          | ABA 10mg + MTX          | 0.42631        | 0.18692        | 1.02712        |
| ETN + MTX             | ABA 10mg + MTX          | 2.27385        | 1.10589        | 5.00869        |
| SARI 200mg + MTX      | ABA 10mg + MTX          | 1.23956        | 0.78383        | 1.95802        |
| CZP + MTX             | ABA 10mg + MTX          | 1.65984        | 0.87975        | 3.35988        |
| PBO + MTX             | ABA SUBCUT + MTX        | 0.2195         | 0.14952        | 0.32236        |
| <b>BARI 4mg + MTX</b> | <b>ABA SUBCUT + MTX</b> | <b>1.09364</b> | <b>0.73106</b> | <b>1.63628</b> |
| ADA 40mg + MTX        | ABA SUBCUT + MTX        | 1.00131        | 0.73415        | 1.37077        |
| ABA 10mg + MTX        | ABA SUBCUT + MTX        | 0.77503        | 0.47786        | 1.25716        |
| ABA SUBCUT + MTX      | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX         | ABA SUBCUT + MTX        | 0.76757        | 0.47468        | 1.24248        |
| RTX 1000mg + MTX      | ABA SUBCUT + MTX        | 0.72001        | 0.41518        | 1.26053        |
| GOL 50mg + MTX        | ABA SUBCUT + MTX        | 0.75978        | 0.44937        | 1.29816        |
| cDMARD + MTX          | ABA SUBCUT + MTX        | 0.33125        | 0.141          | 0.81138        |
| ETN + MTX             | ABA SUBCUT + MTX        | 1.76353        | 0.83637        | 3.97621        |
| SARI 200mg + MTX      | ABA SUBCUT + MTX        | 0.95973        | 0.57374        | 1.60912        |
| CZP + MTX             | ABA SUBCUT + MTX        | 1.28743        | 0.65733        | 2.6908         |
| PBO + MTX             | IFX 3mg + MTX           | 0.28586        | 0.21067        | 0.38323        |
| <b>BARI 4mg + MTX</b> | <b>IFX 3mg + MTX</b>    | <b>1.4248</b>  | <b>0.95344</b> | <b>2.11341</b> |
| ADA 40mg + MTX        | IFX 3mg + MTX           | 1.30503        | 0.89618        | 1.88886        |
| ABA 10mg + MTX        | IFX 3mg + MTX           | 1.00904        | 0.71026        | 1.4229         |
| ABA SUBCUT + MTX      | IFX 3mg + MTX           | 1.30281        | 0.80484        | 2.1067         |
| IFX 3mg + MTX         | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX      | IFX 3mg + MTX           | 0.93819        | 0.56848        | 1.56362        |
| GOL 50mg + MTX        | IFX 3mg + MTX           | 0.98788        | 0.61292        | 1.60039        |
| cDMARD + MTX          | IFX 3mg + MTX           | 0.43052        | 0.18862        | 1.0265         |
| ETN + MTX             | IFX 3mg + MTX           | 2.29326        | 1.11913        | 5.00545        |
| SARI 200mg + MTX      | IFX 3mg + MTX           | 1.24964        | 0.7906         | 1.96818        |
| CZP + MTX             | IFX 3mg + MTX           | 1.67576        | 0.89599        | 3.3616         |
| PBO + MTX             | RTX 1000mg + MTX        | 0.30488        | 0.19822        | 0.45956        |
| <b>BARI 4mg + MTX</b> | <b>RTX 1000mg + MTX</b> | <b>1.51813</b> | <b>0.92038</b> | <b>2.47158</b> |
| ADA 40mg + MTX        | RTX 1000mg + MTX        | 1.39188        | 0.86461        | 2.21098        |
| ABA 10mg + MTX        | RTX 1000mg + MTX        | 1.07583        | 0.64156        | 1.78332        |
| ABA SUBCUT + MTX      | RTX 1000mg + MTX        | 1.38888        | 0.79332        | 2.40861        |
| IFX 3mg + MTX         | RTX 1000mg + MTX        | 1.06588        | 0.63954        | 1.75909        |
| RTX 1000mg + MTX      | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX        | RTX 1000mg + MTX        | 1.05443        | 0.6064         | 1.82295        |
| cDMARD + MTX          | RTX 1000mg + MTX        | 0.46083        | 0.19217        | 1.13047        |
| ETN + MTX             | RTX 1000mg + MTX        | 2.46032        | 1.12833        | 5.52308        |
| SARI 200mg + MTX      | RTX 1000mg + MTX        | 1.33517        | 0.76715        | 2.3064         |
| CZP + MTX             | RTX 1000mg + MTX        | 1.79062        | 0.89467        | 3.76726        |
| PBO + MTX             | GOL 50mg + MTX          | 0.28909        | 0.1963         | 0.42225        |
| <b>BARI 4mg + MTX</b> | <b>GOL 50mg + MTX</b>   | <b>1.44039</b> | <b>0.90268</b> | <b>2.27143</b> |
| ADA 40mg + MTX        | GOL 50mg + MTX          | 1.3214         | 0.85185        | 2.036          |
| ABA 10mg + MTX        | GOL 50mg + MTX          | 1.02069        | 0.6279         | 1.6512         |
| ABA SUBCUT + MTX      | GOL 50mg + MTX          | 1.31618        | 0.77032        | 2.22535        |
| IFX 3mg + MTX         | GOL 50mg + MTX          | 1.01227        | 0.62485        | 1.63153        |
| RTX 1000mg + MTX      | GOL 50mg + MTX          | 0.94838        | 0.54856        | 1.64906        |
| GOL 50mg + MTX        | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX          | GOL 50mg + MTX          | 0.43704        | 0.18424        | 1.04154        |
| ETN + MTX             | GOL 50mg + MTX          | 2.33387        | 1.09127        | 5.11437        |
| SARI 200mg + MTX      | GOL 50mg + MTX          | 1.26488        | 0.74888        | 2.13111        |
| CZP + MTX             | GOL 50mg + MTX          | 1.69967        | 0.8696         | 3.48432        |
| PBO + MTX             | cDMARD + MTX            | 0.66326        | 0.28975        | 1.44771        |
| <b>BARI 4mg + MTX</b> | <b>cDMARD + MTX</b>     | <b>3.30477</b> | <b>1.39487</b> | <b>7.50679</b> |
| ADA 40mg + MTX        | cDMARD + MTX            | 3.02547        | 1.29432        | 6.75504        |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ABA 10mg + MTX        | cDMARD + MTX            | 2.34573        | 0.9736         | 5.34977        |
| ABA SUBCUT + MTX      | cDMARD + MTX            | 3.01883        | 1.23246        | 7.09211        |
| IFX 3mg + MTX         | cDMARD + MTX            | 2.32279        | 0.97419        | 5.30166        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 2.16999        | 0.88459        | 5.20384        |
| GOL 50mg + MTX        | cDMARD + MTX            | 2.28813        | 0.96012        | 5.42775        |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 5.33574        | 3.40226        | 8.52667        |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.91955        | 1.16856        | 6.75753        |
| CZP + MTX             | cDMARD + MTX            | 3.89857        | 1.50284        | 10.3388        |
| PBO + MTX             | ETN + MTX               | 0.12461        | 0.05982        | 0.24377        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.62139</b> | <b>0.28686</b> | <b>1.26021</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.56934        | 0.26717        | 1.12682        |
| ABA 10mg + MTX        | ETN + MTX               | 0.43978        | 0.19965        | 0.90425        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.56704        | 0.2515         | 1.19565        |
| IFX 3mg + MTX         | ETN + MTX               | 0.43606        | 0.19978        | 0.89355        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.40645        | 0.18106        | 0.88626        |
| GOL 50mg + MTX        | ETN + MTX               | 0.42847        | 0.19553        | 0.91636        |
| cDMARD + MTX          | ETN + MTX               | 0.18742        | 0.11728        | 0.29392        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.54737        | 0.23831        | 1.14828        |
| CZP + MTX             | ETN + MTX               | 0.73007        | 0.30384        | 1.78808        |
| PBO + MTX             | SARI 200mg + MTX        | 0.2286         | 0.16075        | 0.32311        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.14103</b> | <b>0.73648</b> | <b>1.75921</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.04483        | 0.68855        | 1.58005        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.80674        | 0.51072        | 1.27579        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 1.04196        | 0.62146        | 1.74295        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.80023        | 0.50808        | 1.26487        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.74897        | 0.43358        | 1.30352        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.79059        | 0.46924        | 1.33533        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.34252        | 0.14798        | 0.85575        |
| ETN + MTX             | SARI 200mg + MTX        | 1.82693        | 0.87087        | 4.19623        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 1.34191        | 0.68806        | 2.80143        |
| PBO + MTX             | CZP + MTX               | 0.17107        | 0.09006        | 0.29887        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>0.85151</b> | <b>0.42504</b> | <b>1.57467</b> |
| ADA 40mg + MTX        | CZP + MTX               | 0.78122        | 0.39698        | 1.41942        |
| ABA 10mg + MTX        | CZP + MTX               | 0.60247        | 0.29763        | 1.13669        |
| ABA SUBCUT + MTX      | CZP + MTX               | 0.77674        | 0.37164        | 1.5213         |
| IFX 3mg + MTX         | CZP + MTX               | 0.59674        | 0.29748        | 1.11609        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.55847        | 0.26544        | 1.11773        |
| GOL 50mg + MTX        | CZP + MTX               | 0.58835        | 0.287          | 1.14995        |
| cDMARD + MTX          | CZP + MTX               | 0.2565         | 0.09672        | 0.66541        |
| ETN + MTX             | CZP + MTX               | 1.36973        | 0.55926        | 3.29117        |
| SARI 200mg + MTX      | CZP + MTX               | 0.74521        | 0.35696        | 1.45336        |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

### 9.1.3. ACR70 response

**Table S14** Primary Analysis: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CRIs) - ACR70 response at week 24- MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.90962</b> | <b>4.1892</b>    | <b>8.46738</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 4.30279        | 3.13894          | 5.97356          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.17438        | 2.12952          | 4.79003          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.10487        | 2.53588          | 6.68776          |
| IFX 3mg + MTX                     | PBO + MTX             | 3.55417        | 2.37697          | 5.40304          |
| RTX 1000mg + MTX                  | PBO + MTX             | 2.6203         | 1.44088          | 4.93619          |
| GOL 50mg + MTX                    | PBO + MTX             | 4.33691        | 2.52618          | 7.74905          |
| cDMARD + MTX                      | PBO + MTX             | 1.55471        | 0.48233          | 5.65011          |
| ETN + MTX                         | PBO + MTX             | 6.61907        | 2.3521           | 21.80178         |
| SARI 200mg + MTX                  | PBO + MTX             | 4.25584        | 3.01852          | 6.06864          |
| CZP + MTX                         | PBO + MTX             | 5.66301        | 2.45465          | 15.43534         |
| PBO + MTX                         | BARI 4mg + MTX        | 0.16922        | 0.1181           | 0.23871          |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.72752        | 0.53526          | 0.9834           |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.53682        | 0.3154           | 0.91589          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.69437        | 0.43106          | 1.11046          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.60233        | 0.35289          | 1.02472          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.44261        | 0.22368          | 0.90395          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.73357        | 0.3897           | 1.42801          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.26203        | 0.07803          | 0.98069          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.11407        | 0.37821          | 3.82348          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.72011        | 0.43627          | 1.17349          |
| CZP + MTX                         | BARI 4mg + MTX        | 0.95794        | 0.38804          | 2.76948          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.23241        | 0.1674           | 0.31858          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ADA 40mg + MTX</b> | <b>1.37453</b> | <b>1.01688</b>   | <b>1.86825</b>   |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.73795        | 0.44408          | 1.23276          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.95444        | 0.65955          | 1.3789           |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.82725        | 0.49446          | 1.37774          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.60862        | 0.31315          | 1.21682          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 1.00859        | 0.54243          | 1.93386          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.36033        | 0.10901          | 1.33238          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.53652        | 0.52915          | 5.14112          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 0.99014        | 0.61852          | 1.58464          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.31606        | 0.54265          | 3.73832          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.31502        | 0.20877          | 0.46959          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.86283</b> | <b>1.09183</b>   | <b>3.17055</b>   |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.35511        | 0.81119          | 2.25187          |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1                | 1                |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.2926         | 0.68843          | 2.42974          |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 1.12181        | 0.72189          | 1.74015          |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.82524        | 0.40494          | 1.72103          |
| GOL 50mg + MTX                    | ABA 10mg + MTX        | 1.36573        | 0.70389          | 2.75068          |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper   |
|-----------------------------------|-------------------------|----------------|----------------|-----------------|
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.489          | 0.14209        | 1.86374         |
| ETN + MTX                         | ABA 10mg + MTX          | 2.08426        | 0.69437        | 7.20118         |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.34121        | 0.78464        | 2.27303         |
| CZP + MTX                         | ABA 10mg + MTX          | 1.78807        | 0.70646        | 5.25484         |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.24361        | 0.14953        | 0.39434         |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.44015</b> | <b>0.90052</b> | <b>2.31987</b>  |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 1.04773        | 0.72522        | 1.51618         |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.77363        | 0.41157        | 1.45257         |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1               |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.86693        | 0.46271        | 1.63136         |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.64112        | 0.29711        | 1.39643         |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 1.05744        | 0.51623        | 2.22824         |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.38036        | 0.10771        | 1.46031         |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.61356        | 0.52512        | 5.7099          |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.03779        | 0.56823        | 1.88664         |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.39165        | 0.52714        | 4.16014         |
| PBO + MTX                         | IFX 3mg + MTX           | 0.28136        | 0.18508        | 0.4207          |
| <b>BARI 4mg + MTX</b>             | <b>IFX 3mg + MTX</b>    | <b>1.66023</b> | <b>0.97588</b> | <b>2.83374</b>  |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.20883        | 0.72583        | 2.02242         |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 0.89141        | 0.57466        | 1.38526         |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.15349        | 0.61299        | 2.16117         |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1               |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.73684        | 0.35883        | 1.54371         |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.21736        | 0.6252         | 2.44052         |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.43707        | 0.12739        | 1.65367         |
| ETN + MTX                         | IFX 3mg + MTX           | 1.8603         | 0.61942        | 6.41905         |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.19713        | 0.69921        | 2.04126         |
| CZP + MTX                         | IFX 3mg + MTX           | 1.59257        | 0.63191        | 4.65816         |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.38164        | 0.20259        | 0.69402         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>2.25934</b> | <b>1.10626</b> | <b>4.4707</b>   |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.64305        | 0.82181        | 3.19337         |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.21176        | 0.58105        | 2.46948         |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.55977        | 0.71611        | 3.36576         |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.35714        | 0.64779        | 2.78687         |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1               |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.65435        | 0.74276        | 3.72542         |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.59257        | 0.16019        | 2.28887         |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.52556        | 0.77569        | 8.97035         |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.62586        | 0.7907         | 3.26308         |
| CZP + MTX                         | RTX 1000mg + MTX        | 2.16587        | 0.77439        | 6.70475         |
| PBO + MTX                         | GOL 50mg + MTX          | 0.23058        | 0.12905        | 0.39586         |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.3632</b>  | <b>0.70027</b> | <b>2.56605</b>  |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 0.99149        | 0.5171         | 1.84355         |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 0.73221        | 0.36355        | 1.42068         |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 0.94568        | 0.44878        | 1.93712         |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 0.82145        | 0.40975        | 1.5995          |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.60447        | 0.26843        | 1.34633         |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1               |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.35855        | 0.09995        | 1.36593         |
| ETN + MTX                         | GOL 50mg + MTX          | 1.5302         | 0.48624        | 5.27018         |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 0.98325        | 0.49571        | 1.86838         |
| CZP + MTX                         | GOL 50mg + MTX          | 1.31051        | 0.48505        | 3.92783         |
| PBO + MTX                         | cDMARD + MTX            | 0.64321        | 0.17699        | 2.07325         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>3.81635</b> | <b>1.01969</b> | <b>12.81611</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 2.77524        | 0.75053        | 9.17349         |
| ABA 10mg + MTX                    | cDMARD + MTX            | 2.045          | 0.53656        | 7.03796         |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ABA SUBCUT + MTX      | cDMARD + MTX            | 2.62911        | 0.68479        | 9.2844         |
| IFX 3mg + MTX         | cDMARD + MTX            | 2.28795        | 0.60471        | 7.85014        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 1.68756        | 0.4369         | 6.24261        |
| GOL 50mg + MTX        | cDMARD + MTX            | 2.789          | 0.7321         | 10.00526       |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 4.25686        | 2.44213        | 7.84486        |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.752          | 0.72016        | 9.23747        |
| CZP + MTX             | cDMARD + MTX            | 3.67318        | 0.85659        | 16.46029       |
| PBO + MTX             | ETN + MTX               | 0.15108        | 0.04587        | 0.42515        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.89761</b> | <b>0.26154</b> | <b>2.64401</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.65082        | 0.19451        | 1.88983        |
| ABA 10mg + MTX        | ETN + MTX               | 0.47979        | 0.13887        | 1.44015        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.61975        | 0.17513        | 1.90433        |
| IFX 3mg + MTX         | ETN + MTX               | 0.53755        | 0.15579        | 1.6144         |
| RTX 1000mg + MTX      | ETN + MTX               | 0.39595        | 0.11148        | 1.28917        |
| GOL 50mg + MTX        | ETN + MTX               | 0.65351        | 0.18975        | 2.05659        |
| cDMARD + MTX          | ETN + MTX               | 0.23492        | 0.12747        | 0.40948        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.64539        | 0.18652        | 1.90243        |
| CZP + MTX             | ETN + MTX               | 0.85835        | 0.21701        | 3.49937        |
| PBO + MTX             | SARI 200mg + MTX        | 0.23497        | 0.16478        | 0.33129        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.38867</b> | <b>0.85216</b> | <b>2.29214</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.00996        | 0.63106        | 1.61677        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.7456         | 0.43994        | 1.27447        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.96359        | 0.53004        | 1.75986        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.83533        | 0.48989        | 1.43019        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.61506        | 0.30646        | 1.2647         |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 1.01703        | 0.53522        | 2.0173         |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.36337        | 0.10825        | 1.38858        |
| ETN + MTX             | SARI 200mg + MTX        | 1.54944        | 0.52564        | 5.36149        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 1.33242        | 0.53458        | 3.87891        |
| PBO + MTX             | CZP + MTX               | 0.17658        | 0.06479        | 0.40739        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>1.04391</b> | <b>0.36108</b> | <b>2.57707</b> |
| ADA 40mg + MTX        | CZP + MTX               | 0.75984        | 0.2675         | 1.84281        |
| ABA 10mg + MTX        | CZP + MTX               | 0.55926        | 0.1903         | 1.4155         |
| ABA SUBCUT + MTX      | CZP + MTX               | 0.71857        | 0.24038        | 1.89703        |
| IFX 3mg + MTX         | CZP + MTX               | 0.62792        | 0.21468        | 1.58251        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.46171        | 0.14915        | 1.29134        |
| GOL 50mg + MTX        | CZP + MTX               | 0.76306        | 0.25459        | 2.06164        |
| cDMARD + MTX          | CZP + MTX               | 0.27224        | 0.06075        | 1.16742        |
| ETN + MTX             | CZP + MTX               | 1.16502        | 0.28577        | 4.60802        |
| SARI 200mg + MTX      | CZP + MTX               | 0.75051        | 0.2578         | 1.87064        |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.



## 9.2. Primary analyses (Simultaneous Random – effects)

### 9.2.1. ACR20 Response

**Table S15** Primary Analysis: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) - ACR20 response at week 24: MTX-IR (Simultaneous Random-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-----------------------|----------------|----------------|----------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1              | 1              |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.35584</b> | <b>3.92299</b> | <b>7.49344</b> |
| ADA 40mg + MTX                    | PBO + MTX             | 4.04785        | 3.24816        | 5.14534        |
| ABA 10mg + MTX                    | PBO + MTX             | 3.65565        | 2.71153        | 4.94564        |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.16303        | 2.74758        | 6.40342        |
| IFX 3mg + MTX                     | PBO + MTX             | 3.2329         | 2.47406        | 4.16245        |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.27508        | 2.29895        | 4.71786        |
| GOL 50mg + MTX                    | PBO + MTX             | 3.74964        | 2.69673        | 5.26016        |
| cDMARD + MTX                      | PBO + MTX             | 1.96546        | 1.01442        | 3.63202        |
| ETN + MTX                         | PBO + MTX             | 9.07524        | 5.16827        | 15.49234       |
| SARI 200mg + MTX                  | PBO + MTX             | 4.11785        | 2.79596        | 6.13754        |
| CZP + MTX                         | PBO + MTX             | 3.50218        | 2.21277        | 5.6458         |
| PBO + MTX                         | BARI 4mg + MTX        | 0.18671        | 0.13345        | 0.25491        |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1              | 1              |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.7553         | 0.53973        | 1.0601         |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.68407        | 0.43409        | 1.05208        |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.77689        | 0.47365        | 1.27108        |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.60353        | 0.39056        | 0.89735        |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.60873        | 0.37919        | 0.98675        |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.69873        | 0.43917        | 1.10684        |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.36577        | 0.17613        | 0.73274        |
| ETN + MTX                         | BARI 4mg + MTX        | 1.69464        | 0.88852        | 3.16414        |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.768          | 0.4612         | 1.26411        |
| CZP + MTX                         | BARI 4mg + MTX        | 0.65326        | 0.37074        | 1.15739        |
| PBO + MTX                         | ADA 40mg + MTX        | 0.24704        | 0.19435        | 0.30787        |
| <b>BARI 4mg + MTX</b>             | <b>ADA 40mg + MTX</b> | <b>1.32398</b> | <b>0.94331</b> | <b>1.85279</b> |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1              | 1              |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.90221        | 0.61655        | 1.29963        |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 1.02776        | 0.70657        | 1.49771        |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.79855        | 0.55642        | 1.10682        |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.80694        | 0.53019        | 1.23253        |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.92346        | 0.61765        | 1.37197        |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.48391        | 0.24029        | 0.92461        |
| ETN + MTX                         | ADA 40mg + MTX        | 2.24358        | 1.22536        | 3.97051        |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 1.02018        | 0.645          | 1.59104        |
| CZP + MTX                         | ADA 40mg + MTX        | 0.86538        | 0.51335        | 1.442          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.27355        | 0.2022         | 0.3688         |
| <b>BARI 4mg + MTX</b>             | <b>ABA 10mg + MTX</b> | <b>1.46183</b> | <b>0.9505</b>  | <b>2.30367</b> |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.10838        | 0.76945        | 1.62194        |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1              | 1              |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.13914        | 0.69183        | 1.91718        |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| IFX 3mg + MTX                     | ABA 10mg + MTX          | 0.88444        | 0.61126        | 1.25984        |
| RTX 1000mg + MTX                  | ABA 10mg + MTX          | 0.89416        | 0.56796        | 1.43754        |
| GOL 50mg + MTX                    | ABA 10mg + MTX          | 1.02256        | 0.66003        | 1.62713        |
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.53481        | 0.26518        | 1.05824        |
| ETN + MTX                         | ABA 10mg + MTX          | 2.48334        | 1.34562        | 4.55605        |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.12485        | 0.69254        | 1.84039        |
| CZP + MTX                         | ABA 10mg + MTX          | 0.95673        | 0.55388        | 1.68935        |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.24021        | 0.15617        | 0.36396        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.28718</b> | <b>0.78673</b> | <b>2.11128</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 0.97299        | 0.66768        | 1.41528        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.87785        | 0.5216         | 1.44545        |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.77545        | 0.46822        | 1.24677        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.78361        | 0.45437        | 1.3625         |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 0.89891        | 0.52379        | 1.5316         |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.47037        | 0.21716        | 0.97988        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 2.17916        | 1.08495        | 4.28379        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 0.99016        | 0.55548        | 1.73709        |
| CZP + MTX                         | ABA SUBCUT + MTX        | 0.84322        | 0.44846        | 1.56888        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.30932        | 0.24024        | 0.40419        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>IFX 3mg + MTX</b>    | <b>1.65691</b> | <b>1.11439</b> | <b>2.56043</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.25227        | 0.90349        | 1.7972         |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 1.13066        | 0.79375        | 1.63596        |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.28958        | 0.80207        | 2.13575        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 1.01241        | 0.66366        | 1.58589        |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.16029        | 0.77625        | 1.77522        |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.6089         | 0.30166        | 1.18882        |
| ETN + MTX                         | IFX 3mg + MTX           | 2.81253        | 1.53142        | 5.10349        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.27327        | 0.8076         | 2.0551         |
| CZP + MTX                         | IFX 3mg + MTX           | 1.08211        | 0.6523         | 1.8689         |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.30534        | 0.21196        | 0.43498        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>1.64276</b> | <b>1.01343</b> | <b>2.63722</b> |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.23925        | 0.81134        | 1.88612        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.11836        | 0.69563        | 1.76068        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.27615        | 0.73395        | 2.20084        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 0.98774        | 0.63056        | 1.50681        |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.14542        | 0.71195        | 1.83143        |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.59969        | 0.28289        | 1.21739        |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.77523        | 1.41943        | 5.18231        |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.26043        | 0.73537        | 2.13838        |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.07131        | 0.60018        | 1.89118        |
| PBO + MTX                         | GOL 50mg + MTX          | 0.26669        | 0.19011        | 0.37082        |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.43118</b> | <b>0.90347</b> | <b>2.27701</b> |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.08288        | 0.72888        | 1.61904        |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 0.97794        | 0.61458        | 1.51508        |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 1.11246        | 0.65291        | 1.90917        |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 0.86186        | 0.56331        | 1.28825        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.87305        | 0.54602        | 1.40458        |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.52491        | 0.24797        | 1.05509        |
| ETN + MTX                         | GOL 50mg + MTX          | 2.43095        | 1.24619        | 4.51476        |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 1.10072        | 0.65262        | 1.84272        |
| CZP + MTX                         | GOL 50mg + MTX          | 0.93755        | 0.5321         | 1.64225        |
| PBO + MTX                         | cDMARD + MTX            | 0.50879        | 0.27533        | 0.98579        |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>2.73399</b> | <b>1.36474</b> | <b>5.67749</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 2.06651        | 1.08153        | 4.16171        |
| ABA 10mg + MTX                    | cDMARD + MTX            | 1.86983        | 0.94497        | 3.77104        |
| ABA SUBCUT + MTX                  | cDMARD + MTX            | 2.12597        | 1.02053        | 4.60488        |
| IFX 3mg + MTX                     | cDMARD + MTX            | 1.6423         | 0.84117        | 3.31503        |
| RTX 1000mg + MTX                  | cDMARD + MTX            | 1.66752        | 0.82143        | 3.53492        |
| GOL 50mg + MTX                    | cDMARD + MTX            | 1.9051         | 0.94779        | 4.03273        |
| cDMARD + MTX                      | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX                         | cDMARD + MTX            | 4.64788        | 2.82639        | 7.5222         |
| SARI 200mg + MTX                  | cDMARD + MTX            | 2.1061         | 1.02021        | 4.52332        |
| CZP + MTX                         | cDMARD + MTX            | 1.78709        | 0.83888        | 4.03127        |
| PBO + MTX                         | ETN + MTX               | 0.11019        | 0.06455        | 0.19349        |
| <b>BARI 4mg + MTX</b>             | <b>ETN + MTX</b>        | <b>0.59009</b> | <b>0.31604</b> | <b>1.12546</b> |
| ADA 40mg + MTX                    | ETN + MTX               | 0.44572        | 0.25186        | 0.81609        |
| ABA 10mg + MTX                    | ETN + MTX               | 0.40268        | 0.21949        | 0.74315        |
| ABA SUBCUT + MTX                  | ETN + MTX               | 0.45889        | 0.23344        | 0.9217         |
| IFX 3mg + MTX                     | ETN + MTX               | 0.35555        | 0.19594        | 0.65299        |
| RTX 1000mg + MTX                  | ETN + MTX               | 0.36033        | 0.19296        | 0.70451        |
| GOL 50mg + MTX                    | ETN + MTX               | 0.41136        | 0.2215         | 0.80244        |
| cDMARD + MTX                      | ETN + MTX               | 0.21515        | 0.13294        | 0.35381        |
| ETN + MTX                         | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX                  | ETN + MTX               | 0.45346        | 0.23223        | 0.89804        |
| CZP + MTX                         | ETN + MTX               | 0.38446        | 0.19224        | 0.79707        |
| PBO + MTX                         | SARI 200mg + MTX        | 0.24284        | 0.16293        | 0.35766        |
| <b>BARI 4mg + MTX</b>             | <b>SARI 200mg + MTX</b> | <b>1.30208</b> | <b>0.79107</b> | <b>2.16827</b> |
| ADA 40mg + MTX                    | SARI 200mg + MTX        | 0.98022        | 0.62852        | 1.55039        |
| ABA 10mg + MTX                    | SARI 200mg + MTX        | 0.88901        | 0.54336        | 1.44396        |
| ABA SUBCUT + MTX                  | SARI 200mg + MTX        | 1.00994        | 0.57568        | 1.80026        |
| IFX 3mg + MTX                     | SARI 200mg + MTX        | 0.78538        | 0.48659        | 1.23824        |
| RTX 1000mg + MTX                  | SARI 200mg + MTX        | 0.79338        | 0.46764        | 1.35985        |
| GOL 50mg + MTX                    | SARI 200mg + MTX        | 0.9085         | 0.54267        | 1.53229        |
| cDMARD + MTX                      | SARI 200mg + MTX        | 0.47481        | 0.22108        | 0.98019        |
| ETN + MTX                         | SARI 200mg + MTX        | 2.20529        | 1.11354        | 4.30603        |
| SARI 200mg + MTX                  | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX                         | SARI 200mg + MTX        | 0.84964        | 0.46686        | 1.57357        |
| PBO + MTX                         | CZP + MTX               | 0.28554        | 0.17712        | 0.45192        |
| <b>BARI 4mg + MTX</b>             | <b>CZP + MTX</b>        | <b>1.53078</b> | <b>0.86401</b> | <b>2.69728</b> |
| ADA 40mg + MTX                    | CZP + MTX               | 1.15556        | 0.69348        | 1.948          |
| ABA 10mg + MTX                    | CZP + MTX               | 1.04522        | 0.59194        | 1.80543        |
| ABA SUBCUT + MTX                  | CZP + MTX               | 1.18593        | 0.6374         | 2.22987        |
| IFX 3mg + MTX                     | CZP + MTX               | 0.92412        | 0.53507        | 1.53305        |
| RTX 1000mg + MTX                  | CZP + MTX               | 0.93344        | 0.52877        | 1.66618        |
| GOL 50mg + MTX                    | CZP + MTX               | 1.06661        | 0.60892        | 1.87936        |
| cDMARD + MTX                      | CZP + MTX               | 0.55957        | 0.24806        | 1.19207        |
| ETN + MTX                         | CZP + MTX               | 2.60102        | 1.2546         | 5.20184        |
| SARI 200mg + MTX                  | CZP + MTX               | 1.17697        | 0.6355         | 2.14195        |
| CZP + MTX                         | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

## 9.2.2. ACR50 Response

**Table S16** Primary Analysis: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) – ACR50 response at week 24: MTX-IR (Simultaneous Random effects-model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.05962</b> | <b>3.53049</b>   | <b>7.52433</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 4.71494        | 3.60397          | 6.52315          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.5264         | 2.44954          | 5.07112          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.68506        | 2.93347          | 7.90648          |
| IFX 3mg + MTX                     | PBO + MTX             | 3.4878         | 2.42097          | 4.98225          |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.32256        | 2.10945          | 5.3351           |
| GOL 50mg + MTX                    | PBO + MTX             | 3.46788        | 2.30761          | 5.32052          |
| cDMARD + MTX                      | PBO + MTX             | 1.54725        | 0.6731           | 3.89247          |
| ETN + MTX                         | PBO + MTX             | 8.18398        | 3.98304          | 18.29486         |
| SARI 200mg + MTX                  | PBO + MTX             | 4.37612        | 2.76577          | 6.86395          |
| CZP + MTX                         | PBO + MTX             | 5.94439        | 3.11934          | 12.02306         |
| PBO + MTX                         | BARI 4mg + MTX        | 0.19764        | 0.1329           | 0.28325          |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.92822        | 0.65255          | 1.39266          |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.69828        | 0.40804          | 1.15789          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.92354        | 0.53908          | 1.64233          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.6893         | 0.40011          | 1.14307          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.65503        | 0.36327          | 1.19257          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.68519        | 0.38747          | 1.19079          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.30696        | 0.1233           | 0.81985          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.61983        | 0.71757          | 3.85302          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.86529        | 0.46886          | 1.5228           |
| CZP + MTX                         | BARI 4mg + MTX        | 1.17462        | 0.55193          | 2.54545          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.21209        | 0.1533           | 0.27747          |
| <b>BARI 4mg + MTX</b>             | <b>ADA 40mg + MTX</b> | <b>1.07733</b> | <b>0.71805</b>   | <b>1.53244</b>   |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.74978        | 0.45839          | 1.15376          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.99318        | 0.65263          | 1.50163          |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.73981        | 0.44883          | 1.13692          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.70237        | 0.40925          | 1.21328          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.73496        | 0.43905          | 1.2021           |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.32895        | 0.13568          | 0.83026          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.73026        | 0.79953          | 3.97687          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 0.929          | 0.52052          | 1.53316          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.26021        | 0.61114          | 2.62781          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.28358        | 0.1972           | 0.40824          |
| <b>BARI 4mg + MTX</b>             | <b>ABA 10mg + MTX</b> | <b>1.4321</b>  | <b>0.86364</b>   | <b>2.45075</b>   |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.33373        | 0.86673          | 2.18156          |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1                | 1                |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.32629        | 0.73838          | 2.49913          |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 0.98749        | 0.64337          | 1.50654          |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.93935        | 0.52506          | 1.72004          |
| GOL 50mg + MTX                    | ABA 10mg + MTX        | 0.98459        | 0.56929          | 1.71025          |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.43907        | 0.17766        | 1.1649         |
| ETN + MTX                         | ABA 10mg + MTX          | 2.31787        | 1.03543        | 5.55429        |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.2379         | 0.69507        | 2.19931        |
| CZP + MTX                         | ABA 10mg + MTX          | 1.68478        | 0.80678        | 3.68825        |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.21344        | 0.12648        | 0.34089        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.08279</b> | <b>0.60889</b> | <b>1.85503</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 1.00686        | 0.66594        | 1.53225        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.75398        | 0.40014        | 1.35431        |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.7433         | 0.39166        | 1.33034        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.70906        | 0.3587         | 1.38202        |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 0.73946        | 0.3847         | 1.38197        |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.33145        | 0.12784        | 0.89828        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.74963        | 0.73875        | 4.31087        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 0.93376        | 0.46696        | 1.77315        |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.2718         | 0.55847        | 2.90257        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.28671        | 0.20071        | 0.41306        |
| <b>BARI 4mg + MTX</b>             | <b>IFX 3mg + MTX</b>    | <b>1.45075</b> | <b>0.87483</b> | <b>2.49933</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.3517         | 0.87957        | 2.22803        |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 1.01267        | 0.66377        | 1.55431        |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.34536        | 0.75169        | 2.55326        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.95097        | 0.54175        | 1.73398        |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 0.99298        | 0.58405        | 1.73865        |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.44532        | 0.1786         | 1.19551        |
| ETN + MTX                         | IFX 3mg + MTX           | 2.34642        | 1.06832        | 5.69848        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.25319        | 0.70763        | 2.2699         |
| CZP + MTX                         | IFX 3mg + MTX           | 1.70722        | 0.83149        | 3.73733        |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.30097        | 0.18744        | 0.47406        |
| <b>BARI 4mg + MTX</b>             | <b>RTX 1000mg + MTX</b> | <b>1.52664</b> | <b>0.83853</b> | <b>2.75279</b> |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.42375        | 0.82421        | 2.44351        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.06456        | 0.58138        | 1.90455        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.41032        | 0.72358        | 2.78783        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.05155        | 0.57671        | 1.84587        |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.04306        | 0.56302        | 1.91748        |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.46992        | 0.18135        | 1.26209        |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.47438        | 1.04839        | 6.00596        |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.31565        | 0.6699         | 2.49993        |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.7942         | 0.8076         | 4.04698        |
| PBO + MTX                         | GOL 50mg + MTX          | 0.28836        | 0.18795        | 0.43335        |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.45945</b> | <b>0.83978</b> | <b>2.58083</b> |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.36062        | 0.83188        | 2.27767        |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 1.01565        | 0.58471        | 1.75657        |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 1.35233        | 0.72361        | 2.59941        |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 1.00707        | 0.57516        | 1.71218        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.95872        | 0.52152        | 1.77613        |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.44748        | 0.17702        | 1.16485        |
| ETN + MTX                         | GOL 50mg + MTX          | 2.37344        | 1.04336        | 5.6369         |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 1.2614         | 0.66821        | 2.33281        |
| CZP + MTX                         | GOL 50mg + MTX          | 1.71654        | 0.8022         | 3.74982        |
| PBO + MTX                         | cDMARD + MTX            | 0.64631        | 0.25691        | 1.48567        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>3.25776</b> | <b>1.21973</b> | <b>8.11059</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 3.03994        | 1.20445        | 7.37022        |
| ABA 10mg + MTX                    | cDMARD + MTX            | 2.27754        | 0.85844        | 5.62859        |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ABA SUBCUT + MTX      | cDMARD + MTX            | 3.01702        | 1.11324        | 7.8225         |
| IFX 3mg + MTX         | cDMARD + MTX            | 2.24559        | 0.83646        | 5.59925        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 2.12804        | 0.79234        | 5.51429        |
| GOL 50mg + MTX        | cDMARD + MTX            | 2.23473        | 0.85848        | 5.64903        |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 5.28318        | 3.09649        | 9.05222        |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.82397        | 0.99702        | 7.25722        |
| CZP + MTX             | cDMARD + MTX            | 3.81651        | 1.28293        | 11.26545       |
| PBO + MTX             | ETN + MTX               | 0.12219        | 0.05466        | 0.25106        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.61735</b> | <b>0.25954</b> | <b>1.39359</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.57795        | 0.25145        | 1.25073        |
| ABA 10mg + MTX        | ETN + MTX               | 0.43143        | 0.18004        | 0.96578        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.57155        | 0.23197        | 1.35365        |
| IFX 3mg + MTX         | ETN + MTX               | 0.42618        | 0.17549        | 0.93605        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.40414        | 0.1665         | 0.95384        |
| GOL 50mg + MTX        | ETN + MTX               | 0.42133        | 0.1774         | 0.95844        |
| cDMARD + MTX          | ETN + MTX               | 0.18928        | 0.11047        | 0.32295        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.53387        | 0.21185        | 1.26211        |
| CZP + MTX             | ETN + MTX               | 0.71999        | 0.26997        | 1.97338        |
| PBO + MTX             | SARI 200mg + MTX        | 0.22851        | 0.14569        | 0.36156        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.15568</b> | <b>0.65668</b> | <b>2.13281</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.07643        | 0.65225        | 1.92116        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.80782        | 0.45469        | 1.43871        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 1.07094        | 0.56397        | 2.14153        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.79796        | 0.44055        | 1.41316        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.76008        | 0.40001        | 1.49276        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.79277        | 0.42867        | 1.49654        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.35411        | 0.13779        | 1.00299        |
| ETN + MTX             | SARI 200mg + MTX        | 1.8731         | 0.79232        | 4.72029        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 1.36106        | 0.61802        | 3.1824         |
| PBO + MTX             | CZP + MTX               | 0.16823        | 0.08317        | 0.32058        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>0.85134</b> | <b>0.39286</b> | <b>1.81181</b> |
| ADA 40mg + MTX        | CZP + MTX               | 0.79352        | 0.38054        | 1.6363         |
| ABA 10mg + MTX        | CZP + MTX               | 0.59355        | 0.27113        | 1.2395         |
| ABA SUBCUT + MTX      | CZP + MTX               | 0.78629        | 0.34452        | 1.79061        |
| IFX 3mg + MTX         | CZP + MTX               | 0.58575        | 0.26757        | 1.20265        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.55735        | 0.2471         | 1.23824        |
| GOL 50mg + MTX        | CZP + MTX               | 0.58257        | 0.26668        | 1.24657        |
| cDMARD + MTX          | CZP + MTX               | 0.26202        | 0.08877        | 0.77946        |
| ETN + MTX             | CZP + MTX               | 1.38891        | 0.50674        | 3.70408        |
| SARI 200mg + MTX      | CZP + MTX               | 0.73472        | 0.31423        | 1.61807        |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

### 9.2.3. ACR70 Response

**Table S17** Primary Analysis: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) – ACR70 response at week 24: MTX-IR (Simultaneous Random-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.99949</b> | <b>3.89412</b>   | <b>9.43604</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 4.45311        | 3.14472          | 6.53227          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.15344        | 2.0251           | 5.06409          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.25696        | 2.40728          | 7.72965          |
| IFX 3mg + MTX                     | PBO + MTX             | 3.5556         | 2.26623          | 5.74016          |
| RTX 1000mg + MTX                  | PBO + MTX             | 2.6467         | 1.4103           | 5.11074          |
| GOL 50mg + MTX                    | PBO + MTX             | 4.41461        | 2.46602          | 7.99231          |
| cDMARD + MTX                      | PBO + MTX             | 1.57919        | 0.46192          | 6.06897          |
| ETN + MTX                         | PBO + MTX             | 6.56235        | 2.2271           | 22.95701         |
| SARI 200mg + MTX                  | PBO + MTX             | 4.27001        | 2.69688          | 6.77139          |
| CZP + MTX                         | PBO + MTX             | 5.76595        | 2.33877          | 16.14244         |
| PBO + MTX                         | BARI 4mg + MTX        | 0.16668        | 0.10598          | 0.2568           |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.73854        | 0.4985           | 1.1517           |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.52596        | 0.2808           | 0.98767          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.70744        | 0.38761          | 1.34833          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.59242        | 0.31427          | 1.12215          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.44083        | 0.20669          | 0.96924          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.73606        | 0.35154          | 1.54149          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.26297        | 0.07359          | 1.09184          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.09068        | 0.35497          | 4.12043          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.70946        | 0.37587          | 1.33512          |
| CZP + MTX                         | BARI 4mg + MTX        | 0.96564        | 0.35456          | 2.95602          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.22456        | 0.15309          | 0.31799          |
| <b>BARI 4mg + MTX</b>             | <b>ADA 40mg + MTX</b> | <b>1.35402</b> | <b>0.86828</b>   | <b>2.006</b>     |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.70794        | 0.39466          | 1.25806          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.95703        | 0.59666          | 1.5291           |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.80106        | 0.44609          | 1.42484          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.59414        | 0.28836          | 1.23561          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.99195        | 0.49813          | 1.95006          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.35102        | 0.10245          | 1.40869          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.46089        | 0.48838          | 5.34211          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 0.96112        | 0.51901          | 1.68695          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.29341        | 0.48886          | 3.84633          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.31711        | 0.19747          | 0.4938           |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.90129</b> | <b>1.01248</b>   | <b>3.56128</b>   |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.41255        | 0.79487          | 2.53383          |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1                | 1                |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.34928        | 0.64478          | 2.83265          |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 1.12749        | 0.68179          | 1.85542          |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.83686        | 0.38951          | 1.84333          |
| GOL 50mg + MTX                    | ABA 10mg + MTX        | 1.39106        | 0.67501          | 2.91992          |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper   |
|-----------------------------------|-------------------------|----------------|----------------|-----------------|
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.50076        | 0.13904        | 2.01995         |
| ETN + MTX                         | ABA 10mg + MTX          | 2.0884         | 0.65862        | 7.50109         |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.35247        | 0.7013         | 2.53506         |
| CZP + MTX                         | ABA 10mg + MTX          | 1.82239        | 0.65664        | 5.58319         |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.23491        | 0.12937        | 0.41541         |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.41355</b> | <b>0.74166</b> | <b>2.57992</b>  |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 1.0449         | 0.65398        | 1.676           |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.74114        | 0.35303        | 1.55091         |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1               |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.83475        | 0.39536        | 1.75185         |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.62109        | 0.26392        | 1.48116         |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 1.0364         | 0.45598        | 2.33588         |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.36738        | 0.10039        | 1.57529         |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.52324        | 0.47262        | 5.88766         |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.00238        | 0.46875        | 2.07595         |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.36253        | 0.46172        | 4.38882         |
| PBO + MTX                         | IFX 3mg + MTX           | 0.28125        | 0.17421        | 0.44126         |
| <b>BARI 4mg + MTX</b>             | <b>IFX 3mg + MTX</b>    | <b>1.68798</b> | <b>0.89115</b> | <b>3.18201</b>  |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.24835        | 0.70184        | 2.24169         |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 0.88692        | 0.53896        | 1.46673         |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.19797        | 0.57083        | 2.52931         |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1               |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.74288        | 0.35062        | 1.63201         |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.23824        | 0.59646        | 2.59212         |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.44371        | 0.12165        | 1.80291         |
| ETN + MTX                         | IFX 3mg + MTX           | 1.84599        | 0.57245        | 6.75431         |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.20341        | 0.61932        | 2.28153         |
| CZP + MTX                         | IFX 3mg + MTX           | 1.63021        | 0.58152        | 5.07075         |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.37783        | 0.19567        | 0.70907         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>2.26847</b> | <b>1.03174</b> | <b>4.83813</b>  |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.6831         | 0.80932        | 3.46788         |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.19494        | 0.5425         | 2.5673          |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.61008        | 0.67515        | 3.78907         |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.34611        | 0.61274        | 2.85205         |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1               |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.65655        | 0.72573        | 3.87633         |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.59683        | 0.15583        | 2.50117         |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.50407        | 0.74393        | 9.38908         |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.61628        | 0.70886        | 3.52271         |
| CZP + MTX                         | RTX 1000mg + MTX        | 2.18702        | 0.72178        | 6.99874         |
| PBO + MTX                         | GOL 50mg + MTX          | 0.22652        | 0.12512        | 0.40551         |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.35859</b> | <b>0.64872</b> | <b>2.84465</b>  |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.00812        | 0.5128         | 2.0075          |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 0.71888        | 0.34248        | 1.48147         |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 0.96488        | 0.4281         | 2.19309         |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 0.8076         | 0.38579        | 1.67656         |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.60366        | 0.25798        | 1.37793         |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1               |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.36092        | 0.0958         | 1.46571         |
| ETN + MTX                         | GOL 50mg + MTX          | 1.49195        | 0.44116        | 5.45612         |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 0.97066        | 0.454          | 2.05147         |
| CZP + MTX                         | GOL 50mg + MTX          | 1.31444        | 0.45339        | 4.13035         |
| PBO + MTX                         | cDMARD + MTX            | 0.63324        | 0.16477        | 2.16487         |
| <b>BARI 4mg + MTX</b>             | <b>cDMARD + MTX</b>     | <b>3.80276</b> | <b>0.91589</b> | <b>13.58789</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 2.84883        | 0.70988        | 9.76039         |
| ABA 10mg + MTX                    | cDMARD + MTX            | 1.99698        | 0.49506        | 7.19239         |



| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ABA SUBCUT + MTX      | cDMARD + MTX            | 2.72195        | 0.6348         | 9.9614         |
| IFX 3mg + MTX         | cDMARD + MTX            | 2.25373        | 0.55466        | 8.22048        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 1.67551        | 0.39981        | 6.41705        |
| GOL 50mg + MTX        | cDMARD + MTX            | 2.77069        | 0.68226        | 10.43877       |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 4.14899        | 2.21399        | 8.21638        |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.70861        | 0.65193        | 10.05903       |
| CZP + MTX             | cDMARD + MTX            | 3.69516        | 0.76806        | 17.18589       |
| PBO + MTX             | ETN + MTX               | 0.15238        | 0.04356        | 0.44901        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.91686</b> | <b>0.24269</b> | <b>2.81715</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.68451        | 0.18719        | 2.04757        |
| ABA 10mg + MTX        | ETN + MTX               | 0.47883        | 0.13331        | 1.51832        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.6565         | 0.16985        | 2.11585        |
| IFX 3mg + MTX         | ETN + MTX               | 0.54171        | 0.14805        | 1.74687        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.39935        | 0.10651        | 1.34421        |
| GOL 50mg + MTX        | ETN + MTX               | 0.67027        | 0.18328        | 2.26675        |
| cDMARD + MTX          | ETN + MTX               | 0.24102        | 0.12171        | 0.45167        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.65197        | 0.17464        | 2.08737        |
| CZP + MTX             | ETN + MTX               | 0.87477        | 0.20694        | 3.67255        |
| PBO + MTX             | SARI 200mg + MTX        | 0.23419        | 0.14768        | 0.3708         |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.40953</b> | <b>0.74899</b> | <b>2.66048</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.04045        | 0.59279        | 1.92674        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.73939        | 0.39447        | 1.42592        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.99762        | 0.48171        | 2.13332        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.83097        | 0.4383         | 1.61466        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.6187         | 0.28387        | 1.41072        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 1.03022        | 0.48746        | 2.20266        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.36919        | 0.09941        | 1.53391        |
| ETN + MTX             | SARI 200mg + MTX        | 1.53381        | 0.47907        | 5.72597        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 1.35235        | 0.48489        | 4.29779        |
| PBO + MTX             | CZP + MTX               | 0.17343        | 0.06195        | 0.42758        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>1.03558</b> | <b>0.33829</b> | <b>2.8204</b>  |
| ADA 40mg + MTX        | CZP + MTX               | 0.77315        | 0.25999        | 2.04557        |
| ABA 10mg + MTX        | CZP + MTX               | 0.54873        | 0.17911        | 1.52291        |
| ABA SUBCUT + MTX      | CZP + MTX               | 0.73393        | 0.22785        | 2.16582        |
| IFX 3mg + MTX         | CZP + MTX               | 0.61342        | 0.19721        | 1.71963        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.45724        | 0.14288        | 1.38546        |
| GOL 50mg + MTX        | CZP + MTX               | 0.76078        | 0.24211        | 2.20561        |
| cDMARD + MTX          | CZP + MTX               | 0.27062        | 0.05819        | 1.30198        |
| ETN + MTX             | CZP + MTX               | 1.14316        | 0.27229        | 4.83225        |
| SARI 200mg + MTX      | CZP + MTX               | 0.73945        | 0.23268        | 2.06233        |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

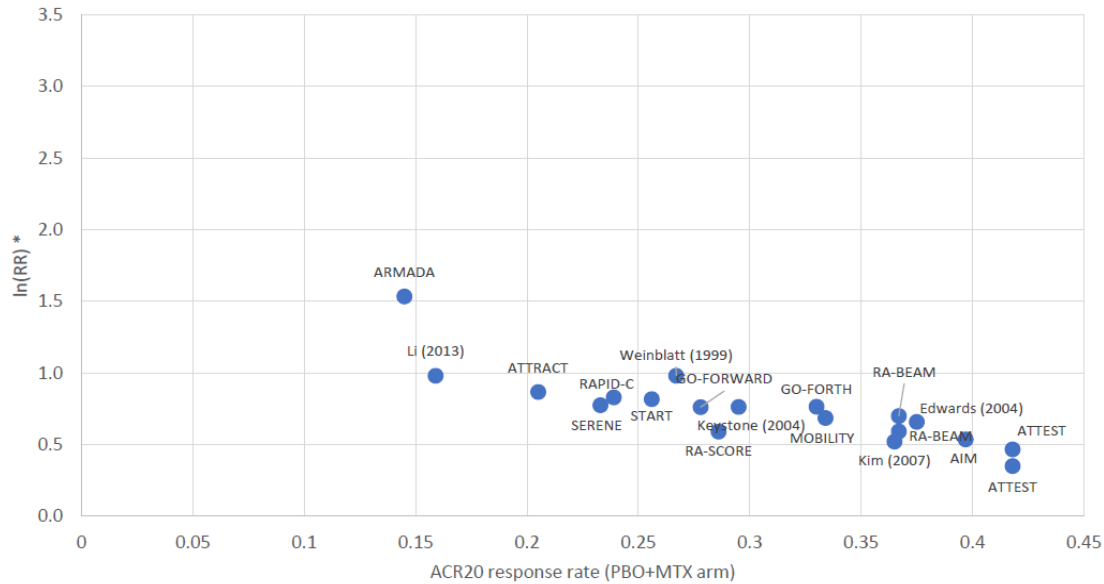
Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

## 10. Results – Sensitivity Analyses

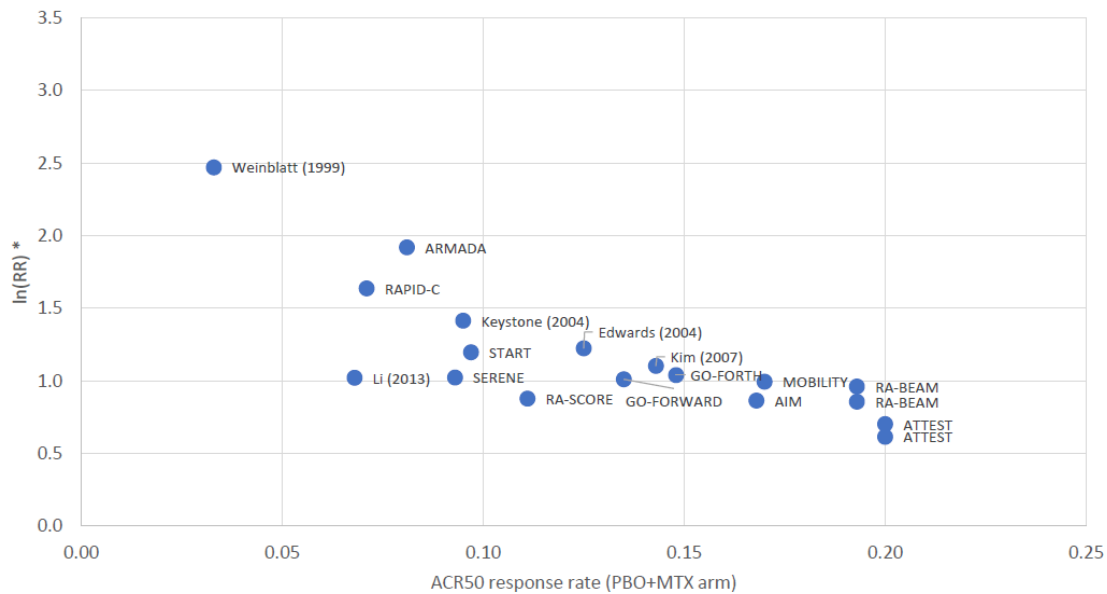
### 10.1. Baseline-risk adjustment

**Figure S2** Response rate in PBO+MTX arm vs.  $\ln(\text{Risk Ratio})$  - Primary analysis

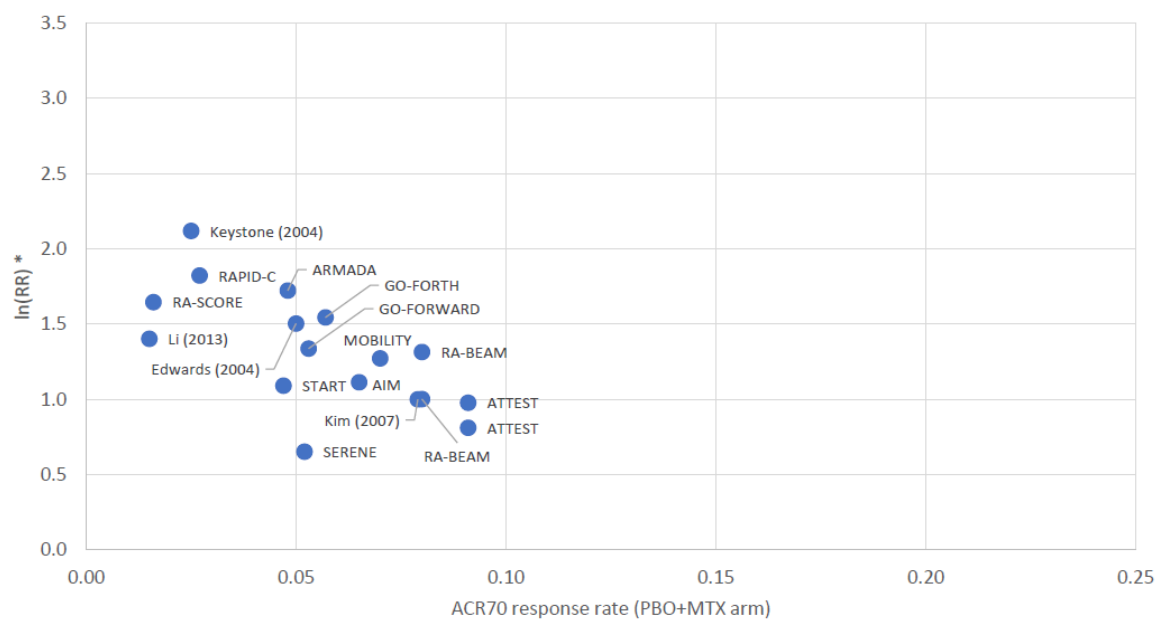
#### (A) ACR20



#### (B) ACR50



### (C) ACR70



\*Risk ratio of bDMARD/tsDMARD comparator over PBO+MTX arm in respective trial

Note: size of trials is not considered in these figures

### 10.1.1. ACR20 Response

**Table S18** Baseline Risk-adjustment (Primary analysis): Relative treatment effect of pairwise

comparisons expressed as Post. Median odds ratios (with 95% Crls)

- ACR20 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% Crl<br>Lower | 95% Crl<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.61288</b> | <b>4.22089</b>   | <b>7.23663</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 4.15006        | 3.32835          | 4.99813          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.90596        | 2.90983          | 5.02336          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.26135        | 2.94373          | 6.03455          |
| IFX 3mg + MTX                     | PBO + MTX             | 3.26426        | 2.63732          | 4.03507          |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.1634         | 2.3469           | 4.37628          |
| GOL 50mg + MTX                    | PBO + MTX             | 3.56656        | 2.67969          | 4.93361          |
| cDMARD + MTX                      | PBO + MTX             | 2.03623        | 1.12003          | 3.44583          |
| ETN + MTX                         | PBO + MTX             | 9.32367        | 5.63475          | 14.84963         |
| SARI 200mg + MTX                  | PBO + MTX             | 4.32623        | 3.07169          | 5.86031          |
| CZP + MTX                         | PBO + MTX             | 3.35824        | 2.36959          | 5.04304          |
| PBO + MTX                         | BARI 4mg + MTX        | 0.17816        | 0.13819          | 0.23692          |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.73874        | 0.56488          | 0.96999          |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.69594        | 0.49344          | 0.97378          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.75933        | 0.51022          | 1.13152          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.58211        | 0.42048          | 0.82588          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.56365        | 0.37878          | 0.88178          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.63635        | 0.42577          | 0.99869          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.36143        | 0.19797          | 0.65755          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.65451        | 0.97959          | 2.84056          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.7695         | 0.52257          | 1.1421           |
| CZP + MTX                         | BARI 4mg + MTX        | 0.59792        | 0.38997          | 1.01254          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.24096        | 0.20007          | 0.30045          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ADA 40mg + MTX</b> | <b>1.35366</b> | <b>1.03094</b>   | <b>1.7703</b>    |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.94385        | 0.68706          | 1.26349          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 1.02832        | 0.75524          | 1.40491          |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.78766        | 0.60071          | 1.06449          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.76372        | 0.53758          | 1.14076          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.8605         | 0.60831          | 1.29224          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.49033        | 0.27293          | 0.8594           |
| ETN + MTX                         | ADA 40mg + MTX        | 2.24396        | 1.35757          | 3.71403          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 1.04386        | 0.72554          | 1.49221          |
| CZP + MTX                         | ADA 40mg + MTX        | 0.80847        | 0.54952          | 1.3115           |
| PBO + MTX                         | ABA 10mg + MTX        | 0.25602        | 0.19907          | 0.34366          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.4369</b>  | <b>1.02692</b>   | <b>2.02659</b>   |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.05949        | 0.79146          | 1.45548          |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1                | 1                |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.08921        | 0.72486          | 1.66977          |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 0.83738        | 0.61741          | 1.17258          |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.8097         | 0.54452          | 1.28672          |
| GOL 50mg + MTX                    | ABA 10mg + MTX        | 0.91286        | 0.60968          | 1.45515          |
| cDMARD + MTX                      | ABA 10mg + MTX        | 0.51946        | 0.28586          | 0.94094          |
| ETN + MTX                         | ABA 10mg + MTX        | 2.37521        | 1.43211          | 4.10002          |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.10663        | 0.75606        | 1.64792        |
| CZP + MTX                         | ABA 10mg + MTX          | 0.85829        | 0.56218        | 1.47782        |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.23467        | 0.16571        | 0.33971        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.31695</b> | <b>0.88377</b> | <b>1.95993</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 0.97246        | 0.71179        | 1.32408        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.9181         | 0.59889        | 1.37957        |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.76704        | 0.51302        | 1.16374        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.74287        | 0.46861        | 1.22628        |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 0.83832        | 0.53145        | 1.39131        |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.4761         | 0.24833        | 0.89536        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 2.18015        | 1.22487        | 3.89872        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.01283        | 0.63748        | 1.6072         |
| CZP + MTX                         | ABA SUBCUT + MTX        | 0.78779        | 0.48485        | 1.38824        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.30635        | 0.24783        | 0.37917        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>IFX 3mg + MTX</b>    | <b>1.71789</b> | <b>1.21083</b> | <b>2.37822</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.26959        | 0.93942        | 1.6647         |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 1.1942         | 0.85282        | 1.61968        |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.30372        | 0.8593         | 1.94925        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.96869        | 0.67567        | 1.42289        |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.09025        | 0.77195        | 1.6069         |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.62351        | 0.33251        | 1.0934         |
| ETN + MTX                         | IFX 3mg + MTX           | 2.84925        | 1.66636        | 4.73111        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.32428        | 0.88717        | 1.90837        |
| CZP + MTX                         | IFX 3mg + MTX           | 1.0293         | 0.68708        | 1.62337        |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.31612        | 0.2285         | 0.42609        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>1.77415</b> | <b>1.13407</b> | <b>2.64006</b> |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.30938        | 0.87661        | 1.86017        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.23502        | 0.77717        | 1.83647        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.34612        | 0.81547        | 2.13395        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.03232        | 0.70279        | 1.48           |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.12652        | 0.75278        | 1.71388        |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.6438         | 0.32245        | 1.17526        |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.94537        | 1.61273        | 5.03143        |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.3681         | 0.83679        | 2.09181        |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.06379        | 0.66779        | 1.71125        |
| PBO + MTX                         | GOL 50mg + MTX          | 0.28038        | 0.20269        | 0.37318        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>GOL 50mg + MTX</b>   | <b>1.57146</b> | <b>1.00132</b> | <b>2.34868</b> |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.16212        | 0.77385        | 1.64389        |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 1.09546        | 0.68721        | 1.64019        |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 1.19286        | 0.71875        | 1.88164        |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 0.91722        | 0.62232        | 1.29542        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.88769        | 0.58347        | 1.32842        |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.57106        | 0.28406        | 1.03623        |
| ETN + MTX                         | GOL 50mg + MTX          | 2.61746        | 1.41488        | 4.42977        |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 1.21249        | 0.73969        | 1.86216        |
| CZP + MTX                         | GOL 50mg + MTX          | 0.94586        | 0.59217        | 1.49091        |
| PBO + MTX                         | cDMARD + MTX            | 0.4911         | 0.29021        | 0.89283        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>2.76679</b> | <b>1.5208</b>  | <b>5.05114</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 2.03943        | 1.1636         | 3.66398        |
| ABA 10mg + MTX                    | cDMARD + MTX            | 1.92509        | 1.06277        | 3.49822        |
| ABA SUBCUT + MTX                  | cDMARD + MTX            | 2.1004         | 1.11687        | 4.02687        |
| IFX 3mg + MTX                     | cDMARD + MTX            | 1.60383        | 0.91458        | 3.0074         |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| RTX 1000mg + MTX      | cDMARD + MTX            | 1.55329        | 0.85088        | 3.10123        |
| GOL 50mg + MTX        | cDMARD + MTX            | 1.75112        | 0.96503        | 3.52043        |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 4.59128        | 2.96425        | 7.1646         |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.13044        | 1.14463        | 4.02233        |
| CZP + MTX             | cDMARD + MTX            | 1.64639        | 0.88811        | 3.46441        |
| PBO + MTX             | ETN + MTX               | 0.10725        | 0.06734        | 0.17747        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.60441</b> | <b>0.35204</b> | <b>1.02084</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.44564        | 0.26925        | 0.73661        |
| ABA 10mg + MTX        | ETN + MTX               | 0.42101        | 0.2439         | 0.69827        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.45868        | 0.25649        | 0.81641        |
| IFX 3mg + MTX         | ETN + MTX               | 0.35097        | 0.21137        | 0.60011        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.33952        | 0.19875        | 0.62007        |
| GOL 50mg + MTX        | ETN + MTX               | 0.38205        | 0.22575        | 0.70678        |
| cDMARD + MTX          | ETN + MTX               | 0.2178         | 0.13958        | 0.33735        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.4658         | 0.26152        | 0.81517        |
| CZP + MTX             | ETN + MTX               | 0.35983        | 0.2043         | 0.70098        |
| PBO + MTX             | SARI 200mg + MTX        | 0.23115        | 0.17064        | 0.32555        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.29954</b> | <b>0.87558</b> | <b>1.91363</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 0.95798        | 0.67015        | 1.37828        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.90365        | 0.60683        | 1.32264        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.98733        | 0.6222         | 1.56867        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.75513        | 0.52401        | 1.12719        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.73094        | 0.47805        | 1.19504        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.82475        | 0.53701        | 1.35191        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.46939        | 0.24861        | 0.87365        |
| ETN + MTX             | SARI 200mg + MTX        | 2.14683        | 1.22674        | 3.82379        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 0.77682        | 0.48954        | 1.35288        |
| PBO + MTX             | CZP + MTX               | 0.29777        | 0.19829        | 0.42201        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>1.67246</b> | <b>0.98761</b> | <b>2.56433</b> |
| ADA 40mg + MTX        | CZP + MTX               | 1.23691        | 0.76248        | 1.81978        |
| ABA 10mg + MTX        | CZP + MTX               | 1.1651         | 0.67667        | 1.77877        |
| ABA SUBCUT + MTX      | CZP + MTX               | 1.26938        | 0.72034        | 2.06251        |
| IFX 3mg + MTX         | CZP + MTX               | 0.97153        | 0.616          | 1.45543        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.94004        | 0.58437        | 1.49748        |
| GOL 50mg + MTX        | CZP + MTX               | 1.05724        | 0.67073        | 1.68872        |
| cDMARD + MTX          | CZP + MTX               | 0.60739        | 0.28865        | 1.12599        |
| ETN + MTX             | CZP + MTX               | 2.77906        | 1.42657        | 4.89484        |
| SARI 200mg + MTX      | CZP + MTX               | 1.2873         | 0.73916        | 2.04272        |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

## 10.1.2. ACR50 Response

**Table S19** Baseline Risk-adjustment (Primary analysis): Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs)

– ACR50 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>3.39252</b> | <b>2.23534</b>   | <b>4.78553</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 3.19596        | 2.16428          | 4.34566          |
| ABA 10mg + MTX                    | PBO + MTX             | 2.72293        | 1.9526           | 3.61762          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 3.14516        | 2.11087          | 4.60369          |
| IFX 3mg + MTX                     | PBO + MTX             | 2.59997        | 1.90052          | 3.4192           |
| RTX 1000mg + MTX                  | PBO + MTX             | 2.37222        | 1.73028          | 3.34283          |
| GOL 50mg + MTX                    | PBO + MTX             | 2.51628        | 1.83186          | 3.47054          |
| cDMARD + MTX                      | PBO + MTX             | 1.43807        | 0.80879          | 2.4282           |
| ETN + MTX                         | PBO + MTX             | 4.1003         | 2.39357          | 7.05307          |
| SARI 200mg + MTX                  | PBO + MTX             | 3.69429        | 2.21377          | 6.05666          |
| CZP + MTX                         | PBO + MTX             | 3.25418        | 2.1391           | 5.16891          |
| PBO + MTX                         | BARI 4mg + MTX        | 0.29477        | 0.20896          | 0.44736          |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.94328        | 0.80538          | 1.08759          |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.81128        | 0.63441          | 0.98284          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.93838        | 0.72989          | 1.17049          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.7751         | 0.59546          | 0.96274          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.713          | 0.5079           | 0.95438          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.75471        | 0.5517           | 0.97694          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.43134        | 0.22385          | 0.73805          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.20527        | 0.9164           | 1.73047          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 1.10683        | 0.78969          | 1.43133          |
| CZP + MTX                         | BARI 4mg + MTX        | 0.96726        | 0.71682          | 1.36975          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.3129         | 0.23011          | 0.46205          |
| <b>BARI 4mg + MTX</b>             | <b>ADA 40mg + MTX</b> | <b>1.06013</b> | <b>0.91947</b>   | <b>1.24164</b>   |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.86217        | 0.68665          | 1.02952          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.99409        | 0.81842          | 1.18936          |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.82232        | 0.64806          | 1.00096          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.75747        | 0.55262          | 0.99765          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.80098        | 0.60288          | 1.01929          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.45926        | 0.24158          | 0.76967          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.28301        | 0.97642          | 1.83843          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 1.17196        | 0.83391          | 1.55956          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.02483        | 0.77883          | 1.44433          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.36725        | 0.27643          | 0.51214          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.23262</b> | <b>1.01746</b>   | <b>1.57627</b>   |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.15986        | 0.97132          | 1.45634          |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1                | 1                |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.15154        | 0.89718          | 1.54095          |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 0.95634        | 0.77232          | 1.18448          |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.87992        | 0.64935          | 1.19336          |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| GOL 50mg + MTX                    | ABA 10mg + MTX          | 0.93022        | 0.70333        | 1.23406        |
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.53595        | 0.28639        | 0.89636        |
| ETN + MTX                         | ABA 10mg + MTX          | 1.49181        | 1.10017        | 2.29094        |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.36199        | 0.96175        | 1.90528        |
| CZP + MTX                         | ABA 10mg + MTX          | 1.18783        | 0.89798        | 1.77349        |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.31795        | 0.21722        | 0.47374        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.06566</b> | <b>0.85434</b> | <b>1.37007</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 1.00595        | 0.84079        | 1.22187        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.8684         | 0.64895        | 1.1146         |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.82928        | 0.61312        | 1.08021        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.76379        | 0.53121        | 1.05268        |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 0.80822        | 0.57542        | 1.08612        |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.46273        | 0.2373         | 0.79801        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.29022        | 0.94438        | 1.94264        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.17643        | 0.80922        | 1.67194        |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.03273        | 0.74783        | 1.51692        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.38462        | 0.29247        | 0.52617        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>IFX 3mg + MTX</b>    | <b>1.29016</b> | <b>1.0387</b>  | <b>1.67938</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.21607        | 0.99904        | 1.54306        |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 1.04565        | 0.84425        | 1.29479        |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.20586        | 0.92575        | 1.63101        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.92118        | 0.68464        | 1.23403        |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 0.97325        | 0.74153        | 1.27497        |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.56128        | 0.29676        | 0.92896        |
| ETN + MTX                         | IFX 3mg + MTX           | 1.56284        | 1.13014        | 2.40814        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.42307        | 0.96456        | 2.09261        |
| CZP + MTX                         | IFX 3mg + MTX           | 1.24673        | 0.9426         | 1.82252        |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.42155        | 0.29915        | 0.57794        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>1.40253</b> | <b>1.0478</b>  | <b>1.9689</b>  |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.32019        | 1.00236        | 1.80957        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.13647        | 0.83797        | 1.54001        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.30927        | 0.94996        | 1.88251        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.08557        | 0.81035        | 1.46063        |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.0559         | 0.7711         | 1.45824        |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.61133        | 0.31561        | 1.02864        |
| ETN + MTX                         | RTX 1000mg + MTX        | 1.70512        | 1.16625        | 2.72863        |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.54657        | 0.96731        | 2.45403        |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.35702        | 0.98572        | 2.04072        |
| PBO + MTX                         | GOL 50mg + MTX          | 0.39741        | 0.28814        | 0.54589        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>GOL 50mg + MTX</b>   | <b>1.32501</b> | <b>1.0236</b>  | <b>1.81258</b> |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.24847        | 0.98107        | 1.65869        |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 1.07501        | 0.81033        | 1.42181        |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 1.23728        | 0.92071        | 1.73786        |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 1.02749        | 0.78433        | 1.34856        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.94706        | 0.68576        | 1.29685        |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.57802        | 0.30135        | 0.96385        |
| ETN + MTX                         | GOL 50mg + MTX          | 1.61243        | 1.12849        | 2.52955        |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 1.46044        | 0.95247        | 2.26043        |
| CZP + MTX                         | GOL 50mg + MTX          | 1.28368        | 0.94778        | 1.90323        |
| PBO + MTX                         | cDMARD + MTX            | 0.69538        | 0.41183        | 1.23641        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>2.31837</b> | <b>1.35492</b> | <b>4.46736</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 2.17741        | 1.29926        | 4.13937        |



| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ABA 10mg + MTX        | cDMARD + MTX            | 1.86585        | 1.11562        | 3.49176        |
| ABA SUBCUT + MTX      | cDMARD + MTX            | 2.16107        | 1.25311        | 4.21411        |
| IFX 3mg + MTX         | cDMARD + MTX            | 1.78165        | 1.07647        | 3.36978        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 1.63577        | 0.97215        | 3.16842        |
| GOL 50mg + MTX        | cDMARD + MTX            | 1.73005        | 1.03751        | 3.31838        |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 2.85382        | 1.71201        | 4.99605        |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.56682        | 1.3512         | 5.12597        |
| CZP + MTX             | cDMARD + MTX            | 2.23345        | 1.29891        | 4.62453        |
| PBO + MTX             | ETN + MTX               | 0.24388        | 0.14178        | 0.41779        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.82969</b> | <b>0.57788</b> | <b>1.09123</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.77942        | 0.54394        | 1.02415        |
| ABA 10mg + MTX        | ETN + MTX               | 0.67033        | 0.4365         | 0.90895        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.77506        | 0.51476        | 1.0589         |
| IFX 3mg + MTX         | ETN + MTX               | 0.63986        | 0.41526        | 0.88485        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.58647        | 0.36648        | 0.85745        |
| GOL 50mg + MTX        | ETN + MTX               | 0.62018        | 0.39533        | 0.88614        |
| cDMARD + MTX          | ETN + MTX               | 0.35041        | 0.20016        | 0.58411        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.92459        | 0.55741        | 1.24906        |
| CZP + MTX             | ETN + MTX               | 0.80195        | 0.5317         | 1.16588        |
| PBO + MTX             | SARI 200mg + MTX        | 0.27069        | 0.16511        | 0.45172        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>0.90348</b> | <b>0.69865</b> | <b>1.26633</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 0.85327        | 0.64121        | 1.19917        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.73422        | 0.52486        | 1.03977        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.85003        | 0.59811        | 1.23576        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.70271        | 0.47787        | 1.03674        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.64659        | 0.40749        | 1.0338         |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.68473        | 0.44239        | 1.0499         |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.38959        | 0.19509        | 0.74008        |
| ETN + MTX             | SARI 200mg + MTX        | 1.08156        | 0.8006         | 1.79402        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 0.87537        | 0.5796         | 1.49622        |
| PBO + MTX             | CZP + MTX               | 0.3073         | 0.19346        | 0.46749        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>1.03385</b> | <b>0.73006</b> | <b>1.39506</b> |
| ADA 40mg + MTX        | CZP + MTX               | 0.97577        | 0.69236        | 1.28398        |
| ABA 10mg + MTX        | CZP + MTX               | 0.84187        | 0.56386        | 1.11361        |
| ABA SUBCUT + MTX      | CZP + MTX               | 0.96831        | 0.65923        | 1.3372         |
| IFX 3mg + MTX         | CZP + MTX               | 0.8021         | 0.54869        | 1.06089        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.73691        | 0.49002        | 1.01449        |
| GOL 50mg + MTX        | CZP + MTX               | 0.77901        | 0.52542        | 1.05509        |
| cDMARD + MTX          | CZP + MTX               | 0.44774        | 0.21624        | 0.76988        |
| ETN + MTX             | CZP + MTX               | 1.24696        | 0.85772        | 1.88076        |
| SARI 200mg + MTX      | CZP + MTX               | 1.14238        | 0.66835        | 1.72532        |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

### 10.1.3. ACR70 Response

**Table S20** Baseline Risk-adjustment (Primary analysis): Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% Crls) – ACR70 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% Crl<br>Lower | 95% Crl<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.37039</b> | <b>3.80805</b>   | <b>7.34374</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 3.91128        | 2.81506          | 5.17215          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.02855        | 2.00323          | 4.32636          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 3.5559         | 2.22037          | 5.5719           |
| IFX 3mg + MTX                     | PBO + MTX             | 3.21707        | 2.23195          | 4.74214          |
| RTX 1000mg + MTX                  | PBO + MTX             | 2.25232        | 1.31318          | 4.01331          |
| GOL 50mg + MTX                    | PBO + MTX             | 3.66982        | 2.2815           | 6.16858          |
| cDMARD + MTX                      | PBO + MTX             | 1.02396        | 0.39914          | 2.43945          |
| ETN + MTX                         | PBO + MTX             | 4.30089        | 1.87691          | 9.12553          |
| SARI 200mg + MTX                  | PBO + MTX             | 5.54668        | 1.41529          | 12.83707         |
| CZP + MTX                         | PBO + MTX             | 3.93328        | 2.0289           | 8.53184          |
| PBO + MTX                         | BARI 4mg + MTX        | 0.18621        | 0.13617          | 0.2626           |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.72682        | 0.5391           | 0.97834          |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.56331        | 0.34207          | 0.90605          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.66427        | 0.41508          | 1.05198          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.59979        | 0.37219          | 1.00288          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.41954        | 0.22825          | 0.82304          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.6838         | 0.38948          | 1.28118          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.19105        | 0.07265          | 0.47647          |
| ETN + MTX                         | BARI 4mg + MTX        | 0.80072        | 0.33846          | 1.78609          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 1.02695        | 0.26927          | 2.4107           |
| CZP + MTX                         | BARI 4mg + MTX        | 0.73479        | 0.35676          | 1.71888          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.25567        | 0.19334          | 0.35523          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ADA 40mg + MTX</b> | <b>1.37585</b> | <b>1.02214</b>   | <b>1.85496</b>   |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.77351        | 0.48305          | 1.22868          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.91339        | 0.63375          | 1.30918          |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.8223         | 0.52642          | 1.36541          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.57712        | 0.31817          | 1.12706          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.94056        | 0.5475           | 1.74803          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.26273        | 0.10082          | 0.64417          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.10245        | 0.47216          | 2.41817          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 1.41359        | 0.38518          | 3.25349          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.00706        | 0.498            | 2.35264          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.33019        | 0.23114          | 0.49919          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.77521</b> | <b>1.10369</b>   | <b>2.92341</b>   |
| ADA 40mg + MTX                    | ABA 10mg + MTX        | 1.2928         | 0.81388          | 2.07017          |
| ABA 10mg + MTX                    | ABA 10mg + MTX        | 1              | 1                | 1                |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX        | 1.18236        | 0.66541          | 2.09828          |
| IFX 3mg + MTX                     | ABA 10mg + MTX        | 1.06993        | 0.70215          | 1.66386          |
| RTX 1000mg + MTX                  | ABA 10mg + MTX        | 0.74303        | 0.39433          | 1.5244           |
| GOL 50mg + MTX                    | ABA 10mg + MTX        | 1.21583        | 0.67518          | 2.37555          |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper   |
|-----------------------------------|-------------------------|----------------|----------------|-----------------|
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.33966        | 0.12809        | 0.85696         |
| ETN + MTX                         | ABA 10mg + MTX          | 1.4248         | 0.59649        | 3.2626          |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.83622        | 0.4865         | 4.16198         |
| CZP + MTX                         | ABA 10mg + MTX          | 1.30166        | 0.627          | 3.17597         |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.28122        | 0.17947        | 0.45038         |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.50542</b> | <b>0.95059</b> | <b>2.40917</b>  |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 1.09482        | 0.76384        | 1.5779          |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.84577        | 0.47658        | 1.50284         |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1               |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.9047         | 0.51104        | 1.65393         |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.63313        | 0.31648        | 1.34542         |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 1.03171        | 0.5412         | 2.08277         |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.28729        | 0.10472        | 0.75502         |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.20471        | 0.48891        | 2.84945         |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.53721        | 0.40246        | 3.85169         |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.1063         | 0.50045        | 2.76322         |
| PBO + MTX                         | IFX 3mg + MTX           | 0.31084        | 0.21088        | 0.44804         |
| <b>BARI 4mg + MTX</b>             | <b>IFX 3mg + MTX</b>    | <b>1.66724</b> | <b>0.99713</b> | <b>2.68677</b>  |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.2161         | 0.73238        | 1.89961         |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 0.93464        | 0.60101        | 1.4242          |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.10534        | 0.60462        | 1.95681         |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1               |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.6994         | 0.36382        | 1.3685          |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.14041        | 0.62558        | 2.13688         |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.31706        | 0.11576        | 0.79948         |
| ETN + MTX                         | IFX 3mg + MTX           | 1.33166        | 0.5375         | 3.04323         |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.70803        | 0.41044        | 4.32007         |
| CZP + MTX                         | IFX 3mg + MTX           | 1.22334        | 0.57233        | 2.86981         |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.44399        | 0.24917        | 0.76151         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>2.38356</b> | <b>1.21501</b> | <b>4.38113</b>  |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.73275        | 0.88726        | 3.14299         |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.34584        | 0.656          | 2.53597         |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.57945        | 0.74326        | 3.15977         |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.4298         | 0.73072        | 2.74858         |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1               |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.63224        | 0.79596        | 3.3749          |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.45448        | 0.15061        | 1.24607         |
| ETN + MTX                         | RTX 1000mg + MTX        | 1.90866        | 0.68915        | 4.68683         |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 2.44256        | 0.52517        | 6.82748         |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.75717        | 0.7376         | 4.3872          |
| PBO + MTX                         | GOL 50mg + MTX          | 0.27249        | 0.16211        | 0.43831         |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.46241</b> | <b>0.78053</b> | <b>2.56755</b>  |
| ADA 40mg + MTX                    | GOL 50mg + MTX          | 1.06319        | 0.57207        | 1.82649         |
| ABA 10mg + MTX                    | GOL 50mg + MTX          | 0.82249        | 0.42096        | 1.48108         |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX          | 0.96926        | 0.48013        | 1.84773         |
| IFX 3mg + MTX                     | GOL 50mg + MTX          | 0.87688        | 0.46797        | 1.59851         |
| RTX 1000mg + MTX                  | GOL 50mg + MTX          | 0.61266        | 0.29631        | 1.25634         |
| GOL 50mg + MTX                    | GOL 50mg + MTX          | 1              | 1              | 1               |
| cDMARD + MTX                      | GOL 50mg + MTX          | 0.27891        | 0.09419        | 0.74006         |
| ETN + MTX                         | GOL 50mg + MTX          | 1.17213        | 0.4335         | 2.77635         |
| SARI 200mg + MTX                  | GOL 50mg + MTX          | 1.48871        | 0.3356         | 4.07866         |
| CZP + MTX                         | GOL 50mg + MTX          | 1.07761        | 0.46751        | 2.59276         |
| PBO + MTX                         | cDMARD + MTX            | 0.9766         | 0.40993        | 2.50541         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>     | <b>5.23431</b> | <b>2.09877</b> | <b>13.76403</b> |
| ADA 40mg + MTX                    | cDMARD + MTX            | 3.80614        | 1.55237        | 9.91831         |
| ABA 10mg + MTX                    | cDMARD + MTX            | 2.94408        | 1.16691        | 7.80695         |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ABA SUBCUT + MTX      | cDMARD + MTX            | 3.4808         | 1.32446        | 9.54948        |
| IFX 3mg + MTX         | cDMARD + MTX            | 3.15397        | 1.25082        | 8.63824        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 2.20033        | 0.80252        | 6.63947        |
| GOL 50mg + MTX        | cDMARD + MTX            | 3.58542        | 1.35125        | 10.61633       |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 4.1695         | 2.42734        | 7.49767        |
| SARI 200mg + MTX      | cDMARD + MTX            | 5.34794        | 1.22074        | 16.34544       |
| CZP + MTX             | cDMARD + MTX            | 3.86171        | 1.31893        | 13.2175        |
| PBO + MTX             | ETN + MTX               | 0.23251        | 0.10958        | 0.53279        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>1.24888</b> | <b>0.55988</b> | <b>2.95459</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.90707        | 0.41354        | 2.11791        |
| ABA 10mg + MTX        | ETN + MTX               | 0.70185        | 0.3065         | 1.67647        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.83008        | 0.35094        | 2.04536        |
| IFX 3mg + MTX         | ETN + MTX               | 0.75094        | 0.3286         | 1.86047        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.52393        | 0.21336        | 1.45106        |
| GOL 50mg + MTX        | ETN + MTX               | 0.85315        | 0.36019        | 2.30681        |
| cDMARD + MTX          | ETN + MTX               | 0.23984        | 0.13337        | 0.41197        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 1.28379        | 0.3081         | 3.48771        |
| CZP + MTX             | ETN + MTX               | 0.91828        | 0.34305        | 2.87751        |
| PBO + MTX             | SARI 200mg + MTX        | 0.18029        | 0.0779         | 0.70657        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>0.97376</b> | <b>0.41482</b> | <b>3.7137</b>  |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 0.70742        | 0.30736        | 2.59622        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.5446         | 0.24027        | 2.05549        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.65053        | 0.25963        | 2.48473        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.58547        | 0.23148        | 2.43639        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.40941        | 0.14647        | 1.90413        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.67172        | 0.24518        | 2.97977        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.18699        | 0.06118        | 0.81918        |
| ETN + MTX             | SARI 200mg + MTX        | 0.77894        | 0.28672        | 3.24574        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| CZP + MTX             | SARI 200mg + MTX        | 0.72157        | 0.24352        | 3.64066        |
| PBO + MTX             | CZP + MTX               | 0.25424        | 0.11721        | 0.49288        |
| <b>BARI 4mg + MTX</b> | <b>CZP + MTX</b>        | <b>1.36094</b> | <b>0.58177</b> | <b>2.80297</b> |
| ADA 40mg + MTX        | CZP + MTX               | 0.99299        | 0.42505        | 2.00804        |
| ABA 10mg + MTX        | CZP + MTX               | 0.76825        | 0.31486        | 1.59491        |
| ABA SUBCUT + MTX      | CZP + MTX               | 0.90391        | 0.3619         | 1.9982         |
| IFX 3mg + MTX         | CZP + MTX               | 0.81743        | 0.34845        | 1.74724        |
| RTX 1000mg + MTX      | CZP + MTX               | 0.5691         | 0.22794        | 1.35574        |
| GOL 50mg + MTX        | CZP + MTX               | 0.92798        | 0.38569        | 2.13901        |
| cDMARD + MTX          | CZP + MTX               | 0.25895        | 0.07566        | 0.75819        |
| ETN + MTX             | CZP + MTX               | 1.089          | 0.34752        | 2.91499        |
| SARI 200mg + MTX      | CZP + MTX               | 1.38586        | 0.27468        | 4.1064         |
| CZP + MTX             | CZP + MTX               | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

## 10.2. Inclusion of Trials with Prior bDMARD use of up to 20%

### 10.2.1. ACR20 Response

**Table S21** Sensitivity analysis including trials with prior bDMARD use of up to 20%: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) - ACR20 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-----------------------|----------------|----------------|----------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1              | 1              |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>5.14605</b> | <b>3.98323</b> | <b>6.66296</b> |
| ADA 40mg + MTX                    | PBO + MTX             | 3.695          | 3.08144        | 4.42057        |
| ABA 10mg + MTX                    | PBO + MTX             | 3.63351        | 2.80299        | 4.74228        |
| ABA SUBCUT + MTX                  | PBO + MTX             | 3.83972        | 2.67139        | 5.47883        |
| IFX 3mg + MTX                     | PBO + MTX             | 3.33178        | 2.64076        | 4.19838        |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.39909        | 2.42594        | 4.77651        |
| GOL 50mg + MTX                    | PBO + MTX             | 3.95352        | 2.87804        | 5.47676        |
| CZP + MTX                         | PBO + MTX             | 6.29142        | 4.9836         | 8.0343         |
| TCZ 8mg + MTX                     | PBO + MTX             | 3.56961        | 2.83119        | 4.51707        |
| cDMARD + MTX                      | PBO + MTX             | 3.0954         | 1.86082        | 5.19699        |
| ETN + MTX                         | PBO + MTX             | 6.78865        | 4.22745        | 10.99119       |
| SARI 200mg + MTX                  | PBO + MTX             | 4.13448        | 2.94363        | 5.81072        |
| TOFA 5mg + MTX                    | PBO + MTX             | 3.81824        | 2.99152        | 4.85959        |
| PBO + MTX                         | BARI 4mg + MTX        | 0.19432        | 0.15008        | 0.25105        |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1              | 1              |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.71719        | 0.54509        | 0.94123        |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.70529        | 0.48981        | 1.01946        |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.74506        | 0.49049        | 1.12596        |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.64642        | 0.45798        | 0.91216        |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.66035        | 0.43425        | 1.00754        |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.76846        | 0.51257        | 1.16187        |
| CZP + MTX                         | BARI 4mg + MTX        | 1.22187        | 0.86067        | 1.74395        |
| TCZ 8mg + MTX                     | BARI 4mg + MTX        | 0.69383        | 0.49226        | 0.98196        |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.60181        | 0.33928        | 1.06752        |
| ETN + MTX                         | BARI 4mg + MTX        | 1.32074        | 0.77283        | 2.27778        |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.80136        | 0.52597        | 1.22853        |
| TOFA 5mg + MTX                    | BARI 4mg + MTX        | 0.74096        | 0.53312        | 1.02875        |
| PBO + MTX                         | ADA 40mg + MTX        | 0.27064        | 0.22622        | 0.32452        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ADA 40mg + MTX</b> | <b>1.39433</b> | <b>1.06244</b> | <b>1.83455</b> |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1              | 1              |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.98354        | 0.72173        | 1.34947        |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 1.03861        | 0.75418        | 1.42491        |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.90044        | 0.67326        | 1.20553        |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.92005        | 0.6318         | 1.34921        |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 1.07145        | 0.74825        | 1.54809        |
| CZP + MTX                         | ADA 40mg + MTX        | 1.70305        | 1.26974        | 2.3152         |
| TCZ 8mg + MTX                     | ADA 40mg + MTX        | 0.96586        | 0.72291        | 1.29729        |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.83693        | 0.4948         | 1.44061        |
| ETN + MTX                         | ADA 40mg + MTX        | 1.83699        | 1.12805        | 3.04914        |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| SARI 200mg + MTX                  | ADA 40mg + MTX          | 1.11736        | 0.76509        | 1.64239        |
| TOFA 5mg + MTX                    | ADA 40mg + MTX          | 1.03326        | 0.83087        | 1.28233        |
| PBO + MTX                         | ABA 10mg + MTX          | 0.27522        | 0.21087        | 0.35676        |
| <b>BARI 4mg + MTX</b>             | <b>ABA 10mg + MTX</b>   | <b>1.41786</b> | <b>0.98092</b> | <b>2.04161</b> |
| ADA 40mg + MTX                    | ABA 10mg + MTX          | 1.01674        | 0.74103        | 1.38557        |
| ABA 10mg + MTX                    | ABA 10mg + MTX          | 1              | 1              | 1              |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX          | 1.05697        | 0.67628        | 1.63348        |
| IFX 3mg + MTX                     | ABA 10mg + MTX          | 0.91543        | 0.66852        | 1.25547        |
| RTX 1000mg + MTX                  | ABA 10mg + MTX          | 0.93437        | 0.60982        | 1.43697        |
| GOL 50mg + MTX                    | ABA 10mg + MTX          | 1.08788        | 0.72105        | 1.65015        |
| CZP + MTX                         | ABA 10mg + MTX          | 1.73091        | 1.20653        | 2.48518        |
| TCZ 8mg + MTX                     | ABA 10mg + MTX          | 0.982          | 0.69056        | 1.39299        |
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.84836        | 0.48282        | 1.51665        |
| ETN + MTX                         | ABA 10mg + MTX          | 1.86915        | 1.09767        | 3.23373        |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.13401        | 0.74169        | 1.74126        |
| TOFA 5mg + MTX                    | ABA 10mg + MTX          | 1.04936        | 0.73669        | 1.48654        |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.26044        | 0.18252        | 0.37434        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.34217</b> | <b>0.88813</b> | <b>2.03879</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 0.96282        | 0.7018         | 1.32594        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.9461         | 0.61219        | 1.47867        |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.86737        | 0.56688        | 1.32944        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.88698        | 0.54589        | 1.44116        |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 1.03093        | 0.64212        | 1.667          |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.63984        | 1.07016        | 2.54286        |
| TCZ 8mg + MTX                     | ABA SUBCUT + MTX        | 0.93006        | 0.60996        | 1.42913        |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.80501        | 0.44036        | 1.50306        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.77082        | 0.99976        | 3.20037        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 1.07609        | 0.65989        | 1.76545        |
| TOFA 5mg + MTX                    | ABA SUBCUT + MTX        | 0.9937         | 0.67935        | 1.46316        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.30014        | 0.23819        | 0.37868        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>IFX 3mg + MTX</b>    | <b>1.54697</b> | <b>1.0963</b>  | <b>2.18348</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.11057        | 0.82951        | 1.48531        |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 1.09238        | 0.79651        | 1.49585        |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.15291        | 0.7522         | 1.76405        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 1.02033        | 0.68095        | 1.53516        |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.18904        | 0.80453        | 1.76781        |
| CZP + MTX                         | IFX 3mg + MTX           | 1.88948        | 1.36374        | 2.63193        |
| TCZ 8mg + MTX                     | IFX 3mg + MTX           | 1.07217        | 0.77513        | 1.48737        |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.92836        | 0.53516        | 1.63085        |
| ETN + MTX                         | IFX 3mg + MTX           | 2.03998        | 1.2085         | 3.45108        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.24125        | 0.82493        | 1.87317        |
| TOFA 5mg + MTX                    | IFX 3mg + MTX           | 1.14728        | 0.82039        | 1.59071        |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.2942         | 0.20936        | 0.41221        |
| <b>BARI 4mg + MTX</b>             | <b>RTX 1000mg + MTX</b> | <b>1.51435</b> | <b>0.99252</b> | <b>2.30284</b> |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.0869         | 0.74118        | 1.58278        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.07024        | 0.69591        | 1.63982        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.12742        | 0.69389        | 1.83189        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 0.98007        | 0.6514         | 1.46854        |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.16293        | 0.73728        | 1.84862        |
| CZP + MTX                         | RTX 1000mg + MTX        | 1.84968        | 1.23537        | 2.77505        |
| TCZ 8mg + MTX                     | RTX 1000mg + MTX        | 1.0497         | 0.69749        | 1.5787         |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.9111         | 0.49808        | 1.66289        |
| ETN + MTX                         | RTX 1000mg + MTX        | 1.99957        | 1.12836        | 3.54835        |

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-----------------------|----------------|----------------|----------------|
| SARI 200mg + MTX                  | RTX 1000mg + MTX      | 1.21641        | 0.75306        | 1.95597        |
| TOFA 5mg + MTX                    | RTX 1000mg + MTX      | 1.12244        | 0.74158        | 1.68833        |
| PBO + MTX                         | GOL 50mg + MTX        | 0.25294        | 0.18259        | 0.34746        |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b> | <b>1.3013</b>  | <b>0.86068</b> | <b>1.95095</b> |
| ADA 40mg + MTX                    | GOL 50mg + MTX        | 0.93332        | 0.64596        | 1.33645        |
| ABA 10mg + MTX                    | GOL 50mg + MTX        | 0.91922        | 0.60601        | 1.38687        |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX        | 0.96999        | 0.59988        | 1.55735        |
| IFX 3mg + MTX                     | GOL 50mg + MTX        | 0.84102        | 0.56567        | 1.24296        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX        | 0.8599         | 0.54094        | 1.35634        |
| GOL 50mg + MTX                    | GOL 50mg + MTX        | 1              | 1              | 1              |
| CZP + MTX                         | GOL 50mg + MTX        | 1.58914        | 1.07779        | 2.34946        |
| TCZ 8mg + MTX                     | GOL 50mg + MTX        | 0.90295        | 0.60805        | 1.32911        |
| cDMARD + MTX                      | GOL 50mg + MTX        | 0.7819         | 0.43197        | 1.41916        |
| ETN + MTX                         | GOL 50mg + MTX        | 1.7199         | 0.97529        | 3.00735        |
| SARI 200mg + MTX                  | GOL 50mg + MTX        | 1.04373        | 0.65167        | 1.66993        |
| TOFA 5mg + MTX                    | GOL 50mg + MTX        | 0.96512        | 0.64669        | 1.42595        |
| PBO + MTX                         | CZP + MTX             | 0.15895        | 0.12447        | 0.20066        |
| <b>BARI 4mg + MTX</b>             | <b>CZP + MTX</b>      | <b>0.81842</b> | <b>0.57341</b> | <b>1.16189</b> |
| ADA 40mg + MTX                    | CZP + MTX             | 0.58718        | 0.43193        | 0.78756        |
| ABA 10mg + MTX                    | CZP + MTX             | 0.57773        | 0.40239        | 0.82882        |
| ABA SUBCUT + MTX                  | CZP + MTX             | 0.60982        | 0.39326        | 0.93444        |
| IFX 3mg + MTX                     | CZP + MTX             | 0.52925        | 0.37995        | 0.73328        |
| RTX 1000mg + MTX                  | CZP + MTX             | 0.54063        | 0.36035        | 0.80947        |
| GOL 50mg + MTX                    | CZP + MTX             | 0.62927        | 0.42563        | 0.92783        |
| CZP + MTX                         | CZP + MTX             | 1              | 1              | 1              |
| TCZ 8mg + MTX                     | CZP + MTX             | 0.56758        | 0.40657        | 0.79157        |
| cDMARD + MTX                      | CZP + MTX             | 0.49204        | 0.28078        | 0.84771        |
| ETN + MTX                         | CZP + MTX             | 1.08097        | 0.63714        | 1.80931        |
| SARI 200mg + MTX                  | CZP + MTX             | 0.65672        | 0.43034        | 0.99834        |
| TOFA 5mg + MTX                    | CZP + MTX             | 0.6067         | 0.43154        | 0.84505        |
| PBO + MTX                         | TCZ 8mg + MTX         | 0.28014        | 0.22138        | 0.35321        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>TCZ 8mg + MTX</b>  | <b>1.44127</b> | <b>1.01838</b> | <b>2.03144</b> |
| ADA 40mg + MTX                    | TCZ 8mg + MTX         | 1.03534        | 0.77084        | 1.3833         |
| ABA 10mg + MTX                    | TCZ 8mg + MTX         | 1.01833        | 0.71788        | 1.4481         |
| ABA SUBCUT + MTX                  | TCZ 8mg + MTX         | 1.0752         | 0.69973        | 1.63944        |
| IFX 3mg + MTX                     | TCZ 8mg + MTX         | 0.93269        | 0.67233        | 1.29011        |
| RTX 1000mg + MTX                  | TCZ 8mg + MTX         | 0.95265        | 0.63343        | 1.43371        |
| GOL 50mg + MTX                    | TCZ 8mg + MTX         | 1.10749        | 0.75238        | 1.64461        |
| CZP + MTX                         | TCZ 8mg + MTX         | 1.76188        | 1.26331        | 2.4596         |
| TCZ 8mg + MTX                     | TCZ 8mg + MTX         | 1              | 1              | 1              |
| cDMARD + MTX                      | TCZ 8mg + MTX         | 0.8648         | 0.49644        | 1.51521        |
| ETN + MTX                         | TCZ 8mg + MTX         | 1.90306        | 1.13013        | 3.22819        |
| SARI 200mg + MTX                  | TCZ 8mg + MTX         | 1.15629        | 0.76606        | 1.74478        |
| TOFA 5mg + MTX                    | TCZ 8mg + MTX         | 1.06889        | 0.76493        | 1.48863        |
| PBO + MTX                         | cDMARD + MTX          | 0.32306        | 0.19242        | 0.5374         |
| <b>BARI 4mg + MTX</b>             | <b>cDMARD + MTX</b>   | <b>1.66165</b> | <b>0.93675</b> | <b>2.9474</b>  |
| ADA 40mg + MTX                    | cDMARD + MTX          | 1.19485        | 0.69415        | 2.02102        |
| ABA 10mg + MTX                    | cDMARD + MTX          | 1.17874        | 0.65935        | 2.07117        |
| ABA SUBCUT + MTX                  | cDMARD + MTX          | 1.24222        | 0.66531        | 2.27088        |
| IFX 3mg + MTX                     | cDMARD + MTX          | 1.07717        | 0.61318        | 1.86859        |
| RTX 1000mg + MTX                  | cDMARD + MTX          | 1.09758        | 0.60136        | 2.00769        |
| GOL 50mg + MTX                    | cDMARD + MTX          | 1.27894        | 0.70464        | 2.31498        |
| CZP + MTX                         | cDMARD + MTX          | 2.03235        | 1.17965        | 3.56145        |
| TCZ 8mg + MTX                     | cDMARD + MTX          | 1.15634        | 0.65997        | 2.01435        |
| cDMARD + MTX                      | cDMARD + MTX          | 1              | 1              | 1              |
| ETN + MTX                         | cDMARD + MTX          | 2.19566        | 1.61672        | 3.00106        |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| SARI 200mg + MTX      | cDMARD + MTX            | 1.33686        | 0.7167         | 2.44778        |
| TOFA 5mg + MTX        | cDMARD + MTX            | 1.2353         | 0.70797        | 2.13365        |
| PBO + MTX             | ETN + MTX               | 0.1473         | 0.09098        | 0.23655        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.75715</b> | <b>0.43902</b> | <b>1.29395</b> |
| ADA 40mg + MTX        | ETN + MTX               | 0.54437        | 0.32796        | 0.88648        |
| ABA 10mg + MTX        | ETN + MTX               | 0.535          | 0.30924        | 0.91102        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.56471        | 0.31246        | 1.00024        |
| IFX 3mg + MTX         | ETN + MTX               | 0.4902         | 0.28976        | 0.82747        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.50011        | 0.28182        | 0.88625        |
| GOL 50mg + MTX        | ETN + MTX               | 0.58143        | 0.33252        | 1.02533        |
| CZP + MTX             | ETN + MTX               | 0.9251         | 0.5527         | 1.56952        |
| TCZ 8mg + MTX         | ETN + MTX               | 0.52547        | 0.30977        | 0.88486        |
| cDMARD + MTX          | ETN + MTX               | 0.45544        | 0.33322        | 0.61854        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.60872        | 0.33836        | 1.07547        |
| TOFA 5mg + MTX        | ETN + MTX               | 0.56259        | 0.33335        | 0.93953        |
| PBO + MTX             | SARI 200mg + MTX        | 0.24187        | 0.1721         | 0.33972        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.24788</b> | <b>0.81398</b> | <b>1.90127</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 0.89497        | 0.60887        | 1.30703        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.88183        | 0.5743         | 1.34827        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.92929        | 0.56643        | 1.5154         |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.80564        | 0.53386        | 1.21223        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.82209        | 0.51126        | 1.32791        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.9581         | 0.59883        | 1.53453        |
| CZP + MTX             | SARI 200mg + MTX        | 1.52272        | 1.00167        | 2.32373        |
| TCZ 8mg + MTX         | SARI 200mg + MTX        | 0.86483        | 0.57314        | 1.30537        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.74802        | 0.40853        | 1.39529        |
| ETN + MTX             | SARI 200mg + MTX        | 1.6428         | 0.92982        | 2.95541        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| TOFA 5mg + MTX        | SARI 200mg + MTX        | 0.92446        | 0.6094         | 1.39578        |
| PBO + MTX             | TOFA 5mg + MTX          | 0.2619         | 0.20578        | 0.33428        |
| <b>BARI 4mg + MTX</b> | <b>TOFA 5mg + MTX</b>   | <b>1.34959</b> | <b>0.97206</b> | <b>1.87576</b> |
| ADA 40mg + MTX        | TOFA 5mg + MTX          | 0.96781        | 0.77983        | 1.20356        |
| ABA 10mg + MTX        | TOFA 5mg + MTX          | 0.95297        | 0.6727         | 1.35742        |
| ABA SUBCUT + MTX      | TOFA 5mg + MTX          | 1.00634        | 0.68345        | 1.47199        |
| IFX 3mg + MTX         | TOFA 5mg + MTX          | 0.87163        | 0.62865        | 1.21893        |
| RTX 1000mg + MTX      | TOFA 5mg + MTX          | 0.89092        | 0.5923         | 1.34846        |
| GOL 50mg + MTX        | TOFA 5mg + MTX          | 1.03614        | 0.70129        | 1.54634        |
| CZP + MTX             | TOFA 5mg + MTX          | 1.64825        | 1.18336        | 2.3173         |
| TCZ 8mg + MTX         | TOFA 5mg + MTX          | 0.93555        | 0.67176        | 1.30731        |
| cDMARD + MTX          | TOFA 5mg + MTX          | 0.80952        | 0.46868        | 1.41249        |
| ETN + MTX             | TOFA 5mg + MTX          | 1.77749        | 1.06437        | 2.99987        |
| SARI 200mg + MTX      | TOFA 5mg + MTX          | 1.08171        | 0.71645        | 1.64096        |
| TOFA 5mg + MTX        | TOFA 5mg + MTX          | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous; TCZ tocilizumab; TOFA tofacitinib.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.



## 10.2.2. ACR50 Response

**Table S22** Sensitivity analysis including trials with prior bDMARD use of up to 20%: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) – ACR50 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>4.92284</b> | <b>3.80091</b>   | <b>6.38747</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 4.4108         | 3.59902          | 5.41705          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.6226         | 2.69699          | 4.89807          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.44791        | 3.09176          | 6.40423          |
| IFX 3mg + MTX                     | PBO + MTX             | 3.57207        | 2.65987          | 4.80206          |
| RTX 1000mg + MTX                  | PBO + MTX             | 3.37328        | 2.25             | 5.1324           |
| GOL 50mg + MTX                    | PBO + MTX             | 3.55103        | 2.45449          | 5.18692          |
| CZP + MTX                         | PBO + MTX             | 6.07995        | 4.6487           | 8.09874          |
| TCZ 8mg + MTX                     | PBO + MTX             | 4.81264        | 3.60205          | 6.49512          |
| cDMARD + MTX                      | PBO + MTX             | 2.21111        | 1.23228          | 4.04475          |
| ETN + MTX                         | PBO + MTX             | 6.90245        | 4.07536          | 12.02721         |
| SARI 200mg + MTX                  | PBO + MTX             | 4.48144        | 3.17723          | 6.37388          |
| TOFA 5mg + MTX                    | PBO + MTX             | 5.16828        | 3.96623          | 6.78726          |
| PBO + MTX                         | BARI 4mg + MTX        | 0.20313        | 0.15656          | 0.26309          |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.89609        | 0.69411          | 1.15565          |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.73589        | 0.49877          | 1.0928           |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.9048         | 0.60339          | 1.34518          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.72532        | 0.49013          | 1.0727           |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.68561        | 0.42426          | 1.12108          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.7214         | 0.46295          | 1.12754          |
| CZP + MTX                         | BARI 4mg + MTX        | 1.23667        | 0.85545          | 1.80824          |
| TCZ 8mg + MTX                     | BARI 4mg + MTX        | 0.97867        | 0.6663           | 1.45581          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.44888        | 0.23897          | 0.85552          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.40231        | 0.7886           | 2.5587           |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.9094         | 0.59491          | 1.40896          |
| TOFA 5mg + MTX                    | BARI 4mg + MTX        | 1.05117        | 0.76128          | 1.45157          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.22672        | 0.1846           | 0.27785          |
| <b>BARI 4mg + MTX</b>             | <b>ADA 40mg + MTX</b> | <b>1.11596</b> | <b>0.86531</b>   | <b>1.4407</b>    |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.82114        | 0.5761           | 1.17107          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 1.0089         | 0.73968          | 1.36986          |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.81           | 0.56947          | 1.15375          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.76507        | 0.48911          | 1.20547          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 0.80348        | 0.53252          | 1.22401          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.37873        | 0.99631          | 1.93743          |
| TCZ 8mg + MTX                     | ADA 40mg + MTX        | 1.09144        | 0.77095          | 1.56067          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.50082        | 0.27474          | 0.92864          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.56353        | 0.90734          | 2.77454          |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 1.01735        | 0.6841           | 1.52205          |
| TOFA 5mg + MTX                    | ADA 40mg + MTX        | 1.17222        | 0.94438          | 1.45672          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.27605        | 0.20416          | 0.37078          |
| <b>BARI 4mg + MTX</b>             | <b>ABA 10mg + MTX</b> | <b>1.3589</b>  | <b>0.91508</b>   | <b>2.00491</b>   |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ADA 40mg + MTX        | ABA 10mg + MTX          | 1.21782        | 0.85392        | 1.73581        |
| ABA 10mg + MTX        | ABA 10mg + MTX          | 1              | 1              | 1              |
| ABA SUBCUT + MTX      | ABA 10mg + MTX          | 1.22674        | 0.76788        | 1.95755        |
| IFX 3mg + MTX         | ABA 10mg + MTX          | 0.98526        | 0.69937        | 1.39538        |
| RTX 1000mg + MTX      | ABA 10mg + MTX          | 0.93132        | 0.56196        | 1.54313        |
| GOL 50mg + MTX        | ABA 10mg + MTX          | 0.97873        | 0.61414        | 1.58276        |
| CZP + MTX             | ABA 10mg + MTX          | 1.67751        | 1.12524        | 2.53607        |
| TCZ 8mg + MTX         | ABA 10mg + MTX          | 1.32944        | 0.88014        | 2.02991        |
| cDMARD + MTX          | ABA 10mg + MTX          | 0.60913        | 0.32071        | 1.1868         |
| ETN + MTX             | ABA 10mg + MTX          | 1.90447        | 1.0505         | 3.56155        |
| SARI 200mg + MTX      | ABA 10mg + MTX          | 1.23737        | 0.78521        | 1.95407        |
| TOFA 5mg + MTX        | ABA 10mg + MTX          | 1.4265         | 0.96279        | 2.12469        |
| PBO + MTX             | ABA SUBCUT + MTX        | 0.22482        | 0.15615        | 0.32344        |
| <b>BARI 4mg + MTX</b> | <b>ABA SUBCUT + MTX</b> | <b>1.10522</b> | <b>0.74339</b> | <b>1.65732</b> |
| ADA 40mg + MTX        | ABA SUBCUT + MTX        | 0.99118        | 0.73           | 1.35194        |
| ABA 10mg + MTX        | ABA SUBCUT + MTX        | 0.81517        | 0.51084        | 1.30228        |
| ABA SUBCUT + MTX      | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX         | ABA SUBCUT + MTX        | 0.80382        | 0.50421        | 1.28067        |
| RTX 1000mg + MTX      | ABA SUBCUT + MTX        | 0.75773        | 0.44445        | 1.312          |
| GOL 50mg + MTX        | ABA SUBCUT + MTX        | 0.79768        | 0.48006        | 1.34176        |
| CZP + MTX             | ABA SUBCUT + MTX        | 1.36911        | 0.87903        | 2.15469        |
| TCZ 8mg + MTX         | ABA SUBCUT + MTX        | 1.08445        | 0.68586        | 1.72942        |
| cDMARD + MTX          | ABA SUBCUT + MTX        | 0.49689        | 0.25508        | 0.98441        |
| ETN + MTX             | ABA SUBCUT + MTX        | 1.55083        | 0.83994        | 2.96651        |
| SARI 200mg + MTX      | ABA SUBCUT + MTX        | 1.00843        | 0.61287        | 1.67343        |
| TOFA 5mg + MTX        | ABA SUBCUT + MTX        | 1.16308        | 0.80083        | 1.69437        |
| PBO + MTX             | IFX 3mg + MTX           | 0.27995        | 0.20824        | 0.37596        |
| <b>BARI 4mg + MTX</b> | <b>IFX 3mg + MTX</b>    | <b>1.3787</b>  | <b>0.93223</b> | <b>2.04029</b> |
| ADA 40mg + MTX        | IFX 3mg + MTX           | 1.23457        | 0.86674        | 1.75602        |
| ABA 10mg + MTX        | IFX 3mg + MTX           | 1.01496        | 0.71665        | 1.42987        |
| ABA SUBCUT + MTX      | IFX 3mg + MTX           | 1.24405        | 0.78084        | 1.98329        |
| IFX 3mg + MTX         | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX      | IFX 3mg + MTX           | 0.94452        | 0.57359        | 1.56298        |
| GOL 50mg + MTX        | IFX 3mg + MTX           | 0.99468        | 0.62054        | 1.59289        |
| CZP + MTX             | IFX 3mg + MTX           | 1.70285        | 1.15004        | 2.55664        |
| TCZ 8mg + MTX         | IFX 3mg + MTX           | 1.34883        | 0.89188        | 2.04576        |
| cDMARD + MTX          | IFX 3mg + MTX           | 0.62032        | 0.32617        | 1.19851        |
| ETN + MTX             | IFX 3mg + MTX           | 1.93269        | 1.06856        | 3.58053        |
| SARI 200mg + MTX      | IFX 3mg + MTX           | 1.25532        | 0.79664        | 1.98886        |
| TOFA 5mg + MTX        | IFX 3mg + MTX           | 1.44794        | 0.97942        | 2.14531        |
| PBO + MTX             | RTX 1000mg + MTX        | 0.29645        | 0.19484        | 0.44444        |
| <b>BARI 4mg + MTX</b> | <b>RTX 1000mg + MTX</b> | <b>1.45854</b> | <b>0.89199</b> | <b>2.35705</b> |
| ADA 40mg + MTX        | RTX 1000mg + MTX        | 1.30707        | 0.82955        | 2.04452        |
| ABA 10mg + MTX        | RTX 1000mg + MTX        | 1.07374        | 0.64804        | 1.77947        |
| ABA SUBCUT + MTX      | RTX 1000mg + MTX        | 1.31974        | 0.7622         | 2.24997        |
| IFX 3mg + MTX         | RTX 1000mg + MTX        | 1.05874        | 0.6398         | 1.74342        |
| RTX 1000mg + MTX      | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX        | RTX 1000mg + MTX        | 1.05323        | 0.60636        | 1.81817        |
| CZP + MTX             | RTX 1000mg + MTX        | 1.80122        | 1.11696        | 2.91667        |
| TCZ 8mg + MTX         | RTX 1000mg + MTX        | 1.42642        | 0.86808        | 2.36546        |
| cDMARD + MTX          | RTX 1000mg + MTX        | 0.65717        | 0.32754        | 1.32075        |
| ETN + MTX             | RTX 1000mg + MTX        | 2.04799        | 1.06692        | 3.97474        |
| SARI 200mg + MTX      | RTX 1000mg + MTX        | 1.32663        | 0.77032        | 2.28573        |
| TOFA 5mg + MTX        | RTX 1000mg + MTX        | 1.53329        | 0.94717        | 2.47234        |
| PBO + MTX             | GOL 50mg + MTX          | 0.28161        | 0.19279        | 0.40742        |
| <b>BARI 4mg + MTX</b> | <b>GOL 50mg + MTX</b>   | <b>1.38619</b> | <b>0.88688</b> | <b>2.16005</b> |

| Treatment 1                       | Treatment 2          | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|----------------------|----------------|----------------|----------------|
| ADA 40mg + MTX                    | GOL 50mg + MTX       | 1.24458        | 0.81699        | 1.87786        |
| ABA 10mg + MTX                    | GOL 50mg + MTX       | 1.02173        | 0.63181        | 1.6283         |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX       | 1.25363        | 0.74529        | 2.08308        |
| IFX 3mg + MTX                     | GOL 50mg + MTX       | 1.00534        | 0.62779        | 1.61149        |
| RTX 1000mg + MTX                  | GOL 50mg + MTX       | 0.94946        | 0.55           | 1.64918        |
| GOL 50mg + MTX                    | GOL 50mg + MTX       | 1              | 1              | 1              |
| CZP + MTX                         | GOL 50mg + MTX       | 1.71448        | 1.09551        | 2.70376        |
| TCZ 8mg + MTX                     | GOL 50mg + MTX       | 1.35578        | 0.8498         | 2.16762        |
| cDMARD + MTX                      | GOL 50mg + MTX       | 0.62187        | 0.3149         | 1.23578        |
| ETN + MTX                         | GOL 50mg + MTX       | 1.94412        | 1.03205        | 3.70368        |
| SARI 200mg + MTX                  | GOL 50mg + MTX       | 1.26104        | 0.75305        | 2.11303        |
| TOFA 5mg + MTX                    | GOL 50mg + MTX       | 1.45644        | 0.92728        | 2.27755        |
| PBO + MTX                         | CZP + MTX            | 0.16447        | 0.12348        | 0.21511        |
| <b>BARI 4mg + MTX</b>             | <b>CZP + MTX</b>     | <b>0.80862</b> | <b>0.55302</b> | <b>1.16898</b> |
| ADA 40mg + MTX                    | CZP + MTX            | 0.72531        | 0.51615        | 1.0037         |
| ABA 10mg + MTX                    | CZP + MTX            | 0.59612        | 0.39431        | 0.8887         |
| ABA SUBCUT + MTX                  | CZP + MTX            | 0.7304         | 0.4641         | 1.13762        |
| IFX 3mg + MTX                     | CZP + MTX            | 0.58725        | 0.39114        | 0.86954        |
| RTX 1000mg + MTX                  | CZP + MTX            | 0.55518        | 0.34286        | 0.89528        |
| GOL 50mg + MTX                    | CZP + MTX            | 0.58327        | 0.36985        | 0.91282        |
| CZP + MTX                         | CZP + MTX            | 1              | 1              | 1              |
| TCZ 8mg + MTX                     | CZP + MTX            | 0.79151        | 0.53255        | 1.17142        |
| cDMARD + MTX                      | CZP + MTX            | 0.3646         | 0.19294        | 0.68112        |
| ETN + MTX                         | CZP + MTX            | 1.13694        | 0.63847        | 2.02104        |
| SARI 200mg + MTX                  | CZP + MTX            | 0.73631        | 0.46765        | 1.15689        |
| TOFA 5mg + MTX                    | CZP + MTX            | 0.85048        | 0.58286        | 1.23035        |
| PBO + MTX                         | TCZ 8mg + MTX        | 0.20779        | 0.15396        | 0.27762        |
| <b>BARI 4mg + MTX</b>             | <b>TCZ 8mg + MTX</b> | <b>1.02179</b> | <b>0.6869</b>  | <b>1.50083</b> |
| ADA 40mg + MTX                    | TCZ 8mg + MTX        | 0.91622        | 0.64075        | 1.2971         |
| ABA 10mg + MTX                    | TCZ 8mg + MTX        | 0.7522         | 0.49263        | 1.13618        |
| ABA SUBCUT + MTX                  | TCZ 8mg + MTX        | 0.92213        | 0.57823        | 1.45803        |
| IFX 3mg + MTX                     | TCZ 8mg + MTX        | 0.74138        | 0.48881        | 1.12123        |
| RTX 1000mg + MTX                  | TCZ 8mg + MTX        | 0.70105        | 0.42275        | 1.15197        |
| GOL 50mg + MTX                    | TCZ 8mg + MTX        | 0.73758        | 0.46133        | 1.17675        |
| CZP + MTX                         | TCZ 8mg + MTX        | 1.26341        | 0.85366        | 1.87775        |
| TCZ 8mg + MTX                     | TCZ 8mg + MTX        | 1              | 1              | 1              |
| cDMARD + MTX                      | TCZ 8mg + MTX        | 0.4592         | 0.24022        | 0.88222        |
| ETN + MTX                         | TCZ 8mg + MTX        | 1.4335         | 0.78914        | 2.63642        |
| SARI 200mg + MTX                  | TCZ 8mg + MTX        | 0.93048        | 0.58856        | 1.47132        |
| TOFA 5mg + MTX                    | TCZ 8mg + MTX        | 1.0731         | 0.72387        | 1.57837        |
| PBO + MTX                         | cDMARD + MTX         | 0.45226        | 0.24723        | 0.81151        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>  | <b>2.22775</b> | <b>1.16888</b> | <b>4.18461</b> |
| ADA 40mg + MTX                    | cDMARD + MTX         | 1.99672        | 1.07684        | 3.63984        |
| ABA 10mg + MTX                    | cDMARD + MTX         | 1.64168        | 0.8426         | 3.11804        |
| ABA SUBCUT + MTX                  | cDMARD + MTX         | 2.01251        | 1.01584        | 3.92029        |
| IFX 3mg + MTX                     | cDMARD + MTX         | 1.61206        | 0.83437        | 3.06592        |
| RTX 1000mg + MTX                  | cDMARD + MTX         | 1.52167        | 0.75715        | 3.05303        |
| GOL 50mg + MTX                    | cDMARD + MTX         | 1.60804        | 0.80921        | 3.17566        |
| CZP + MTX                         | cDMARD + MTX         | 2.74276        | 1.46816        | 5.18299        |
| TCZ 8mg + MTX                     | cDMARD + MTX         | 2.17768        | 1.1335         | 4.16291        |
| cDMARD + MTX                      | cDMARD + MTX         | 1              | 1              | 1              |
| ETN + MTX                         | cDMARD + MTX         | 3.12087        | 2.2574         | 4.32991        |
| SARI 200mg + MTX                  | cDMARD + MTX         | 2.03566        | 1.01224        | 3.92905        |
| TOFA 5mg + MTX                    | cDMARD + MTX         | 2.34048        | 1.23516        | 4.35614        |
| PBO + MTX                         | ETN + MTX            | 0.14488        | 0.08314        | 0.24538        |
| <b>BARI 4mg + MTX</b>             | <b>ETN + MTX</b>     | <b>0.71311</b> | <b>0.39082</b> | <b>1.26806</b> |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ADA 40mg + MTX        | ETN + MTX               | 0.63958        | 0.36042        | 1.10213        |
| ABA 10mg + MTX        | ETN + MTX               | 0.52508        | 0.28078        | 0.95192        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.64481        | 0.3371         | 1.19057        |
| IFX 3mg + MTX         | ETN + MTX               | 0.51741        | 0.27929        | 0.93584        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.48828        | 0.25159        | 0.93727        |
| GOL 50mg + MTX        | ETN + MTX               | 0.51437        | 0.27           | 0.96894        |
| CZP + MTX             | ETN + MTX               | 0.87955        | 0.49479        | 1.56624        |
| TCZ 8mg + MTX         | ETN + MTX               | 0.69759        | 0.3793         | 1.2672         |
| cDMARD + MTX          | ETN + MTX               | 0.32042        | 0.23095        | 0.44299        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.65088        | 0.33482        | 1.20984        |
| TOFA 5mg + MTX        | ETN + MTX               | 0.74823        | 0.41359        | 1.32875        |
| PBO + MTX             | SARI 200mg + MTX        | 0.22314        | 0.15689        | 0.31474        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.09963</b> | <b>0.70974</b> | <b>1.68094</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 0.98295        | 0.65701        | 1.46178        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.80817        | 0.51175        | 1.27355        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.99164        | 0.59758        | 1.63168        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.79661        | 0.5028         | 1.25527        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.75379        | 0.4375         | 1.29817        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.793          | 0.47325        | 1.32793        |
| CZP + MTX             | SARI 200mg + MTX        | 1.35812        | 0.86438        | 2.13836        |
| TCZ 8mg + MTX         | SARI 200mg + MTX        | 1.07471        | 0.67966        | 1.69905        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.49124        | 0.25451        | 0.9879         |
| ETN + MTX             | SARI 200mg + MTX        | 1.53638        | 0.82656        | 2.9867         |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| TOFA 5mg + MTX        | SARI 200mg + MTX        | 1.15364        | 0.74323        | 1.78556        |
| PBO + MTX             | TOFA 5mg + MTX          | 0.19349        | 0.14733        | 0.25213        |
| <b>BARI 4mg + MTX</b> | <b>TOFA 5mg + MTX</b>   | <b>0.95132</b> | <b>0.68891</b> | <b>1.31358</b> |
| ADA 40mg + MTX        | TOFA 5mg + MTX          | 0.85308        | 0.68647        | 1.05889        |
| ABA 10mg + MTX        | TOFA 5mg + MTX          | 0.70102        | 0.47066        | 1.03865        |
| ABA SUBCUT + MTX      | TOFA 5mg + MTX          | 0.85979        | 0.59019        | 1.24871        |
| IFX 3mg + MTX         | TOFA 5mg + MTX          | 0.69064        | 0.46613        | 1.02101        |
| RTX 1000mg + MTX      | TOFA 5mg + MTX          | 0.65219        | 0.40447        | 1.05578        |
| GOL 50mg + MTX        | TOFA 5mg + MTX          | 0.6866         | 0.43907        | 1.07842        |
| CZP + MTX             | TOFA 5mg + MTX          | 1.17581        | 0.81278        | 1.71568        |
| TCZ 8mg + MTX         | TOFA 5mg + MTX          | 0.93188        | 0.63357        | 1.38146        |
| cDMARD + MTX          | TOFA 5mg + MTX          | 0.42726        | 0.22956        | 0.80961        |
| ETN + MTX             | TOFA 5mg + MTX          | 1.3365         | 0.75259        | 2.41785        |
| SARI 200mg + MTX      | TOFA 5mg + MTX          | 0.86682        | 0.56005        | 1.34548        |
| TOFA 5mg + MTX        | TOFA 5mg + MTX          | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous; TCZ tocilizumab; TOFA tofacitinib.

<sup>1</sup>statistically significantly favouring BARI.

Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.

### 10.2.3. ACR70 Response

**Table S23** Sensitivity analysis including trials with prior bDMARD use of up to 20%: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) – ACR70 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1                       | Treatment 2           | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------------------|-----------------------|----------------|------------------|------------------|
| PBO + MTX                         | PBO + MTX             | 1              | 1                | 1                |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>PBO + MTX</b>      | <b>6.21014</b> | <b>4.42976</b>   | <b>8.81452</b>   |
| ADA 40mg + MTX                    | PBO + MTX             | 4.58825        | 3.42443          | 6.18615          |
| ABA 10mg + MTX                    | PBO + MTX             | 3.32687        | 2.22952          | 5.04195          |
| ABA SUBCUT + MTX                  | PBO + MTX             | 4.42208        | 2.76583          | 7.07758          |
| IFX 3mg + MTX                     | PBO + MTX             | 3.71296        | 2.47455          | 5.68175          |
| RTX 1000mg + MTX                  | PBO + MTX             | 2.90505        | 1.56695          | 5.52338          |
| GOL 50mg + MTX                    | PBO + MTX             | 4.74344        | 2.78178          | 8.34182          |
| CZP + MTX                         | PBO + MTX             | 8.32686        | 5.42892          | 13.58279         |
| TCZ 8mg + MTX                     | PBO + MTX             | 7.7413         | 4.6842           | 13.56946         |
| cDMARD + MTX                      | PBO + MTX             | 1.69706        | 0.64449          | 4.68677          |
| ETN + MTX                         | PBO + MTX             | 6.87779        | 2.86605          | 17.41077         |
| SARI 200mg + MTX                  | PBO + MTX             | 4.31033        | 3.05637          | 6.13804          |
| TOFA 5mg + MTX                    | PBO + MTX             | 6.98925        | 4.7874           | 10.29918         |
| PBO + MTX                         | BARI 4mg + MTX        | 0.16103        | 0.11345          | 0.22575          |
| BARI 4mg + MTX                    | BARI 4mg + MTX        | 1              | 1                | 1                |
| ADA 40mg + MTX                    | BARI 4mg + MTX        | 0.73899        | 0.54471          | 0.99842          |
| ABA 10mg + MTX                    | BARI 4mg + MTX        | 0.53563        | 0.31546          | 0.91053          |
| ABA SUBCUT + MTX                  | BARI 4mg + MTX        | 0.71069        | 0.44051          | 1.14128          |
| IFX 3mg + MTX                     | BARI 4mg + MTX        | 0.5987         | 0.34951          | 1.02381          |
| RTX 1000mg + MTX                  | BARI 4mg + MTX        | 0.46731        | 0.23244          | 0.96101          |
| GOL 50mg + MTX                    | BARI 4mg + MTX        | 0.76394        | 0.41057          | 1.45986          |
| CZP + MTX                         | BARI 4mg + MTX        | 1.34424        | 0.78146          | 2.3955           |
| TCZ 8mg + MTX                     | BARI 4mg + MTX        | 1.24548        | 0.67596          | 2.39299          |
| cDMARD + MTX                      | BARI 4mg + MTX        | 0.27222        | 0.09944          | 0.78376          |
| ETN + MTX                         | BARI 4mg + MTX        | 1.10323        | 0.43711          | 2.91861          |
| SARI 200mg + MTX                  | BARI 4mg + MTX        | 0.69367        | 0.42641          | 1.13232          |
| TOFA 5mg + MTX                    | BARI 4mg + MTX        | 1.12606        | 0.74676          | 1.68326          |
| PBO + MTX                         | ADA 40mg + MTX        | 0.21795        | 0.16165          | 0.29202          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ADA 40mg + MTX</b> | <b>1.35321</b> | <b>1.00159</b>   | <b>1.83585</b>   |
| ADA 40mg + MTX                    | ADA 40mg + MTX        | 1              | 1                | 1                |
| ABA 10mg + MTX                    | ADA 40mg + MTX        | 0.72514        | 0.44105          | 1.19788          |
| ABA SUBCUT + MTX                  | ADA 40mg + MTX        | 0.96279        | 0.66275          | 1.38928          |
| IFX 3mg + MTX                     | ADA 40mg + MTX        | 0.81021        | 0.4901           | 1.34816          |
| RTX 1000mg + MTX                  | ADA 40mg + MTX        | 0.63177        | 0.32443          | 1.26628          |
| GOL 50mg + MTX                    | ADA 40mg + MTX        | 1.03482        | 0.5672           | 1.93573          |
| CZP + MTX                         | ADA 40mg + MTX        | 1.81387        | 1.09684          | 3.14225          |
| TCZ 8mg + MTX                     | ADA 40mg + MTX        | 1.68681        | 0.9459           | 3.15286          |
| cDMARD + MTX                      | ADA 40mg + MTX        | 0.36912        | 0.13743          | 1.03661          |
| ETN + MTX                         | ADA 40mg + MTX        | 1.49331        | 0.60899          | 3.8783           |
| SARI 200mg + MTX                  | ADA 40mg + MTX        | 0.94037        | 0.5948           | 1.48988          |
| TOFA 5mg + MTX                    | ADA 40mg + MTX        | 1.52386        | 1.1514           | 2.01755          |
| PBO + MTX                         | ABA 10mg + MTX        | 0.30058        | 0.19834          | 0.44853          |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>ABA 10mg + MTX</b> | <b>1.86697</b> | <b>1.09826</b>   | <b>3.17</b>      |

| Treatment 1                       | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------------------|-------------------------|----------------|----------------|----------------|
| ADA 40mg + MTX                    | ABA 10mg + MTX          | 1.37904        | 0.83481        | 2.26734        |
| ABA 10mg + MTX                    | ABA 10mg + MTX          | 1              | 1              | 1              |
| ABA SUBCUT + MTX                  | ABA 10mg + MTX          | 1.32614        | 0.71544        | 2.46851        |
| IFX 3mg + MTX                     | ABA 10mg + MTX          | 1.1183         | 0.71823        | 1.72602        |
| RTX 1000mg + MTX                  | ABA 10mg + MTX          | 0.87564        | 0.41671        | 1.85469        |
| GOL 50mg + MTX                    | ABA 10mg + MTX          | 1.42562        | 0.72586        | 2.83534        |
| CZP + MTX                         | ABA 10mg + MTX          | 2.50669        | 1.38285        | 4.67101        |
| TCZ 8mg + MTX                     | ABA 10mg + MTX          | 2.32693        | 1.21334        | 4.62482        |
| cDMARD + MTX                      | ABA 10mg + MTX          | 0.50771        | 0.17903        | 1.5208         |
| ETN + MTX                         | ABA 10mg + MTX          | 2.05802        | 0.78726        | 5.66625        |
| SARI 200mg + MTX                  | ABA 10mg + MTX          | 1.29648        | 0.75744        | 2.20831        |
| TOFA 5mg + MTX                    | ABA 10mg + MTX          | 2.09959        | 1.20454        | 3.6667         |
| PBO + MTX                         | ABA SUBCUT + MTX        | 0.22614        | 0.14129        | 0.36155        |
| <b>BARI 4mg + MTX</b>             | <b>ABA SUBCUT + MTX</b> | <b>1.40708</b> | <b>0.87621</b> | <b>2.27012</b> |
| ADA 40mg + MTX                    | ABA SUBCUT + MTX        | 1.03865        | 0.7198         | 1.50886        |
| ABA 10mg + MTX                    | ABA SUBCUT + MTX        | 0.75407        | 0.4051         | 1.39773        |
| ABA SUBCUT + MTX                  | ABA SUBCUT + MTX        | 1              | 1              | 1              |
| IFX 3mg + MTX                     | ABA SUBCUT + MTX        | 0.84295        | 0.4514         | 1.57895        |
| RTX 1000mg + MTX                  | ABA SUBCUT + MTX        | 0.65767        | 0.30851        | 1.44292        |
| GOL 50mg + MTX                    | ABA SUBCUT + MTX        | 1.07727        | 0.53102        | 2.22381        |
| CZP + MTX                         | ABA SUBCUT + MTX        | 1.89571        | 1.0115         | 3.62642        |
| TCZ 8mg + MTX                     | ABA SUBCUT + MTX        | 1.75643        | 0.88873        | 3.61398        |
| cDMARD + MTX                      | ABA SUBCUT + MTX        | 0.38285        | 0.13412        | 1.15269        |
| ETN + MTX                         | ABA SUBCUT + MTX        | 1.54975        | 0.59801        | 4.33397        |
| SARI 200mg + MTX                  | ABA SUBCUT + MTX        | 0.97733        | 0.54639        | 1.75442        |
| TOFA 5mg + MTX                    | ABA SUBCUT + MTX        | 1.58011        | 0.998          | 2.52479        |
| PBO + MTX                         | IFX 3mg + MTX           | 0.26933        | 0.176          | 0.40411        |
| <b>BARI 4mg + MTX</b>             | <b>IFX 3mg + MTX</b>    | <b>1.67029</b> | <b>0.97674</b> | <b>2.86112</b> |
| ADA 40mg + MTX                    | IFX 3mg + MTX           | 1.23425        | 0.74175        | 2.04038        |
| ABA 10mg + MTX                    | IFX 3mg + MTX           | 0.89422        | 0.57937        | 1.3923         |
| ABA SUBCUT + MTX                  | IFX 3mg + MTX           | 1.18631        | 0.63333        | 2.21534        |
| IFX 3mg + MTX                     | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX                  | IFX 3mg + MTX           | 0.78261        | 0.37205        | 1.664          |
| GOL 50mg + MTX                    | IFX 3mg + MTX           | 1.27638        | 0.64666        | 2.56369        |
| CZP + MTX                         | IFX 3mg + MTX           | 2.24302        | 1.23868        | 4.18801        |
| TCZ 8mg + MTX                     | IFX 3mg + MTX           | 2.08821        | 1.08183        | 4.15328        |
| cDMARD + MTX                      | IFX 3mg + MTX           | 0.45509        | 0.1611         | 1.34926        |
| ETN + MTX                         | IFX 3mg + MTX           | 1.83743        | 0.71284        | 5.05965        |
| SARI 200mg + MTX                  | IFX 3mg + MTX           | 1.16119        | 0.67462        | 1.9854         |
| TOFA 5mg + MTX                    | IFX 3mg + MTX           | 1.87668        | 1.07225        | 3.28402        |
| PBO + MTX                         | RTX 1000mg + MTX        | 0.34423        | 0.18105        | 0.63818        |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>RTX 1000mg + MTX</b> | <b>2.1399</b>  | <b>1.04057</b> | <b>4.30218</b> |
| ADA 40mg + MTX                    | RTX 1000mg + MTX        | 1.58287        | 0.78972        | 3.08235        |
| ABA 10mg + MTX                    | RTX 1000mg + MTX        | 1.14202        | 0.53917        | 2.39974        |
| ABA SUBCUT + MTX                  | RTX 1000mg + MTX        | 1.52053        | 0.69304        | 3.24135        |
| IFX 3mg + MTX                     | RTX 1000mg + MTX        | 1.27778        | 0.60096        | 2.68781        |
| RTX 1000mg + MTX                  | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX                    | RTX 1000mg + MTX        | 1.63562        | 0.72024        | 3.71365        |
| CZP + MTX                         | RTX 1000mg + MTX        | 2.87632        | 1.3584         | 6.09418        |
| TCZ 8mg + MTX                     | RTX 1000mg + MTX        | 2.66991        | 1.18472        | 6.00828        |
| cDMARD + MTX                      | RTX 1000mg + MTX        | 0.58256        | 0.18728        | 1.83563        |
| ETN + MTX                         | RTX 1000mg + MTX        | 2.35472        | 0.8256         | 6.98465        |
| SARI 200mg + MTX                  | RTX 1000mg + MTX        | 1.48131        | 0.71229        | 3.05109        |
| TOFA 5mg + MTX                    | RTX 1000mg + MTX        | 2.40889        | 1.15987        | 4.89592        |
| PBO + MTX                         | GOL 50mg + MTX          | 0.21082        | 0.11988        | 0.35948        |
| <b>BARI 4mg + MTX</b>             | <b>GOL 50mg + MTX</b>   | <b>1.30899</b> | <b>0.685</b>   | <b>2.43563</b> |

| Treatment 1                       | Treatment 2          | Median OR      | 95% CrI Lower  | 95% CrI Upper   |
|-----------------------------------|----------------------|----------------|----------------|-----------------|
| ADA 40mg + MTX                    | GOL 50mg + MTX       | 0.96635        | 0.5166         | 1.76306         |
| ABA 10mg + MTX                    | GOL 50mg + MTX       | 0.70145        | 0.35269        | 1.37767         |
| ABA SUBCUT + MTX                  | GOL 50mg + MTX       | 0.92827        | 0.44968        | 1.88317         |
| IFX 3mg + MTX                     | GOL 50mg + MTX       | 0.78347        | 0.39006        | 1.5464          |
| RTX 1000mg + MTX                  | GOL 50mg + MTX       | 0.61139        | 0.26928        | 1.38842         |
| GOL 50mg + MTX                    | GOL 50mg + MTX       | 1              | 1              | 1               |
| CZP + MTX                         | GOL 50mg + MTX       | 1.75685        | 0.88286        | 3.52941         |
| TCZ 8mg + MTX                     | GOL 50mg + MTX       | 1.63659        | 0.77318        | 3.50045         |
| cDMARD + MTX                      | GOL 50mg + MTX       | 0.35671        | 0.11972        | 1.0907          |
| ETN + MTX                         | GOL 50mg + MTX       | 1.44747        | 0.52758        | 4.12747         |
| SARI 200mg + MTX                  | GOL 50mg + MTX       | 0.90941        | 0.46668        | 1.72805         |
| TOFA 5mg + MTX                    | GOL 50mg + MTX       | 1.47017        | 0.75467        | 2.80173         |
| PBO + MTX                         | CZP + MTX            | 0.12009        | 0.07362        | 0.1842          |
| <b>BARI 4mg + MTX</b>             | <b>CZP + MTX</b>     | <b>0.74391</b> | <b>0.41745</b> | <b>1.27966</b>  |
| ADA 40mg + MTX                    | CZP + MTX            | 0.55131        | 0.31824        | 0.91171         |
| ABA 10mg + MTX                    | CZP + MTX            | 0.39893        | 0.21409        | 0.72314         |
| ABA SUBCUT + MTX                  | CZP + MTX            | 0.52751        | 0.27575        | 0.98863         |
| IFX 3mg + MTX                     | CZP + MTX            | 0.44583        | 0.23878        | 0.80731         |
| RTX 1000mg + MTX                  | CZP + MTX            | 0.34767        | 0.16409        | 0.73616         |
| GOL 50mg + MTX                    | CZP + MTX            | 0.5692         | 0.28333        | 1.13269         |
| CZP + MTX                         | CZP + MTX            | 1              | 1              | 1               |
| TCZ 8mg + MTX                     | CZP + MTX            | 0.92861        | 0.47681        | 1.83099         |
| cDMARD + MTX                      | CZP + MTX            | 0.20291        | 0.07175        | 0.57852         |
| ETN + MTX                         | CZP + MTX            | 0.82369        | 0.31731        | 2.17246         |
| SARI 200mg + MTX                  | CZP + MTX            | 0.51753        | 0.28282        | 0.90726         |
| TOFA 5mg + MTX                    | CZP + MTX            | 0.83765        | 0.46628        | 1.45809         |
| PBO + MTX                         | TCZ 8mg + MTX        | 0.12918        | 0.07369        | 0.21348         |
| <b>BARI 4mg + MTX</b>             | <b>TCZ 8mg + MTX</b> | <b>0.8029</b>  | <b>0.41789</b> | <b>1.47939</b>  |
| ADA 40mg + MTX                    | TCZ 8mg + MTX        | 0.59284        | 0.31717        | 1.05719         |
| ABA 10mg + MTX                    | TCZ 8mg + MTX        | 0.42975        | 0.21622        | 0.82417         |
| ABA SUBCUT + MTX                  | TCZ 8mg + MTX        | 0.56934        | 0.2767         | 1.12521         |
| IFX 3mg + MTX                     | TCZ 8mg + MTX        | 0.47888        | 0.24077        | 0.92436         |
| RTX 1000mg + MTX                  | TCZ 8mg + MTX        | 0.37454        | 0.16644        | 0.84408         |
| GOL 50mg + MTX                    | TCZ 8mg + MTX        | 0.61103        | 0.28568        | 1.29336         |
| CZP + MTX                         | TCZ 8mg + MTX        | 1.07688        | 0.54615        | 2.09726         |
| TCZ 8mg + MTX                     | TCZ 8mg + MTX        | 1              | 1              | 1               |
| cDMARD + MTX                      | TCZ 8mg + MTX        | 0.21801        | 0.07374        | 0.65852         |
| ETN + MTX                         | TCZ 8mg + MTX        | 0.88432        | 0.32122        | 2.46692         |
| SARI 200mg + MTX                  | TCZ 8mg + MTX        | 0.55674        | 0.28702        | 1.03638         |
| TOFA 5mg + MTX                    | TCZ 8mg + MTX        | 0.90268        | 0.4643         | 1.6837          |
| PBO + MTX                         | cDMARD + MTX         | 0.58925        | 0.21337        | 1.55162         |
| <b>BARI 4mg + MTX<sup>1</sup></b> | <b>cDMARD + MTX</b>  | <b>3.67348</b> | <b>1.27591</b> | <b>10.05613</b> |
| ADA 40mg + MTX                    | cDMARD + MTX         | 2.70915        | 0.96469        | 7.27646         |
| ABA 10mg + MTX                    | cDMARD + MTX         | 1.96962        | 0.65755        | 5.58578         |
| ABA SUBCUT + MTX                  | cDMARD + MTX         | 2.61196        | 0.86753        | 7.45598         |
| IFX 3mg + MTX                     | cDMARD + MTX         | 2.19736        | 0.74114        | 6.2075          |
| RTX 1000mg + MTX                  | cDMARD + MTX         | 1.71655        | 0.54477        | 5.33966         |
| GOL 50mg + MTX                    | cDMARD + MTX         | 2.80343        | 0.91684        | 8.35283         |
| CZP + MTX                         | cDMARD + MTX         | 4.92823        | 1.72854        | 13.93764        |
| TCZ 8mg + MTX                     | cDMARD + MTX         | 4.5869         | 1.51855        | 13.56166        |
| cDMARD + MTX                      | cDMARD + MTX         | 1              | 1              | 1               |
| ETN + MTX                         | cDMARD + MTX         | 4.03019        | 2.56495        | 6.64515         |
| SARI 200mg + MTX                  | cDMARD + MTX         | 2.54929        | 0.86369        | 7.14762         |
| TOFA 5mg + MTX                    | cDMARD + MTX         | 4.12254        | 1.43655        | 11.39452        |
| PBO + MTX                         | ETN + MTX            | 0.1454         | 0.05744        | 0.34891         |
| <b>BARI 4mg + MTX</b>             | <b>ETN + MTX</b>     | <b>0.90643</b> | <b>0.34263</b> | <b>2.28773</b>  |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| ADA 40mg + MTX        | ETN + MTX               | 0.66966        | 0.25785        | 1.64207        |
| ABA 10mg + MTX        | ETN + MTX               | 0.4859         | 0.17648        | 1.27023        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.64527        | 0.23074        | 1.67223        |
| IFX 3mg + MTX         | ETN + MTX               | 0.54424        | 0.19764        | 1.40284        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.42468        | 0.14317        | 1.21124        |
| GOL 50mg + MTX        | ETN + MTX               | 0.69086        | 0.24228        | 1.89546        |
| CZP + MTX             | ETN + MTX               | 1.21405        | 0.46031        | 3.15146        |
| TCZ 8mg + MTX         | ETN + MTX               | 1.13081        | 0.40536        | 3.11316        |
| cDMARD + MTX          | ETN + MTX               | 0.24813        | 0.15049        | 0.38987        |
| ETN + MTX             | ETN + MTX               | 1              | 1              | 1              |
| SARI 200mg + MTX      | ETN + MTX               | 0.62698        | 0.2312         | 1.61207        |
| TOFA 5mg + MTX        | ETN + MTX               | 1.01977        | 0.38195        | 2.5614         |
| PBO + MTX             | SARI 200mg + MTX        | 0.232          | 0.16292        | 0.32719        |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.44161</b> | <b>0.88314</b> | <b>2.34518</b> |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.06341        | 0.67119        | 1.68123        |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.77132        | 0.45283        | 1.32023        |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 1.02319        | 0.56999        | 1.83021        |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.86119        | 0.50368        | 1.48231        |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.67508        | 0.32775        | 1.40393        |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 1.09961        | 0.57869        | 2.14282        |
| CZP + MTX             | SARI 200mg + MTX        | 1.93225        | 1.10223        | 3.53582        |
| TCZ 8mg + MTX         | SARI 200mg + MTX        | 1.79618        | 0.9649         | 3.48409        |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.39227        | 0.13991        | 1.15782        |
| ETN + MTX             | SARI 200mg + MTX        | 1.59495        | 0.62032        | 4.32526        |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1              | 1              |
| TOFA 5mg + MTX        | SARI 200mg + MTX        | 1.62155        | 0.96764        | 2.71326        |
| PBO + MTX             | TOFA 5mg + MTX          | 0.14308        | 0.0971         | 0.20888        |
| <b>BARI 4mg + MTX</b> | <b>TOFA 5mg + MTX</b>   | <b>0.88805</b> | <b>0.59409</b> | <b>1.33912</b> |
| ADA 40mg + MTX        | TOFA 5mg + MTX          | 0.65623        | 0.49565        | 0.86851        |
| ABA 10mg + MTX        | TOFA 5mg + MTX          | 0.47628        | 0.27272        | 0.83019        |
| ABA SUBCUT + MTX      | TOFA 5mg + MTX          | 0.63287        | 0.39607        | 1.002          |
| IFX 3mg + MTX         | TOFA 5mg + MTX          | 0.53285        | 0.3045         | 0.93262        |
| RTX 1000mg + MTX      | TOFA 5mg + MTX          | 0.41513        | 0.20425        | 0.86217        |
| GOL 50mg + MTX        | TOFA 5mg + MTX          | 0.68019        | 0.35692        | 1.32509        |
| CZP + MTX             | TOFA 5mg + MTX          | 1.19382        | 0.68583        | 2.14463        |
| TCZ 8mg + MTX         | TOFA 5mg + MTX          | 1.10782        | 0.59393        | 2.15376        |
| cDMARD + MTX          | TOFA 5mg + MTX          | 0.24257        | 0.08776        | 0.69611        |
| ETN + MTX             | TOFA 5mg + MTX          | 0.98062        | 0.39041        | 2.61816        |
| SARI 200mg + MTX      | TOFA 5mg + MTX          | 0.61669        | 0.36856        | 1.03344        |
| TOFA 5mg + MTX        | TOFA 5mg + MTX          | 1              | 1              | 1              |

Abbreviations: ABA abatacept; ADA adalimumab; BARI baricitinib; ETN etanercept; GOL golimumab; IFX infliximab; MTX methotrexate; PBO placebo; RTX rituximab; SARI sarilumab; SUBCUT subcutaneous; TCZ tocilizumab; TOFA tofacitinib.

<sup>1</sup>statistically significantly favouring BARI.

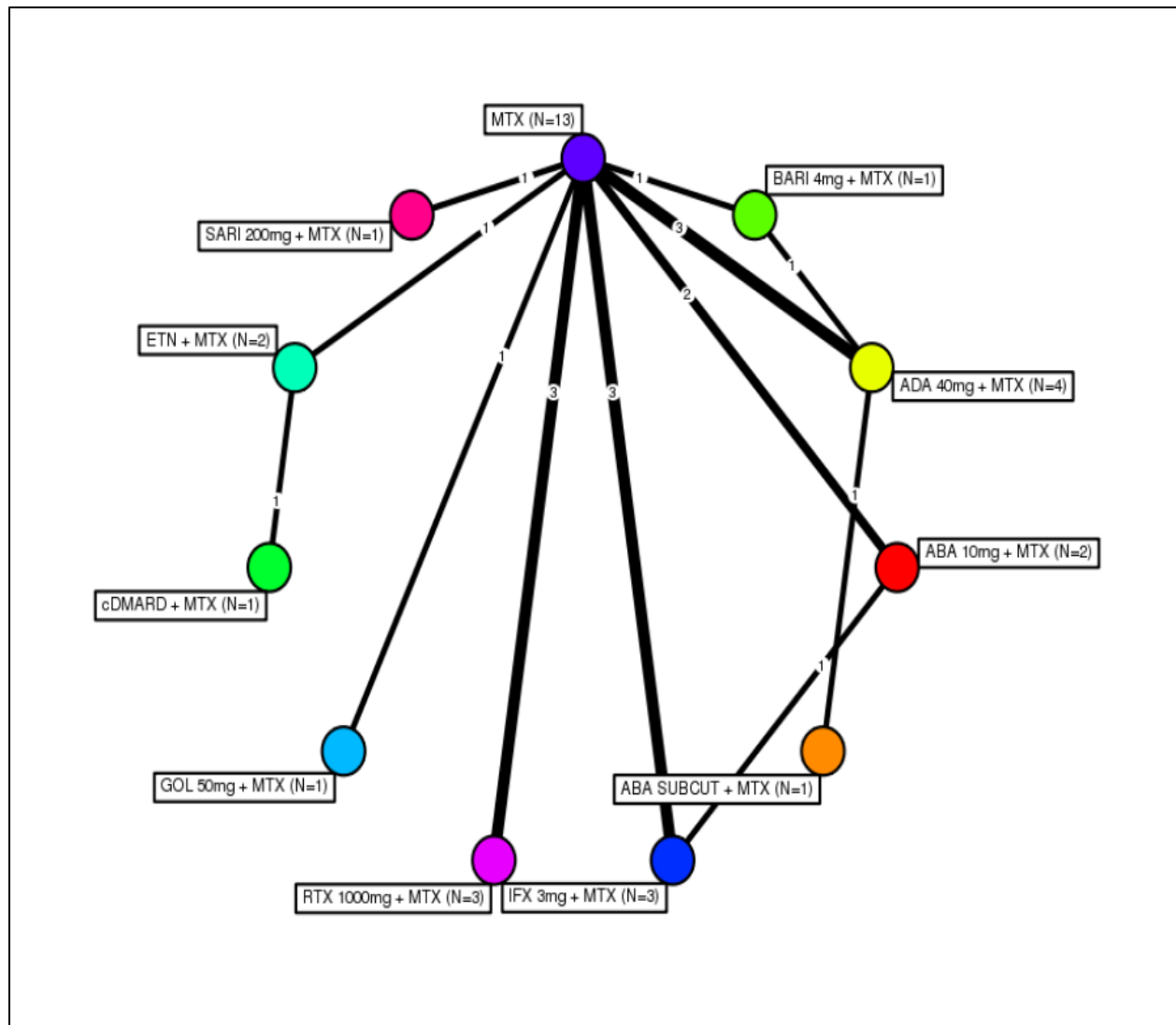
Odds ratios >1 are in favour of Treatment 1; and odds ratios <1 are in favour of Treatment 2.



## 10.3. Trials Conducted in Asia Pacific/Low Dose MTX

### 10.3.1. ACR20 response

**Figure S3** Sensitivity analysis excluding trials conducted solely in Asia-Pacific and/or low MTX dose: Network of Evidence - Simultaneous fixed effects: ACR20



Note: Sensitivity excluding trials conducted solely in Asia-Pacific and/or low MTX dose (N=15 trials for ACR20 and N=14 trials for ACR50/70 (minus ATTRACT [IFX])

**Table S24** Sensitivity analysis excluding trials conducted solely in Asia-Pacific and/or low MTX dose:  
Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% Crls)  
– ACR20 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1           | Treatment 2             | Median OR      | 95% Crl<br>Lower | 95% Crl<br>Upper |
|-----------------------|-------------------------|----------------|------------------|------------------|
| MTX                   | MTX                     | 1              | 1                | 1                |
| <b>BARI 4mg + MTX</b> | <b>MTX</b>              | <b>5.37048</b> | <b>4.16293</b>   | <b>6.97437</b>   |
| ADA 40mg + MTX        | MTX                     | 4.04653        | 3.30839          | 4.96635          |
| ABA 10mg + MTX        | MTX                     | 3.73632        | 2.86435          | 4.84977          |
| ABA SUBCUT + MTX      | MTX                     | 4.14362        | 2.90908          | 5.89238          |
| IFX 3mg + MTX         | MTX                     | 3.19234        | 2.55836          | 3.99711          |
| RTX 1000mg + MTX      | MTX                     | 3.10623        | 2.26495          | 4.33549          |
| GOL 50mg + MTX        | MTX                     | 3.62315        | 2.17581          | 6.12803          |
| cDMARD + MTX          | MTX                     | 1.95595        | 1.10581          | 3.29082          |
| ETN + MTX             | MTX                     | 8.9441         | 5.53275          | 14.09385         |
| SARI 200mg + MTX      | MTX                     | 4.15888        | 3.00172          | 5.75745          |
| MTX                   | BARI 4mg + MTX          | 0.1862         | 0.14338          | 0.24022          |
| BARI 4mg + MTX        | BARI 4mg + MTX          | 1              | 1                | 1                |
| ADA 40mg + MTX        | BARI 4mg + MTX          | 0.75281        | 0.5718           | 0.99825          |
| ABA 10mg + MTX        | BARI 4mg + MTX          | 0.69561        | 0.48486          | 0.98986          |
| ABA SUBCUT + MTX      | BARI 4mg + MTX          | 0.77098        | 0.51537          | 1.15413          |
| IFX 3mg + MTX         | BARI 4mg + MTX          | 0.59349        | 0.42563          | 0.83334          |
| RTX 1000mg + MTX      | BARI 4mg + MTX          | 0.57916        | 0.38661          | 0.87746          |
| GOL 50mg + MTX        | BARI 4mg + MTX          | 0.6743         | 0.3831           | 1.20797          |
| cDMARD + MTX          | BARI 4mg + MTX          | 0.36341        | 0.1975           | 0.6459           |
| ETN + MTX             | BARI 4mg + MTX          | 1.66131        | 0.98309          | 2.78207          |
| SARI 200mg + MTX      | BARI 4mg + MTX          | 0.7746         | 0.51413          | 1.1619           |
| MTX                   | ADA 40mg + MTX          | 0.24713        | 0.20136          | 0.30226          |
| <b>BARI 4mg + MTX</b> | <b>ADA 40mg + MTX</b>   | <b>1.32836</b> | <b>1.00175</b>   | <b>1.74886</b>   |
| ADA 40mg + MTX        | ADA 40mg + MTX          | 1              | 1                | 1                |
| ABA 10mg + MTX        | ADA 40mg + MTX          | 0.92378        | 0.66352          | 1.26569          |
| ABA SUBCUT + MTX      | ADA 40mg + MTX          | 1.02325        | 0.75395          | 1.39196          |
| IFX 3mg + MTX         | ADA 40mg + MTX          | 0.7877         | 0.58913          | 1.05786          |
| RTX 1000mg + MTX      | ADA 40mg + MTX          | 0.76894        | 0.53386          | 1.12031          |
| GOL 50mg + MTX        | ADA 40mg + MTX          | 0.89495        | 0.52492          | 1.56451          |
| cDMARD + MTX          | ADA 40mg + MTX          | 0.48361        | 0.26706          | 0.83406          |
| ETN + MTX             | ADA 40mg + MTX          | 2.20984        | 1.33392          | 3.57495          |
| SARI 200mg + MTX      | ADA 40mg + MTX          | 1.02854        | 0.70288          | 1.50034          |
| MTX                   | ABA 10mg + MTX          | 0.26764        | 0.2062           | 0.34912          |
| <b>BARI 4mg + MTX</b> | <b>ABA 10mg + MTX</b>   | <b>1.43759</b> | <b>1.01025</b>   | <b>2.06244</b>   |
| ADA 40mg + MTX        | ABA 10mg + MTX          | 1.08251        | 0.79008          | 1.50711          |
| ABA 10mg + MTX        | ABA 10mg + MTX          | 1              | 1                | 1                |
| ABA SUBCUT + MTX      | ABA 10mg + MTX          | 1.10821        | 0.72674          | 1.70557          |
| IFX 3mg + MTX         | ABA 10mg + MTX          | 0.85461        | 0.62356          | 1.17594          |
| RTX 1000mg + MTX      | ABA 10mg + MTX          | 0.83263        | 0.55116          | 1.27331          |
| GOL 50mg + MTX        | ABA 10mg + MTX          | 0.97046        | 0.54768          | 1.75083          |
| cDMARD + MTX          | ABA 10mg + MTX          | 0.52148        | 0.28706          | 0.92376          |
| ETN + MTX             | ABA 10mg + MTX          | 2.38602        | 1.433            | 4.01141          |
| SARI 200mg + MTX      | ABA 10mg + MTX          | 1.11273        | 0.74206          | 1.68621          |
| MTX                   | ABA SUBCUT + MTX        | 0.24134        | 0.16971          | 0.34375          |
| <b>BARI 4mg + MTX</b> | <b>ABA SUBCUT + MTX</b> | <b>1.29705</b> | <b>0.86645</b>   | <b>1.94037</b>   |
| ADA 40mg + MTX        | ABA SUBCUT + MTX        | 0.97728        | 0.71841          | 1.32635          |
| ABA 10mg + MTX        | ABA SUBCUT + MTX        | 0.90235        | 0.58631          | 1.376            |
| ABA SUBCUT + MTX      | ABA SUBCUT + MTX        | 1              | 1                | 1                |
| IFX 3mg + MTX         | ABA SUBCUT + MTX        | 0.7698         | 0.51369          | 1.15968          |
| RTX 1000mg + MTX      | ABA SUBCUT + MTX        | 0.75093        | 0.47582          | 1.20294          |
| GOL 50mg + MTX        | ABA SUBCUT + MTX        | 0.87461        | 0.47519          | 1.64567          |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-------------------------|----------------|----------------|----------------|
| cDMARD + MTX          | ABA SUBCUT + MTX        | 0.47109        | 0.24668        | 0.8694         |
| ETN + MTX             | ABA SUBCUT + MTX        | 2.15673        | 1.21811        | 3.7406         |
| SARI 200mg + MTX      | ABA SUBCUT + MTX        | 1.00468        | 0.62345        | 1.60418        |
| MTX                   | IFX 3mg + MTX           | 0.31325        | 0.25018        | 0.39087        |
| <b>BARI 4mg + MTX</b> | <b>IFX 3mg + MTX</b>    | <b>1.68494</b> | <b>1.19999</b> | <b>2.34948</b> |
| ADA 40mg + MTX        | IFX 3mg + MTX           | 1.26952        | 0.9453         | 1.69742        |
| ABA 10mg + MTX        | IFX 3mg + MTX           | 1.17012        | 0.85038        | 1.60371        |
| ABA SUBCUT + MTX      | IFX 3mg + MTX           | 1.29904        | 0.86231        | 1.94671        |
| IFX 3mg + MTX         | IFX 3mg + MTX           | 1              | 1              | 1              |
| RTX 1000mg + MTX      | IFX 3mg + MTX           | 0.97507        | 0.67149        | 1.42778        |
| GOL 50mg + MTX        | IFX 3mg + MTX           | 1.13585        | 0.65765        | 1.99493        |
| cDMARD + MTX          | IFX 3mg + MTX           | 0.61382        | 0.33277        | 1.06373        |
| ETN + MTX             | IFX 3mg + MTX           | 2.80805        | 1.66408        | 4.5755         |
| SARI 200mg + MTX      | IFX 3mg + MTX           | 1.30365        | 0.87628        | 1.92489        |
| MTX                   | RTX 1000mg + MTX        | 0.32193        | 0.23065        | 0.44151        |
| <b>BARI 4mg + MTX</b> | <b>RTX 1000mg + MTX</b> | <b>1.72665</b> | <b>1.13965</b> | <b>2.58658</b> |
| ADA 40mg + MTX        | RTX 1000mg + MTX        | 1.30049        | 0.89261        | 1.87313        |
| ABA 10mg + MTX        | RTX 1000mg + MTX        | 1.20101        | 0.78535        | 1.81434        |
| ABA SUBCUT + MTX      | RTX 1000mg + MTX        | 1.33169        | 0.8313         | 2.10162        |
| IFX 3mg + MTX         | RTX 1000mg + MTX        | 1.02557        | 0.70039        | 1.48923        |
| RTX 1000mg + MTX      | RTX 1000mg + MTX        | 1              | 1              | 1              |
| GOL 50mg + MTX        | RTX 1000mg + MTX        | 1.16663        | 0.64197        | 2.12786        |
| cDMARD + MTX          | RTX 1000mg + MTX        | 0.62863        | 0.3254         | 1.14171        |
| ETN + MTX             | RTX 1000mg + MTX        | 2.88301        | 1.62059        | 4.91039        |
| SARI 200mg + MTX      | RTX 1000mg + MTX        | 1.33724        | 0.84281        | 2.10091        |
| MTX                   | GOL 50mg + MTX          | 0.276          | 0.16318        | 0.4596         |
| <b>BARI 4mg + MTX</b> | <b>GOL 50mg + MTX</b>   | <b>1.48303</b> | <b>0.82783</b> | <b>2.61028</b> |
| ADA 40mg + MTX        | GOL 50mg + MTX          | 1.11738        | 0.63918        | 1.90507        |
| ABA 10mg + MTX        | GOL 50mg + MTX          | 1.03044        | 0.57116        | 1.82588        |
| ABA SUBCUT + MTX      | GOL 50mg + MTX          | 1.14337        | 0.60765        | 2.10443        |
| IFX 3mg + MTX         | GOL 50mg + MTX          | 0.8804         | 0.50127        | 1.52057        |
| RTX 1000mg + MTX      | GOL 50mg + MTX          | 0.85717        | 0.46996        | 1.55772        |
| GOL 50mg + MTX        | GOL 50mg + MTX          | 1              | 1              | 1              |
| cDMARD + MTX          | GOL 50mg + MTX          | 0.53894        | 0.25093        | 1.10286        |
| ETN + MTX             | GOL 50mg + MTX          | 2.4639         | 1.22371        | 4.79625        |
| SARI 200mg + MTX      | GOL 50mg + MTX          | 1.14785        | 0.62058        | 2.08488        |
| MTX                   | cDMARD + MTX            | 0.51126        | 0.30388        | 0.90431        |
| <b>BARI 4mg + MTX</b> | <b>cDMARD + MTX</b>     | <b>2.75168</b> | <b>1.54824</b> | <b>5.06338</b> |
| ADA 40mg + MTX        | cDMARD + MTX            | 2.06779        | 1.19895        | 3.74449        |
| ABA 10mg + MTX        | cDMARD + MTX            | 1.91764        | 1.08253        | 3.48364        |
| ABA SUBCUT + MTX      | cDMARD + MTX            | 2.12274        | 1.15022        | 4.05383        |
| IFX 3mg + MTX         | cDMARD + MTX            | 1.62914        | 0.94008        | 3.00511        |
| RTX 1000mg + MTX      | cDMARD + MTX            | 1.59075        | 0.87588        | 3.07315        |
| GOL 50mg + MTX        | cDMARD + MTX            | 1.8555         | 0.90673        | 3.98519        |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1              |
| ETN + MTX             | cDMARD + MTX            | 4.58387        | 2.98054        | 7.15383        |
| SARI 200mg + MTX      | cDMARD + MTX            | 2.1313         | 1.15538        | 4.04219        |
| MTX                   | ETN + MTX               | 0.11181        | 0.07095        | 0.18074        |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.60193</b> | <b>0.35944</b> | <b>1.0172</b>  |
| ADA 40mg + MTX        | ETN + MTX               | 0.45252        | 0.27972        | 0.74967        |
| ABA 10mg + MTX        | ETN + MTX               | 0.41911        | 0.24929        | 0.69783        |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.46366        | 0.26734        | 0.82095        |
| IFX 3mg + MTX         | ETN + MTX               | 0.35612        | 0.21856        | 0.60093        |
| RTX 1000mg + MTX      | ETN + MTX               | 0.34686        | 0.20365        | 0.61706        |
| GOL 50mg + MTX        | ETN + MTX               | 0.40586        | 0.2085         | 0.81718        |
| cDMARD + MTX          | ETN + MTX               | 0.21816        | 0.13979        | 0.33551        |

| <b>Treatment 1</b>    | <b>Treatment 2</b>      | <b>Median OR</b> | <b>95% CrI<br/>Lower</b> | <b>95% CrI<br/>Upper</b> |
|-----------------------|-------------------------|------------------|--------------------------|--------------------------|
| ETN + MTX             | ETN + MTX               | 1                | 1                        | 1                        |
| SARI 200mg + MTX      | ETN + MTX               | 0.46684          | 0.26562                  | 0.81718                  |
| MTX                   | SARI 200mg + MTX        | 0.24045          | 0.17369                  | 0.33314                  |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.29099</b>   | <b>0.86066</b>           | <b>1.94505</b>           |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 0.97225          | 0.66652                  | 1.42272                  |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.89869          | 0.59304                  | 1.34761                  |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.99534          | 0.62337                  | 1.60399                  |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.76708          | 0.51951                  | 1.14118                  |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.74781          | 0.47599                  | 1.1865                   |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.87119          | 0.47964                  | 1.61139                  |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.4692           | 0.24739                  | 0.86552                  |
| ETN + MTX             | SARI 200mg + MTX        | 2.14208          | 1.22373                  | 3.76474                  |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1                | 1                        | 1                        |

### 10.3.2. ACR50 response

**Table S25** Sensitivity analysis excluding trials conducted solely in Asia-Pacific and/or low MTX dose: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) – ACR50 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1           | Treatment 2           | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-----------------------|----------------|----------------|----------------|
| MTX                   | MTX                   | 1              | 1              | 1              |
| <b>BARI 4mg + MTX</b> | <b>MTX</b>            | <b>4.91902</b> | <b>3.75386</b> | <b>6.46411</b> |
| ADA 40mg + MTX        | MTX                   | 4.46572        | 3.51362        | 5.70599        |
| ABA 10mg + MTX        | MTX                   | 3.48194        | 2.58922        | 4.70285        |
| ABA SUBCUT + MTX      | MTX                   | 4.43214        | 3.01747        | 6.51707        |
| IFX 3mg + MTX         | MTX                   | 3.44204        | 2.56947        | 4.6451         |
| RTX 1000mg + MTX      | MTX                   | 3.13834        | 2.07935        | 4.84871        |
| GOL 50mg + MTX        | MTX                   | 3.70393        | 2.02353        | 6.82704        |
| cDMARD + MTX          | MTX                   | 1.38322        | 0.64269        | 3.1433         |
| ETN + MTX             | MTX                   | 7.35481        | 3.84743        | 15.37692       |
| SARI 200mg + MTX      | MTX                   | 4.39488        | 3.1141         | 6.2253         |
| MTX                   | BARI 4mg + MTX        | 0.20329        | 0.1547         | 0.26639        |
| BARI 4mg + MTX        | BARI 4mg + MTX        | 1              | 1              | 1              |
| ADA 40mg + MTX        | BARI 4mg + MTX        | 0.90752        | 0.69779        | 1.1789         |
| ABA 10mg + MTX        | BARI 4mg + MTX        | 0.70844        | 0.47417        | 1.0588         |
| ABA SUBCUT + MTX      | BARI 4mg + MTX        | 0.90093        | 0.60026        | 1.34672        |
| IFX 3mg + MTX         | BARI 4mg + MTX        | 0.7001         | 0.47011        | 1.04351        |
| RTX 1000mg + MTX      | BARI 4mg + MTX        | 0.63908        | 0.39234        | 1.06024        |
| GOL 50mg + MTX        | BARI 4mg + MTX        | 0.7536         | 0.38906        | 1.46185        |
| cDMARD + MTX          | BARI 4mg + MTX        | 0.28136        | 0.12626        | 0.66247        |
| ETN + MTX             | BARI 4mg + MTX        | 1.49391        | 0.75062        | 3.22924        |
| SARI 200mg + MTX      | BARI 4mg + MTX        | 0.89404        | 0.57709        | 1.38573        |
| MTX                   | ADA 40mg + MTX        | 0.22393        | 0.17525        | 0.28461        |
| <b>BARI 4mg + MTX</b> | <b>ADA 40mg + MTX</b> | <b>1.1019</b>  | <b>0.84824</b> | <b>1.43311</b> |
| ADA 40mg + MTX        | ADA 40mg + MTX        | 1              | 1              | 1              |
| ABA 10mg + MTX        | ADA 40mg + MTX        | 0.7815         | 0.5329         | 1.13377        |
| ABA SUBCUT + MTX      | ADA 40mg + MTX        | 0.99333        | 0.72713        | 1.35705        |
| IFX 3mg + MTX         | ADA 40mg + MTX        | 0.77041        | 0.53121        | 1.12594        |
| RTX 1000mg + MTX      | ADA 40mg + MTX        | 0.70352        | 0.44247        | 1.14264        |
| GOL 50mg + MTX        | ADA 40mg + MTX        | 0.83152        | 0.43202        | 1.58855        |
| cDMARD + MTX          | ADA 40mg + MTX        | 0.31006        | 0.14077        | 0.71576        |
| ETN + MTX             | ADA 40mg + MTX        | 1.64609        | 0.84125        | 3.46877        |
| SARI 200mg + MTX      | ADA 40mg + MTX        | 0.98503        | 0.64435        | 1.50432        |
| MTX                   | ABA 10mg + MTX        | 0.2872         | 0.21264        | 0.38622        |
| <b>BARI 4mg + MTX</b> | <b>ABA 10mg + MTX</b> | <b>1.41155</b> | <b>0.94447</b> | <b>2.10893</b> |
| ADA 40mg + MTX        | ABA 10mg + MTX        | 1.2796         | 0.88201        | 1.87653        |
| ABA 10mg + MTX        | ABA 10mg + MTX        | 1              | 1              | 1              |
| ABA SUBCUT + MTX      | ABA 10mg + MTX        | 1.27182        | 0.78634        | 2.06184        |
| IFX 3mg + MTX         | ABA 10mg + MTX        | 0.98738        | 0.69842        | 1.4006         |
| RTX 1000mg + MTX      | ABA 10mg + MTX        | 0.90207        | 0.54673        | 1.51893        |
| GOL 50mg + MTX        | ABA 10mg + MTX        | 1.06442        | 0.53927        | 2.09933        |
| cDMARD + MTX          | ABA 10mg + MTX        | 0.39693        | 0.17707        | 0.94152        |
| ETN + MTX             | ABA 10mg + MTX        | 2.11145        | 1.0493         | 4.60216        |
| SARI 200mg + MTX      | ABA 10mg + MTX        | 1.26079        | 0.7974         | 1.99003        |
| MTX                   | ABA SUBCUT + MTX      | 0.22562        | 0.15344        | 0.3314         |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------|-------------------------|----------------|------------------|------------------|
| <b>BARI 4mg + MTX</b> | <b>ABA SUBCUT + MTX</b> | <b>1.10996</b> | <b>0.74254</b>   | <b>1.66596</b>   |
| ADA 40mg + MTX        | ABA SUBCUT + MTX        | 1.00671        | 0.73689          | 1.37528          |
| ABA 10mg + MTX        | ABA SUBCUT + MTX        | 0.78627        | 0.485            | 1.27172          |
| ABA SUBCUT + MTX      | ABA SUBCUT + MTX        | 1              | 1                | 1                |
| IFX 3mg + MTX         | ABA SUBCUT + MTX        | 0.77615        | 0.48202          | 1.26144          |
| RTX 1000mg + MTX      | ABA SUBCUT + MTX        | 0.70823        | 0.41129          | 1.25565          |
| GOL 50mg + MTX        | ABA SUBCUT + MTX        | 0.83691        | 0.40963          | 1.71735          |
| cDMARD + MTX          | ABA SUBCUT + MTX        | 0.31332        | 0.13438          | 0.75612          |
| ETN + MTX             | ABA SUBCUT + MTX        | 1.6601         | 0.79646          | 3.67486          |
| SARI 200mg + MTX      | ABA SUBCUT + MTX        | 0.99144        | 0.59026          | 1.6594           |
| MTX                   | IFX 3mg + MTX           | 0.29053        | 0.21528          | 0.38919          |
| <b>BARI 4mg + MTX</b> | <b>IFX 3mg + MTX</b>    | <b>1.42837</b> | <b>0.95831</b>   | <b>2.12716</b>   |
| ADA 40mg + MTX        | IFX 3mg + MTX           | 1.29801        | 0.88815          | 1.88249          |
| ABA 10mg + MTX        | IFX 3mg + MTX           | 1.01278        | 0.71398          | 1.4318           |
| ABA SUBCUT + MTX      | IFX 3mg + MTX           | 1.28841        | 0.79275          | 2.07458          |
| IFX 3mg + MTX         | IFX 3mg + MTX           | 1              | 1                | 1                |
| RTX 1000mg + MTX      | IFX 3mg + MTX           | 0.91347        | 0.555            | 1.52066          |
| GOL 50mg + MTX        | IFX 3mg + MTX           | 1.0766         | 0.54676          | 2.11349          |
| cDMARD + MTX          | IFX 3mg + MTX           | 0.40233        | 0.17828          | 0.94492          |
| ETN + MTX             | IFX 3mg + MTX           | 2.13778        | 1.05255          | 4.61504          |
| SARI 200mg + MTX      | IFX 3mg + MTX           | 1.27657        | 0.80548          | 2.00377          |
| MTX                   | RTX 1000mg + MTX        | 0.31864        | 0.20624          | 0.48092          |
| <b>BARI 4mg + MTX</b> | <b>RTX 1000mg + MTX</b> | <b>1.56474</b> | <b>0.94319</b>   | <b>2.54883</b>   |
| ADA 40mg + MTX        | RTX 1000mg + MTX        | 1.42141        | 0.87517          | 2.26006          |
| ABA 10mg + MTX        | RTX 1000mg + MTX        | 1.10856        | 0.65836          | 1.82907          |
| ABA SUBCUT + MTX      | RTX 1000mg + MTX        | 1.41197        | 0.7964           | 2.43135          |
| IFX 3mg + MTX         | RTX 1000mg + MTX        | 1.09473        | 0.65761          | 1.80179          |
| RTX 1000mg + MTX      | RTX 1000mg + MTX        | 1              | 1                | 1                |
| GOL 50mg + MTX        | RTX 1000mg + MTX        | 1.17927        | 0.56903          | 2.42582          |
| cDMARD + MTX          | RTX 1000mg + MTX        | 0.44167        | 0.18697          | 1.05828          |
| ETN + MTX             | RTX 1000mg + MTX        | 2.35378        | 1.10568          | 5.14459          |
| SARI 200mg + MTX      | RTX 1000mg + MTX        | 1.39665        | 0.79521          | 2.4151           |
| MTX                   | GOL 50mg + MTX          | 0.26998        | 0.14648          | 0.49419          |
| <b>BARI 4mg + MTX</b> | <b>GOL 50mg + MTX</b>   | <b>1.32696</b> | <b>0.68406</b>   | <b>2.57033</b>   |
| ADA 40mg + MTX        | GOL 50mg + MTX          | 1.20261        | 0.62951          | 2.31471          |
| ABA 10mg + MTX        | GOL 50mg + MTX          | 0.93948        | 0.47634          | 1.85436          |
| ABA SUBCUT + MTX      | GOL 50mg + MTX          | 1.19487        | 0.58229          | 2.44122          |
| IFX 3mg + MTX         | GOL 50mg + MTX          | 0.92885        | 0.47315          | 1.82897          |
| RTX 1000mg + MTX      | GOL 50mg + MTX          | 0.84798        | 0.41223          | 1.75739          |
| GOL 50mg + MTX        | GOL 50mg + MTX          | 1              | 1                | 1                |
| cDMARD + MTX          | GOL 50mg + MTX          | 0.37404        | 0.14113          | 1.01528          |
| ETN + MTX             | GOL 50mg + MTX          | 1.99218        | 0.82878          | 5.01129          |
| SARI 200mg + MTX      | GOL 50mg + MTX          | 1.18692        | 0.58417          | 2.39409          |
| MTX                   | cDMARD + MTX            | 0.72295        | 0.31814          | 1.55595          |
| <b>BARI 4mg + MTX</b> | <b>cDMARD + MTX</b>     | <b>3.55418</b> | <b>1.50949</b>   | <b>7.92017</b>   |
| ADA 40mg + MTX        | cDMARD + MTX            | 3.22523        | 1.39711          | 7.10359          |
| ABA 10mg + MTX        | cDMARD + MTX            | 2.51936        | 1.06212          | 5.6474           |
| ABA SUBCUT + MTX      | cDMARD + MTX            | 3.19167        | 1.32255          | 7.44135          |
| IFX 3mg + MTX         | cDMARD + MTX            | 2.4855         | 1.05829          | 5.60925          |
| RTX 1000mg + MTX      | cDMARD + MTX            | 2.26415        | 0.94493          | 5.34845          |
| GOL 50mg + MTX        | cDMARD + MTX            | 2.67348        | 0.98495          | 7.08553          |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1                | 1                |
| ETN + MTX             | cDMARD + MTX            | 5.32332        | 3.38902          | 8.45493          |
| SARI 200mg + MTX      | cDMARD + MTX            | 3.18289        | 1.29418          | 7.24838          |
| MTX                   | ETN + MTX               | 0.13597        | 0.06503          | 0.25991          |
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>0.66939</b> | <b>0.30967</b>   | <b>1.33224</b>   |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------|-------------------------|----------------|------------------|------------------|
| ADA 40mg + MTX        | ETN + MTX               | 0.6075         | 0.28829          | 1.1887           |
| ABA 10mg + MTX        | ETN + MTX               | 0.47361        | 0.21729          | 0.95301          |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.60237        | 0.27212          | 1.25555          |
| IFX 3mg + MTX         | ETN + MTX               | 0.46777        | 0.21668          | 0.95007          |
| RTX 1000mg + MTX      | ETN + MTX               | 0.42485        | 0.19438          | 0.90442          |
| GOL 50mg + MTX        | ETN + MTX               | 0.50196        | 0.19955          | 1.20659          |
| cDMARD + MTX          | ETN + MTX               | 0.18785        | 0.11827          | 0.29507          |
| ETN + MTX             | ETN + MTX               | 1              | 1                | 1                |
| SARI 200mg + MTX      | ETN + MTX               | 0.59788        | 0.26308          | 1.22316          |
| MTX                   | SARI 200mg + MTX        | 0.22754        | 0.16063          | 0.32112          |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.11852</b> | <b>0.72164</b>   | <b>1.73284</b>   |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.0152         | 0.66475          | 1.55195          |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.79315        | 0.50251          | 1.25407          |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 1.00863        | 0.60263          | 1.69416          |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.78335        | 0.49906          | 1.2415           |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.716          | 0.41406          | 1.25753          |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 0.84251        | 0.4177           | 1.71183          |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.31418        | 0.13796          | 0.77269          |
| ETN + MTX             | SARI 200mg + MTX        | 1.67257        | 0.81755          | 3.80115          |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1                | 1                |

### 10.3.3. ACR70 response

**Table S26** Sensitivity analysis excluding trials conducted solely in Asia-Pacific and/or low MTX dose: Relative treatment effect of pairwise comparisons expressed as Post. Median odds ratios (with 95% CrIs) – ACR70 response at week 24: MTX-IR (Simultaneous Fixed-effects model)

| Treatment 1           | Treatment 2           | Median OR      | 95% CrI Lower  | 95% CrI Upper  |
|-----------------------|-----------------------|----------------|----------------|----------------|
| MTX                   | MTX                   | 1              | 1              | 1              |
| <b>BARI 4mg + MTX</b> | <b>MTX</b>            | <b>5.88738</b> | <b>4.13599</b> | <b>8.46163</b> |
| ADA 40mg + MTX        | MTX                   | 4.291          | 3.07796        | 6.0451         |
| ABA 10mg + MTX        | MTX                   | 3.10864        | 2.08679        | 4.68187        |
| ABA SUBCUT + MTX      | MTX                   | 4.06656        | 2.49117        | 6.70514        |
| IFX 3mg + MTX         | MTX                   | 3.46965        | 2.3322         | 5.24931        |
| RTX 1000mg + MTX      | MTX                   | 2.48715        | 1.35321        | 4.71134        |
| GOL 50mg + MTX        | MTX                   | 4.32118        | 1.9055         | 10.36569       |
| cDMARD + MTX          | MTX                   | 1.36336        | 0.42985        | 4.9867         |
| ETN + MTX             | MTX                   | 5.78645        | 2.08325        | 19.43516       |
| SARI 200mg + MTX      | MTX                   | 4.27494        | 3.01698        | 6.08           |
| MTX                   | BARI 4mg + MTX        | 0.16985        | 0.11818        | 0.24178        |
| BARI 4mg + MTX        | BARI 4mg + MTX        | 1              | 1              | 1              |
| ADA 40mg + MTX        | BARI 4mg + MTX        | 0.72977        | 0.53584        | 0.98664        |
| ABA 10mg + MTX        | BARI 4mg + MTX        | 0.52792        | 0.31078        | 0.90004        |
| ABA SUBCUT + MTX      | BARI 4mg + MTX        | 0.69117        | 0.42872        | 1.11327        |
| IFX 3mg + MTX         | BARI 4mg + MTX        | 0.59           | 0.34577        | 1.0111         |
| RTX 1000mg + MTX      | BARI 4mg + MTX        | 0.42243        | 0.21188        | 0.86685        |
| GOL 50mg + MTX        | BARI 4mg + MTX        | 0.73614        | 0.30038        | 1.85482        |
| cDMARD + MTX          | BARI 4mg + MTX        | 0.23171        | 0.07005        | 0.858          |
| ETN + MTX             | BARI 4mg + MTX        | 0.98501        | 0.33681        | 3.32157        |
| SARI 200mg + MTX      | BARI 4mg + MTX        | 0.72614        | 0.43852        | 1.18727        |
| MTX                   | ADA 40mg + MTX        | 0.23305        | 0.16542        | 0.32489        |
| <b>BARI 4mg + MTX</b> | <b>ADA 40mg + MTX</b> | <b>1.37029</b> | <b>1.01354</b> | <b>1.86624</b> |
| ADA 40mg + MTX        | ADA 40mg + MTX        | 1              | 1              | 1              |
| ABA 10mg + MTX        | ADA 40mg + MTX        | 0.72315        | 0.43217        | 1.21345        |
| ABA SUBCUT + MTX      | ADA 40mg + MTX        | 0.94728        | 0.65393        | 1.37147        |
| IFX 3mg + MTX         | ADA 40mg + MTX        | 0.80864        | 0.4844         | 1.36075        |
| RTX 1000mg + MTX      | ADA 40mg + MTX        | 0.57881        | 0.2948         | 1.17028        |
| GOL 50mg + MTX        | ADA 40mg + MTX        | 1.00763        | 0.4161         | 2.52501        |
| cDMARD + MTX          | ADA 40mg + MTX        | 0.31728        | 0.09723        | 1.17116        |
| ETN + MTX             | ADA 40mg + MTX        | 1.34838        | 0.47036        | 4.5089         |
| SARI 200mg + MTX      | ADA 40mg + MTX        | 0.99567        | 0.60774        | 1.61547        |
| MTX                   | ABA 10mg + MTX        | 0.32168        | 0.21359        | 0.4792         |
| <b>BARI 4mg + MTX</b> | <b>ABA 10mg + MTX</b> | <b>1.89424</b> | <b>1.11106</b> | <b>3.21776</b> |
| ADA 40mg + MTX        | ABA 10mg + MTX        | 1.38283        | 0.8241         | 2.31393        |
| ABA 10mg + MTX        | ABA 10mg + MTX        | 1              | 1              | 1              |
| ABA SUBCUT + MTX      | ABA 10mg + MTX        | 1.31278        | 0.69759        | 2.45599        |
| IFX 3mg + MTX         | ABA 10mg + MTX        | 1.11797        | 0.72628        | 1.73653        |
| RTX 1000mg + MTX      | ABA 10mg + MTX        | 0.7989         | 0.3911         | 1.69242        |
| GOL 50mg + MTX        | ABA 10mg + MTX        | 1.39261        | 0.56216        | 3.65692        |
| cDMARD + MTX          | ABA 10mg + MTX        | 0.4393         | 0.13026        | 1.6535         |
| ETN + MTX             | ABA 10mg + MTX        | 1.86273        | 0.63315        | 6.51865        |
| SARI 200mg + MTX      | ABA 10mg + MTX        | 1.37509        | 0.80625        | 2.34229        |



| Treatment 1           | Treatment 2             | Median OR      | 95% CrI Lower  | 95% CrI Upper   |
|-----------------------|-------------------------|----------------|----------------|-----------------|
| MTX                   | ABA SUBCUT + MTX        | 0.24591        | 0.14914        | 0.40142         |
| <b>BARI 4mg + MTX</b> | <b>ABA SUBCUT + MTX</b> | <b>1.44682</b> | <b>0.89826</b> | <b>2.33253</b>  |
| ADA 40mg + MTX        | ABA SUBCUT + MTX        | 1.05565        | 0.72914        | 1.52922         |
| ABA 10mg + MTX        | ABA SUBCUT + MTX        | 0.76174        | 0.40717        | 1.4335          |
| ABA SUBCUT + MTX      | ABA SUBCUT + MTX        | 1              | 1              | 1               |
| IFX 3mg + MTX         | ABA SUBCUT + MTX        | 0.85535        | 0.45278        | 1.59743         |
| RTX 1000mg + MTX      | ABA SUBCUT + MTX        | 0.61058        | 0.28577        | 1.34177         |
| GOL 50mg + MTX        | ABA SUBCUT + MTX        | 1.06638        | 0.41394        | 2.84328         |
| cDMARD + MTX          | ABA SUBCUT + MTX        | 0.33545        | 0.0972         | 1.28433         |
| ETN + MTX             | ABA SUBCUT + MTX        | 1.42589        | 0.47046        | 4.98796         |
| SARI 200mg + MTX      | ABA SUBCUT + MTX        | 1.05136        | 0.57141        | 1.91605         |
| MTX                   | IFX 3mg + MTX           | 0.28821        | 0.1905         | 0.42878         |
| <b>BARI 4mg + MTX</b> | <b>IFX 3mg + MTX</b>    | <b>1.69493</b> | <b>0.98903</b> | <b>2.89213</b>  |
| ADA 40mg + MTX        | IFX 3mg + MTX           | 1.23664        | 0.73489        | 2.06441         |
| ABA 10mg + MTX        | IFX 3mg + MTX           | 0.89448        | 0.57586        | 1.37688         |
| ABA SUBCUT + MTX      | IFX 3mg + MTX           | 1.16911        | 0.62601        | 2.20859         |
| IFX 3mg + MTX         | IFX 3mg + MTX           | 1              | 1              | 1               |
| RTX 1000mg + MTX      | IFX 3mg + MTX           | 0.71571        | 0.34923        | 1.51086         |
| GOL 50mg + MTX        | IFX 3mg + MTX           | 1.24469        | 0.50152        | 3.23029         |
| cDMARD + MTX          | IFX 3mg + MTX           | 0.39219        | 0.11662        | 1.50147         |
| ETN + MTX             | IFX 3mg + MTX           | 1.66469        | 0.56047        | 5.80853         |
| SARI 200mg + MTX      | IFX 3mg + MTX           | 1.2316         | 0.71633        | 2.09185         |
| MTX                   | RTX 1000mg + MTX        | 0.40207        | 0.21225        | 0.73898         |
| <b>BARI 4mg + MTX</b> | <b>RTX 1000mg + MTX</b> | <b>2.36727</b> | <b>1.1536</b>  | <b>4.71956</b>  |
| ADA 40mg + MTX        | RTX 1000mg + MTX        | 1.72767        | 0.8545         | 3.39209         |
| ABA 10mg + MTX        | RTX 1000mg + MTX        | 1.25172        | 0.59087        | 2.55691         |
| ABA SUBCUT + MTX      | RTX 1000mg + MTX        | 1.63778        | 0.74529        | 3.49934         |
| IFX 3mg + MTX         | RTX 1000mg + MTX        | 1.39722        | 0.66187        | 2.86348         |
| RTX 1000mg + MTX      | RTX 1000mg + MTX        | 1              | 1              | 1               |
| GOL 50mg + MTX        | RTX 1000mg + MTX        | 1.74587        | 0.63129        | 4.93995         |
| cDMARD + MTX          | RTX 1000mg + MTX        | 0.55082        | 0.15311        | 2.14165         |
| ETN + MTX             | RTX 1000mg + MTX        | 2.33626        | 0.73524        | 8.32762         |
| SARI 200mg + MTX      | RTX 1000mg + MTX        | 1.72083        | 0.82628        | 3.50401         |
| MTX                   | GOL 50mg + MTX          | 0.23142        | 0.09647        | 0.5248          |
| <b>BARI 4mg + MTX</b> | <b>GOL 50mg + MTX</b>   | <b>1.35844</b> | <b>0.53914</b> | <b>3.32909</b>  |
| ADA 40mg + MTX        | GOL 50mg + MTX          | 0.99243        | 0.39604        | 2.40328         |
| ABA 10mg + MTX        | GOL 50mg + MTX          | 0.71807        | 0.27345        | 1.77886         |
| ABA SUBCUT + MTX      | GOL 50mg + MTX          | 0.93775        | 0.35171        | 2.41582         |
| IFX 3mg + MTX         | GOL 50mg + MTX          | 0.80341        | 0.30957        | 1.99393         |
| RTX 1000mg + MTX      | GOL 50mg + MTX          | 0.57278        | 0.20243        | 1.58405         |
| GOL 50mg + MTX        | GOL 50mg + MTX          | 1              | 1              | 1               |
| cDMARD + MTX          | GOL 50mg + MTX          | 0.31525        | 0.07646        | 1.37442         |
| ETN + MTX             | GOL 50mg + MTX          | 1.34106        | 0.36143        | 5.49629         |
| SARI 200mg + MTX      | GOL 50mg + MTX          | 0.99042        | 0.38411        | 2.41258         |
| MTX                   | cDMARD + MTX            | 0.73348        | 0.20053        | 2.32637         |
| <b>BARI 4mg + MTX</b> | <b>cDMARD + MTX</b>     | <b>4.31578</b> | <b>1.1655</b>  | <b>14.27601</b> |
| ADA 40mg + MTX        | cDMARD + MTX            | 3.15177        | 0.85385        | 10.28475        |
| ABA 10mg + MTX        | cDMARD + MTX            | 2.27635        | 0.60478        | 7.67709         |
| ABA SUBCUT + MTX      | cDMARD + MTX            | 2.98104        | 0.77862        | 10.28779        |
| IFX 3mg + MTX         | cDMARD + MTX            | 2.54976        | 0.66601        | 8.5752          |
| RTX 1000mg + MTX      | cDMARD + MTX            | 1.81548        | 0.46693        | 6.53132         |
| GOL 50mg + MTX        | cDMARD + MTX            | 3.17213        | 0.72758        | 13.07879        |
| cDMARD + MTX          | cDMARD + MTX            | 1              | 1              | 1               |
| ETN + MTX             | cDMARD + MTX            | 4.22977        | 2.42282        | 7.80838         |
| SARI 200mg + MTX      | cDMARD + MTX            | 3.14407        | 0.80513        | 10.54994        |
| MTX                   | ETN + MTX               | 0.17282        | 0.05145        | 0.48002         |

| Treatment 1           | Treatment 2             | Median OR      | 95% CrI<br>Lower | 95% CrI<br>Upper |
|-----------------------|-------------------------|----------------|------------------|------------------|
| <b>BARI 4mg + MTX</b> | <b>ETN + MTX</b>        | <b>1.01522</b> | <b>0.30106</b>   | <b>2.96902</b>   |
| ADA 40mg + MTX        | ETN + MTX               | 0.74163        | 0.22178          | 2.12602          |
| ABA 10mg + MTX        | ETN + MTX               | 0.53685        | 0.15341          | 1.57941          |
| ABA SUBCUT + MTX      | ETN + MTX               | 0.70132        | 0.20048          | 2.1256           |
| IFX 3mg + MTX         | ETN + MTX               | 0.60071        | 0.17216          | 1.78421          |
| RTX 1000mg + MTX      | ETN + MTX               | 0.42803        | 0.12008          | 1.36009          |
| GOL 50mg + MTX        | ETN + MTX               | 0.74568        | 0.18194          | 2.76681          |
| cDMARD + MTX          | ETN + MTX               | 0.23642        | 0.12807          | 0.41274          |
| ETN + MTX             | ETN + MTX               | 1              | 1                | 1                |
| SARI 200mg + MTX      | ETN + MTX               | 0.74056        | 0.20704          | 2.16986          |
| MTX                   | SARI 200mg + MTX        | 0.23392        | 0.16447          | 0.33146          |
| <b>BARI 4mg + MTX</b> | <b>SARI 200mg + MTX</b> | <b>1.37715</b> | <b>0.84227</b>   | <b>2.28042</b>   |
| ADA 40mg + MTX        | SARI 200mg + MTX        | 1.00435        | 0.61902          | 1.64543          |
| ABA 10mg + MTX        | SARI 200mg + MTX        | 0.72723        | 0.42693          | 1.24031          |
| ABA SUBCUT + MTX      | SARI 200mg + MTX        | 0.95115        | 0.52191          | 1.75005          |
| IFX 3mg + MTX         | SARI 200mg + MTX        | 0.81195        | 0.47805          | 1.39601          |
| RTX 1000mg + MTX      | SARI 200mg + MTX        | 0.58112        | 0.28539          | 1.21025          |
| GOL 50mg + MTX        | SARI 200mg + MTX        | 1.00967        | 0.41449          | 2.60342          |
| cDMARD + MTX          | SARI 200mg + MTX        | 0.31806        | 0.09479          | 1.24204          |
| ETN + MTX             | SARI 200mg + MTX        | 1.35034        | 0.46086          | 4.82999          |
| SARI 200mg + MTX      | SARI 200mg + MTX        | 1              | 1                | 1                |

## 11. Model Fit

**Table S27** presents model fit statistics as per the Deviance Information Criterion (DIC) and the overall residual deviance for the primary analyses and main sensitivity analyses.

**Table S27** Model Fit Summary

| Type of analysis                                                | # of trials <sup>1</sup> | # of data points <sup>1</sup> | ACR20  |                 | ACR50  |                 | ACR70 |                 |
|-----------------------------------------------------------------|--------------------------|-------------------------------|--------|-----------------|--------|-----------------|-------|-----------------|
|                                                                 |                          |                               | DIC    | $\bar{D}_{res}$ | DIC    | $\bar{D}_{res}$ | DIC   | $\bar{D}_{res}$ |
| Primary analysis (Sim-FE)                                       | 19 / 18                  | 40 / 38                       | 71.42  | 46.00           | 67.78  | 42.39           | 62.31 | 36.70           |
| Primary analysis (Sim-RE)                                       | 19 / 18                  | 40 / 38                       | 71.35  | 44.67           | 67.19  | 40.21           | 61.98 | 35.64           |
| Baseline-risk adjustment (Sim-FE)                               | 19 / 18                  | 40 / 38                       | 72.50  | 45.90           | 68.19  | 41.85           | 64.47 | 38.92           |
| Primary analysis (Ind-FE)                                       | 19 / 18                  | 40 / 38                       | 75.67  | 45.67           | 71.76  | 42.60           | 65.73 | 37.51           |
| Primary analysis (Ind-RE)                                       | 19 / 18                  | 40 / 38                       | 75.57  | 43.38           | 71.02  | 39.66           | 65.59 | 36.29           |
|                                                                 |                          |                               |        |                 |        |                 |       |                 |
| Inclusion of trials with prior bDMARD use of up to 20% (Sim-FE) | 29 / 28                  | 61 / 58                       | 137.90 | 100.65          | 114.02 | 78.00           | 95.31 | 58.59           |
| Removal of Asian-Pacific trials/low MTX dose (Sim-FE)           | 15 / 14                  | 32 / 30                       | 60.89  | 40.54           | 58.46  | 37.32           | 52.45 | 31.10           |

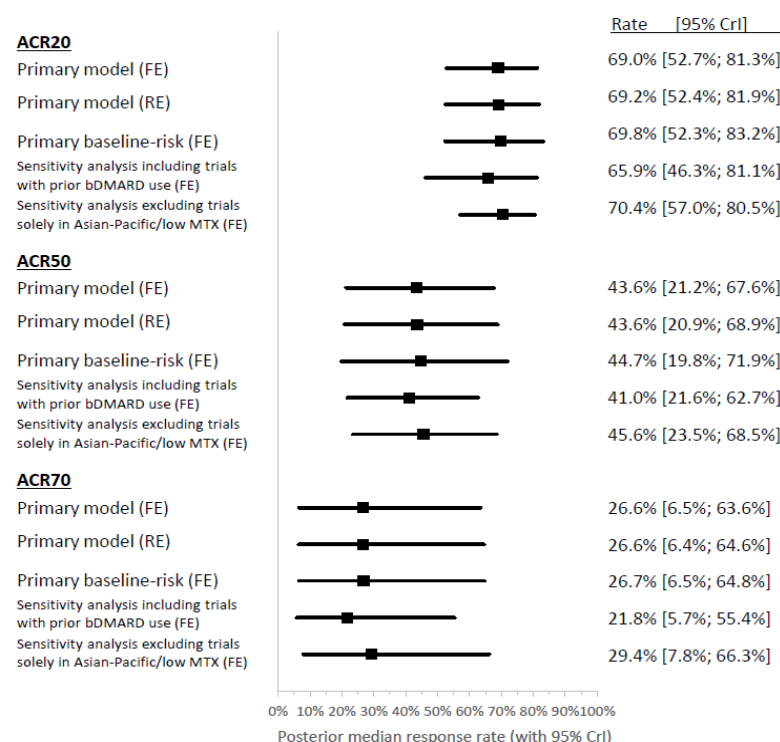
Abbreviations: DIC Deviance Information Criterion;  $\bar{D}_{res}$  overall residual deviance; MTX methotrexate; Sim-FE simultaneous fixed-effects model; Sim-RE simultaneous random-effects model; Ind-FE independent fixed-effects model; Ind-RE independent random-effects model.

1- numbers before “/” are for ACR20, numbers after “/” are for ACR50 and ACR70.

## 12. Posterior Median ACR response, by Treatment and Analysis (Forest Plots)

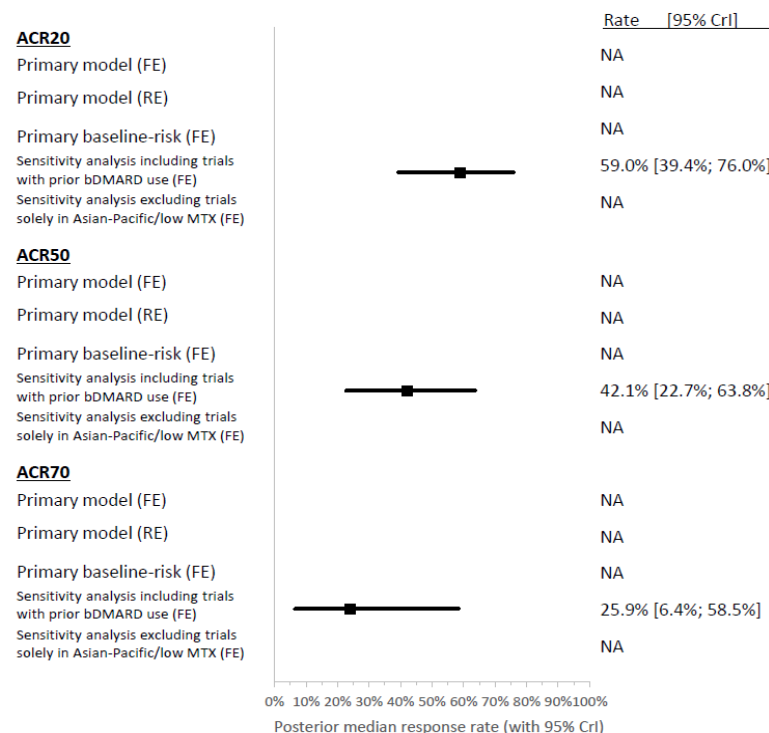
The following figures present the estimated median ACR response rates, plus corresponding 95% CrIs, across the primary and main sensitivity analyses, separately for each of the treatments.

**Figure S4** BARI 4mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: Overall, for baricitinib, there was 1 trial (RA-BEAM). It was part of the primary and all sensitivity analyses.

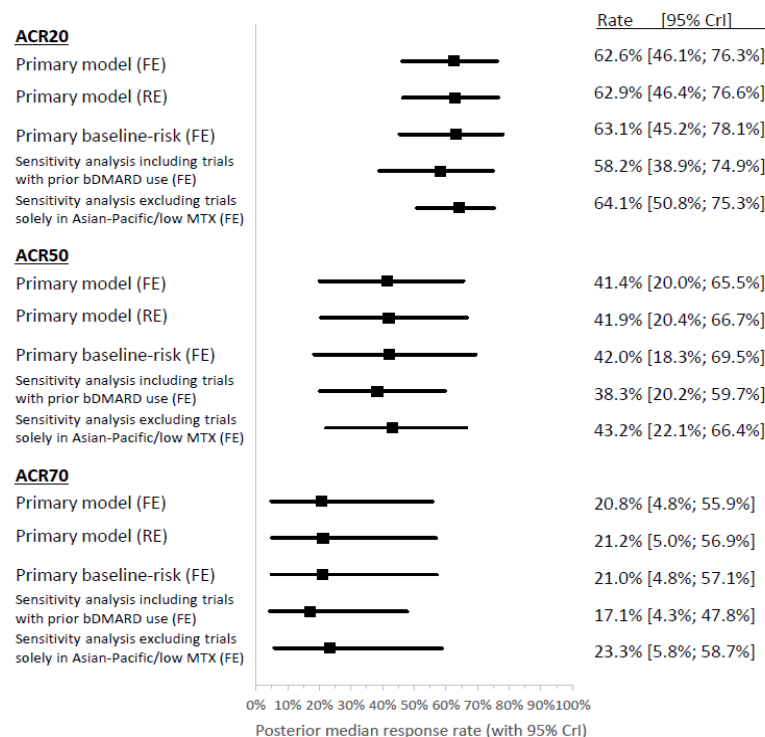
**Figure S5** TOFA 5mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



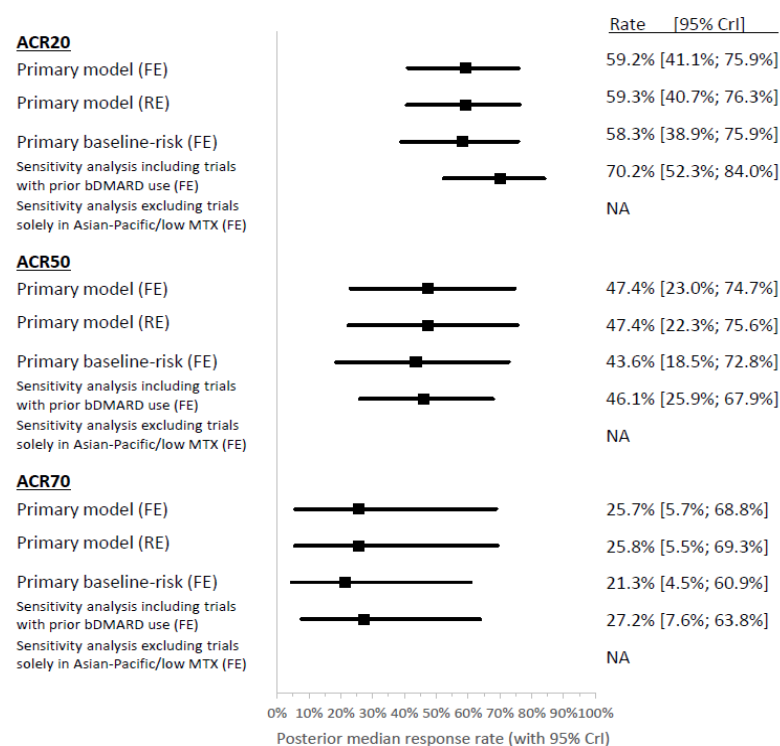
Note: Overall, for tofacitinib there were 3 trials (ORAL SCAN, ORAL STANDARD, ORAL STRATEGY). All allowed for prior bDMARD use of up to 20%, and thus could only be analyzed via the corresponding sensitivity analysis.

Abbreviations: BARI baricitinib; Cr-Int Credible Interval; FE fixed-effects model; MTX methotrexate; RE random-effects model; TOFA tofacitinib.

**Figure S6** ADA 40mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



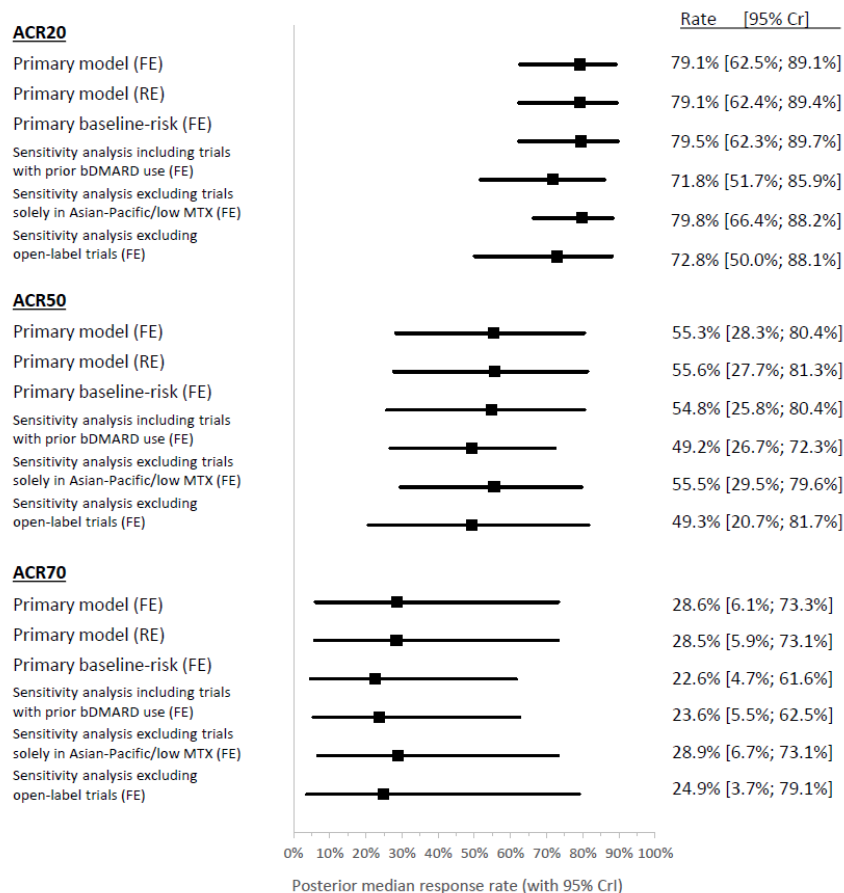
**Figure S7** CZP + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: For certolizumab there was only 1 trial in the primary analysis (RAPID-C, Asian-Pacific), and 4 trials (J-RAPID, Kang 2013, RAPID1, RAPID2) that were added via the sensitivity analysis allowing for trials with prior bDMARD use of up to 20% of patients.

Abbreviations: ADA adalimumab; Cr-Int Credible Interval; CZP certolizumab; FE fixed-effects model; MTX methotrexate; RE random-effects model.

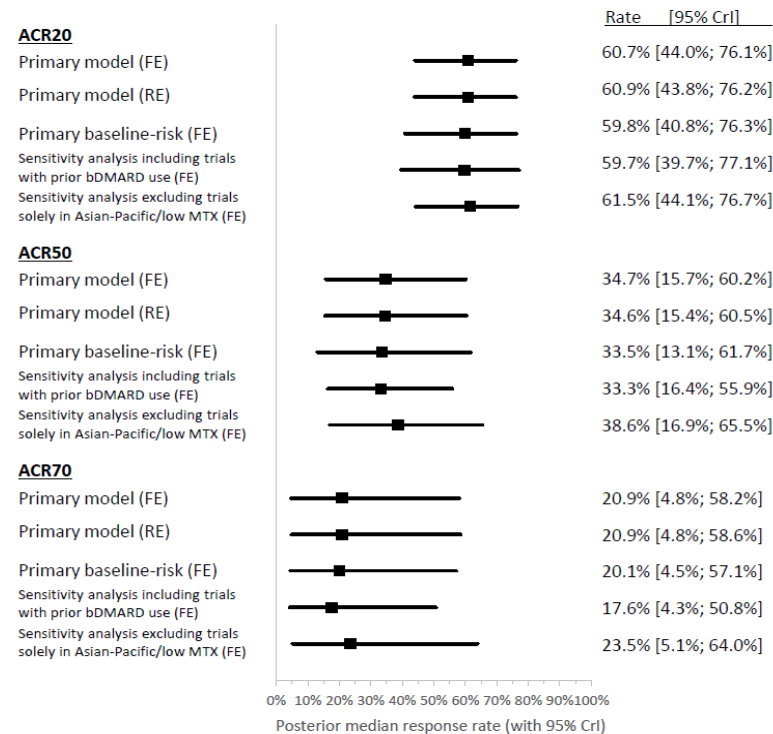
**Figure S8** ETN + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: The primary analysis included 2 trials (Machado 2014, Weinblatt 1999), one of which was an open-label trial (Machado 2014) not directly connected to the reference treatment (PBO+MTX). Overall, there were 3 ETN trials, and 2 of them compared ETN+MTX against cDMARD+MTX.

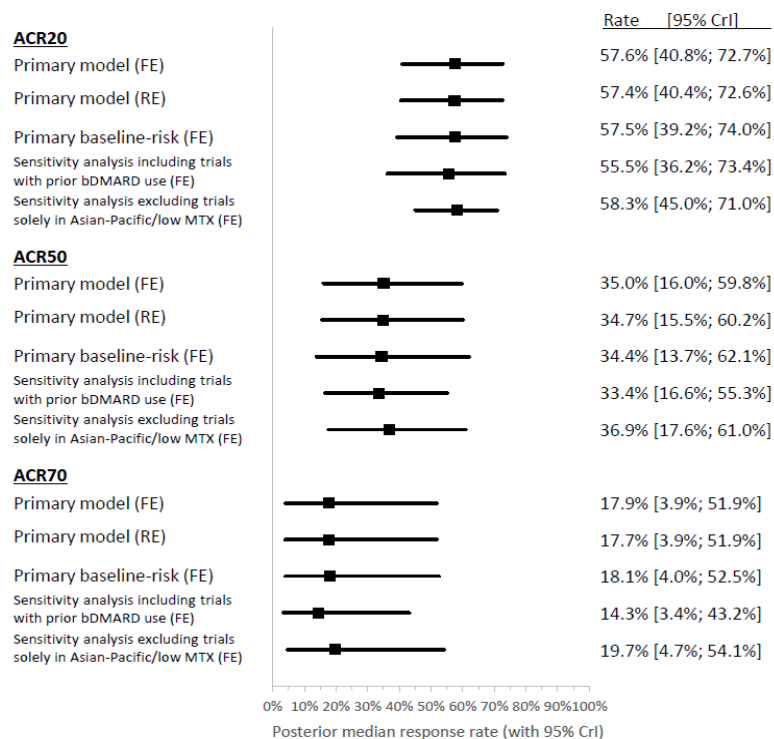
Abbreviations: Cr-Int Credible Interval; ETN eterncept; FE fixed-effects model; GOL golimumab; MTX methotrexate; RE random-effects model.

**Figure S9** GOL 50mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: The primary analysis included only 1 trial (GO-FORTH). Two additional trials (GO-FORTH, Li 2013) were added via the sensitivity analysis allowing for prior bDMARD use of up to 20%.

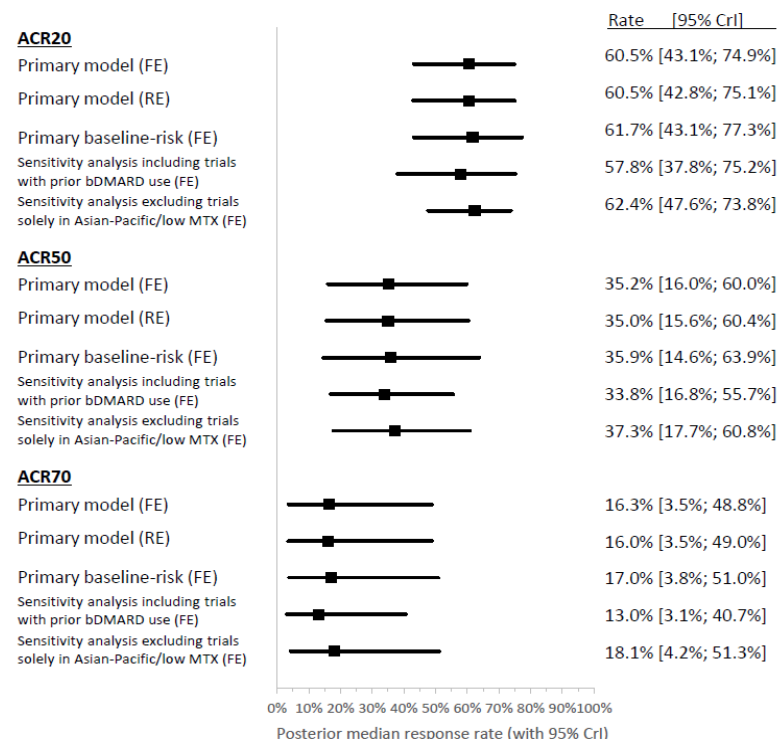
**Figure S10** IFX 3mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: Overall, for infliximab, there were 2 trials (ATTRACT, START), which were part of the primary and all sensitivity analyses. In ATTRACT, only ACR20 was reported.

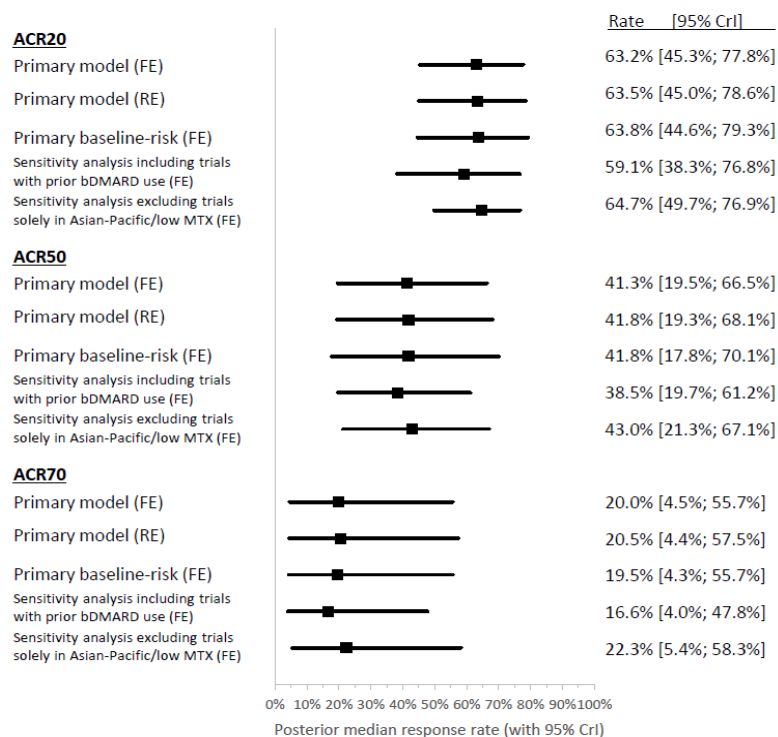
Abbreviations: ABA abatacept; Cr-Int Credible Interval; FE fixed-effects model; IFX infliximab; MTX methotrexate; RE random-effects model.

**Figure S11** ABA 10mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: Overall, for abatacept 10mg, there were 2 trials (AIM, ATTEST), which were part of the primary and all sensitivity analyses.

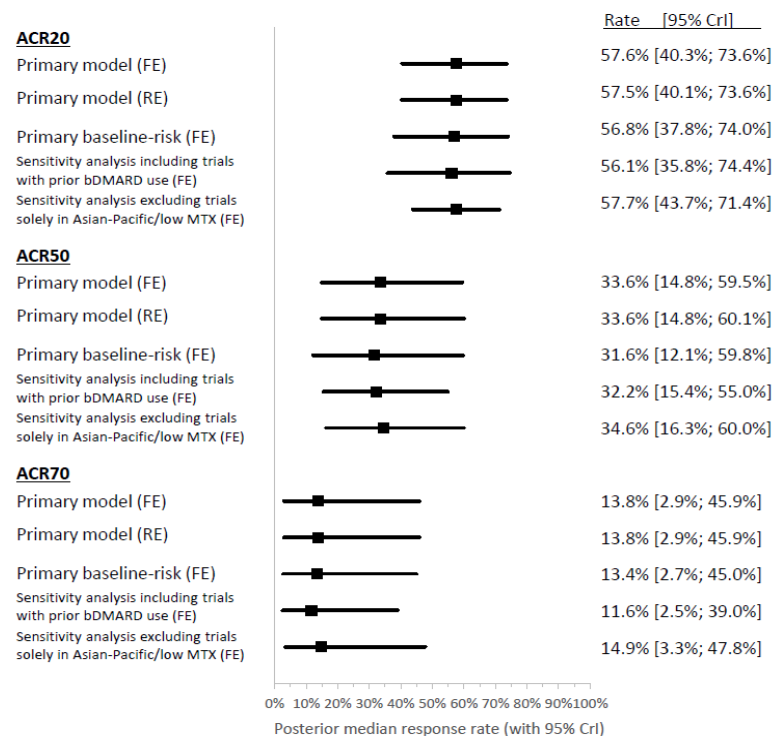
**Figure S12** ABA SUBCUT + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: Overall, for abatacept subcutaneous, there was 1 trial (AMPLE). It compared ADA SUBCUT + MTX vs ADA 40mg + MTX and was part of the primary and all sensitivity analyses.

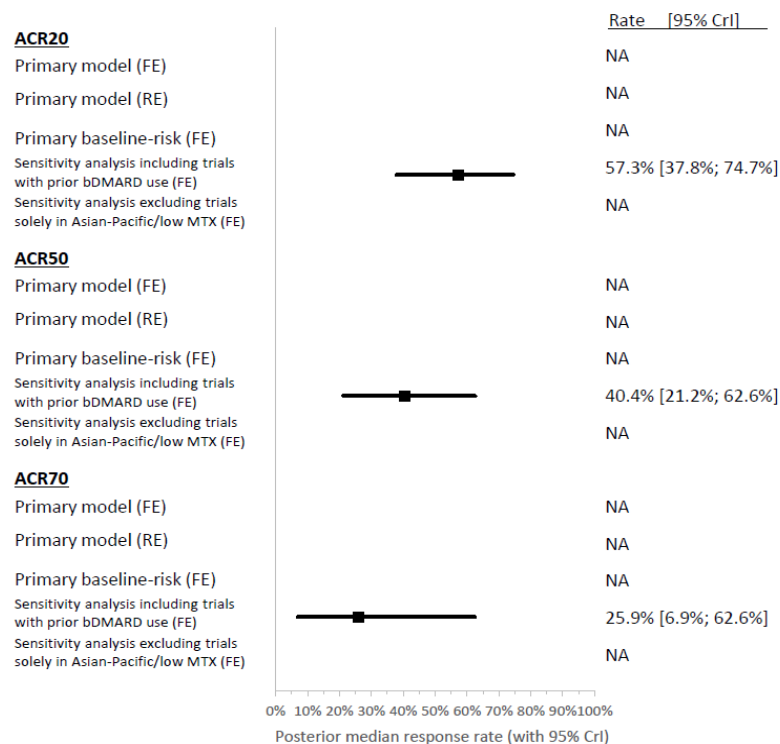
Abbreviations: ABA abatacept; Cr-Int Credible Interval; FE fixed-effects model; MTX methotrexate; RE random-effects model; RTX rituximab; SUBCUT subcutaneous.

**Figure S13** RTX + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses





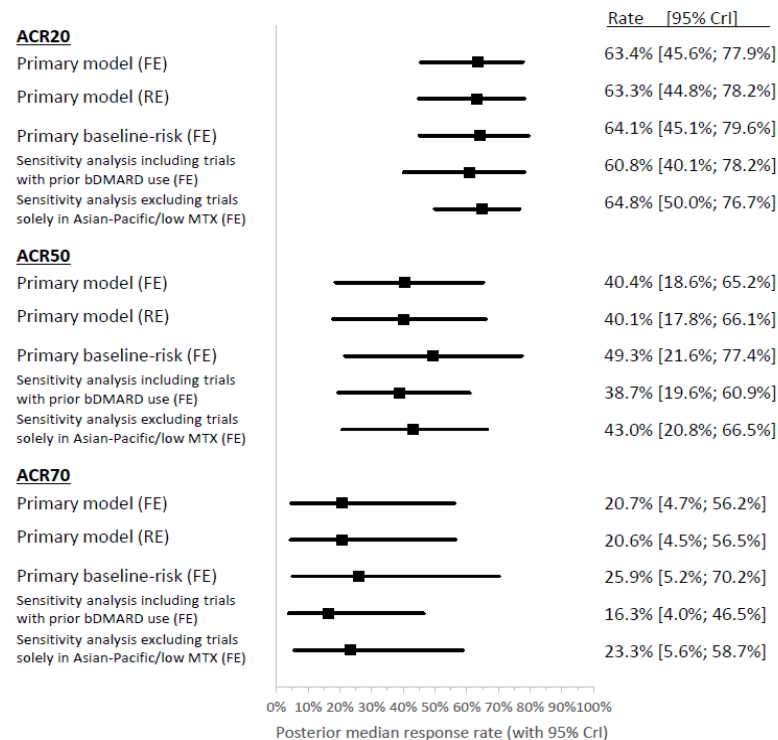
**Figure S14** TCZ + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: Overall, for tocilizumab there were only 2 trials (LITHE, OPTION). Both allowed for prior bDMARD use of up to 20%, and thus could only be analyzed via the corresponding sensitivity analysis.

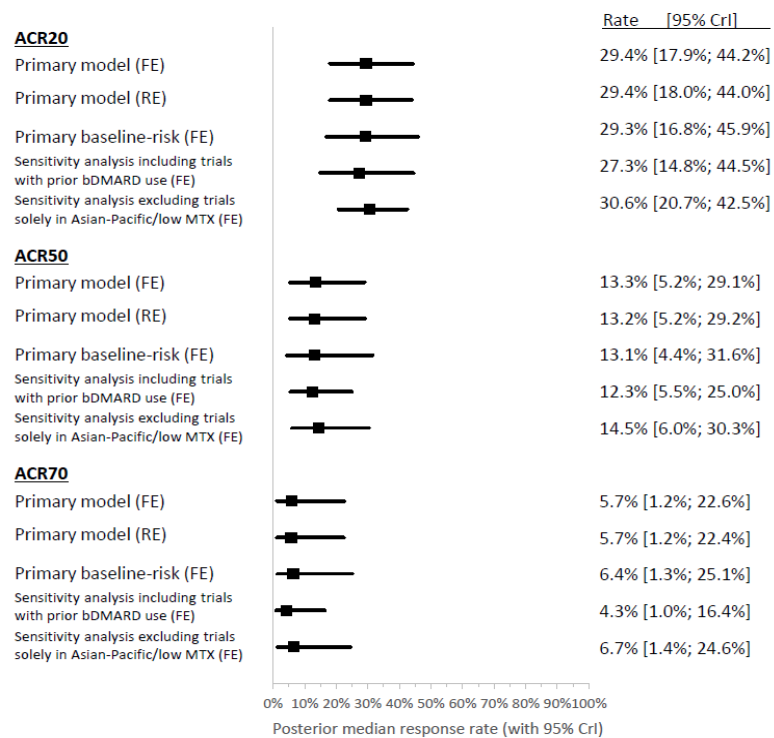
Abbreviations: Cr-Int Credible Interval; FE fixed-effects model; MTX methotrexate; RE random-effects model; SARI sarilumab; TCZ tocilizumab.

**Figure S15** SARI 200mg + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Note: Overall, for sarilumab, there was 1 trial (MOBILITY). Only results from the subpopulation of MOBILITY patients who were bDMARD-naïve were used in all analyses (primary and all sensitivity).

**Figure S16** PBO + MTX: Estimated posterior median ACR response rates across primary and main sensitivity analyses



Abbreviations: Cr-Int Credible Interval; FE fixed-effects model; PBO placebo; MTX methotrexate; RE random-effects model.

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