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Section 5 References
Section 1: Search strategy and PICO's

1.1 Rheumatoid and Psoriatic Arthritis: Efficacy

1.1.1 Medline

1. exp arthritis, rheumatoid/

2. ((rheumatoid or reumatoid or rheumat$ or reumat$) adj3 (arthrit$ or artrit$ or diseas$ or condition$ or nodule$)).tw.

3. (felty$ adj2 syndrome).tw.

4. (caplan$ adj2 syndrome).tw.

5. psoriatic arthritis/

6. (psoria$ adj (arthriti$ or arthropath$)).tw.

7. ((arthriti$ or arthropath$) adj psoria$).tw.

8. oligoarthritis$.tw.

9. or/1-8

10 Janus Kinase Inhibitors/

11 janus kinase inhibitor$.tw.

12 JAK inhibitor$.tw.

13 Tofacitinib.tw.

14 (Tofacitinib or xeljanz or tasocitinib).tw.

15 (Baricitinib or olumiant).tw.

16 (Filgotinib or cyclopropanecarboxamide).tw.
Peficitinib.tw.
Decernotinib.tw.
(Ruxolitinib or jaka?i).tw.
or/10-19
randomized controlled trial.pt.
controlled clinical trial.pt.
randomized.ab.
placebo.ab.
drug therapy.fs.
randomly.ab.
trial.ab.
groups.ab.
or/21-28
exp animals/ not humans.sh.
29 not 30
(safe or safety).tw.
side effect$.tw.
((adverse or undesirable or harms$ or serious or toxic) adj3 (effect$ or reaction$ or event$ or outcome$)).tw.
exp product surveillance, postmarketing/
exp adverse drug reaction reporting systems/
clinical trials, phase iv/
Clinical Trials, Phase III/
exp poisoning/
exp substance-related disorders/
exp drug toxicity/
exp abnormalities, drug induced/
exp drug monitoring/
exp drug hypersensitivity/
(toxicity or complication$ or noxious or tolerability).tw.
exp Postoperative Complications/
exp Intraoperative Complications/
or/32-47
exp animals/ not humans.sh.
48 not 49
31 or 50
and/9,20,51
#1.1.2  EMBASE

#45. #8 AND #18 AND #44 AND [humans]/lim AND ([article]/lim OR [article in press]/lim OR [review]/lim)

#44. #8 AND #18 AND #44

#43. #28 OR #43

#42. #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42

#41. 'peroperative complication'/de

#40. 'postoperative complication'/exp

#39. toxicity:ab,ti OR complication*:ab,ti OR noxious:ab,ti OR tolerability:ab,ti

#38. 'drug hypersensitivity'/exp

#37. 'drug monitoring'/de

#36. 'congenital malformation'/exp

#35. 'drug toxicity'/exp

#34. 'intoxication'/exp

#33. 'phase 4 clinical trial (topic)'/de

#32. 'postmarketing surveillance'/exp

#31. (adverse OR undesirable OR harms* OR serious OR toxic) NEAR/3 (effect* OR reaction* OR event* OR outcome*):ab,ti

#30. 'side effect':ab,ti OR 'side effects':ab,ti

#29. safe:ab,ti OR safety:ab,ti

#28. 'adverse drug reaction'/lnk OR 'complication'/lnk OR 'side effect'/lnk

#27. #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
#26. 'single-blind procedure'
#25. crossover*:ab,ti OR 'cross over*':ab,ti
#24. placebo*:ab,ti
#23. (doubl* NEAR/2 blind*):ab,ti
#22. allocat*:ab,ti
#21. trial:ti
#20. 'randomized controlled trial'/exp
#19. random*:ab,ti
#18. #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
#17. ruxolitinib:ab,ti OR jaka?:ab,ti
#16. decernotinib:ab,ti
#15. peficitinib:ab,ti
#14. filgotinib:ab,ti OR cyclopropanecarboxamide:ab,ti
#13. baricitinib:ab,ti OR olumiant:ab,ti
#12. tofacitinib:ab,ti OR xeljanz:ab,ti OR tasocitinib:ab,ti
#11. 'jak inhibitor*':ab,ti
#10. 'janus kinase inhibitor*':ab,ti
#9. 'janus kinase inhibitor'/exp
#8. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#7. oligoarthritis*:ab,ti
#6. (psoria* NEAR/2 (arthriti* OR arthropath*)):ab,ti
#5. 'psoriatic arthritis'/de
#4. (caplan* NEAR/2 syndrome):ab,ti
#3. (felty* NEAR/2 syndrome):ab,ti
#2. ((rheumatoid OR reumatoid OR rheumat* OR reumat*) NEAR/3 (arthrit* OR artrit* OR diseas* OR condition* OR nodule*)):ab,ti
#1. 'rheumatoid arthritis'/exp

1.1.3 The Cochrane Library
#1 MeSH descriptor: [Arthritis, Rheumatoid] explode all trees
#2 ((rheumatoid or reumatoid or rheumat* or reumat*) near/3 (arthrit* or artrit* or diseas* or condition* or nodule*)):ti,ab
#3 (felty* near/2 syndrome):ti,ab
#4 (caplan* near/2 syndrome):ti,ab
#5 MeSH descriptor: [Arthritis, Psoriatic] this term only
#6 (psoria* next (arthriti* or arthropath*)):ti,ab
#7 ((arthriti* or arthropath*) next psoria*):ti,ab
#8 oligoarthriti*:ti,ab
#9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10 MeSH descriptor: [Janus Kinase Inhibitors] this term only
#11 "janus kinase inhibitor*":ti,ab
#12 "JAK inhibitor*":ti,ab
#13  Tofacitinib:ti,ab
#14  (Tofacitinib or xeljanz or tasocitinib):ti,ab
#15  (Baricitinib or olumiant):ti,ab
#16  (Filgotinib or cyclopropanecarboxamide):ti,ab
#17  Peficitinib:ti,ab
#18  Decernotinib:ti,ab
#19  (Ruxolitinib or jaka?i):ti,ab
#20  #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21  #9 AND #20
1.2 Systemic Lupus Erythematosus: Efficacy and Safety

1.2.1 Medline

1 exp lupus erythematosus, systemic/
2 systemic lupus erythematosus.tw.
3 sle.tw.
4 ((libman-sacks or libman sacks) adj disease).tw.
5 (lupus adj (Nephritis or Vasculitis)).tw.
6 or/1-5
7 Janus Kinase Inhibitors/
8 janus kinase inhibitor$.tw.
9 JAK inhibitor$.tw.
10 Tofacitinib.tw.
11 (Tofacitinib or xeljanz or tasocitinib).tw.
12 (Baricitinib or olumiant).tw.
13 (Filgotinib or cyclopropanecarboxamide).tw.
14 Peficitinib.tw.
15 Decernotinib.tw.
16 (Ruxolitinib or jaka?).tw.
17 or/7-16
18 randomized controlled trial.pt.
controlled clinical trial.pt.
randomized.ab.
placebo.ab.
drug therapy.fs.
randomly.ab.
trial.ab.
groups.ab.
or/18-25
exp animals/ not humans.sh.
26 not 27 (3798143)
(safe or safety).tw.
side effect$.tw.
((adverse or undesirable or harms$ or serious or toxic) adj3 (effect$ or reaction$ or event$ or outcome$)).tw.
exp product surveillance, postmarketing/
exp adverse drug reaction reporting systems/
clinical trials, phase iv/
Clinical Trials, Phase III/
exp poisoning/
exp substance-related disorders/
exp drug toxicity/
39 exp abnormalities, drug induced/
40 exp drug monitoring/
41 exp drug hypersensitivity/
42 (toxicity or complication$ or noxious or tolerability).tw.
43 exp Postoperative Complications/
44 exp Intraoperative Complications/
45 or/29-44
46 exp animals/ not humans.sh
47 45 not 46
48 28 or 47
49 and/6,17,48

1.2.2 EMBASE
#43. #17 AND #41 AND [humans]/lim
#42. #17 AND #41
#41. #27 OR #40
#40. #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39
#39. toxicity:ab,ti OR complication*:ab,ti OR noxious:ab,ti OR tolerability:ab,ti
#38. 'drug hypersensitivity'/exp
#37. 'drug monitoring'/de
#36. 'congenital malformation'/exp
#35. 'drug toxicity'/exp
#34. 'intoxication'/exp
#33. 'phase 4 clinical trial (topic)'/de
#32. 'postmarketing surveillance'/exp
#31. ((adverse OR undesirable OR harms* OR serious OR toxic) NEAR/3 (effect* OR reaction* OR event* OR outcome*)):ab,ti
#30. 'side effect':ab,ti OR 'side effects':ab,ti
#29. safe:ab,ti OR safety:ab,ti
#28. 'adverse drug reaction'/lnk OR 'complication'/lnk OR 'side effect'/lnk
#27. #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
#26. 'crossover procedure'/de
#25. 'single-blind procedure'
#24. crossover*:ab,ti OR 'cross over*':ab,ti
#23. placebo*:ab,ti
#22. (doubl* NEAR/2 blind*):ab,ti
#21. allocat*:ab,ti
#20. trial:ti
#19. 'randomized controlled trial'/exp
#18. random*:ab,ti
#17. #6 AND #16
#16. #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
#15. ruxolitinib:ab,ti OR jaka?:ab,ti
#14. decernotinib:ab,ti
#13. peficitinib:ab,ti
#12. filgotinib:ab,ti OR cyclopropanecarboxamide:ab,ti
#11. baricitinib:ab,ti OR olumiant:ab,ti
#10. tofacitinib:ab,ti OR xeljanz:ab,ti OR tasocitinib:ab,ti
#9. 'jak inhibitor*':ab,ti
#8. 'janus kinase inhibitor*':ab,ti
#7. 'janus kinase inhibitor'/exp
#6. #1 OR #2 OR #3 OR #4 OR #5
#5. (lupus NEAR/2 (nephritis OR vasculitis)):ab,ti
#4. ('libman sacks' OR 'libman sacks') NEAR/2 disease):ab,ti
#3. sle:ab,ti
#2. 'systemic lupus erythematosus':ab,ti
#1. 'systemic lupus erythematosus'/exp

1.2.3 The Cochrane Library
#1 MeSH descriptor: [Systemic Lupus Erythematos] explode all trees
#2 "systemic lupus erythematosus":ti,ab
#3 sle:ti,ab
#4 ("libman sacks" OR libman sacks) NEXT disease):ti,ab
1.3 Ankylosing spondylitis, Psoriasis, Alopecia, Crohn’s disease, Ulcerative Colitis: Efficacy & Safety

1.3.1 Medline: Efficacy

1 Spondylitis, Ankylosing/ (13986)

2 ankylos$ spondyl$.tw. (13166)

3 (Seronegative adj (arthrit$ or arthropath$ or spondyl$)).tw. (1097)

4 colitis, ulcerative/ or crohn disease/ (58297)
(Crohn$ adj (disease or enteritis)).tw. (41405)
ulcerative colitis.tw. (35215)
psoriasis/ (32971)
Chronic plaque psoriasis.tw. (962)
((atopic$ or disseminated) adj (dermatit$ or neurodermat$ or eczema)).tw. (20777)
Alopecia Areata/ (3021)
(aloepecia adj (Areat$ or circumscripta or universalis)).tw. (3576)
or/1-11 (149579)
Janus Kinase Inhibitors/ (127)
janus kinase inhibitor$.tw. (429)
JAK inhibitor$.tw. (1131)
Tofacitinib.tw. (798)
(Tofacitinib or xeljanz or tasocitinib).tw. (808)
(Baricitinib or olumiant).tw. (135)
(Filgotinib or cyclopropanecarboxamide).tw. (61)
Peficitinib.tw. (19)
Decernotinib.tw. (13)
(Ruxolitinib or jaka?).tw. (906)
or/13-21 (2055)
randomized controlled trial.pt. (477193)
controlled clinical trial.pt. (92945)
randomized.ab. (436251)
placebo.ab. (195836)
drug therapy.fs. (2088187)
randomly.ab. (306614)
trial.ab. (455752)
groups.ab. (1887119)
or/24-31 (4389362)
exp animals/ not humans.sh. (4554122)
32 not 33 (3795778)
and/12,23,34 (254)

1.3.2 Medline: Safety
1 Spondylitis, Ankylosing/ (13986)
2 ankylos$ spondyl$.tw. (13166)
3 (Seronegative adj (arthrit$ or arthropath$ or spondyl$)).tw. (1097)
4 colitis, ulcerative/ or crohn disease/ (58297)
5 (Crohn$ adj (disease or enteritis)).tw. (41405)
6 ulcerative colitis.tw. (35215)
7 psoriasis/ (32971)
8 Chronic plaque psoriasis.tw. (962)
((atopic$ or disseminated) adj (dermatit$ or neurodermat$ or eczema)).tw. (20777)

Alopecia Areata/ (3021)

(aloepecia adj (Areat$ or circumscripta or universalis)).tw. (3576)

or/1-11 (149579)

Janus Kinase Inhibitors/ (127)

janus kinase inhibitor$.tw. (429)

JAK inhibitor$.tw. (1131)

Tofacitinib.tw. (798)

(Tofacitinib or xeljanz or tasocitinib).tw. (808)

(Baricitinib or olumiant).tw. (135)

(Filgotinib or cyclopropanecarboxamide).tw. (61)

Peficitinib.tw. (19)

Decernotinib.tw. (13)

(Ruxolitinib or jaka?).tw. (906)

or/13-21 (2055)

(safe or safety).tw. (689909)

side effect$.tw. (228583)

((adverse or undesirable or harms$ or serious or toxic) adj3 (effect$ or reaction$ or event$ or outcome$)).tw. (457115)

exp product surveillance, postmarketing/ (14223)

exp adverse drug reaction reporting systems/ (7055)
clinical trials, phase iv/ (272)
Clinical Trials, Phase III/ (8565)
exp poisoning/ (151822)
exp substance-related disorders/ (264092)
exp drug toxicity/ (108814)
exp abnormalities, drug induced/ (14396)
exp drug monitoring/ (19339)
exp drug hypersensitivity/ (44141)
(toxicity or complication$ or noxious or tolerability).tw. (1205908)
exp Postoperative Complications/ (511878)
exp Intraoperative Complications/ (49901)
or/24-39 (2932032)
and/12,23,40 (151)
exp animals/ not humans.sh. (4554122)
41 not 42 (149)

1.3.3 EMBASE: Efficacy
#34. #23 AND #33 AND [humans]/lim
#33. #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32
#32. 'crossover procedure'/de
#31. 'single-blind procedure'
#30. crossover*:ab,ti OR 'cross over*':ab,ti
#29. placebo*:ab,ti
#28. (doubl* NEAR/2 blind*):ab,ti
#27. allocat*:ab,ti
#26. trial:ti
#25. 'randomized controlled trial'/exp
#24. random*:ab,ti
#23. #12 AND #22
#22. #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#21. ruxolitinib:ab,ti OR jaka?:ab,ti
#20. decernotinib:ab,ti
#19. peficitinib:ab,ti
#18. filgotinib:ab,ti OR cyclopropanecarboxamide:ab,ti
#17. baricitinib:ab,ti OR olumiant:ab,ti
#16. tofacitinib:ab,ti OR xeljanz:ab,ti OR tasocitinib:ab,ti
#15. 'jak inhibitor*':ab,ti
#14. 'janus kinase inhibitor*':ab,ti
#13. 'janus kinase inhibitor'/exp
#12. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#11. (alopecia NEAR/2 (areat* OR circumscripta OR universalis)):ab,ti
#10. 'alopecia areata'/de
#9. ((atopic* OR disseminated) NEAR/2 (dermatit* OR neurodermat* OR eczema)):ab,ti
#8. 'chronic plaque psoriasis':ab,ti
#7. 'psoriasis'/de
#6. 'ulcerative colitis':ab,ti
#5. (crohn* NEAR/2 (disease OR enteritis)):ab,ti
#4. 'ulcerative colitis'/exp OR 'crohn disease'/exp
#3. (seronegative NEAR/2 (arthrit* OR arthropath* OR spondyl*)):ab,ti
#2. (ankylos* NEAR/2 spondyl*):ab,ti
#1. 'ankylosing spondylitis'/de

1.3.4 EMBASE: Safety
#41. #39 NOT #40 AND [humans]/lim
#40. #23 AND #38 AND [review]/lim
#39. #23 AND #38
#38. #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37
#37. 'peroperative complication'/de
#36. 'postoperative complication'/exp
#35. toxicity:ab,ti OR complication*:ab,ti OR noxious:ab,ti OR tolerability:ab,ti
#34. 'drug hypersensitivity'/exp
#33. 'drug monitoring'/de
#32. 'congenital malformation'/exp
#31. 'drug toxicity'/exp
#30. 'intoxication'/exp
#29. 'phase 4 clinical trial (topic)'/de
#28. 'postmarketing surveillance'/exp
#27. ((adverse OR undesirable OR harms* OR serious OR toxic) NEAR/3 (effect* OR reaction* OR event* OR outcome*)):ab,ti
#26. 'side effect':ab,ti OR 'side effects':ab,ti
#25. safe:ab,ti OR safety:ab,ti
#24. 'adverse drug reaction'/lnk OR 'complication'/lnk OR 'side effect'/lnk
#23. #12 AND #22
#22. #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#21. ruxolitinib:ab,ti OR jaka?:ab,ti
#20. decernotinib:ab,ti
#19. peficitinib:ab,ti
#18. filgotinib:ab,ti OR cyclopropanecarboxamide:ab,ti
#17. baricitinib:ab,ti OR olumiant:ab,ti
#16. tofacitinib:ab,ti OR xeljanz:ab,ti OR tasocitinib:ab,ti
#15. 'jak inhibitor*':ab,ti
#14. 'janus kinase inhibitor*':ab,ti
1.3.5  The Cochrane Library: Efficacy & Safety

#1  MeSH descriptor: [Spondylitis, Ankylosing] this term only
#2  (ankylos* NEXT spondyl*):ti,ab
#3  (Seronegative next (arthrit* or arthropath* or spondyl*)):ti,ab
#4  MeSH descriptor: [Spondylitis, Ankylosing] this term only
#5  MeSH descriptor: [Crohn Disease] this term only
#6 (Crohn* NEXT (disease or enteritis)):ti,ab
#7 "ulcerative colitis":ti,ab
#8 MeSH descriptor: [Psoriasis] this term only
#9 "Chronic plaque psoriasis":ti,ab
#10 ((atopic* or disseminated) NEXT (dermatit* or neurodermat* or eczema)):ti,ab
#11 MeSH descriptor: [Alopecia Areata] this term only
#12 (alopecia NEXT(Areat* or circumscripta or universalis)):ti,ab
#13 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 MeSH descriptor: [Janus Kinase Inhibitors] this term only
#15 "janus kinase inhibitor*":ti,ab
#16 "JAK inhibitor*":ti,ab
#17 Tofacitinib:ti,ab
#18 (Tofacitinib or xeljanz or tasocitinib):ti,ab
#19 (Baricitinib or olumiant):ti,ab
#20 (Filgotinib or cyclopropenecarboxamide):ti,ab
#21 Peficitinib:ti,ab
#22 Decernotinib:ti,ab
#23 (Ruxolitinib or jak?)i:ti,ab
#24 #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
#25 #13 AND #24
1.4 Patients, Interventions, Control, Outcomes (PICOs)

1.4.1 Definitions

1.4.1.1 Populations and efficacy measures

1.4.1.1.1 Rheumatoid Arthritis (RA)
- Core set variables: SJC, TJC, Pain, Patient global assessment, Physician global, HAQ, CRP, ESR
- Composite measures: ACR 20/50/70, DAS28-CRP, DAS28-ESR, CDAI, SDAI, EULAR responses, ACR/EULAR remission
- Structural damage: Sharp score (including modifications), Larsen score, No. of patients achieving radiographic non-progression (as defined in individual studies)

1.4.1.1.2 Psoriatic arthritis (PsA)
- Core set variables as in 1.4.1.1.1 but additionally: Enthesitis (MASES, LEI), Dactylitis, PASI
- Composite measures: ACR 20/50/70, DAPSA, PASDAS, PsARC, MDA
- Structural damage: PsA modified Sharp van der Heijde Score, No. of patients achieving radiographic non-progression (as defined in individual studies)

1.4.1.1.3 Axial spondylarthritis (axSpA)
- Core set variables: Patient global assessment, back pain, nocturnal pain, duration of morning stiffness, fatigue, CRP, Enthesitis (MASES), SJC, Spinal mobility (Chest expansion, lateral spinal flexion, modified Schober, occiput to wall distance, cervical rotation), BASDAI, BASFI, BASMI
- Composite measures: ASAS 20/40, ASAS 5/6, ASDAS(CRP)
- Inflammation: SPARCC MRI Index of the SI Joints, Berlin modification of ASspiMRI
- Structural damage: mSASSS. mNY SI joints

1.4.1.1.4 Crohn’s disease (CD)
- Core set variables: no. of soft/liquid stools, abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need of antidiarrheal drugs, abdominal masses, hematocrit, body weight, CRP
- Composite measures: Crohn’s Disease Activity Index
1.4.1.5 Ulcerative colitis (UC)
- **Core set variables**: Stool frequency, rectal bleeding, Mayo endoscopic subscore (endoscopic proctosigmoidoscopy findings), physician global assessment
- **Composite measures**: Mayo score (remission/clinical response/deep remission), partial mayo score

1.4.1.6 Psoriasis (PsO)
- **Outcome measures**: Physician Global Assessment Score, PASI 75/90/100, BSA, NAPSI, DLQI

1.4.1.7 Atopic dermatitis (AD)
- **Outcome measures**: Eczema Area and Severity Index (EASI), Physician Global Assessment Score, BSA

1.4.1.8 Alopecia areata (AA)
- **Outcome measures**: Physician Global Assessment, Patient Global Assessment

1.4.1.2 Safety measures
- **Global**: Number of AEs, Number of serious adverse events, deaths, withdrawals due to AEs
- **Infections**: Serious infections, Opportunistic infections, Tuberculosis, Herpes zoster, CMV, nontuberculous mycobacteria, fungal
- **Malignancies**: lymphoma, skin-cancer non-melanoma, solid tumors, other haematological malignancies
- **Venous thromboembolic events**: DVT, Pulmonary embolism
- **Haematologic**: anemia, neutropenia, lymphopenia, thrombocytosis
- **Cardiac**: Congestive heart failure, Cardio-vascular disease (coronary heart disease including angina, MI, stroke), MACE
- **Lipid levels**
- **Renal**
- **Hepatic** effects: elevation of transaminases and bilirubin
- **Gastro-intestinal**
- **Demyelinating** disease
- **Teratogenicity**
1.4.1.3 Interventions
- baricitinib (BARI)
- decernotinib (DEC)
- filgotinib (FILGO)
- fostamatinib (FOSTA)
- peficitinib (PEF)
- ruxolitinib (RUXO)
- tofacitinib (TOFA)
- upadacitinib (UPA)

1.4.1.4 Controls
- **Biologic DMARDs (bDMARDs):** Etanercept (ETA), Adalimumab (ADA), Golimumab (GOL), Certolizumab pegol (CZP), Rituximab (RTX), Abatacept (ABA), Tocilizumab (TCZ), Sarilumab (SAR), Secukinumab (SCM), Brodalumab (BLM), Ixekizumab (IXE), Ustekinumab (UKM), Tildrakizumab (TKM), Briakinumab (BKM), Vedolizumab (VDM)
- **Conventional synthetic DMARDs (csDMARDs):** Methotrexate (MTX), leflunomide (LEF), sulfasalazine (SZP), hydroxychloroquine (HCQ), injectable gold (GOLD), chloroquine (CQ)
- **Any combination of the previous**
### 1.4.2 Research questions: Efficacy

| #  | Research question                                                                 | Population | Intervention | Control | Outcome |
|----|-----------------------------------------------------------------------------------|------------|--------------|---------|---------|
| 1  | What is the efficacy of JAKi compared to bDMARDs (combined with csDMARDs) in csDMARD insufficient responders (IRs)? |            |              |         |         |
| 2  | What is the efficacy of JAKi compared to csDMARDs in csDMARD naïve patients?       |            |              |         |         |
| 3  | What is the efficacy of JAKi compared to placebo in csDMARD IRs?                   |            |              |         |         |
| 4  | What are the efficacy differences between different patient populations (MTX-naïve, MTX-IR, csDMARD-IR, bDMARD-IR)? |            |              |         |         |
| 5  | Are there differences in efficacy between JAK inhibitors with different selectivity to JAK1/2/3 inhibition with clinically meaningful differences? |            |              |         |         |
| 6  | What is the evidence for switching between different JAKs because of LoE or AEs?   |            |              |         |         |
| 7  | If a patient achieves a sustained ACR/EULAR remission with a JAK, can the dose be reduced and the remission be maintained? |            |              |         |         |
| 8  | Would a patient who is treated with a JAK initially with no or little response, be able to respond to a bDMARD? |            |              |         |         |
| 9  | Are JAKs effective or detrimental in patients with interstitial lung disease?      |            |              |         |         |
| 10 | What is the efficacy of JAKi combination therapy with csDMARDs (SZP, LEF) other than MTX? |            |              |         |         |
### 1.4.3 Research questions: Safety

| #  | Research question                                                                                                                                                                                                 | Population | Intervention | Control | Outcome |
|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|--------------|---------|---------|
| 1  | What is the risk for infections of 1) herpes zoster, 2) tuberculosis, 3) nontuberculous mycobacteria, 4) CMV, and 5) fungal infections of patients treated with JAKi as compared to bDMARDs? |             |              |         |         |
| 2  | What is the risk of serious infections with JAK inhibitors as compared to bDMARDs + MTX?                                                                                                                                 |             |              |         |         |
| 3  | Are there differences in safety signals (VTEs, anemia, zoster) between JAK inhibitors with different selectivity to JAK1/2/3 inhibition?                                                                                   |             |              |         |         |
| 4  | Is there a specific dosage dependent effect of JAKi comediations (csDMARDS/corticosteroids) on the risk of infection?                                                                                                    |             |              |         |         |
| 5  | Are there differences in safety between different patient populations (MTX-naïve, MTX-IR, csDMARD-IR, bDMARD-IR)?                                                                                                    |             |              |         |         |
| 6  | What is the risk of VTEs of JAKi compared to other 1) JAKi 2) bDMARDs?                                                                                                                                              |             |              |         |         |
| 7  | What is the comparative risk of malignancy (excluding NMSC) between JAKs and bDMARDs?                                                                                                                            |             |              |         |         |
| 8  | What is the comparative risk of NMSC between JAKs and bDMARDs?                                                                                                                                                     |             |              |         |         |
| 9  | What is the risk of severe lymphopenia or neutropenia during JAK inhibition?                                                                                                                                        |             |              |         |         |
| 10 | What are the rates of MACE events across JAKs, and how to they compare to those seen with bDMARDs?                                                                                                                  |             |              |         |         |
| 11 | There have been reports that GC in combination with a JAK increase SIE and HZ – is there a dose of GC below which this is not a problem?                                                                            |             |              |         |         |
| 12 | Can a JAK be used during pregnancy/lactation?                                                                                                                                                                     |             |              |         |         |
| 13 | Should a JAK be discontinued before pregnancy? If yes, how long?                                                                                                                                                  |             |              |         |         |
| 14 | What is the comparative risk for perioperative infections in patients undergoing elective surgery of patients treated with JAKi compared to bDMARDs?                                                                |             |              |         |         |
| 15 | Should JAKi therapy be paused before elective surgery? If yes, for how long? When should therapy be reinitiated                                                                                                     |             |              |         |         |
|   | Question                                                                 |
|---|-------------------------------------------------------------------------|
|16 | Is there a difference between infection risks in patients vaccinated against zoster? |
|17 | Is Shingrix vaccine of value in patients treated with a JAK? How effective and for how long? |
|18 | How should patients be vaccinated for pneumonia and flu while on a JAK? Are other vaccinations necessary? |
|19 | Which screening tests should be performed before starting a JAK? |
Section 2: Characteristics of articles and abstracts included: Efficacy

2.1. Details of articles and abstracts selected for inclusion

Table S2.1.1: Rheumatoid arthritis

| Study                | Treatment                  | Target  | Population                      |
|---------------------|----------------------------|---------|---------------------------------|
| Kremer 2009 [1]     | Tofacitinib                | JAK-1-3 | Mixed csDMARD / TNF-IR          |
| Tanaka 2011a [2]    | Tofacitinib                | JAK-1-3 | MTX-IR; Japanese                |
| Fleischmann 2012 [3]| Tofacitinib                | JAK-1-3 | DMARD-IR                        |
| Fleischmann 2012 [4]| Tofacitinib                | JAK-1-3 | Biologic / non-biologic DMARD IR|
| Kremer 2012 [5]     | Tofacitinib                | JAK-1-3 | MTX-IR                          |
| Van Vollenhoven 2012 [6]| Tofacitinib vs. Adalimumab| JAK-1-3 vs. TNF | MTX-IR |
| Burmester 2013 [7]  | Tofacitinib                | JAK-1-3 | TNF-IR                          |
| Kremer 2013 [8]     | Tofacitinib                | JAK-1-3 | DMARD-IR                        |
| Van der Heijde 2013 [9, 10]| Tofacitinib            | JAK-1-3 | MTX-IR                          |
| Lee 2014 [11]       | Tofacitinib                | JAK-1-3 | MTX naive                        |
| Tanaka 2015 [12]    | Tofacitinib                | JAK-1-3 | DMARD-IR; Japanese              |
| Fleischmann 2015 [13]| Decernotinib             | JAK-3   | csDMARD-IR / TNF-IR             |
| Genovese 2016a [14] | Baricitinib                | JAK-1/2 | bDMARD-IR                       |
| Study                                | Treatment            | JAK-1/2 | IR Treatment       |
|--------------------------------------|----------------------|---------|--------------------|
| Genovese 2016b [15]                 | Upadacitinib         |         | MTX-IR             |
| Genovese 2016c [16]                 | Decernotinib         |         | MTX-IR             |
| Genovese 2016d [17]                 | Decernotinib         |         | csDMARD-IR         |
| Kremer 2016 [18]                    | Upadacitinib         | JAK-1/2 | TNFi-IR            |
| Takeuchi 2016 [19]                  | Peficitinib          | JAK-1   | csDMARD-IR / TNF-IR; Japanese |
| Tanaka 2016 [20]                    | Baricitinib          | JAK-1/2 | MTX-IR; Japanese   |
| Dougados 2017 (RA-BUILD) [21]       | Baricitinib          | JAK-1/2 | csDMARD-IR         |
| Fleischmann 2017a (ORAL-Strategy) [22] | Tofacitinib vs. Adalimumab | JAK-1-3 vs. TNF | MTX-IR |
| Fleischmann 2017b (RA-BEGIN) [23]   | Baricitinib          | JAK-1/2 | csDMARD naïve      |
| Genovese 2017 [24]                  | Peficitinib          | JAK-1   | minimal csDMARD exposure; MTX naïve |
| Kivitz 2017 [25]                    | Peficitinib          | JAK-1   | MTX-IR             |
| Kavanaugh 2017 (DARWIN 2) [26]      | Filgotinib           | JAK-1   | MTX-IR             |
| Taylor 2017 (RA-BEAM) [27]          | Baricitinib vs. Adalimumab | JAK-1/2 vs. TNF | MTX-IR |
| Vanhouotte 2017 [28]                | Filgotinib           | JAK-1   | MTX-IR             |
| Westhovens 2017 (DARWIN 1) [29]     | Filgotinib           | JAK-1   | MTX-IR             |
| Burmester 2018 (SELECT-NEXT) [30]   | Upadacitinib         | JAK-1/2 | csDMARD-IR         |
| Fleischmann 2018 (SELECT-COMPARE) [31, 32] | Upadacitinib vs. Adalimumab | JAK-1/2 vs. TNF | MTX-IR |
| Genovese 2018 (SELECT-BEYOND) [33]  | Upadacitinib         | JAK-1/2 | bDMARD-IR          |
| Kivitz ACR 2018 [34]                | GS-9876, Filgotinib  |         | SYK; JAK-1         | MTX-IR |
| Study                                      | Drug               | JAK Isoform | MTX Form     |
|-------------------------------------------|--------------------|-------------|--------------|
| Hu 2018 (RA-BALANCE) [35, 36]             | Baricitinib        | JAK-1/2     | MTX-IR       |
| Smolen 2018 (SELECT-MONOTHERAPY) [37, 38] | Upadacitinib       | JAK-1/2     | MTX-IR       |
| Tanaka 2018 (SELECT-SUNRISE) [39, 40]     | Upadacitinib       | JAK-1/2     | csDMARD-IR   |
| Tanaka & Takeuchi 2018 [41, 42]           | Peficitinib        | JAK-1       | MTX-naïve    |
| Takeuchi 2018 [43, 44]                    | Peficitinib        | JAK-1       | MTX-IR       |
| van Vollenhoven ACR 2018 (SELECT-EARLY)   | Upadacitinib       | JAK-1       | MTX-naïve    |
| Takeuchi 2019 (RA-BEYOND) [46, 47]        | Baricitinib; Tapering to 2mg vs. BARI 4mg continuation | JAK-1/2    | BARI 4mg + CDAI<10 |
| Tanaka 2019 [48]                          | Tofacitinib        | JAK-1-3     | MTX-IR       |
Table S2.1.2: Psoriatic arthritis

| Study                          | Treatment          | Target   | Population       |
|-------------------------------|--------------------|----------|------------------|
| Mease 2017 (OPAL Broaden) [49]| Tofacitinib / Adalimumab | JAK-1-3 / TNF | csDMARD-IR      |
| Gladman 2017 (OPAL Beyond) [50]| Tofacitinib      | JAK-1-3  | TNFi-IR         |
| Mease 2018d (EQUATOR) [51]    | Filgotinib        | JAK-1    | csDMARD-IR      |

Table S2.1.3: Ankylosing spondylitis

| Study                          | Treatment          | Target | Population       |
|-------------------------------|--------------------|--------|------------------|
| Van der Heijde 2017 [52]      | Tofacitinib        | JAK-1-3| NSAID-IR        |
| Van der Heijde 2018 [53]      | Filgotinib        | JAK-1  | NSAID-IR        |

Table S2.1.4: Systemic Lupus Erythematosus

| Study                          | Treatment          | Target     | Population                          |
|-------------------------------|--------------------|------------|-------------------------------------|
| Kahl 2016 [54]                | Solcitinib (GSK2586184) | JAK-1      | SELENA-SLEDAI score ≥ 8; ANA OR dsDNA positivity |
| Wallace 2018 [55]             | Baricitinib        | JAK-1/2    | SLEDAI-2K ≥ 4; active arthritis or rash; ANA OR |


|              |              |              | dsDNA positivity |
|--------------|--------------|--------------|------------------|

| Study                  | Treatment                  | Target   | Population                                                                 |
|------------------------|----------------------------|----------|-----------------------------------------------------------------------------|
| Papp 2012 [56]         | Tofacitinib                | JAK-1-3  | Candidates for systemic therapy or phototherapy                            |
| Bachelez 2015 [57]     | Tofacitinib / Etanercept  | JAK-1-3; TNF-R | Candidates for systemic therapy or phototherapy + PASI > 12 + PGA moderate/severe + csDMARD-IR/intolerance |
| Bissonnette 2014 [58]  | Tofacitinib (withdrawal study) | JAK-1-3  | Candidates for systemic therapy or phototherapy; PASI75 + PGA clear/almost clear after 24 weeks |
| Papp 2015 [59]         | Peficitinib (ASP015K)      | JAK-1    | Candidates for systemic therapy or phototherapy                            |
| Papp 2015 [60]         | Tofacitinib                | JAK-1-3  | Candidates for systemic therapy or phototherapy                            |
| Bissonnette 2016 [61]  | Itacitinib (INCB039110)    | JAK-1    | Inadequate response to topical therapies                                    |
| Papp 2016 [62]         | Baricitinib                | JAK-1/2  | Candidates for systemic therapy or phototherapy                            |
| Papp 2016 [63]         | Topical tofacitinib        | JAK-1-3  | PGA mild or moderate; 2-20% BSA                                             |
| Zhang 2017 [64]        | Tofacitinib                | JAK-1-3  | Candidates for systemic therapy or phototherapy                            |
Table S2.1.6: Alopecia & Atopic Dermatitis

| Study                        | Treatment                  | Target            | Population                                                                 |
|------------------------------|----------------------------|-------------------|-----------------------------------------------------------------------------|
| Guttman-Yassky 2018 [66]     | PF-06651600 / PF-06700841 | JAK-3 / TYK2+JAK1 | Alopecia areata; ≥50 scalp affection                                         |
| Bissonette 2016 [67]         | Topical tofacitinib        | JAK-1-3           | Atopic dermatitis; PGA mild or moderate + 2-20% BSA + lichenification score ≤ 1 in each Eczema Area and Severity Index (EASI) body region with treatment-eligible AD |
| De Bruin-Weller 2018 [68, 69]| Upadacitinib               | JAK-1             | Atopic dermatitis; Eczema Area and Severity Index ≥ 16, BSA ≥ 10%, Investigator’s Global Assessment ≥ 3 |
| Guttman-Yassky 2018 [70]     | Baricitinib                | JAK-1/2           | Atopic dermatitis; Eczema Area and Severity Index ≥12 and >10% body, diagnosis ≥2 years, IR emollients, systemic corticosteroids or |
| Study                  | Treatment  | Target | Population                                                                 |
|------------------------|------------|--------|-----------------------------------------------------------------------------|
| Nakagawa 2018 [71]     | Topical JTE-052 | JAK-1-3 | Atopic dermatitis; Eczema Area Severity Index (EASI) score ≥ 10; Investigator’s Global Assessment ≥ 3; BSA ≥ 10-30% |

**Table S2.1.7: Ulcerative Colitis**

| Study                  | Treatment | Target | Population                                                                 |
|------------------------|-----------|--------|-----------------------------------------------------------------------------|
| Sandborn 2012 [72]     | Tofacitinib | JAK-1-3 | Mayo score 6-12 + endoscopy subscore 2-3; GC/DMARD-IR                      |
| Sandborn 2017 [73]     | Tofacitinib | JAK-1-3 | Mayo score 6-12 + endoscopy subscore 2-3 + rectal bleeding subscore 1-3; GC/DMARD-IR |
| Sandborn 2018 [74, 75] | Upadacitinib | JAK-1  | Mayo score (without EGA) 5-9 + endoscopy subscore 2-3; GC/DMARD-IR          |
| Sands 2018 [76]        | Peficitinib | JAK-1  | Mayo score 6-12 + endoscopy subscore 2-3; GC/DMARD-IR                      |
| Study                  | Treatment | Target | Population                                                                 |
|------------------------|-----------|--------|-----------------------------------------------------------------------------|
| Sandborn 2014 [77]     | Tofacitinib | JAK-1-3 | Crohn’s Disease Activity Index (CDAI) score of 220 to 450                   |
| Panés 2017 [78]        | Tofacitinib | JAK-1-3 | CDAI ≥220 to ≤450 + intestinal ulceration (colonoscopy within six weeks prior screening), DMARD-IR |
| Sandborn 2017 / Panés 2018 [79-81] | Upadacitinib | JAK-1 | CDAI 220–450, average daily liquid/soft stool frequency ≥2.5 or daily abdominal pain score ≥2.0 + Simplified Endoscopic Score for CD (SES-CD) ≥6 (or ≥4 for those with isolated ileal disease); GC/DMARD-IR |
| Vermeire 2017 [82]    | Filgotinib  | JAK-1  | CDAI ≥220 to ≤450 + intestinal ulceration (colonoscopy within six weeks prior screening), GC/DMARD-IR |
### 2.2 Risk of bias analysis: Efficacy

#### Table S2.2.1: Rheumatoid arthritis

| Study                  | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary          | Comment                                                                 |
|------------------------|----------------------------|------------------------|----------------------------------------|-------------------------------|------------------------|---------------------|---------------------|-------------------|-------------------------------------------------------------------------|
| Kremer 2009 [1]        | Unclear                   | Unclear                | Low                                    | Low                           | Low                    | Low                 | Low                 | Unclear          |                                                                           |
| Tanaka 2011a [2]       | Unclear                   | Unclear                | Low                                    | Low                           | Low                    | Low                 | Low                 | Unclear          |                                                                           |
| Fleischmann 2012 [3]   | Low                       | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               |                                                                           |
| Fleischmann 2012 [4]   | Low                       | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               |                                                                           |
| Kremer 2012 [5]        | Unclear                   | Unclear                | Low                                    | Low                           | Low                    | Low                 | Low                 | Unclear          | Randomization sequence generation and allocation not reported           |
| Van Vollenhoven 2012 [6]| Low                      | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               | Analyses with and without advancement penalty                           |
| Burmester 2013 [7]     | Low                       | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               |                                                                           |
| Kremer 2013 [8]        | Low                       | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               |                                                                           |
| Van der Heijde 2013 [9, 10]| Low                | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               |                                                                           |
| Lee 2014 [11]          | Low                       | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low               |                                                                           |
| Study                        | Initiation | Compliance | Maintenance | Viability | Recruitment | Randomization | Blinding | Analysis |
|------------------------------|------------|------------|-------------|-----------|-------------|--------------|----------|----------|
| Tanaka 2015 [12]             | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Fleischmann 2015 [13]        | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Genovese 2016a [14]          | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Genovese 2016b [15]          | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Genovese 2016c [16]          | Unclear    | Unclear    | Low         | Low       | Low         | Low          | Low      | Unclear  |
| Genovese 2016d [17]          | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Kremer 2016 [18]             | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Takeuchi 2016 [19]           | Unclear    | Unclear    | Low         | Low       | Low         | Low          | Low      | Unclear  |
| Tanaka 2016 [20]             | Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Dougados 2017 (RA-BUILD) [21]| Low        | Low        | Low         | Low       | Low         | Low          | Low      | Low      |
| Fleischmann 2017a (ORAL-Strategy) [22] | Low | Low | Low | Low | Low | Low | Low | Low |
| Fleischmann 2017b (RA-BEGIN) [23] | Low | Low | Low | Low | Low | Low | Low | Low |
| Genovese 2017 [24]           | Unclear    | Low        | Low         | Low       | Low         | Unclear      | Unclear  | protocol changes after study initiation and enrollment of 97 patients (excluding
| Study                                | Type                  | Blind | Sample Size | Power | Blinding | Allocation | Allocation | Blinding | Allocation | Allocation |
|--------------------------------------|-----------------------|-------|-------------|-------|----------|------------|------------|----------|------------|------------|
| Kivitz 2017 [25]                     | Unclear               | Low   | Low         | Low   | Low      | Unclear    | Unclear    | Low      | Unclear    | Unclear    |
| Kavanaugh 2017 (DARWIN 2) [26]       | Low                   | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Taylor 2017 (RA-BEAM) [27]           | Low                   | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Vanhoutte 2017 [28]                  | Unclear               | Unclear | Low        | Low   | Low      | Low        | Low        | Unclear  | Low        | Unclear    |
| Westhovens 2017 (DARWIN 1) [29]      | Low                   | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Burmester 2018 (SELECT-NEXT) [30]    | Low                   | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Fleischmann 2018 (SELECT-COMPARE) [31, 32] | Low                | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Genovese 2018 (SELECT-BEYOND) [33]   | Low                   | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Kivitz ACR 2018 [34]                 | Abstract              | Abstract | Abstract  | Abstract | Abstract | Abstract   | Abstract   | Abstract | Abstract   | Abstract   |
| Hu 2018 (RA-BALANCE) [35]            | Abstract              | Abstract | Abstract  | Abstract | Abstract | Abstract   | Abstract   | Abstract | Abstract   | Abstract   |
| Smolen 2018 (SELECT-MONOTHERAPY)     | Low                   | Low   | Low         | Low   | Low      | Low        | Low        | Low      | Low        | Low        |
| Reference | Year | Low | Low | Low | Low | Low | Low | Low | Low |
|-----------|------|-----|-----|-----|-----|-----|-----|-----|-----|
| Tanaka 2018a (SELECT-SUNRISE) [39, 40] | 2018 | Low | Low | Low | Low | Low | Low | Low | Low |
| Tanaka & Takeuchi 2018 [41, 42] | 2018 | Low | Low | Low | Low | Low | Low | Low | Low |
| Takeuchi 2018 [43, 44] | 2018 | Low | Low | Low | Low | Low | Low | Low | Low |
| van Vollenhoven ACR 2018 (SELECT-EARLY) [45] | 2018 | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract |
| Tanaka 2019 [48] | 2019 | Low | Low | Low | Low | Low | Low | Low | Low |
| Takeuchi 2019 (RA-BEYOND) [47] | 2019 | Low | Low | Low | Low | Low | Low | Low | Low |
### Table S2.2.2: Psoriatic arthritis

| Study                          | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary | Comment |
|--------------------------------|-----------------------------|------------------------|---------------------------------------|--------------------------------|-------------------------|---------------------|---------------------|---------|---------|
| Mease 2017 (OPAL Broaden) [49] | Low                         | Low                    | Low                                   | Low                            | Low                     | Low                 | Low                 | Low     |         |
| Gladman 2017 (OPAL Beyond) [50]| Low                         | Low                    | Low                                   | Low                            | Low                     | Low                 | Low                 | Low     |         |
| Mease 2018 (EQUATOR) [51]     | Low                         | Low                    | Low                                   | Low                            | Low                     | Low                 | Low                 | Low     |         |

### Table S2.2.3: Ankylosing spondylitis

| Study                      | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary | Comment                                           |
|----------------------------|-----------------------------|------------------------|---------------------------------------|--------------------------------|-------------------------|---------------------|---------------------|---------|---------------------------------------------------|
| Van der Heijde 2017 [52]   | Unclear                     | Unclear                | Low                                   | Low                            | Low                     | Low                 | Low                 | Unclear | Randomization sequence generation and allocation not reported |
| Van der Heijde             | Low                         | Low                    | Low                                   | Low                            | Low                     | Low                 | Low                 | Low     |         |
Table S2.2.4: Systemic lupus erythematosus

| Study          | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary | Comment                                                                 |
|---------------|-----------------------------|------------------------|----------------------------------------|-------------------------------|------------------------|---------------------|---------------------|---------|-------------------------------------------------------------------------|
| Kahl 2016 [54]| Unclear                     | Unclear                | Low                                    | Low                           | High                   | High                | High                | High    | Randomization sequence generation and allocation not reported; study terminated early; outcomes not completely reported; |
| Wallace 2018 [55] | Low                         | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low     |                                                                 |

Table S2.2.5: Psoriasis

| Study         | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary | Comment |
|---------------|-----------------------------|------------------------|----------------------------------------|-------------------------------|------------------------|---------------------|---------------------|---------|---------|
| Papp 2012 [56] | Low                         | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low     |         |
| Bachelez 2015 | Low                         | Low                    | Low                                    | Low                           | Low                    | Low                 | Low                 | Low     |         |
| Study                  | Allocation | Randomization | Reporting | Quality | Bias | Confound. | Funding | Int. | Setting |
|-----------------------|------------|---------------|-----------|---------|------|-----------|---------|------|---------|
| Bissonnette 2014      | Low        | Low           | Low       | Low     | Low  | Low       | Low     | Low  | Low     |
| Papp 2015 [59]        | Low        | Low           | Low       | Low     | Low  | Low       | Low     | Low  | Low     |
| Papp 2015 [60]        | Low        | Low           | Low       | Low     | Low  | Low       | Low     | Low  | Low     |
| Bissonnette 2016 [61] | Unclear    | Unclear       | Low       | Low     | Low  | Low       | Low     | Unclear | Randomization sequence generation and allocation not reported |
| Papp 2016 [62]        | Low        | Low           | Low       | Low     | Low  | Low       | Low     | Low  | Low     |
| Papp 2016 [63]        | Unclear    | Unclear       | High      | High    | Low  | Low       | Low     | High | Randomization sequence generation and allocation not reported; “neither investigators nor patients were blinded to regimen” |
| Zhang 2017 [64]       | Low        | Low           | Low       | Low     | Low  | Low       | Low     | Low  | Low     |
| Papp 2018 [65]        | Low        | Low           | Low       | Low     | Low  | Low       | Low     | Low  | Low     |
Table S2.2.6: Alopecia & Atopic Dermatitis

| Study                     | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary | Comment |
|---------------------------|-----------------------------|------------------------|----------------------------------------|-------------------------------|-------------------------|---------------------|----------------------|---------|---------|
| Guttman-Yassky 2018 [66]  | Abstract                    | Abstract               | Abstract                               | Abstract                      | Abstract                | Abstract            | Abstract            | Abstract |         |
| Bissonette 2016 [67]      | Low                         | Low                    | Low                                    | Low                           | Low                     | Low                 | Low                 | Low     |         |
| De Bruin-Weller 2018 [68, 69] | Low                        | Low                    | Low                                    | Low                           | Low                     | Low                 | Low                 | Low     |         |
| Guttman-Yassky 2018 [70]  | Low                         | Low                    | Low                                    | Low                           | Low                     | Low                 | Low                 | Low     |         |
| Nakagawa 2018 [71]        | Low                         | Low                    | High                                   | Low                           | Low                     | Low                 | Low                 | High    | appearance of each strength of the JTE-052 ointments and vehicle ointment different |

Table S2.2.7: Ulcerative Colitis

| Study                     | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary | Comment |
|---------------------------|-----------------------------|------------------------|----------------------------------------|-------------------------------|-------------------------|---------------------|----------------------|---------|---------|
| Study                        | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias | Summary     | Comment                                         |
|------------------------------|----------------------------|------------------------|----------------------------------------|------------------------------|------------------------|---------------------|---------------------|-------------|------------------------------------------------|
| Sandborn 2012 [72]          | Low                        | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |
| Sandborn 2017 [73]          | Low                        | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |
| Sandborn 2018 [74, 75]      | Low                        | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |
| Sands 2018 [76]             | Low                        | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |
| Sandborn 2014 [77]          | Unclear                    | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Unclear    | Randomization sequence generation not reported |
| Panés 2017 [78]             | Low                        | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |
| Sandborn 2017 / Panés 2018 [79-81] | Low              | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |
| Vermeire 2017 [82]          | Low                        | Low                    | Low                                    | Low                          | Low                    | Low                 | Low                 | Low         |                                                 |

Table S2.2.8: Crohn’s disease
Table S2.3: Baseline characteristics: Efficacy

Table S2.3.1: Rheumatoid arthritis

| Study                  | Treatment                  | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean DAS28 | Mean CDAI  | Mean HAQ | Mean mTSS |
|------------------------|----------------------------|---------------------|------------------|------------------------------|------------|------------|----------|-----------|
| Kremer 2009 [1]        | Placebo                    | 65                  | 47.9             | 8.7                          | 6.0        | 1.71       |          |           |
|                        | TOFA 5mg BID               | 61                  | 51.8             | 10.2                         | 6.17       | 1.75       |          |           |
|                        | TOFA 15mg BID              | 69                  | 51.1             | 9.6                          | 5.69       | 1.66       |          |           |
|                        | TOFA 30mg BID              | 69                  | 51.3             | 9.9                          | 5.91       | 1.61       |          |           |
| Tanaka 2011a [2]       | Placebo + MTX             | 28                  | 50.6             | 8.4                          | 4.9        | 1.3        |          |           |
|                        | TOFA 1mg BID + MTX        | 28                  | 52.0             | 5.7                          | 5.0        | 1.1        |          |           |
|                        | TOFA 3mg BID + MTX        | 27                  | 53.3             | 8.7                          | 5.1        | 1.3        |          |           |
|                        | TOFA 5mg BID + MTX        | 27                  | 50.0             | 8.3                          | 5.0        | 1.2        |          |           |
|                        | TOFA 10mg BID + MTX       | 26                  | 50.6             | 7.1                          | 4.9        | 1.2        |          |           |
| Fleischmann 2012 [3]   | Placebo                   | 59                  | 53               | 10.8                         | 5.62       | 1.54       |          |           |
|                        | TOFA 1mg BID              | 54                  | 55               | 9.4                          | 5.51       | 1.57       |          |           |
|                        | TOFA 3mg BID              | 51                  | 53               | 9.9                          | 5.37       | 1.53       |          |           |
|                        | TOFA 5mg BID              | 49                  | 54               | 8.1                          | 5.58       | 1.4        |          |           |
|                        | TOFA 10mg BID             | 61                  | 52               | 8.6                          | 5.46       | 1.49       |          |           |
| Study                  | Group Description                          | N  | A   | B   | C   | D   |
|-----------------------|--------------------------------------------|----|-----|-----|-----|-----|
| Fleischmann 2012 [4]   | Placebo                                    | 122| 49.7| 7.7 | 5.56| 1.53|
|                       | TOFA 5mg BID                                | 243| 52.2| 8   | 5.68| 1.53|
|                       | TOFA 10mg BID                               | 245| 52.4| 8.6 | 5.6 | 1.5  |
| Kremer 2012 [5]        | Placebo + MTX                              | 69 | 53  | 9.2 | 5.3 | 1.2  |
|                       | TOFA 1mg BID + MTX                          | 70 | 52  | 11.8| 5.5 | 1.58 |
|                       | TOFA 3mg BID + MTX                          | 68 | 51  | 9.4 | 5.3 | 1.36 |
|                       | TOFA 5mg BID + MTX                          | 71 | 52  | 9.0 | 5.1 | 1.44 |
|                       | TOFA 10mg BID + MTX                         | 74 | 56  | 7.5 | 5.3 | 1.33 |
|                       | TOFA 15mg BID + MTX                         | 75 | 54  | 10.8| 5.4 | 1.41 |
|                       | TOFA 20mg BID + MTX                         | 80 | 54  | 9.8 | 5.3 | 1.46 |
| Van Vollenhoven 2012 [6]| Placebo + MTX (cross-over to TOFA 5mg BID + MTX after 3 months) | 56 | 55.5| 6.9 | 5.6 | 1.5  |
|                       | Placebo + MTX (cross-over to TOFA 10mg BID + MTX after 3 months) | 52 | 51.9| 9   | 5.3 | 1.4  |
|                       | TOFA 5mg BID + MTX                          | 204| 53  | 7.6 | 5.4 | 1.5  |
|                       | TOFA 10mg BID + MTX                         | 201| 52.9| 7.4 | 5.4 | 1.5  |
|                       | ADA 40mg EOW + MTX                          | 204| 52.5| 8.1 | 5.3 | 1.5  |
|                       | Placebo + MTX (Combination)                 | 106|     |     |     |      |
| Study                          | Group Description                                         | n  | Mean | SD  | CV | SE  |
|-------------------------------|-----------------------------------------------------------|----|------|-----|----|-----|
| Burmester 2013 [7]            | Placebo + MTX                                             | 132| 54.4 | 11.3| 5.4| 1.6 |
|                              | TOFA 5mg BID + MTX                                        | 133| 55.4 | 13  | 5.4| 1.6 |
|                              | TOFA 10mg BID + MTX                                       | 134| 55.1 | 12.6| 5.3| 1.5 |
| Kremer 2013 [8]               | Placebo + DMARD (Combination group)                       | 159|      |     |    |     |
|                              | Placebo + DMARD (cross-over to TOFA 5mg BID + DMARD after 3/6 months) | 79 | 50.8 | 9.5 | 6.44|     |
|                              | Placebo + DMARD (cross-over to TOFA 10mg BID + DMARD after 3/6 months) | 80 | 53.3 | 10.2| 6.14|     |
|                              | TOFA 5mg BID + DMARD                                      | 315| 52.7 | 8.1 | 6.27| 1.44|
|                              | TOFA 10mg BID + DMARD                                     | 318| 51.9 | 9.2 | 6.36| 1.43|
| Van der Heijde 2013 [9]      | Placebo + DMARD (Combination group)                       | 160|      |     |    |     |
|                              | Placebo + DMARD (cross-over to TOFA 5mg BID + DMARD after 3/6 months) | 81 | 53.2 | 8.8 | 5.14| 1.4 | 35 |
|                              | Placebo + DMARD (cross-over to TOFA 10mg BID + DMARD after 3/6 months) | 79 | 52.1 | 9.5 | 5.18| 1.23 | 30.1 |
|                              | TOFA 5mg BID + DMARD                                      | 321| 53.7 | 8.9 | 5.22| 1.41 | 31.1 |
|                              | TOFA 10mg BID + DMARD                                     | 316| 52   | 9   | 5.2 | 1.39 | 37.3 |
| Study               | Treatment      | N   | Mean ESR | Standard Deviation | Mean CRP | Standard Deviation |
|---------------------|----------------|-----|----------|--------------------|----------|--------------------|
| Lee 2014 [11]       | MTX            | 186 | 48.8     | 2.7                | 6.6      | 1.5                |
|                     | TOFA 5mg BID   | 373 | 50.3     | 2.9                | 6.6      | 1.5                |
|                     | TOFA 10mg BID  | 397 | 49.3     | 3.4                | 6.5      | 1.5                |
| Tanaka 2015 [12]    | Placebo        | 52  | 53.3     | 6.4                | 6.0      | 1.21               |
|                     | TOFA 1mg BID   | 53  | 53.3     | 8.1                | 6.1      | 1.25               |
|                     | TOFA 3mg BID   | 53  | 52.8     | 6.8                | 6.4      | 1.19               |
|                     | TOFA 5mg BID   | 52  | 52.6     | 11.0               | 6.1      | 1.5                |
|                     | TOFA 10mg BID  | 53  | 54.7     | 7.3                | 6.2      | 1.2                |
|                     | TOFA 15mg BID  | 54  | 53.6     | 7.4                | 5.8      | 1.2                |
| Fleischmann 2015    | Placebo        | 41  | 54.9     | 10.6               | 6.0      | 1.6                |
| [13]                | DEC 25mg BID   | 41  | 56.8     | 9.5                | 6.2      | 1.7                |
|                     | DEC 50mg BID   | 41  | 55.6     | 11.3               | 6.2      | 1.6                |
|                     | DEC 100mg BID  | 40  | 56.5     | 8.9                | 6.0      | 1.6                |
|                     | DEC 150mg BID  | 41  | 57       | 9.3                | 6.1      | 1.7                |
| Genovese 2016a      | Placebo + csDMARD | 176 | 56     | 14              | 5.9      | 41        | 1.78        |
| [14]                | BARI 2mg + csDMARD | 174 | 55     | 14              | 6        | 43        | 1.71        |
|                     | BARI 4mg + csDMARD | 177 | 56     | 14              | 5.9      | 40        | 1.74        |
| Genovese 2016b      | Placebo + MTX  | 50  | 55      | 5.9              | 5.6      | 40        | 1.4         |
| [15]                | UPA 3mg BID + MTX | 50  | 53      | 3.9              | 5.5      | 38        | 1.3         |
|                     | UPA 6mg BID + MTX | 50  | 55      | 7                | 5.8      | 43        | 1.6         |
| Study               | Treatment                  | N  | Mean  | SD   | Median | IQR  |
|---------------------|----------------------------|----|-------|------|--------|------|
| Genovese 2016c [16] | Placebo + MTX             | 71 | 52.7  | 13.2 | 7.2    | 1.7  |
|                     | DEC 100mg OD + MTX        | 71 | 53.5  | 11.3 | 6.5    | 1.5  |
|                     | DEC 150mg OD + MTX        | 72 | 50.1  | 11.8 | 8.1    | 1.2  |
|                     | DEC 200mg OD + MTX        | 72 | 53.2  | 13.2 | 7.2    | 1.5  |
|                     | DEC 100mg BID + MTX       | 72 | 55.7  | 12.2 | 7.7    | 1.6  |
| Genovese 2016d [17] | Placebo + csDMARD         | 12 | 52.8  | 12.3 | 6.3    |      |
|                     | DEC 100mg BID + csDMARD   | 11 | 56.7  | 6.5  | 5.4    |      |
|                     | DEC 200mg BID + csDMARD   | 10 | 50.5  | 11.9 | 5.8    |      |
|                     | DEC 300mg BID + csDMARD   | 10 | 54.9  | 5    | 6.1    |      |
| Kremer 2016 [18]    | Placebo                   | 56 | 58    | 12.1 | 5.8    | 41   |
|                     | UPA 3 mg + MTX            | 55 | 57    | 11.8 | 5.7    | 40   |
|                     | UPA 6 mg + MTX            | 55 | 56    | 12.3 | 5.9    | 42   |
|                     | UPA 12 mg + MTX           | 55 | 59    | 12.2 | 5.7    | 40   |
|                     | UPA 18 mg + MTX           | 55 | 57    | 10.9 | 5.8    | 41   |
| Takeuchi 2016 [19]  | Placebo                   | 56 | 54.2  | 12.1 | 5.1    | 0.9  |
|                     | PEF 25mg OD               | 55 | 52.9  | 9.5  | 5.3    | 0.9  |
|                     | PEF 50mg OD               | 57 | 54.2  | 11.6 | 5.26   | 0.9  |
| Study                        | Drug Combinations       | N  | Platelet (x10^9) | WBC (x10^9) | Hb (g/L) | Ht (%) |
|------------------------------|-------------------------|----|-----------------|-------------|---------|-------|
| **Tanaka 2016 [20]**         | PEF 100mg OD            | 55 | 52.1            | 12.1        | 5.34    | 1.0   |
|                              | PEF 150mg OD            | 58 | 51.6            | 12.1        | 5.41    | 1.0   |
|                              | Placebo + MTX           | 49 | 51.1            | 5.06        | 4.72    | 0.855 |
|                              | BARI 1mg OD + MTX       | 24 | 52.7            | 6.22        | 4.6     | 1.005 |
|                              | BARI 2mg OD + MTX       | 24 | 56.1            | 6.32        | 4.94    | 0.948 |
|                              | BARI 4mg OD + MTX       | 24 | 57.5            | 5.86        | 4.96    | 0.974 |
|                              | BARI 8mg OD + MTX       | 24 | 53.6            | 5.55        | 4.67    | 0.63  |
| **Dougados 2017 (RA-BUILD) [21, 83]** | Placebo + csDMARD      | 228| 51              | 7           | 5.5     | 36    | 1.5   | 19    |
|                              | BARI 2mg + csDMARD      | 229| 52              | 8           | 5.6     | 37    | 1.51  | 26    |
|                              | BARI 4mg + csDMARD      | 227| 52              | 8           | 5.6     | 36    | 1.55  | 24    |
| **Fleischmann 2017a (ORAL-Strategy) [22]** | TOFA 5mg BID + PLC      | 384| 49.7            | 6.1         | 5.7     | 38.6  | 1.6   |
|                              | TOFA 5mg BID + MTX      | 376| 50              | 5.4         | 5.8     | 39.7  | 1.6   |
|                              | ADA 40mg Q2W + MTX      | 386| 50.7            | 6           | 5.7     | 38.2  | 1.7   |
| **Fleischmann 2017b (RA-BEGIN) [23]** | Placebo + MTX           | 210| 51              | 1.3         | 5.9     | 39    | 1.7   | 11.8  |
|                              | BARI 4mg + Placebo      | 159| 51              | 1.9         | 5.9     | 40    | 1.6   | 13.3  |
|                              | BARI 4mg + MTX          | 215| 49              | 1.3         | 5.9     | 40    | 1.6   | 11.4  |
| **Genovese 2017 [24]**       | Placebo + HCQ/SZP       | 51 | 52.7            | 9.8         | 5.9     | 40.8  | 1.6   |
|                              | PEF 25mg + HCQ/SZP      | 59 | 52.6            | 10.4        | 5.8     | 40.8  | 1.4   |
|                              | PEF 50mg + HCQ/SZP      | 57 | 54.8            | 10.3        | 5.9     | 42    | 1.6   |
|                              | PEF 100mg + HCQ/SZP     | 58 | 54.9            | 11          | 5.7     | 40.4  | 1.4   |
| Study | Treatment | N | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) |
|-------|-----------|---|-----------|-----------|-----------|-----------|
|       |           |   | Placebo + MTX                          | Placebo + MTX                          | Placebo + MTX                          | Placebo + MTX                          |
|       |           |   | 72 52 10 6.22 42 1.8                    | 72 52 9 6.03 41 1.8                    | 72 52 9 6.09 42 1.8                    | 72 52 10 6.22 42 1.8                    |
| Kivitz 2017 [25] | PEF 150mg + HCQ/SZP | 64 | 54.4 10.5 5.9 41.6 1.5 | 54.4 10.5 5.9 41.6 1.5 | 54.4 10.5 5.9 41.6 1.5 | 54.4 10.5 5.9 41.6 1.5 |
|       |           |   | PEF 25mg + MTX                          | PEF 25mg + MTX                          | PEF 25mg + MTX                          | PEF 25mg + MTX                          |
|       |           |   | 66 52.8 8.1 5.5 37.6 1.4                | 66 52.8 8.1 5.5 37.6 1.4                | 66 52.8 8.1 5.5 37.6 1.4                | 66 52.8 8.1 5.5 37.6 1.4                |
|       |           |   | PEF 50mg + MTX                          | PEF 50mg + MTX                          | PEF 50mg + MTX                          | PEF 50mg + MTX                          |
|       |           |   | 78 52.3 8 5.6 37.8 1.3                  | 78 52.3 8 5.6 37.8 1.3                  | 78 52.3 8 5.6 37.8 1.3                  | 78 52.3 8 5.6 37.8 1.3                  |
|       |           |   | PEF 100mg + MTX                         | PEF 100mg + MTX                         | PEF 100mg + MTX                         | PEF 100mg + MTX                         |
|       |           |   | 84 54.5 7.5 5.6 39.4 1.3                | 84 54.5 7.5 5.6 39.4 1.3                | 84 54.5 7.5 5.6 39.4 1.3                | 84 54.5 7.5 5.6 39.4 1.3                |
|       |           |   | PEF 150mg + MTX                         | PEF 150mg + MTX                         | PEF 150mg + MTX                         | PEF 150mg + MTX                         |
|       |           |   | 78 54.2 7.3 5.6 38.8 1.3                | 78 54.2 7.3 5.6 38.8 1.3                | 78 54.2 7.3 5.6 38.8 1.3                | 78 54.2 7.3 5.6 38.8 1.3                |
| Kavanaugh 2017 (DARWIN 2) [26] | Placebo | 72 | 52 10 6.22 42 1.8 | 72 52 9 6.03 41 1.8 | 72 52 9 6.09 42 1.8 | 72 52 10 6.22 42 1.8 |
|       |           |   | FILGO 50mg OD                           | FILGO 50mg OD                           | FILGO 50mg OD                           | FILGO 50mg OD                           |
|       |           |   | 72 52 9 6.03 41 1.8                    | 72 52 9 6.03 41 1.8                    | 72 52 9 6.03 41 1.8                    | 72 52 9 6.03 41 1.8                    |
|       |           |   | FILGO 100mg OD                          | FILGO 100mg OD                          | FILGO 100mg OD                          | FILGO 100mg OD                          |
|       |           |   | 70 53 9 6.18 44 1.8                    | 70 53 9 6.18 44 1.8                    | 70 53 9 6.18 44 1.8                    | 70 53 9 6.18 44 1.8                    |
|       |           |   | FILGO 200mg OD                          | FILGO 200mg OD                          | FILGO 200mg OD                          | FILGO 200mg OD                          |
|       |           |   | 69 52 9 6.09 42 1.8                    | 69 52 9 6.09 42 1.8                    | 69 52 9 6.09 42 1.8                    | 69 52 9 6.09 42 1.8                    |
| Taylor 2017 (RA-BEAM) [27] | Placebo + MTX | 488 | 53 10 5.7 38 1.55 45 | 488 53 10 5.7 38 1.55 45 | 488 53 10 5.7 38 1.55 45 | 488 53 10 5.7 38 1.55 45 |
|       |           |   | BARI 4mg + MTX                          | BARI 4mg + MTX                          | BARI 4mg + MTX                          | BARI 4mg + MTX                          |
|       |           |   | 487 54 10 5.8 38 1.57 43                | 487 54 10 5.8 38 1.57 43                | 487 54 10 5.8 38 1.57 43                | 487 54 10 5.8 38 1.57 43                |
|       |           |   | ADA 40mg Q2W + MTX                      | ADA 40mg Q2W + MTX                      | ADA 40mg Q2W + MTX                      | ADA 40mg Q2W + MTX                      |
|       |           |   | 330 53 10 5.8 38 1.59 44                | 330 53 10 5.8 38 1.59 44                | 330 53 10 5.8 38 1.59 44                | 330 53 10 5.8 38 1.59 44                |
| Vanhoutte 2017 [28]  | Study 1: Placebo + MTX | 12 | 47 5.6 6.3 2.0 | 12 52 7.5 6.4 2.1 | 12 52 7.5 6.4 2.1 | 12 52 7.5 6.4 2.1 |
|       |           |   | Study 1: FILGO 200mg OD + MTX           | Study 1: FILGO 200mg OD + MTX           | Study 1: FILGO 200mg OD + MTX           | Study 1: FILGO 200mg OD + MTX           |
|       |           |   | 12 52 7.5 6.4 2.1                      | 12 52 7.5 6.4 2.1                      | 12 52 7.5 6.4 2.1                      | 12 52 7.5 6.4 2.1                      |
|       |           |   | Study 1: FILGO 100mg BID + MTX          | Study 1: FILGO 100mg BID + MTX          | Study 1: FILGO 100mg BID + MTX          | Study 1: FILGO 100mg BID + MTX          |
|       |           |   | 12 53 9.7 6.6 1.9                     | 12 53 9.7 6.6 1.9                     | 12 53 9.7 6.6 1.9                     | 12 53 9.7 6.6 1.9                     |
|       |           |   | Study 2: Placebo + MTX                 | Study 2: Placebo + MTX                 | Study 2: Placebo + MTX                 | Study 2: Placebo + MTX                 |
|       |           |   | 17 44 4.4 6.1 1.7                     | 17 44 4.4 6.1 1.7                     | 17 44 4.4 6.1 1.7                     | 17 44 4.4 6.1 1.7                     |
|       |           |   | Study 2: FILGO 30mg OD + MTX           | Study 2: FILGO 30mg OD + MTX           | Study 2: FILGO 30mg OD + MTX           | Study 2: FILGO 30mg OD + MTX           |
|       |           |   | 17 52 8.0 5.7 1.5                     | 17 52 8.0 5.7 1.5                     | 17 52 8.0 5.7 1.5                     | 17 52 8.0 5.7 1.5                     |
|       |           |   | Study 2: FILGO 75mg OD + MTX           | Study 2: FILGO 75mg OD + MTX           | Study 2: FILGO 75mg OD + MTX           | Study 2: FILGO 75mg OD + MTX           |
|       |           |   | 22 50 7.9 5.9 1.4                     | 22 50 7.9 5.9 1.4                     | 22 50 7.9 5.9 1.4                     | 22 50 7.9 5.9 1.4                     |
| Study 2: FILGO 150mg OD + MTX | 15 | 55 | 10.0 | 6.4 | 1.8 |
| Study 2: FILGO 300mg OD + MTX | 20 | 51.5 | 9.7 | 5.8 | 1.8 |
| Westhovens 2017 (DARWIN 1) [29] | Placebo + MTX | 86 | 52 | 8 | 5.98 | 42 | 1.7 |
| FILGO 50mg OD + MTX | 82 | 53 | 7 | 6.08 | 41 | 1.7 |
| FILGO 100mg OD + MTX | 85 | 52 | 8 | 6.14 | 43 | 1.7 |
| FILGO 200mg OD + MTX | 86 | 55 | 9 | 6.22 | 43 | 1.8 |
| FILGO 25mg BID + MTX | 86 | 52 | 9 | 6.05 | 41 | 1.7 |
| FILGO 50mg BID + MTX | 85 | 55 | 8 | 6.1 | 42 | 1.8 |
| FILGO 100mg BID + MTX | 84 | 54 | 10 | 6.14 | 42 | 1.8 |
| Burmester 2018 (SELECT-NEXT) [30] | Placebo + csDMARD | 221 | 56 | 7.2 | 5.6 | 37.8 | 1.4 |
| UPA 15mg + csDMARD | 221 | 55.3 | 7.3 | 5.7 | 38.3 | 1.5 |
| UPA 30mg + csDMARD | 219 | 55.8 | 7.3 | 5.7 | 38.6 | 1.5 |
| Fleischmann 2018 (SELECT-COMpare) [31, 32] | Placebo + MTX | 651 | 54 | 8 | 5.8 | 40 | 1.6 |
| UPA 15mg OD + MTX | 651 | 54 | 8 | 5.8 | 40 | 1.6 |
| ADA 40mg Q2W + MTX | 327 | 54 | 8 | 5.9 | 40 | 1.6 |
| Genovese 2018 (SELECT-BEYOND) [33] | Placebo + csDMARD | 169 | 57.6 | 14.5 | 5.8 | 41 | 1.6 |
| UPA 15mg + csDMARD | 164 | 56.3 | 12.4 | 5.9 | 41.7 | 1.7 |
| UPA 30mg + csDMARD | 165 | 57.3 | 12.7 | 5.8 | 40.1 | 1.6 |
| Kivitz ACR 2018 [34] | Placebo + MTX | 22 | 54 | 5.51 | 1.5 |
| Study                          | Treatment                        | N  | % females | ACR20   | ESR   | CRP   |
|-------------------------------|----------------------------------|----|----------|---------|-------|-------|
| **GS-9876 10mg OD + MTX**     | 20                               | 56 | 5.65     | 1.5     |
| **GS-9876 30mg OD + MTX**     | 20                               | 58 | 5.78     | 1.4     |
| **Hu 2018 (RA-BALANCE) [35, 36]** | Placebo + MTX                  | 145| 48.9     | 9.1     | 1.52  |
|                               | BARI 4mg + MTX                   | 145| 49.5     | 10.7    | 1.59  |
| **Smolen 2018 (SELECT-MONOTHERAPY) [37, 38]** | Continued MTX              | 216| 55.3     | 5.8     | 5.6   | 37.8  | 1.5   |
|                               | UPA 15mg OD                      | 217| 54.5     | 7.5     | 5.6   | 38    | 1.5   |
|                               | UPA 30mg OD                      | 215| 53.1     | 6.5     | 5.6   | 38.4  | 1.5   |
| **Tanaka 2018a (SELECT-SUNRISE) [39, 40]** | Placebo + csDMARDs            | 49 | 54.3     | 2.1     | 5.2   | 31.0  | 1.0   |
|                               | UPA 7.5mg + csDMARDs            | 49 | 55.8     | 4.0     | 5.1   | 29.1  | 0.9   |
|                               | UPA 15mg + csDMARDs             | 49 | 56.0     | 2.9     | 5.1   | 32.1  | 1.0   |
|                               | UPA 30mg + csDMARDs             | 50 | 54.7     | 2.8     | 5.0   | 29.8  | 0.9   |
| **Tanaka & Takeuchi 2018 [41, 42]** | Placebo ± csDMARDs           | 101| 56.3     | 6.98    | 5.43  | 33.2  | 1.00  |
|                               | PEF 100mg OD ± csDMARDs         | 104| 54.1     | 8.75    | 5.29  | 31.3  | 0.92  |
|                               | PEF 150mg OD ± csDMARDs         | 102| 55.0     | 10.39   | 5.41  | 31.6  | 1.03  |
|                               | Open-label ETA 50mg QW ± csDMARDs| 200| 54.5     | 9.56    | 5.35  | 31.4  | 0.97  |
| **Takeuchi 2018 [43, 44]**    | Placebo + MTX                   | 170| 55.3     | 4.3     | 5.41  | 31.56 | 1.05  | 28.4  |
|                               | PEF 100mg OD + MTX              | 174| 58.5     | 4.4     | 5.21  | 29.88 | 0.91  | 25.2  |
|                               | PEF 150mg OD + MTX              | 174| 56.2     | 4.4     | 5.36  | 31.51 | 1.025 | 25    |
| **van Vollenhoven ACR 2018 (SELECT-)** | Placebo + MTX                 | 314| 53.3     | 2.6     | 5.9   | 1.6   | 13.3  |
|                               | UPA 15mg + MTX                  | 317| 51.9     | 2.9     | 5.9   | 1.6   | 18.1  |
| Study                          | Treatment                      | N  | ADA   | ETA   | Q2W   | OD   | BID   |
|-------------------------------|--------------------------------|----|-------|-------|-------|------|-------|
| EARLY) [45]*                  | UPA 30mg + MTX                 | 314| 54.9  | 2.8   | 5.8   | 1.5  | 17.2  |
| Tanaka 2019 [48]              | TOFA 11mg modified release OD + MTX | 104| 57.1  | 9.5   | 5.1   | 1.0  |       |
|                               | TOFA 5mg immediate release BID + MTX | 105| 58.9  | 9.4   | 5.0   | 0.9  |       |
| van der Heijde 2019 (ORAL Scan) [10] | TOFA 5mg + MTX                 | 321| 53.7  | 8.9   | 5.22  | 1.41 | 31.1  |
|                               | TOFA 10mg + MTX                | 316| 52    | 9     | 5.2   | 1.39 | 37.3  |
|                               | Placebo->TOFA 5mg + MTX        | 81 | 53.2  | 8.8   | 5.14  | 1.4  | 35    |
|                               | Placebo->TOFA 10mg + MTX       | 79 | 52.1  | 9.5   | 5.18  | 1.23 | 30.1  |

*Data extracted from clinicaltrials.gov database (NCT02706873); ADA: Adalimumab; ETA: etanercept; Q2W: every other week; OD: once daily; BID: twice daily; TOFA: tofacitinib, BARI: baricitinib; UPA: upadacitinib;
**Table S2.3.2: Psoriatic arthritis**

| Study                     | Treatment                             | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean SJC66 | Mean TJC68 | Mean EGA | Mean CRP (mg/dL) | PASI (mean) | Dactylitis (%) | Enthesitis (%) | Mean HAQ | Mean mTSS |
|---------------------------|---------------------------------------|---------------------|------------------|-----------------------------|------------|------------|----------|----------------|-------------|---------------|---------------|---------|----------|
| Mease 2017 (OPAL Broaden) [49] | Placebo ± csDMARD | 105                | 47.7             | 6.4                         | 11.5       | 20.6       | 53.8      | 6.6             | 55          | 62           | 1.1          | 17.6    |          |
|                           | TOFA 5mg BID ± csDMARD                | 107                | 49.4             | 7.3                         | 12.9       | 20.5       | 54.6      | 5.6             | 57          | 70           | 1.2          | 17.1    |          |
|                           | TOFA 10mg BID ± csDMARD               | 104                | 46.9             | 5.4                         | 11.7       | 20.3       | 55.2      | 7.8             | 58          | 62           | 1.1          | 10.4    |          |
|                           | ADA 40mg Q2W ± csDMARD                | 106                | 47.4             | 5.3                         | 9.8        | 12.9       | 50.5      | 7               | 55          | 72           | 1.1          | 14.4    |          |
| Gladman 2017 (OPAL Beyond) [50] | Placebo ± csDMARD                     | 131                | 49               | 9.4                         | 10.5       | 19.8       | 53.7      | 0.44            | 7.1         | 48           | 71           | 1.3     |          |
|                           | TOFA 5mg BID ± csDMARD                | 131                | 49.5             | 9.6                         | 12.1       | 20.5       | 53.5      | 0.57            | 7.6         | 50           | 63           | 1.3     |          |
|                           | TOFA 10mg BID ± csDMARD               | 132                | 51.3             | 9.1                         | 12.8       | 25.5       | 55.8      | 0.49            | 8.8         | 49           | 75           | 1.4     |          |
| Mease 2018d (EQUATOR) [51] | Placebo ± csDMARD                     | 66                 | 50               | 7                           | 12.7       | 21.6       | 66        | 10.9            | 6.9         |              |              | 1.36    |          |
|                           | FILGO 200mg OD ± csDMARD              | 65                 | 49               | 7                           | 11.6       | 18.3       | 66.1      | 13.9            | 6.5         |              |              | 1.43    |          |

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Table S2.3.3: Ankylosing spondylitis

| Study                  | Treatment                        | No. of patients (n) | Mean age (years) | Mean disease duration (years) | HLA-B27 pos. (%) | ASDAS  | BASDAI | BASFI | BASMI | SPARCC spine | SPARCC sacroiliac joint | Enthesitis (%) | MASES score | CRP (mg/L) |
|------------------------|----------------------------------|---------------------|------------------|-------------------------------|------------------|--------|--------|-------|-------|--------------|--------------------------|----------------|-------------|------------|
| Van der Heijde 2017 [52] | Placebo ± csDMARD               | 51                  | 41.9             | 3.0                           | 86.3             | 3.7    | 6.3    | 5.7   | 4.0   | 16.2         | 9.6                      |                |             |            |
|                        | TOFA 2mg BID ± csDMARD           | 52                  | 41.8             | 4.1                           | 84.6             | 3.6    | 7.0    | 5.5   | 4.0   | 17.1         | 12.8                     |                |             |            |
|                        | TOFA 5mg BID ± csDMARD           | 52                  | 41.2             | 3.5                           | 84.6             | 3.7    | 6.5    | 5.8   | 3.8   | 19.6         | 13.5                     |                |             |            |
|                        | TOFA 10mg BID ± csDMARD          | 52                  | 41.6             | 1.5                           | 94.2             | 3.7    | 6.9    | 5.7   | 3.9   | 17.0         | 10.7                     |                |             |            |
| Van der Heijde 2018 [53] | Placebo ± csDMARD               | 58                  | 42               | 8                             | 88               | 4.2    | 7.0    | 6.9   | 5.3   | 13.8         | 5.3                      | 81             | 2.9         | 21.2       |
|                        | FILGO 200mg OD ± csDMARD         | 58                  | 41               | 6                             | 88               | 4.2    | 6.9    | 7.0   | 5.1   | 19.0         | 6.8                      | 83             | 2.8         | 19.6       |

csDMARD: conventional synthetic disease modifying drug; BID: twice daily; OD: once daily; FILGO: filgotinib; TOFA: tofacitinib; HLA: human leukocyte antigen; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; SPARCC: Spondyloarthritis Research Consortium of Canada Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; CRP: C-reactive protein;
## Table S2.3.4: Systemic Lupus Erythematosus

| Study            | Treatment                        | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean SELENA-SLEDAI | Mean SLEDAI-2K | Steroids at baseline (%) |
|------------------|----------------------------------|---------------------|------------------|------------------------------|--------------------|----------------|--------------------------|
| **Kahl 2016 [54]** | Placebo ± csDMARD                | 11                  | 36.9             | 6.1                          | 9.8                |                | 91                       |
|                  | Solcitinib 50mg BID ± csDMARD    | 9                   | 38.0             | 6.5                          | 9.9                |                | 67                       |
|                  | Solcitinib 100mg BID ± csDMARD   | 10                  | 43.1             | 5.4                          | 11.1               |                | 100                      |
|                  | Solcitinib 200mg BID ± csDMARD   | 10                  | 37.3             | 5.8                          | 12.0               |                | 100                      |
|                  | Solcitinib 400mg BID ± csDMARD   | 10                  | 47.5             | 8.6                          | 10.6               |                | 90                       |
| **Wallace 2018 [55]** | Placebo ± csDMARD               | 105                 | 44.9             | 9.7                          | 8.9                | 8.9            | 73                       |
|                  | BARI 2mg OD ± csDMARD            | 105                 | 43.2             | 11.8                         | 8.8                | 8.8            | 75                       |
|                  | BARI 4mg OD ± csDMARD            | 104                 | 45.0             | 11.5                         | 9.0                | 9.0            | 71                       |

csDMARD: conventional synthetic disease modifying drug; BID: twice daily; OD: once daily
### Table S2.3.5: Psoriasis

| Study              | Treatment               | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean PASI | Mean BSA | PGA mild (%) | PGA moderate (%) | PGA severe (%) | Mean DLQI |
|--------------------|-------------------------|---------------------|------------------|------------------------------|-----------|---------|--------------|------------------|----------------|-----------|
| Papp 2012 [56]     | Placebo                 | 50                  | 43.9             | 17.2                         | 21.5      | 29.8    | 12.0          | 82.0             | 6.0            |           |
|                    | TOFA 2mg BID            | 49                  | 45.7             | 16.5                         | 21.5      | 29.8    | 16.3          | 79.6             | 4.1            |           |
|                    | TOFA 5mg BID            | 49                  | 44.0             | 16.4                         | 21.2      | 30.1    | 22.4          | 67.3             | 10.2           |           |
|                    | TOFA 15mg BID           | 49                  | 43.6             | 16.9                         | 22.6      | 31.9    | 18.8          | 68.8             | 12.5           |           |
| Bachelez 2015 [57] | Placebo                 | 107                 | 46.0             | 16.0                         | 21.0      | 26.0    | 3             | 82               | 15            | 11.5      |
|                    | TOFA 5mg BID            | 329                 | 44.0             | 17.0                         | 21.0      | 28.0    | 2             | 80               | 18            | 12.0      |
|                    | TOFA 10mg BID           | 330                 | 44.0             | 18.0                         | 19.4      | 28.0    | 1             | 83               | 16            | 13.0      |
|                    | ETA 50mg twice weekly   | 335                 | 42.0             | 17.0                         | 19.5      | 25.0    | 1             | 81               | 18            | 12.0      |
| Bissonnette 2014 [58] | TOFA 5mg BID          | 331                 | 45               | 15.0                         | 18.0      | 22.0    | 0.9           | 84.6             | 14.5          | 12.0      |
|                    | TOFA 10mg BID           | 335                 | 47               | 16.0                         | 18.6      | 21.0    | 0.9           | 86.9             | 12.2          | 12.0      |
| Papp 2015 [59]     | Placebo                 | 29                  | 53.1             | 17.4                         | 21.7      |         |               |                  |                |           |
|                    | PEF 10mg BID            | 19                  | 39.1             | 11.8                         | 14.6      |         |               |                  |                |           |
|                    | PEF 25mg BID            | 21                  | 47.5             | 15.4                         | 22.1      |         |               |                  |                |           |
|                    | PEF 60mg BID            | 19                  | 46.4             | 14.1                         | 19.1      |         |               |                  |                |           |
|                    | PEF 100mg BID           | 17                  | 51.1             | 17.0                         | 19.0      |         |               |                  |                |           |
|                    | PEF 50mg OD             | 19                  | 49.1             | 15.9                         | 24.1      |         |               |                  |                |           |
| Study 1: Placebo       | 177 | 45.0 | 15.7 | 19.8 | 25.0 | 0   | 95.5 | 4.5 | 14 |
|-----------------------|-----|------|------|------|------|-----|------|-----|----|
| Study 1: TOFA 5mg BID | 363 | 46.0 | 16.0 | 19.5 | 24   | 0.3 | 88.2 | 11.6| 12 |
| Study 1: TOFA 10mg BID| 360 | 46.0 | 16.9 | 20.4 | 26.5 | 0.3 | 88.9 | 10.8| 12 |
| Study 2: Placebo      | 196 | 45.0 | 18.4 | 20.1 | 23.6 | 0.5 | 80.6 | 18.9| 13 |
| Study 2: TOFA 5mg BID | 382 | 47.0 | 15.2 | 20.7 | 26.0 | 0   | 82.5 | 17.3| 12 |
| Study 2: TOFA 10mg BID| 381 | 44.0 | 15.2 | 19.3 | 24.0 | 0.3 | 81.6 | 18.4| 12 |

| Placebo               | 12  | 49.1 | 8.9  | 7.6  |      |     |      |     | 5.0|
| Itacitinib 100mg OD   | 9   | 47.8 | 9.6  | 7.8  |      |     |      |     | 4.0|
| Itacitinib 200mg OD   | 9   | 46.9 | 8.6  | 6.8  |      |     |      |     | 7.0|
| Itacitinib 200mg BID  | 9   | 52.8 | 9.8  | 8.5  |      |     |      |     | 12.0|
| Itacitinib 600mg OD   | 11  | 46.0 | 12.4 | 9.9  |      |     |      |     | 7.0|

| Placebo               | 34  | 46.7 | 16.4 | 19.1 | 23.2 | 52.9| 47.1 | 0   |     |
| BARI 2mg              | 32  | 47.8 | 15.0 | 21.4 | 30.8 | 62.5| 34.4 | 3.1 |     |
| BARI 4mg              | 72  | 47.2 | 19.9 | 20.6 | 28.6 | 65.3| 33.3 | 1.4 |     |
| BARI 8mg              | 64  | 47.4 | 16.6 | 20.2 | 28.2 | 59.4| 39.1 | 1.6 |     |
| BARI 10mg             | 69  | 47.4 | 16.6 | 19.0 | 24.5 | 53.6| 44.9 | 1.4 |     |

| Vehicle BID           | 71  | 48.8 | 8.5  | 6.5  | 29.6 | 70.4| 9.3  |     |     |
| 2% TOFA BID           | 71  | 47.6 | 9.5  | 7.6  | 28.2 | 71.8| 10.6 |     |     |
| 1% TOFA BID           | 70  | 50.4 | 8.5  | 6.4  | 30.0 | 70.0| 8.6  |     |     |
| Vehicle OD            | 74  | 48.9 | 9.6  | 8.0  | 27.0 | 73.0| 10.2 |     |     |
|                  | 2% TOFA OD | 1% TOFA OD | Zhang 2017 [64] | Papp 2018 [65] |
|------------------|------------|------------|----------------|----------------|
|                  |            |            | Placebo        | Placebo        |
|                  | 70         | 74         | 88             | 45             |
|                  | 50.7       | 47.8       | 41.7           | 46             |
|                  | 9.9        | 10.1       | 13.2           | 18             |
|                  | 7.8        | 8.4        | 26.1           | 19             |
|                  | 32.9       | 27.0       | 35.8           | 24             |
|                  | 67.1       | 73.0       | 76.1           | 24             |
|                  |            |            | 23.9           | 13             |
|                  |            |            | 12.3           |                |
|                  |            |            | TOFA 5mg BID   |                |
|                  | 88         | 88         | 40.7           | 44             |
|                  |            |            | 15.6           | 41             |
|                  |            |            | 25.3           | 18             |
|                  |            |            | 37.4           | 17             |
|                  |            |            | 87.5           | 20             |
|                  |            |            | 12.5           |                |
|                  |            |            | 13.5           |                |
|                  |            |            | TOFA 10mg BID  |                |
|                  | 90         | 90         | 41.0           | 45             |
|                  |            |            | 14.4           | 46             |
|                  |            |            | 25.3           | 13             |
|                  |            |            | 36.4           | 18             |
|                  |            |            | 85.6           | 24             |
|                  |            |            | 14.4           |                |
|                  |            |            | 14.1           |                |
|                  |            |            |                |                |
|                  |            |            | BMS-986165 3mg EOD | 44         |
|                  |            |            | 44             | 41             |
|                  |            |            | 18             | 17             |
|                  |            |            | 19             | 19             |
|                  |            |            | 24             | 24             |
|                  |            |            | 20             |                |
|                  |            |            | 12             |                |
|                  |            |            | BMS-986165 3mg OD | 44         |
|                  |            |            | 44             | 45             |
|                  |            |            | 13             | 18             |
|                  |            |            | 18             | 23             |
|                  |            |            | 23             |                |
|                  |            |            | 12             |                |
|                  |            |            | BMS-986165 3mg BID | 45         |
|                  |            |            | 45             | 46             |
|                  |            |            | 13             | 13             |
|                  |            |            | 19             | 24             |
|                  |            |            | 24             |                |
|                  |            |            | 13             |                |
|                  |            |            | BMS-986165 6mg BID | 45         |
|                  |            |            | 45             | 43             |
|                  |            |            | 15             | 15             |
|                  |            |            | 18             | 18             |
|                  |            |            | 25             |                |
|                  |            |            | 11             |                |
|                  |            |            | BMS-986165 12mg OD | 44         |
|                  |            |            | 44             | 47             |
|                  |            |            | 20             | 20             |
|                  |            |            | 18             | 18             |
|                  |            |            | 21             |                |
|                  |            |            | 13             |                |
Table S2.3.6: Alopecia & Atopic Dermatitis

| Study                      | Treatment                          | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean EASI | Mean BSA | PGA mild (%) | PGA moderate (%) | PGA severe (%) | Itch severity item |
|----------------------------|------------------------------------|---------------------|------------------|-------------------------------|-----------|----------|--------------|-----------------|-----------------|-------------------|
| Guttman-Yassky 2018 [66]   | Placebo                            | 142                 |                  |                               |           |          |              |                 |                 |                   |
|                            | PF-06651600 200mg OD (4 weeks) / 50mg OD (20 weeks) |                     |                  |                               |           |          |              |                 |                 |                   |
|                            | PF-06700841 60mg OD (4 weeks) /30mg OD (20 weeks) |                     |                  |                               |           |          |              |                 |                 |                   |
| Bissonette 2016 [67]       | Topical TOFA 2% BID                 | 35                  | 32.4             | 21                            | 14.7      | 6.4      | 29           | 71              | 0               | 6.5               |
|                            | Topical Vehicle BID                | 34                  | 30.4             | 22                            | 14.5      | 7.1      | 26           | 74              | 0               | 5.5               |
| De Bruin-Weller 2018 [68, 69] | Placebo                            | 41                  | 39.9             | 26.8                          | 32.6      | 45.7     | 44           | 56              | 6.5             |
|                            | UPA 7.5mg OD                       | 42                  | 41.5             | 30.4                          | 31.4      | 46.9     | 69           | 31              | 6.8             |
|                            | UPA 15mg OD                        | 42                  | 38.5             | 22.6                          | 31.4      | 50.6     | 45           | 55              | 6.4             |
|                            | UPA 30mg OD                        | 42                  | 39.9             | 24.2                          | 28.2      | 42.1     | 74           | 26              | 6.3             |
| Guttman-Yassky 2018 [70]   | Placebo + topical steroids         | 49                  | 35               | 17.7                          | 22.1      |          |              |                 |                 | 7                 |
|                            | BARI 2mg OD + topical steroids     | 37                  | 42               | 26.4                          | 22.1      |          |              |                 |                 | 6                 |
|                            | BARI 4mg OD + topical steroids     | 38                  | 32.5             | 22.0                          | 19.5      |          |              |                 |                 | 6.5               |
| Nakagawa 2018 [71]         | Vehicle                            | 31                  | 31.6             | 25.0                          | 16        | 24       | 84           | 16              | 5.4             |
|                            | Topical JTE-052 0.25%              | 69                  | 31.5             | 23.4                          | 17.2      | 24.5     | 88           | 12              | 5.1             |
|                      |       |     |    |    |    |       |     |
|----------------------|-------|-----|----|----|----|-------|-----|
| Topical JTE-052 0.5% | 65    | 29.5| 20.9| 16.6| 23.8| 94    | 6   |
| Topical JTE-052 1%  | 66    | 28.6| 20.8| 17.8| 25.3| 85    | 15  |
| Topical JTE-052 3%  | 65    | 32.3| 25.2| 16.5| 24.5| 86    | 14  |
| Topical tacrolimus  | 30    | 33.1| 23.0| 16.7| 24.1| 87    | 13  |
| Study            | Treatment                              | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean CRP (mg/L) | Mean Mayo score | Fecal calprotectin (mg/kg) | Rectosigmoid involvement (%) | Left-sided involvement (%) | Extensive involvement (%) |
|------------------|----------------------------------------|---------------------|------------------|-------------------------------|----------------|-----------------|---------------------------|----------------------------|-----------------------------|---------------------------|
| Sandborn 2012 [72] | Placebo ± Mesalamine                   | 48                  | 42.5             | 8.8                           | 9.7            | 8.2             | 1733                      | 30                         | 26                          | 43                        |
|                  | TOFA 0.5mg BID ± Mesalamine            | 31                  | 43.8             | 8.8                           | 18.8           | 8.6             | 1440                      | 43                         | 27                          | 30                        |
|                  | TOFA 3mg BID ± Mesalamine              | 33                  | 42.5             | 8.9                           | 12.6           | 8.3             | 1474                      | 28                         | 34                          | 38                        |
|                  | TOFA 10mg BID ± Mesalamine             | 33                  | 43.2             | 10.9                          | 11.3           | 8.0             | 1145                      | 23                         | 35                          | 42                        |
|                  | TOFA 15mg BID ± Mesalamine             | 49                  | 41.2             | 7.6                           | 17.1           | 8.0             | 1523                      | 39                         | 24                          | 37                        |
| Sandborn 2017 [73] | OCTAVE Induction 1: Placebo            | 122                 | 41.8             | 6.0                           | 4.7            | 9.1             | 15.6                      | 30.3                       | 54.1                        |                          |
|                  | OCTAVE Induction 1: TOFA 10mg BID      | 476                 | 41.3             | 6.5                           | 4.4            | 9.0             | 13.7                      | 33.3                       | 53.1                        |                          |
|                  | OCTAVE Induction 2: Placebo            | 112                 | 40.4             | 6.2                           | 5.0            | 8.9             | 14.4                      | 35.1                       | 50.5                        |                          |
|                  | OCTAVE Induction 2: TOFA 10mg BID      | 429                 | 41.1             | 6.0                           | 4.6            | 9.0             | 15.7                      | 34.8                       | 49.3                        |                          |
|                  | OCTAVE Sustain: Placebo                | 198                 | 43.4             | 7.2                           | 1.0            | 3.3             | 10.6                      | 34.3                       | 54.5                        |                          |
|                  | OCTAVE Sustain: TOFA 5mg BID           | 198                 | 41.9             | 6.5                           | 0.7            | 3.3             | 14.3                      | 33.7                       | 52.0                        |                          |
|                  | OCTAVE Sustain: TOFA 10mg BID          | 197                 | 42.9             | 6.8                           | 0.9            | 3.4             | 16.8                      | 30.6                       | 52.6                        |                          |
| Sandborn 2018 [74, 75] | Placebo                              | 46                  | 40               | 5.19                          | 5.4            | 9.3             | 2100                      | 0                          | 41.3                        | 58.7                       |
|                  | UPA 7.5mg OD                           | 47                  | 41               | 6.59                          | 4.9            | 9.0             | 1576                      | 2.1                        | 44.7                        | 53.2                       |
| Treatment          | N | Age | HR | CR | Duration | LVEF | BNP | 6MWT | BDI | Zung |
|--------------------|---|-----|----|----|----------|------|-----|------|-----|------|------|
| UPA 15mg OD        | 49| 47  | 4.58| 8.7| 1843     | 0    | 51.0| 49.0 |     |      |      |
| UPA 30mg OD        | 52| 42  | 6.06| 6.7| 1648     | 0    | 44.2| 55.8 |     |      |      |
| UPA 45mg OD        | 56| 37  | 6.46| 6.3| 1666     | 0    | 46.4| 53.6 |     |      |      |
| Sands 2018 [76]    |   |     |     |    |          |      |     |      |     |      |      |
| Placebo            | 43| 39  | 4.0 | 5.87| 9.0      | 868  | 58.1| 41.9 |     |      |      |
| Peficitinib 25mg OD| 44| 45  | 6.0 | 4.08| 9.0      | 763  | 47.7| 52.3 |     |      |      |
| Peficitinib 75mg OD| 44| 43  | 6.5 | 2.43| 9.0      | 498  | 59.1| 40.9 |     |      |      |
| Peficitinib 150mg OD| 44| 44  | 5.0 | 3.39| 8.0      | 617  | 63.6| 36.4 |     |      |      |
| Peficitinib 75mg BID| 44| 38.5| 5.0 | 4.32| 8.0      | 613  | 52.3| 47.7 |     |      |
Table S2.3.8: Crohn’s disease

| Study        | Treatment   | No. of patients (n) | Mean age (years) | Mean disease duration (years) | Mean CRP (mg/L) | Mean Crohn's Disease Activity Index | Fecal calprotectin (mg/kg) | Ileal involvement (%) | Colonic involvement (%) | Ileocolonic involvement (%) | Upper gastrointestinal involvement (%) |
|--------------|-------------|---------------------|------------------|------------------------------|----------------|-------------------------------------|---------------------------|---------------------|----------------------|--------------------------|---------------------------------|
| Sandborn 2014 [77] | Placebo     | 34                  | 35.7             | 8.2                          | 17.1           | 306.4                               | 1422                      | 26                  | 41                   | 47                       | 0                               |
|              | TOFA 1mg BID| 36                  | 36.6             | 11.1                         | 18.3           | 300.3                               | 1409                      | 17                  | 56                   | 42                       | 3                               |
|              | TOFA 5mg BID| 34                  | 38.7             | 10.9                         | 17.5           | 297.7                               | 482                       | 9                   | 53                   | 32                       | 0                               |
|              | TOFA 15mg BID | 35              | 38.1             | 11.2                         | 26.1           | 308.0                               | 1175                      | 29                  | 49                   | 49                       | 0                               |
| Panés 2017 [78]   | Induction: Placebo | 91                | 37.2             | 10.9                         | 5.5            | 313                                 | 246                       | 11                  | 5.5                  | 27.5                     | 0                               |
|              | Induction: TOFA 5mg BID | 86            | 40.2             | 11.2                         | 5.9            | 314                                 | 398                       | 16.3                | 4.7                  | 14                       | 0                               |
|              | Induction: TOFA 10mg BID | 86           | 39.3             | 11.3                         | 5.5            | 320                                 | 430                       | 8.1                 | 5.8                  | 17.4                     | 0                               |
|              | Induction: TOFA 15mg BID | 16           | 41.3             | 11.1                         | 20.0           | 328                                 | 363                       | 6.3                 | 12.5                 | 18.8                     | 0                               |
|              | Maintenance: Placebo | 59            | 41.5             | 12.5                         | 3.7            | 140                                 | 212                       | 10.2                | 6.8                  | 25.4                     | 0                               |
|              | Maintenance: TOFA 5mg BID | 60           | 38.1             | 11.2                         | 2.7            | 131                                 | 277                       | 10.0                | 5.0                  | 21.7                     | 0                               |
|              | Maintenance: TOFA 10mg BID | 61           | 39.0             | 12.6                         | 3.2            | 129                                 | 322                       | 8.2                 | 4.9                  | 21.3                     | 0                               |
| Study                  | Treatment | Placebo | 3mg | 6mg | 12mg | 24mg | Placebo | 200mg OD |
|------------------------|-----------|---------|-----|-----|------|------|---------|----------|
| Sandborn 2017 / Panés 2018 [79-81] | UPA 3mg BID | 39 | 37 | 10.7 | 6.0 | 288.0 | 916.0 | 25.6 | 23.1 | 51.3 |
|                        | UPA 6mg BID | 37 | 39 | 8.8 | 11.7 | 296.0 | 1602.5 | 16.2 | 35.1 | 48.6 |
|                        | UPA 12mg BID | 36 | 41 | 9.1 | 16.6 | 280.0 | 1622.0 | 13.9 | 30.6 | 55.6 |
|                        | UPA 24mg BID | 36 | 44 | 14.1 | 5.9 | 277.5 | 1377.0 | 16.7 | 30.6 | 52.8 |
|                        | UPA 24mg OD | 35 | 41 | 10.8 | 7.4 | 305.0 | 814.0 | 28.6 | 28.6 | 42.9 |
| Vermeire 2017 [82]     | Placebo   | 44 | 35.1 | 6.8 | 19.8 | 298.6 | 264.0 | 16 | 14 | 70 |
|                        | FILGO 200mg OD | 130 | 37.4 | 8.8 | 14.2 | 291.3 | 270.5 | 18 | 22 | 59 |
### Section 3: Efficacy outcomes

#### Table S3.1: Rheumatoid Arthritis

| Study          | Treatment               | No. of patients (n) | Timepoint (weeks) | ACR20 (%) | ACR50 (%) | ACR70 (%) | DAS28 <2.6 (%) | CDAI ≤2.8 (%) | ACR/EULAR Boolean rem. (%) | ΔHAQ | ΔmTSS |
|----------------|-------------------------|---------------------|-------------------|-----------|-----------|-----------|----------------|----------------|----------------------------|------|-------|
| Kremer 2009 [1] | Placebo                 | 65                  |                   | 29.2      | 2.6       | 1.3       |                |                |                            | -0.3 |       |
|                | TOFA 5mg BID            | 61                  | 6                 | 70.5      | 12.2      | 4.88      |                |                |                            | -0.6 |       |
|                | TOFA 15mg BID           | 69                  |                   | 81.2      | 25.53     | 10.35     |                |                |                            | -0.7 |       |
|                | TOFA 30mg BID           | 69                  |                   | 76.8      | 24.15     | 13.11     |                |                |                            | -0.7 |       |
| Tanaka 2011a [2] | Placebo + MTX          | 28                  |                   | 14.3      | 14.3      | 3.6       |                |                |                            | -0.05|       |
|                | TOFA 1mg BID + MTX      | 28                  | 12                | 64.3      | 32.1      | 7.1       |                |                |                            | -0.4 |       |
|                | TOFA 3mg BID + MTX      | 27                  |                   | 77.8      | 44.4      | 14.8      |                |                |                            | -0.4 |       |
|                | TOFA 5mg BID + MTX      | 27                  |                   | 96.3      | 81.5      | 33.3      |                |                |                            | -0.5 |       |
|                | TOFA 10mg BID + MTX     | 26                  |                   | 80.8      | 57.7      | 34.6      |                |                |                            | -0.6 |       |
| Fleischmann 2012 [3] | Placebo               | 59                  | 12                | 23.73     | 10.17     | 3.39      | 3.6            |                |                            | -0.25|       |
|                | TOFA 1mg BID            | 54                  |                   | 31.48     | 11.11     | 5.56      | 7.7            |                |                            |       |       |
|                  | 51   | 49   | 61   | 57   | 53   | 122  | 243  | 245  | 69   | 70   | 68   | 71   | 74   | 75   | 80   |
|------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| **TOFA 3mg BID** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 5mg BID** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 10mg BID**|      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 15mg BID**|      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **ADA 40mg EOW** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **Fleischmann 2012 [4]** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **Placebo**      | 45.1 | 25.49| 11.76| 5.9  |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 3mg BID** | 61.22| 38.78| 14.29| 12.5 |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 5mg BID** | 72.13| 45.9 | 24.59| 14.8 |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 10mg BID**| 71.93| 50.88| 26.32| 19.3 |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 15mg BID**| 39.62| 20.75| 3.77 | 3.9  |      |      |      |      |      |      |      |      |      |      |      |
| **Kremer 2012 [5]** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **Placebo + MTX**|      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 1mg BID + MTX** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 3mg BID + MTX** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 5mg BID + MTX** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 10mg BID + MTX** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 15mg BID + MTX** |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| **TOFA 20mg**    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|                  | 53.8 | 20.8 | 20.8 | 5.3  |      |      |      |      |      |      |      |      |      |      |      |

**Notes:**
- BID: Twice a day
- MTX: Methotrexate
| Study                     | Treatment                        | N  | Y-axis | X-axis 1 | X-axis 2 | X-axis 3 | X-axis 4 | Change |
|---------------------------|----------------------------------|----|--------|----------|----------|----------|----------|--------|
| Van Vollenhoven 2012 [6]  | TOFA 5mg BID + MTX               | 204|        | 51.53    | 36.73    | 19.9     | 6.21     | -0.55  |
|                           | TOFA 10mg BID + MTX              | 201| 24     | 52.55    | 34.69    | 21.94    | 12.5     | -0.61  |
|                           | ADA 40mg EOW + MTX               | 204|        | 47.24    | 27.64    | 9.05     | 6.74     | -0.49  |
|                           | Placebo + MTX (Combination group)| 106|        | 28.3     | 12.26    | 1.89     | 1.09     | -0.24  |
| Burmester 2013 [7]        | Placebo + MTX                   | 132|        | 24.4     | 8.4      | 1.5      | 1.7      | 0      | -0.18  |
|                           | TOFA 5mg BID + MTX               | 133| 12     | 41.7     | 26.5     | 13.6     | 6.7      | 6.1    | -0.43  |
|                           | TOFA 10mg BID + MTX              | 134|        | 48.1     | 27.8     | 10.5     | 8.8      | 4.5    | -0.46  |
| Kremer 2013 [8]           | Placebo + DMARD                  | 159|        | 31.21    | 12.74    | 3.18     | 2.6      | -0.16  |
|                           | TOFA 5mg BID + DMARD             | 315| 24     | 52.73    | 33.76    | 13.18    | 8.5      | -0.44  |
|                           | TOFA 10mg BID + DMARD            | 318|        | 58.25    | 36.57    | 16.18    | 12.5     | -0.53  |
| Van der Heijde 2013 [9]   | Placebo + DMARD (Combination group)| 160|        | 25.32    | 8.44     | 1.3      |          |        |
|                           | Placebo + DMARD                  | 81 |        |          |          |          |          |        |
| Study                        | Treatment 1                           | n  | Treatment 2                           | n  | Treatment 3                           | n  | Treatment 4                           | n  |
|-----------------------------|--------------------------------------|----|--------------------------------------|----|--------------------------------------|----|--------------------------------------|----|
| DMARD (cross-over to TOFA 5mg BID + DMARD after 3/6 months) | Placebo + DMARD (cross-over to TOFA 10mg BID + DMARD after 3/6 months) | 79 | TOFA 5mg BID + DMARD                 | 321| TOFA 10mg BID + DMARD                 | 316|                                       |    |
|                             |                                       |    | 51.46                                |    | 32.36                                |    | 14.56                                |    |
| Lee 2014 [11]               | MTX                                  | 186|                                       |    |                                       |    |                                       |    |
|                             | TOFA 5mg BID                          | 373|                                       |    |                                       |    |                                       |    |
|                             | TOFA 10mg BID                         | 397|                                       |    |                                       |    |                                       |    |
|                             |                                       |    | 50.5                                 |    | 26.6                                 |    | 12                                   |    |
|                             |                                       |    |                                       |    |                                       |    |                                       |    |
| Tanaka 2015 [12]            | Placebo                              | 52 |                                       |    |                                       |    |                                       |    |
|                             | TOFA 1mg BID                          | 53 |                                       |    |                                       |    |                                       |    |
|                             | TOFA 3mg BID                          | 53 |                                       |    |                                       |    |                                       |    |
|                             | TOFA 5mg BID                          | 52 |                                       |    |                                       |    |                                       |    |
|                             | TOFA 10mg                             | 53 |                                       |    |                                       |    |                                       |    |
|                             |                                       |    | 15.4                                 |    | 7.7                                  |    | 7.5                                  |    |
|                             |                                       |    |                                       |    |                                       |    |                                       |    |

- MTX: Methotrexate
- TOFA: Tofacitinib
- BID: Twice a day
- DMARD: Disease-modifying antirheumatic drug
| Study                  | Treatment          | N  | Mean (SD)       | Median (SD) | Min-Max |
|-----------------------|--------------------|----|----------------|-------------|---------|
| Fleischmann 2015 [13] | TOFA 15mg BID      | 54 | 90.7 (72.2)     | 1.9         | -0.68   |
|                       | Placebo            | 41 | 28 (7)          | 2           | 7.3     | -0.12   |
|                       | DEC 25mg BID       | 41 | 39 (17)         | 7           | -0.24   |
|                       | DEC 50mg BID       | 41 | 61 (32)         | 12          | -0.5    |
|                       | DEC 100mg BID      | 40 | 65 (38)         | 18          | 35      | -0.52   |
|                       | DEC 150mg BID      | 41 | 66 (49)         | 22          | 36.6    | -0.64   |
| Genovese 2016a [14]   | Placebo + csDMARD | 176| 27 (8)          | 2           | 1.7     | -0.2    |
|                       | BARI 2mg + csDMARD | 174| 49 (20)         | 13          | 11      | 3       |
|                       | BARI 4mg + csDMARD | 177| 55 (28)         | 11          | 16      | 6       | 5.1     | -0.42   |
| Genovese 2016b [15]   | Placebo + MTX     | 50 | 46 (18)         | 6           | 14      | 4       | -0.4    |
|                       | UPA 3mg BID + MTX  | 50 | 62 (38)         | 22          | 36      | 12      | -0.6    |
|                       | UPA 6mg BID + MTX  | 50 | 68 (46)         | 28          | 36      | 14      | -0.7    |
|                       | UPA 12mg BID + MTX | 50 | 80 (50)         | 16          | 34      | 6       | -0.8    |
|                       | UPA 18mg BID       | 50 | 64 (40)         | 26          | 40      | 14      | -0.6    |
|                | + MTX |                |                |                |                |                |
|----------------|-------|----------------|----------------|----------------|----------------|----------------|
| **UPA 24mg QD**| 49    | 76             | 39             | 22             | 22             | 6              | -0.6           |
| **UPA + MTX**  | 71    | 16.9           | 7              | 2.8            | 5.6            | -0.6           |
| **Placebo + MTX** | 71  | 60.6           | 38             | 16.9           | 21.1           | -0.62          |
| **DEC 100mg OD + MTX** | 72 | 61.1           | 38.9           | 18.1           | 29.2           | -0.65          |
| **DEC 200mg OD + MTX** | 72 | 61.1           | 40.3           | 15.3           | 27.8           | -0.79          |
| **DEC 300mg OD + MTX** | 72 | 62.5           | 47.2           | 25             | 31.9           | -0.75          |
| **DEC 100mg BID + MTX** | 72 | 63             | 27.3           | 18.2           |                |                |
| **DEC 200mg BID + csDMARD** | 10 | 60             | 30             | 10             |                |                |
| **DEC 300mg BID + csDMARD** | 10 | 60             | 60             | 20             |                |                |
| **Placebo + csDMARD** | 12 | 25             | 8.3            | 8.3            |                |                |
| **UPA 3 mg + MTX** | 55    | 53             | 24             | 13             | 24             | 9              | -0.3           |
| **UPA + MTX**  | 56    | 34             | 16             | 4              | 13             | 7              | -0.2           |
| **Placebo**   | 56    | 34             | 16             | 4              | 13             | 7              | -0.2           |
| **UPA 3 mg + MTX** | 55 | 53             | 24             | 13             | 24             | 9              | -0.3           |

Genovese 2016c [16]

Genovese 2016d [17]

Kremer 2016 [18]
| Study               | Group                          | n  | UPA 6 mg + MTX | UPA 12 mg + MTX | UPA 18 mg + MTX | Placebo | Placebo + MTX | BARI 1mg OD + MTX | BARI 2mg OD + MTX | BARI 4mg OD + MTX | BARI 8mg OD + MTX | Placebo + csDMARD | BARI 2mg + csDMARD |
|---------------------|-------------------------------|----|----------------|----------------|----------------|---------|---------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| Takeuchi 2016 [19]  |                               |    |                |                |                |         | 56            | 10.7               | 10.7               | 10.7               | 10.7               | 10.7               | 10.7               |
|                     | Placebo                       | 56 | 58             | 67             | 67             | 56      | 12           | 5.4                | 3.1                | 1.8                | 1.8                | 3.1                | 3.1                |
|                     | PEF 25mg OD                   | 55 | 58             | 71             | 67             | 55      | 15           | 23.6               | 31.6               | 31.6               | 31.6               | 23.6               | 31.6               |
|                     | PEF 50mg OD                   | 57 | 58             | 71             | 67             | 57      | 15           | 23.6               | 31.6               | 31.6               | 31.6               | 23.6               | 31.6               |
|                     | PEF 100mg OD                  | 55 |                |                |                | 55      | 15           | 54.5               | 54.5               | 54.5               | 54.5               | 54.5               | 54.5               |
|                     | PEF 150mg OD                  | 58 |                |                |                | 58      | 15           | 65.5               | 65.5               | 65.5               | 65.5               | 65.5               | 65.5               |
| Tanaka 2016 [20]    | Placebo + MTX                | 49 |                |                |                | 49      | 12           | 0                  | 0                  | 0                  | 0                  | 0                  | 0                  |
|                     | BARI 1mg OD + MTX             | 24 |                |                |                | 24      | 12           | 0                  | 13                 | 10                 | 13                 | 13                 | 13                 |
|                     | BARI 2mg OD + MTX             | 24 |                |                |                | 24      | 12           | 0                  | 13                 | 10                 | 13                 | 13                 | 13                 |
|                     | BARI 4mg OD + MTX             | 24 |                |                |                | 24      | 12           | 0                  | 29                 | 29                 | 29                 | 29                 | 29                 |
|                     | BARI 8mg OD + MTX             | 24 |                |                |                | 24      | 12           | 0                  | 29                 | 29                 | 29                 | 29                 | 29                 |
| Dougados 2017 [21]  | Placebo + csDMARD             | 228| 12/24^a        | 39.47          | 3.07           | 228     | 12/24^a      | 12.72              | 0.44               | -0.3               | 0.70^a             | -0.3               | 0.70^a             |
|                     | BARI 2mg + csDMARD            | 229|                | 65.94          | 17.9           |         | 12/24^a      | 33.62              | 6.99               | -0.52              | 0.33^a             | 6.99               | -0.52              | 0.33^a             |
| Study                                      | Treatment                          | N   | ACP       | PGA        | ESR        | CRP        | Subjective | CDAI       |
|-------------------------------------------|------------------------------------|-----|-----------|------------|------------|------------|------------|------------|
| Fleischmann 2017a [22]                    | BARI 4mg + csDMARD                 | 227 | 61.67     | 33.48      | 18.06      | 6.61       | -0.52      | 0.15²      |
|                                           | TOFA 5mg BID + PLC                 | 384 | 64.8      | 38.3       | 18.2       | 21.1       | 10.2       | 7          | -0.52      |
|                                           | TOFA 5mg BID + MTX                 | 376 | 73.1      | 46         | 25         | 30.6       | 13.8       | 8.2        | -0.58      |
|                                           | ADA 40mg Q2W + MTX                 | 386 | 71        | 43.8       | 20.7       | 28         | 13.2       | 8.8        | -0.54      |
| Fleischmann 2017b (RA-BEGIN) [23]         | Placebo + MTX                      | 210 | 61.9      | 43.3       | 21.4       | 23.8       | 11         | -0.74      | 0.61       |
|                                           | BARI 4mg + Placebo                 | 159 | 76.7      | 59.7       | 42.1       | 40.3       | 21.4       | -1.04      | 0.39       |
|                                           | BARI 4mg + MTX                     | 215 | 78.1      | 63.3       | 39.5       | 40.5       | 22.3       | -1.03      | 0.29       |
| Genovese 2017 [24]                        | Placebo + HCO/SZP                  | 51  | 29.4      | 9.8        | 7.8        | 9.8        |            |            |
|                                           | PEF 25mg + HCO/SZP                 | 59  | 22        | 15.3       | 6.8        | 6.8        |            |            |
|                                           | PEF 50mg + HCO/SZP                 | 57  | 36.8      | 24.6       | 15.8       | 12.5       |            |            |
|                                           | PEF 100mg + HCO/SZP                | 58  | 48.3      | 27.6       | 19         | 22.8       |            |            |
|                                           | PEF 150mg + HCO/SZP                | 64  | 56.3      | 28.1       | 10.9       | 20.3       |            |            |
| Kivitz 2017 [25]                          | Placebo + MTX                      | 72  | 44.4      | 26.4       | 11.1       |            |            |            |
|                                           | PEF 25mg +                         | 66  | 43.9      | 18.2       | 9.1        |            |            |            |
| Study                                                                 | Treatment                         | N  | Median | IQR  | Mean | Median Difference | p Value |
|----------------------------------------------------------------------|-----------------------------------|----|--------|------|------|-------------------|---------|
| Kavanaugh 2017 (DARWIN 2) [26]                                       | Placebo                          | 72 | 29.2   | 11.1 | 6.9  | 2.8               | 1.4     |
|                                                                      | FILGO 50mg OD                    | 72 | 66.7   | 34.7 | 8.3  | 12.5              | 2.8     |
|                                                                      | FILGO 100mg OD                   | 70 | 65.7   | 37.1 | 18.6 | 14.3              | 5.7     |
|                                                                      | FILGO 200mg OD                   | 69 | 72.5   | 43.5 | 13   | 17.4              | 8.7     |
| Taylor 2017 (RA-BEAM) [27]                                          | Placebo + MTX                    | 488| 40.2   | 16.8 | 4.7  | 4                 | 2       |
|                                                                      | BARI 4mg + MTX                   | 487| 69.6   | 45   | 18.9 | 24                | 8       |
|                                                                      | ADA 40mg Q2W + MTX               | 330| 61.2   | 34.8 | 12.7 | 19                | 7       |
| Vanhoutte 2017 [28]                                                 | Study 1: Placebo + MTX           | 12 | 33.3   | 8.3  | 0    |                   | -0.11   |
|                                                                      | Study 1: FILGO 200mg OD + MTX    | 12 | 75.0   | 16.7 | 16.7 |                   | -0.57   |
| Study 1: FILGO 100mg BID + MTX | 12 | 91.7 | 33.3 | 25 | -0.52 |
| Study 2: Placebo + MTX | 17 | 41.2 | 5.9 | 5.9 | -0.31 |
| Study 2: FILGO 30mg OD + MTX | 17 | 35.3 | 11.8 | 11.8 | -0.15 |
| Study 2: FILGO 75mg OD + MTX | 22 | 54.5 | 27.3 | 13.6 | -0.47 |
| Study 2: FILGO 150mg OD + MTX | 15 | 40.0 | 0 | 0 | -0.26 |
| Study 2: FILGO 300mg OD + MTX | 20 | 65.0 | 45.0 | 25 | -0.68 |
| Westhovens 2017 (DARWIN 1) [29] | | | | | |
| Placebo + MTX | 86 | 44.19 | 15.12 | 8.14 | 6.98 | 2.33 | 3.49 | -0.38 |
| FILGO 50mg OD + MTX | 82 | 56.1 | 32.93 | 15.85 | 12.2 | 7.32 | 3.66 | -0.58 |
| FILGO 100mg OD + MTX | 85 | 63.53 | 37.65 | 21.18 | 22.35 | 8.24 | 3.53 | -0.65 |
| FILGO 200mg OD + MTX | 86 | 68.6 | 43.02 | 24.42 | 22.09 | 10.47 | 5.81 | -0.75 |
| FILGO 25mg BID + MTX | 86 | 56.98 | 27.91 | 13.95 | 15.12 | 10.47 | 4.65 | -0.59 |
| Study                                      | Treatment                               | N  | Week 12 | Week 26 | Week 34 | Week 40 | Week 52 | Week 60 | Week 72 | Week 84 | Adj. p-value |
|--------------------------------------------|-----------------------------------------|----|---------|---------|---------|---------|---------|---------|---------|---------|--------------|
| Burmester 2018 (SELECT-NEXT) [30]          | FILGO 50mg BID + MTX                    | 85 | 60      | 34.12   | 18.82   | 17.65   | 8.24    | 4.71    | -0.58   |         |              |
|                                            | FILGO 100mg BID + MTX                   | 84 | 78.57   | 54.76   | 30.95   | 35.71   | 17.86   | 9.52    | -0.84   |         |              |
|                                            | Placebo + csDMARD                        | 221| 36      | 15      | 6       | 10      | 3       | 4       | -0.26   |         |              |
|                                            | UPA 15mg + csDMARD                       | 221| 64      | 38      | 21      | 31      | 9       | 10      | -0.61   |         |              |
|                                            | UPA 30mg + csDMARD                       | 219| 66      | 43      | 27      | 28      | 12      | 9       | -0.55   |         |              |
| Fleischmann 2018 (SELECT-COMPARE) [31, 32]| Placebo + MTX                           | 651| 36.4    | 14.9    | 4.9     | 6.1     | 3.1     | 2       | -0.28   | 0.92*    |              |
|                                            | UPA 15mg OD + MTX                        | 651| 70.5    | 45.2    | 24.9    | 28.7    | 13.4    | 9.8     | -0.6    | 0.24*    |              |
|                                            | ADA 40mg Q2W + MTX                       | 327| 63      | 29.1    | 13.5    | 18      | 7.6     | 4       | -0.49   | 0.1*     |              |
| Genovese 2018 (SELECT-BEYOND) [33]         | Placebo + csDMARD                        | 169| 28      | 34      | 7       |         |         |         |         |         | -0.16        |
|                                            | UPA 15mg + csDMARD                       | 164| 65      | 36      | 12      |         |         |         |         |         | -0.41        |
|                                            | UPA 30mg + csDMARD                       | 165| 93      | 12      | 23      |         |         |         |         |         | -0.44        |
| Kivitz ACR 2018 [34]                       | Placebo + MTX                           | 22 | 40.9    | 22.7    | 13.6    |         |         |         |         |         | -0.39        |
|                                            | GS-9876 10mg OD + MTX                    | 20 | 25      | 20      | 15      |         |         |         |         |         | -0.18        |
|                                            | GS-9876 30mg                             | 20 | 35      | 20      | 5       |         |         |         |         |         | -0.46        |
| Study                                      | Treatment          | N   | Week | ACR20 | ACR50 | ACR70 | ESR | DAS28 | SF36physical | SF36mental | Change in DAS28 |
|-------------------------------------------|--------------------|-----|------|-------|-------|-------|-----|-------|---------------|-------------|-----------------|
| Hu 2018 (RA-BALANCE) [35, 36]            | OD + MTX          |     |      |       |       |       |     |       |               |             |                 |
| Placebo + MTX                            | 145               | 12  |      | 28.3  | 8.3   | 1.4   | 2.8 |       |               |             |                 |
| BARI 4mg + MTX                           | 145               | 12  |      | 58.6  | 30.3  | 9.7   | 11.7|       |               |             |                 |
| Smolen 2018 (SELECT-MONOTHERAPY) [37, 38]| Continued MTX     | 216 | 14   | 41.2  | 15.3  | 2.8   | 8.3 | 1     | 0.9           | -0.32       |                 |
| UPA 15mg OD                              | 217               |     |      | 67.7  | 41.9  | 22.6  | 28.1| 13    | 9.2           | -0.65       |                 |
| UPA 30mg OD                              | 215               |     |      | 71.2  | 52.1  | 33    | 40.5| 19    | 19.1          | -0.73       |                 |
| Tanaka 2018a (SELECT-SUNRISE) [39, 40]   | Placebo + csDMARDs| 49  |      | 42.9  | 16.3  | 2     | 6.1 | 2     | -0.1          |             |                 |
| UPA 7.5mg + csDMARDs                     | 49                | 12  |      | 75.5  | 40.6  | 20.4  | 36.7| 10    | -0.41         |             |                 |
| UPA 15mg + csDMARDs                      | 49                |     |      | 83.7  | 65.3  | 34.7  | 57.1| 18    | -0.45         |             |                 |
| UPA 30mg + csDMARDs                      | 50                |     |      | 80    | 58    | 28    | 50  | 18    | -0.49         |             |                 |
| Tanaka & Takeuchi 2018 [41, 42]          | Placebo ± csDMARDs| 101 |      | 30.7  | 8.9   | 1.0   | 5   | 0     |               |             |                 |
| PEF 100mg OD ± csDMARDs                  | 104               | 12  |      | 57.7  | 30.8  | 13.5  | 24.5| 8.7   |               |             |                 |
| PEF 150mg OD ± csDMARDs                  | 102               |     |      | 74.5  | 42.2  | 27.5  | 34.7| 9.9   |               |             |                 |
| Open-label ETA 50mg QW ± csDMARDs        | 200               |     |      | 83.5  | 52.5  | 30.5  | 45.5| 19.0  |               |             |                 |
| Study                                      | Treatment                        | n   | Time  | ACR20          | ACR50  | ACR70  | ACR10  | ADA30  | ADA50  | ADA70  | ADA10  | Change |
|-------------------------------------------|----------------------------------|-----|-------|----------------|--------|--------|--------|--------|--------|--------|--------|--------|
| Takeuchi 2018 [43, 44]                    | Placebo + MTXs                   | 170 | 12b/28c | 21.8b          | 7.6b   | 2.4b   | 7.7b   | 0.6    | 0.6    | 0.0    | 3.37c  |
|                                           | PEF 100mg OD + MTXs              | 174 |       | 58.6b          | 29.9b  | 12.1b  | 31.4b  | 4.7    | 5.8    | -0.25  | 1.62d  |
|                                           | PEF 150mg OD + MTXs              | 174 |       | 64.4b          | 46b    | 23.6b  | 35.1b  | 14.6   | 9.9    | -0.38  | 1.03d  |
| van Vollenhoven ACR 2018 (SELECT-EARLY)  | Placebo + MTX                    | 314 | 12/24d | 54.1           | 28.3   | 14     | 18.5d  | 6.4    | 6.4    | -0.49  | 0.67d  |
|                                           | UPA 15mg + MTX                   | 317 |       | 75.7           | 52.1   | 32.5   | 48.3d  | 16.1   | 12.9   | -0.83  | 0.14d  |
|                                           | UPA 30mg + MTX                   | 314 |       | 77.1           | 56.4   | 36.9   | 50d    | 21.3   | 15.3   | -0.86  | 0.07d  |
| Tanaka 2019 [48]                          | TOFA 11mg modified-release OD + MTX | 104 | 12      | 84.5           | 68     | 31.1   | 50.5   | 18.5   | 11.7   | -0.44  |
|                                           | TOFA 5mg immediate-release BID + MTX | 105 |         | 79.8           | 68.3   | 46.2   | 69.2   | 36.5   | 29.8   | -0.46  |
| van der Heijde 2019 (ORAL Scan) [10]      | TOFA 5mg + MTX                   | 321 | 96     | 2.8            | 2.7    | 2.2    | 1.9    | 1.9    | 1.7    | -0.5   |
|                                           | TOFA 10mg + MTX                  | 316 |       | 2.8            | 2.8    | 2.6    | 2.2    | 2.3    | 2      | -0.7   |
|                                           | Placebo->TOFA 5mg + MTX          | 81  |       | 5.5            | 5.5    | 4.6    | 3.3    | 3.7    | 3.9    | -0.6   |
| Placebo-TOFA 10mg + MTX | 79 | 5.7 | 5.6 | 5.1 | 4.5 | 4.8 | 4.7 | -0.6 |

ADA: Adalimumab; BARI: Baricitinib; TOFA: Tofacitinib; UPA: Upadacitinib; BID: twice daily; OD: once daily; Q2W: every two weeks; MTX: Methotrexate
## Table S3.2: Psoriatic Arthritis

| Study | Treatment | No. of patients (n) | Timepoint (weeks) | ACR20 (%) | ACR50 (%) | ACR70 (%) | ΔDAPSA (%) | MDA (%) | PASI 75 (%) | ΔHAQ-DI | ΔmTSS | Resolution of dactylitis (%) | Resolution of enthesitis (%) |
|-------|-----------|---------------------|-------------------|-----------|-----------|-----------|------------|---------|-------------|---------|--------|----------------------------|-----------------------------|
| Mease 2017 (OPAL Broaden) [49] | Placebo ± csDMARD | 105 | 12 | 33 | 10 | 5 | -0.8 | 7 | 15 | -0.18 | 0.00<sup>b,c</sup>/ 0.09<sup>b,d</sup> | 32.8 | 21.5 |
| | TOFA 5mg BID ± csDMARD | 107 | | 50 | 28 | 17 | -1.3 | 26 | 43 | -0.35 | 0.01<sup>b</sup> | | 34.4 | 33.3 |
| | TOFA 10mg BID ± csDMARD | 104 | | 61 | 40 | 14 | -1.6 | 26 | 44 | -0.4 | -0.01<sup>b</sup> | | 60 | 40.6 |
| | ADA 40mg Q2W ± csDMARD | 106 | | 52 | 33 | 19 | -1.5 | 25 | 39 | -0.38 | -0.07<sup>b</sup> | | 46.6 | 47.4 |
| Gladman 2017 (OPAL Beyond) [50] | Placebo ± csDMARD | 131 | 24 | 24 | 15 | 10 | 14.5 | 14 | -0.14 | 28.6 | 21.5 |
| | TOFA 5mg BID ± csDMARD | 131 | | 50 | 30 | 17 | 22.9 | 21 | -0.39 | 51.5 | 39.8 |
| | TOFA 10mg BID ± csDMARD | 132 | | 47 | 28 | 14 | 21.2 | 43 | -0.35 | 50.8 | 32.3 |
| Mease 2018 (EQUATOR) [51] | Placebo ± csDMARD | 66 | 16 | 33.3 | 15.2 | 6.1 | 15 | -0.28 | | | | |
| | FILGO 200mg OD ± csDMARD | 65 | | 80 | 47.7 | 23.1 | | 45.2 | -0.57 | | |

* week 24; <sup>a</sup> week 52; <sup>b</sup> Placebo advancing to TOFA 5mg BID; <sup>c</sup> Placebo advancing to TOFA 10mg BID; ABA: abatacept; ACR: American College of Rheumatology response; ADA: adalimumab; APR: apremilast; bDMARD: biological disease modifying drug; BID: twice daily; BL: baseline; CKM: clazakizumab; CRP: C-reactive protein; csDMARD: conventional synthetic disease modifying drug; CZP: certolizumab pegol; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score using 28-joint count assessment and CRP; ETA: etanercept; FILGO: filgotinib; GLM: golimumab; GKM: guselkumab; IXE: ixekizumab; MDA: minimal disease activity; mTSS: PsA modified total Sharp score; MTX: methotrexate; QNW: every N weeks; RKM: risankizumab; SEC: secukinumab; TOFA: tofacitinib; UKM: ustekinumab;
Table S3.3: Ankylosing Spondylitis

| Study                  | Treatment                | No. of patients (n) | Time-point (weeks) | ASAS 20 (%) | ASAS 40 (%) | ASAS 5/6 (%) | ΔASDAS (%) | ΔBASDAI (%) | ΔBASFI (%) | ΔBASMI (%) | ΔSPARCC spine | ΔSPARCC sacroiliac joint | ΔCRP (mg/L) |
|------------------------|--------------------------|---------------------|--------------------|-------------|-------------|-------------|------------|-------------|------------|------------|----------------|--------------------------|-------------|
| Van der Heijde 2017 [52] | Placebo ± csDMARD       | 51                  | 12                 | 40.1        | 19.6        | 15.7        | -0.7       | -1.9        | -1.4       | -0.2       | -0.1          | -0.8                     | 1.2         |
|                        | TOFA 2mg BID ± csDMARD   | 52                  |                    | 56.0        | 42.3        | 19.2        | 13.5       | -2.8        | -1.9       | -0.3       | -3.1          | -1.7                     | 0.6         |
|                        | TOFA 5mg BID ± csDMARD   | 52                  |                    | 63.0        | 46.2        | 50.0        | 13.5       | -2.9        | -2.4       | -0.4       | -5.5          | -3.2                     | 0.6         |
|                        | TOFA 10mg BID ± csDMARD  | 52                  |                    | 67.4        | 38.5        | 38.5        | 15.4       | -2.7        | -2.2       | -0.6       | -6.6          | -3.6                     | 0.3         |
| Van der Heijde 2018 [53] | Placebo ± csDMARD       | 58                  | 12                 | 40          | 19          | 21          | 0          | -0.57       | -1.44       | -1.23       | -0.39         | 0.52                     | 0.06        | -2.24       |
|                        | FILGO 200mg OD ± csDMARD | 58                  |                    | 76          | 38          | 59          | 5          | -1.47       | -2.41       | -2.45       | -0.75        | -5.76                    | -3.52       | -10.84      |

csDMARD: conventional synthetic disease modifying drug; BID: twice daily; OD: once daily; FILGO: filgotinib; TOFA: tofacitinib; HLA: human leukocyte antigen; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; SPARCC: Spondyloarthritis Research Consortium of Canada Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; CRP: C-reactive protein;
### Table S3.4: Systemic lupus erythematosus

| Study        | Treatment                      | No. of patients (n) | Timepoint (weeks) | ΔSELENA-SLEDAI-2K | ΔSLEDAI-2K | SRI-4 response | Resolution of arthritis/rash (SLEDAI-2K) | LLDAS | ΔCLASI | SLICC/ACR Damage Index score |
|--------------|--------------------------------|---------------------|-------------------|------------------|------------|----------------|------------------------------------------|-------|--------|-------------------------------|
| Kahl 2016 [54] | Placebo ± csDMARD             | 11                  |                   |                  |            |                |                                          |       |        |                               |
|              | Solcitinib 50mg BID ± csDMARD  | 9                   | 12                | -6.2             | 0/5        |                |                                          |       |        |                               |
|              | Solcitinib 100mg BID ± csDMARD | 10                  |                   | -3.6             | 1/4        |                |                                          |       |        |                               |
|              | Solcitinib 200mg BID ± csDMARD | 10                  |                   |                  | 1/4        |                |                                          |       |        |                               |
|              | Solcitinib 400mg BID ± csDMARD | 10                  |                   |                  | 2/5        |                |                                          |       |        |                               |
| Wallace 2018 [55] | Placebo ± csDMARD       | 105                 | 24                | -3.8             | 48         | 53             | 26            | -2.8 | 0.05   |                               |
|              | BARI 2mg OD ± csDMARD         | 105                 |                   | -4.1             | 51         | 58             | 33            | -1.7 | 0.07   |                               |
|              | BARI 4mg OD ± csDMARD         | 104                 |                   | -4.4             | 64         | 67             | 38            | -2.3 | 0.07   |                               |

csDMARD: conventional synthetic disease modifying drug; BID: twice daily; OD: once daily; BARI: baricitinib; SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus: National Assessment—Systemic Lupus Erythematosus Disease Activity Index; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; SRI: Systemic Lupus Erythematosus Responder Index; LLDAS: Lupus Low Disease Activity State; CLASI: Cutaneous Lupus Erythematosus Disease Area and Severity Index; SLICC/ACR: systemic lupus international collaborating clinics American College of Rheumatology

### Table S3.5: Psoriasis

| Study        | Treatment                      | No. of patients | Timepoint | PASI 50 | PASI 75 | PASI 90 | PASI 100 (%) | ΔPASI | PGA | PGA clear |
|--------------|--------------------------------|----------------|-----------|---------|---------|---------|--------------|-------|-----|-----------|

| Study          | Drug/Dose                        | (n) | (weeks) | (%)  | (%)  | (%)  | response |
|---------------|----------------------------------|-----|---------|------|------|------|----------|
| Papp 2012 [56]| Placebo                          | 50  |         | 20.0 | 2.0  | 0    | 10.0     |
|               | TOFA 2mg BID                      | 49  | 12      | 37.5 | 25.0 | 14.6 | 24.5     |
|               | TOFA 5mg BID                      | 49  |         | 63.3 | 40.8 | 18.4 | 40.8     |
|               | TOFA 15mg BID                     | 49  |         | 79.2 | 60.4 | 29.2 | 72.9     |
| Bachelez 2015 [57]| Placebo                          | 107 | 12     | 20.6 | 5.6  | 0.9  | 15.0     | 1.9     |
|               | TOFA 5mg BID                      | 329 |        | 65.7 | 39.5 | 21.0 | 47.1     | 11.2    |
|               | TOFA 10mg BID                     | 330 |        | 80.6 | 63.6 | 36.1 | 68.2     | 25.4    |
|               | ETA 50mg twice weekly             | 335 |        | 80.3 | 58.8 | 32.2 | 66.3     | 19.4    |
| Bissonnette 2014 [58]| TOFA 5mg BID (continued)     | 31  |         | 56.2 |      |      | 49.9     |
|               | TOFA 5mg to Placebo (withdrawal) | 82  |        |      | 23.3 |      | 22.9     |
|               | TOFA 10mg BID (continued)        | 45  |        |      | 62.3 |      | 63.9     |
|               | TOFA 10mg BID to Placebo (withdrawal) | 133 |       |      | 26.1 |      | 18.0     |
| Papp 2015 [59]| Placebo                          | 29  | 6       | 17.2 | 3.4  | 0    |          |
|               | PEF 10mg BID                      | 19  |         | 63.2 | 31.6 | 0    |          |
|               | PEF 25mg BID                      | 21  |         | 47.6 | 14.3 | 4.8  |          |
|               | PEF 60mg BID                      | 19  |         | 57.9 | 21.1 | 21.1 |          |
|               | PEF 100mg BID                     | 17  |         | 64.7 | 58.8 | 58.8 |          |
|               | PEF 50mg BID                      | 19  |         | 47.4 | 15.8 | 0    |          |
| Study | Dose | N  | esAS | CRP  | 21-OH |
|-------|------|----|------|------|-------|
| Study 1: Placebo | 177 | 6.2 | 19.8 | 9.0 |
| Study 1: TOFA 5mg BID | 363 | 39.9 | 39.4 | 41.9 |
| Study 1: TOFA 10mg BID | 360 | 59.2 | 0.6 | 59.2 |
| Study 2: Placebo | 196 | 11.4 | 24.5 | 10.9 |
| Study 2: TOFA 5mg BID | 382 | 46.0 | 38.8 | 46.0 |
| Study 2: TOFA 10mg BID | 381 | 59.6 | 1.6 | 59.1 |

| Study | Dose | N  | esAS | CRP  | 21-OH |
|-------|------|----|------|------|-------|
| Bissonnette 2016 | Placebo | 12 | 8.3 | 0 | 0 |
| Itacitinib 100mg OD | 9 | 22.2 | 11.1 | 11.1 |
| Itacitinib 200mg OD | 9 | 66.7 | 0 | 22.2 |
| Itacitinib 200mg BID | 9 | 44.4 | 22.2 | 33.3 |
| Itacitinib 600mg OD | 11 | 81.8 | 27.3 | 45.5 |

| Study | Dose | N  | esAS | CRP  | 21-OH |
|-------|------|----|------|------|-------|
| Study 1: Placebo | 34 | 17.6 | | | |
| Study 1: BARI 2mg | 32 | 31.3 | | | |
| Study 1: BARI 4mg | 72 | 29.2 | | | |
| Study 1: BARI 8mg | 64 | 43.8 | | | |
| Study 1: BARI 10mg | 69 | 55.1 | | | |

| Study | Dose | N  | esAS | CRP  | 21-OH |
|-------|------|----|------|------|-------|
| Study 1: Placebo | 71 | 8 | -23.5% | 25.2 |
| Study 1: TOFA BID | 71 | 15.2 | -31.8% | 41.8 |
| Study 1: BARI 2mg | 70 | 9.1 | -26.7% | 20.9 |
| Study 1: BARI 4mg | 74 | 8.3 | -19.1% | 13.8 |
| Treatment                      | N  | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 | Week 7 | Week 8 | Week 9 | Week 10 | Week 11 | Week 12 | Week 13 | Week 14 | Week 15 | Week 16 | Week 17 | Week 18 | Week 19 | Week 20 |
|-------------------------------|----|--------|--------|--------|--------|--------|--------|--------|--------|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| 2% TOFA OD                    | 70 | 17.9   |        |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |
| 1% TOFA OD                    | 74 | 7.2    |        |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |
| Zhang 2017 [64]               |    |        |        |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |
| Placebo                       | 88 | 12.5   | 3.4    |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |
| TOFA 5mg BID                  | 88 | 54.6   | 35.2   |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |
| TOFA 10mg BID                 | 90 | 81.1   | 60.0   |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |
| Papp 2018 [65]                |    |        |        |        |        |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |
| Placebo                       | 45 | 31     | 7      | 2      | 0      |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |         |
| BMS-986165 3mg EOD            | 44 | 43     | 9      | 7      | 2      |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |         |
| BMS-986165 3mg OD             | 44 | 68     | 39     | 16     | 0      |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |         |
| BMS-986165 3mg BID            | 45 | 91     | 69     | 44     | 9      |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |         |
| BMS-986165 6mg BID            | 45 | 78     | 67     | 44     | 18     |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |         |
| BMS-986165 12mg OD            | 44 | 89     | 75     | 43     | 25     |        |        |        |        |        |         |         |         |         |         |         |         |         |         |         |         |         |         |
Table S3.6: Alopecia & Atopic Dermatitis

| Study                     | Treatment                        | No. of patients (n) | Timepoint (weeks) | SALT30 (%) | ΔSALT | ΔEASI | PGA clear/almost clear (%) | EASI50 (%) | EASI100 (%) | Itch Severity Item |
|---------------------------|----------------------------------|---------------------|-------------------|------------|-------|-------|-----------------------------|------------|-------------|---------------------|
| Alopecia areata           |                                  |                     |                   |            |       |       |                             |            |             |                     |
| Guttman-Yassky 2018 [66]  | Placebo                          | 142                 | 24                |             |       |       |                             |            |             |                     |
|                           | PF-06651600 200mg OD (4 weeks) / 50mg OD (20 weeks) |                     |                   |             |       |       |                             |            |             |                     |
|                           | PF-06700841 60mg OD (4 weeks) / 30mg OD (20 weeks) |                     |                   |             |       |       |                             |            |             |                     |
|                           |                                  |                     |                   | 48         | 33.6  | -     |                             |            |             |                     |
|                           |                                  |                     |                   | 60         | 49.5  | -     |                             |            |             |                     |
| Atopic dermatitis         |                                  |                     |                   |            |       |       |                             |            |             |                     |
| Bissonette 2016 [67]      | Topical TOFA 2% BID              | 35                  | 4                 | -81.7%     |       |       |                             | 73         |             |                     |
|                           | Topical Vehicle BID              | 34                  |                   | -29.9%     |       |       |                             | 22         |             |                     |
| De Bruin-Weller 2018 [68, 69] | Placebo                         | 41                  | 16                | -23%       |       |       |                             | 0          |             |                     |
|                           | UPA 7.5mg OD                     | 42                  |                   | -39%       |       | -    |                             | 2.4        |             |                     |
|                           | UPA 15mg OD                      | 42                  |                   | -62%       |       | -    |                             | 9.5        |             |                     |
|                           | UPA 30mg OD                      | 42                  |                   | -74%       |       | -    |                             | 24         |             |                     |
| Guttman-Yassky 2018 [70]  | Placebo + topical steroids       | 49                  | 16                | -46%       |       | -    |                             | 37         |             |                     |
|                           | BARI 2mg OD + topical steroids   | 37                  |                   | -64%       |       | -    |                             | 67         |             |                     |
Table S3.7: Ulcerative Colitis

| Study           | Treatment                   | No. of patients (n) | Timepoint (weeks) | Mayo clinical response (%) | Mayo clinical remission (%) | Mayo endoscopic response (%) | Mayo endoscopic remission (%) | ΔCRP (mg/L) | ΔCalprotectin (mg/kg) |
|-----------------|-----------------------------|---------------------|-------------------|----------------------------|----------------------------|------------------------------|------------------------------|-------------|----------------------|
| Sandborn 2012   | Placebo ± Mesalamine        | 48                  |                   | 42                         | 10                         | 46                           | 2                           | 0.9         | -400                 |
|                 | TOFA 0.5mg BID ± Mesalamine | 31                  | 8                 | 32                         | 13                         | 52                           | 10                           | -6.84       | -292                 |
|                 | TOFA 3mg BID ± Mesalamine   | 33                  |                   | 48                         | 33                         | 58                           | 18                           | -3.85       | -570                 |
|                 | TOFA 10mg BID ± Mesalamine  | 33                  |                   | 61                         | 48                         | 67                           | 30                           | -0.12       | -636                 |
|                 | TOFA 15mg BID ±             | 49                  |                   | 78                         | 41                         | 78                           | 27                           | -8.2        | -596                 |
| Nakagawa 2018   | Vehicle                     | 31                  | 4                 | -11.6%                     | 3.2                        | 22.6                         | 0.6                          |             |                      |
|                 | Topical JTE-052 0.25%       | 69                  |                   | -41.2%                     | 10.1                       | 53.6                         | -0.8                         |             |                      |
|                 | Topical JTE-052 0.5%        | 65                  |                   | -58.5%                     | 10.8                       | 63.1                         | -1.7                         |             |                      |
|                 | Topical JTE-052 1%          | 66                  |                   | -54.4%                     | 10.6                       | 65.2                         | -1.5                         |             |                      |
|                 | Topical JTE-052 3%          | 65                  |                   | -72.9%                     | 23.1                       | 86.2                         | -2.4                         |             |                      |
|                 | Topical tacrolimus          | 30                  |                   | -63.1%                     | 6.7                        | 73.3                         | -1.2                         |             |                      |
|                  | Mesalamine                                                                 |
|------------------|---------------------------------------------------------------------------|
| Sandborn 2017    | OCTAVE Induction 1: Placebo                                              |
| [73]             | 122                                                                        |
|                  | OCTAVE Induction 1: TOFA 10mg BID                                        |
|                  | 476                                                                      |
|                  | OCTAVE Induction 2: Placebo                                              |
|                  | 112                                                                      |
|                  | OCTAVE Induction 2: TOFA 10mg BID                                        |
|                  | 429                                                                      |
|                  | OCTAVE Sustain: Placebo                                                  |
|                  | 198                                                                      |
|                  | OCTAVE Sustain: TOFA 5mg BID                                             |
|                  | 198                                                                      |
|                  | OCTAVE Sustain: TOFA 10mg BID                                            |
|                  | 197                                                                      |
| Sandborn 2018    | Placebo                                                                   |
| [74, 75]         | 46                                                                       |
|                  | UPA 7.5mg OD                                                             |
|                  | 47                                                                       |
|                  | UPA 15mg OD                                                              |
|                  | 49                                                                       |
|                  | UPA 30mg OD                                                              |
|                  | 52                                                                       |
|                  | UPA 45mg OD                                                              |
|                  | 56                                                                       |
| Sands 2018       | Placebo                                                                   |
| [76]             | 43                                                                       |
|                  | Peficitinib 25mg OD                                                      |
|                  | 44                                                                       |
|                  | Peficitinib 75mg OD                                                      |
|                  | 44                                                                       |
|                  | Peficitinib 150mg OD                                                     |
|                  | 44                                                                       |
### Table S3.8: Crohn’s Disease

| Study                      | Treatment                          | No. of patients (n) | Timepoint (weeks) | CDAI Response-70 (%) | CDAI Response-100 (%) | CDAI <150 (%) | ΔCDAI | ΔCRP (mg/L) | ΔCalprotectin (mg/kg) |
|----------------------------|------------------------------------|--------------------|------------------|----------------------|-----------------------|--------------|-------|-------------|-----------------------|
| Sandborn 2014 [77]         | Placebo                            | 34                 | 4                | 47.1                 | 29.4                  | 20.6         | -78.38 |             |                       |
|                            | TOFA 1mg BID                        | 36                 |                  | 36.1                 | 30.6                  | 30.6         | -63.85 |             |                       |
|                            | TOFA 5mg BID                        | 34                 |                  | 57.6                 | 45.5                  | 24.2         | -100.28 |             |                       |
|                            | TOFA 15mg BID                       | 35                 |                  | 45.7                 | 37.1                  | 14.3         | -67.19 |             |                       |
| Panés 2017 [78]            | Induction: Placebo                  | 91                 | 8                | 62.2                 | 54.4                  | 36.7         | -117.4 | 0.12        | -0.02 (log)           |
|                            | Induction: TOFA 5mg BID             | 86                 |                  | 76.5                 | 70.6                  | 43.5         | -149.7 | -0.42       | -0.31 (log)           |
|                            | Induction: TOFA 10mg BID            | 86                 |                  | 74.4                 | 68.6                  | 43.0         | -157.3 | -0.73       | -0.30 (log)           |
|                            | Maintenance: Placebo                | 59                 | 26               | 35.7                 | 28.6                  | -69.5        | 1.13   | 1.13 (log)  |                       |
|                            | Maintenance: TOFA 5mg BID           | 60                 |                  | 37.2                 | 37.2                  | -63.5        | 0.57   | 0.57 (log)  |                       |
|                            | Maintenance: TOFA 10mg BID          | 61                 |                  | 55.8                 | 41.9                  | -19.1        | -0.07  | -0.07 (log) |                       |
| Sandborn 2017 / Panés 2018 [79-81] | Induction: Placebo                  | 37                 | 16               | 35.1                 | 16                    | -0.1         | -14.5  |             |                       |
|                            | Induction: UPA 3mg BID              | 39                 |                  | 46.2                 | 21                    | -3.0         | -24.6  |             |                       |
|                            | Induction: UPA 6mg BID              | 37                 |                  | 54.1                 | 30                    | -3.9         | -41.8  |             |                       |
| Condition                          | Dose | Week | Mean | SD  | Mean | SD  |
|-----------------------------------|------|------|------|-----|------|-----|
| **Induction:**                    |      |      |      |     |      |     |
| UPA 12mg BID                       | 36   | 44.4 | 39   | -6.1| -32.1|
| UPA 24mg BID                       | 36   | 61.1 | 31   | -14.8| -44.4|
| UPA 24mg OD                        | 35   | 48.6 | 20   | -2.7 | -22.5|
| **Maintenance:**                  |      |      |      |     |      |     |
| UPA 3mg BID                        | 20   | 55   | 55   | -4.3 | -51.9|
| UPA 6mg BID                        | 8    | 75   | 50   | -7.0 | -524.1|
| UPA 12mg BID                       | 16   | 75   | 69   | -20.4| -3047.5|
| UPA 24mg OD                        | 10   | 40   | 40   | -6.2 | -2371.8|
| Placebo                            | 44   | 41   | 23   |      |      |
| FILGO 200mg OD                     | 130  | 59   | 47   |      |      |

Vermeire 2017 [82]
### Section 4: Safety study characteristics of articles and abstracts included.

### Section 4.1: Details of articles and abstracts selected for inclusion: Safety

#### Table S4.1.1: Rheumatoid Arthritis

| Study                  | Type | Outcome            | Exposure | Control       |
|------------------------|------|--------------------|----------|---------------|
| Kremer 2009 [1]        | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Tanaka 2011a [2]       | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Tanaka 2011b [12, 84]  | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Fleischmann 2012 [3]   | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Fleischmann 2012 [4]   | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Kremer 2012 [5]        | RCT  | RCT Safety Data    | TOFA + MTX | Placebo + MTX |
| Van Vollenhoven 2012 [6]| RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Burmester 2013 [7]     | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Kremer 2013 [8]        | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Van der Heijde 2013 [9]| RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Lee 2014 [11]          | RCT  | RCT Safety Data    | TOFA     | Placebo + MTX |
| Tanaka 2015 [12]       | RCT  | RCT Safety Data    | TOFA     | Placebo       |
| Fleischmann 2015 [13]  | RCT  | RCT Safety Data    | DEC      | Placebo       |
| Charles-Schoeman [85]  | RCT + LTE | Cardiovascular risk factors / | TOFA | Placebo       |
| Study                          | Design Type | Study Type          | Treatment 1          | Treatment 2          |
|-------------------------------|-------------|---------------------|----------------------|----------------------|
| Clowse 2016 [86]              | RCT         | Pregnancy           | TOFA                 | Placebo              |
| Genovese 2016a [14]           | RCT         | RCT Safety Data     | BARI                 | Placebo + csDMARD    |
| Genovese 2016b [15]           | RCT         | RCT Safety Data     | UPA                  | Placebo + MTX       |
| Genovese 2016c [16]           | RCT         | RCT Safety Data     | DEC                  | Placebo + MTX       |
| Genovese 2016d [17]           | RCT         | RCT Safety Data     | DEC                  | Placebo + csDMARD    |
| Kremer 2016 [18]              | RCT         | RCT Safety Data     | UPA + MTX            | Placebo + MTX       |
| Takeuchi 2016 [19]            | RCT         | RCT Safety Data     | PEF                  | Placebo              |
| Tanaka 2016 [20]              | RCT         | RCT Safety Data     | BARI + MTX           | Placebo + MTX       |
| Cohen 2017 [87]               | RCT + LTE   | Integrated Safety Data | TOFA               | -                   |
| Dougados 2017 [RA-BUILD] [21] | RCT         | RCT Safety Data     | BARI                 | Placebo + csDMARD    |
| Fleischmann 2017a [22]        | RCT         | RCT Safety Data     | TOFA; TOFA + MTX    | ADA + MTX            |
| Fleischmann 2017b [RA-BEGIN]  [23] | RCT   | RCT Safety Data     | BARI; BARI + MTX    | Placebo + MTX       |
| Genovese 2017 [24]            | RCT         | RCT Safety Data     | PEF + HCQ/SZP        | Placebo + HCQ/SZP    |
| Kivitz 2017 [25]              | RCT         | RCT Safety Data     | PEF + MTX            | Placebo + MTX       |
| Kavanaugh 2017 [DARWIN 2] [26] | RCT      | RCT Safety Data     | FILGO                | Placebo              |
| Taylor 2017 [RA-BEAM] [27]    | RCT         | RCT Safety Data     | BARI + MTX           | ADA + MTX; Placebo + MTX |
| Study                                    | Design   | Study Type       | Comparator 1 | Comparator 2 |
|------------------------------------------|----------|------------------|--------------|--------------|
| Vanhoutte 2017 [28]                      | RCT      | RCT Safety Data  | FILGO + MTX  | Placebo + MTX|
| Westhovens 2017 (DARWIN 1) [29]         | RCT      | RCT Safety Data  | FILGO + MTX  | Placebo + MTX|
| Burmester 2018 (SELECT-NEXT) [30]       | RCT      | RCT Safety Data  | UPA + csDMARD| Placebo + csDMARD|
| Fleischmann 2018 (SELECT-COMPARE) [31, 32] | RCT      | RCT Safety Data  | UPA + MTX    | ADA + MTX; Placebo + MTX |
| Genovese 2018 (SELECT-BEYOND) [33]      | RCT      | RCT Safety Data  | UPA + csDMARD| Placebo + csDMARD|
| Kivitz ACR 2018 [34]                    | RCT      | RCT Safety Data  | GS-9876 10mg OD + MTX | Placebo + MTX|
| Hu 2018 (RA-BALANCE) [35, 36]           | RCT      | RCT Safety Data  | BARI + MTX   | Placebo + MTX|
| Smolen 2018 (SELECT-MONOTHERAPY) [37, 38] | RCT      | RCT Safety Data  | UPA          | Placebo + MTX|
| Tanaka 2018a (SELECT-SUNRISE) [39, 40]  | RCT      | RCT Safety Data  | UPA + csDMARDs | Placebo + csDMARDs|
| Tanaka & Takeuchi 2018 [41, 42]         | RCT      | RCT Safety Data  | PEF + csDMARDs| Placebo + csDMARDs / Open-label ETA 50mg + csDMARDs|
| Takeuchi 2018 [43, 44]                  | RCT      | RCT Safety Data  | PEF + MTX    | Placebo + MTX|
| van Vollenhoven ACR 2018 (SELECT-EARLY) [45] | RCT      | RCT Safety Data  | UPA          | Placebo + MTX|
| Smolen 2019 [48]                        | RCT + LTE| Integrated Safety Data | BARI | Placebo |
Desai 2019 [89] | Cohort study | Venous thromboembolism | TOFA | TNFi
---|---|---|---|---
BARI: baricitinib; Cs: conventional synthetic; DEC: decernotinib; DMARD: disease modifying anti-rheumatic drug; MTX: methotrexate; TNF: Tumor necrosis factor; PEF: peficitinib; TOFA: tofacitinib; UPA: upadacitinib;

### Table S4.1.2: Psoriatic Arthritis

| Study | Type | Outcome | Exposure | Control |
| --- | --- | --- | --- | --- |
| Mease 2017 (OPAL Broaden) [49] | RCT | RCT Safety Data | TOFA ± csDMARD | ADA ± csDMARD |
| Gladman 2017 (OPAL Beyond) [50] | RCT | RCT Safety Data | TOFA ± csDMARD | Placebo ± csDMARD |
| Mease 2018 (EQUATOR) [51] | RCT | RCT Safety Data | FILGO ± csDMARD | Placebo ± csDMARD |

### Table S4.1.3: Ankylosing Spondylitis

| Study | Type | Outcome | Exposure | Control |
| --- | --- | --- | --- | --- |
| Van der Heijde 2017 [52] | RCT | RCT Safety Data | TOFA ± csDMARD | Placebo ± csDMARD |
| Van der Heijde 2018 [53] | RCT | RCT Safety Data | FILGO ± csDMARD | Placebo ± csDMARD |

### Table S4.1.4: Systemic Lupus Erythematosus

| Study | Type | Outcome | Exposure | Control |
| --- | --- | --- | --- | --- |
| Kahl 2016 [54] | RCT | RCT Safety Data | Solcitinib ± csDMARD | Placebo ± csDMARD |
| Wallace 2018 [55] | RCT | RCT Safety Data | BARI ± csDMARD | Placebo ± csDMARD |
| Study                  | Type       | Outcome                      | Exposure     | Control                  |
|------------------------|------------|------------------------------|--------------|--------------------------|
| Papp 2012 [56]         | RCT        | RCT Safety Data              | TOFA         | Placebo                  |
| Bachelez 2015 [57]     | RCT        | RCT Safety Data              | TOFA         | Placebo / Etanercept     |
| Papp 2015 [59]         | RCT        | RCT Safety Data              | PEF          | Placebo                  |
| Papp 2015 [60]         | RCT        | RCT Safety Data              | TOFA         | Placebo                  |
| Bissonnette 2016 [61]  | RCT        | RCT Safety Data              | Itacinib     | Placebo                  |
| Clowse 2016 [86]       | RCT + LTE  | Pregnancy                    | TOFA         | Placebo                  |
| Papp 2016 [62]         | RCT        | RCT Safety Data              | BARI         | Placebo                  |
| Papp 2016 [63]         | RCT        | RCT Safety Data              | Topical TOFA | Vehicle                  |
| Wu 2016 [90]           | RCT + LTE  | Cardiovascular risk factors / MACE | TOFA     | Placebo                  |
| Winthrop 2017 [91]     | RCT + LTE  | Herpes Zoster                | TOFA         | Placebo                  |
| Zhang 2017 [64]        | RCT        | RCT Safety Data              | TOFA         | Placebo                  |
| Papp 2018 [65]         | RCT        | RCT Safety Data              | BMS-986165   | Placebo                  |
| Strober 2018 [92]      | RCT + LTE  | Integrated Safety Data       | Tofacitinib  | Placebo                  |
### Table S4.1.6: Alopecia & Atopic Dermatitis

| Study                        | Type         | Outcome                | Exposure                           | Control         |
|------------------------------|--------------|------------------------|------------------------------------|-----------------|
| Guttman-Yassky 2018 [66]     | RCT          | RCT Safety Data        | PF-06651600 / PF-06700841          | Placebo         |
| Bissonette 2016 [67]         | RCT          | RCT Safety Data        | Topical TOFA                       | Vehicle         |
| De Bruin-Weller 2018 [68, 69]| RCT          | RCT Safety Data        | UPA                                | Placebo         |
| Guttman-Yassky 2018 [70]     | RCT          | RCT Safety Data        | BARI                               | Placebo         |
| Nakagawa 2018 [71]           | RCT          | RCT Safety Data        | Topical JTE-052                    | Placebo         |

### Table S4.1.7: Ulcerative Colitis

| Study                        | Type         | Outcome                | Exposure                           | Control         |
|------------------------------|--------------|------------------------|------------------------------------|-----------------|
| Sandborn 2012 [72]           | RCT          | RCT Safety Data        | Tofacitinib                        | Placebo         |
| Sandborn 2017 [73]           | RCT          | RCT Safety Data        | Tofacitinib                        | Vehicle         |
| Winthrop 2017 [93, 94]       | RCT + LTE    | Herpes Zoster          | TOFA                              | Placebo         |
| Mahadevan 2018 [95]          | RCT + LTE    | Pregnancy              | Tofacitinib                        | Placebo         |
| Sandborn 2018 [74, 75]       | RCT          | RCT Safety Data        | Upadacitinib                       | Placebo         |
| Sandborn 2018 [96]           | RCT + LTE    | Integrated Safety Data | Tofacitinib                        | Placebo         |
| Sands 2018 [76]              | RCT          | RCT Safety Data        | Peficitinib                        | Placebo         |
| Sands 2018 [97]              | RCT + LTE    | Cardiovascular risk factors / MACE | TOFA                               | Placebo         |
### Table S4.1.8: Crohn’s Disease

| Study                        | Type | Outcome                  | Exposure   | Control  |
|------------------------------|------|--------------------------|------------|----------|
| Sandborn 2014 [77]           | RCT  | RCT Safety Data          | Tofacitinib| Placebo  |
| Panés 2017 [78]               | RCT  | RCT Safety Data          | Tofacitinib| Placebo  |
| Sandborn 2017 / Panés 2018   | RCT  | RCT Safety Data          | Upadacitinib| Placebo  |
| Vermeire 2017 [82]           | RCT  | RCT Safety Data          | Filgotinib | Placebo  |
4.2 Safety outcomes (overall & infections) of randomized controlled trials

Table S4.2.1: Rheumatoid Arthritis

| Study            | Group               | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|------------------|---------------------|-----------------|-------------------|-----------------------|---------|----------------|----------------------|------------------|-------------------|-------------------|
| Kremer 2009 [1]  | Placebo             | 65              | 6                 | 1.5                   | 26.2    | 0              | 6.2                  | 0                |                   |                   |
| TOFA 5mg BID     | 61                  |                 |                   | 1.6                   | 24.6    | 0              | 0                    |                  |                   |                   |
| TOFA 15mg BID    | 69                  |                 |                   | 7.3                   | 30.4    | 1.44           | 4.3                  |                  |                   |                   |
| TOFA 30mg BID    | 69                  |                 |                   | 4.4                   | 30.4    | 0              | 1.4                  |                  |                   |                   |
| Tanaka 2011a [2]| Placebo + MTX      | 28              | 12                | 0                     | 21.4    | 3.6            | 0                    | 3.6              |                   |                   |
| TOFA 1mg BID + MTX | 28              |                 |                   | 3.6                   | 10.7    | 0              | 0                    |                  |                   |                   |
| TOFA 3mg BID + MTX | 27              |                 |                   | 3.7                   | 29.6    | 3.7            | 3.7                  |                  |                   |                   |
| TOFA 5mg BID + MTX | 27              |                 |                   | 3.7                   | 11.1    | 0              | 0                    |                  |                   |                   |
| TOFA 10mg BID + MTX | 26              |                 |                   | 7.7                   | 42.3    | 0              | 0                    |                  |                   |                   |
| Fleischmann 2012 [3]| Placeboa          | 34              | 12\b/24           | 5.9                   | 17.6    | 2.9            | 2.9                  | 2.9              |                   |                   |
| TOFA 1mg BIDa     | 37                  |                 |                   | 5.4                   | 29.7    | 5.9            | 5.4                  |                  |                   |                   |
| Drug Formulation | N | Y1 | Y2 | Y3 | Y4 |
|------------------|---|----|----|----|----|
| TOFA 3mg BID<sup>a</sup> | 34 | 2.9 | 20.6 | 0 | 0 |
| TOFA 5mg BID | 49 | 0 | 34.7 | 0 | 4.1 |
| TOFA 10mg BID | 61 | 1.6 | 34.4 | 0 | 4.92 |
| TOFA 15mg BID | 57 | 7.0 | 33.3 | 1.8 | 5.26 |
| ADA 40mg EOW<sup>b</sup> | 53 | 1.9 | 18.9 | 0 | 0 |
| Fleischmann 2012 [4] | | | | | |
| Placebo | 122 | 4.9 | 0 | 4.9 |
| TOFA 5mg BID | 243 | 0.4 | 0 | 4.5 |
| TOFA 10mg BID | 245 | 2.0 | 0.4 | 3.3 |
| Kremer 2012 [5] | | | | | |
| Placebo + MTX | 69 | 0 | 5.9 | 0 | 2.9 |
| TOFA 1mg BID + MTX | 70 | 2.0 | 14.3 | 0 | 0 |
| TOFA 3mg BID + MTX | 68 | 3.6 | 20.0 | 3.6 | 4.4 |
| TOFA 5mg BID + MTX | 71 | 5.6 | 22.5 | 1.4 | 7.0 |
| TOFA 10mg BID + MTX | 74 | 9.5 | 17.6 | 1.4 | 6.8 |
| TOFA 15mg BID + MTX | 75 | 8.0 | 18.7 | 0 | 2.7 |
| Study                        | Treatment 1                        | N  | Treatment 2                        | N  | ACR 20 | ACR 50 | ACR 70 | EULAR Remission |
|------------------------------|-----------------------------------|----|-----------------------------------|----|--------|--------|--------|-----------------|
| Van Vollenhoven 2012 [6]     | Placebo + MTX (cross-over to TOFA 5mg BID + MTX after 3 months) | 56 | Placebo + MTX (cross-over to TOFA 10mg BID + MTX after 3 months) | 52 |         |         |         |                 |
|                              | TOFA 5mg BID + MTX                | 204|                                  |    | 5.9    | 1.5    | 0      | 4.4             |
|                              | TOFA 10mg BID + MTX               | 201|                                  |    | 5.0    | 2.0    | 1      | 3.5             |
|                              | ADA 40mg EOW + MTX                | 204|                                  |    | 2.5    | 0      | 0      | 3.4             |
|                              | Placebo + MTX (Combination group) | 106|                                  |    | 1.9    | 0.9    | 0      | 0.9             |
| Burmester 2013 [7]           | Placebo + MTX                     | 132|                                  |    | 4.5    | 0      | 0      | 3.0             |
|                              | TOFA 5mg BID + MTX                | 133|                                  |    | 1.5    | 0      | 0      | 3.8             |
|                              | TOFA 10mg BID + MTX               | 134|                                  |    | 1.5    | 0      | 0      | 1.5             |
| Study Year | Group Description | n | N | Treatment | **Baseline** | **12 Weeks** | **24 Weeks** |
|------------|-------------------|---|---|-----------|--------------|--------------|--------------|
| Kremer 2013 [8] | Placebo + DMARD (Combination group) | 52 | 159 | 55.6 | 10.9 (4.9-24.2)* | 1.3 | 12.6* | 6.8* |
| | TOFA 5mg BID + DMARD | | 315 | | 324.6 | 6.9 (4.6-10.5)* | 4.1 | 12.3* | 4.2* |
| | TOFA 10mg BID + DMARD | | 318 | | 321.7 | 7.3 (4.8-11.)* | 4.1 | 14.6* | 0.6* |
| Van der Heijde 2013 [9] | Placebo + DMARD (Combination group) | 12 | 160 | | 3.1 | 3.1 | 0 |
| | TOFA 5mg BID + DMARD | | 321 | | 3.7 | 2.8 | 0.9 |
| | TOFA 10mg BID + DMARD | | 316 | | 3.2 | 2.2 | 1.6 |
| Lee 2014 [11] | MTX | 186 | 288 | | 11.8 | 8.1 | 1.1 |
| | TOFA 5mg BID | | 373 | | 10.7 | 8.0 | 3.5 |
| | TOFA 10mg BID | | 397 | | 10.8 | 9.1 | 4.5 |
| Tanaka 2015 [12] | Placebo | 52 | 12 | | 1.92 | | |
| | TOFA 1mg BID | | 53 | | 0 | | |
| | TOFA 3mg BID | | 53 | | 0 | | |
| | TOFA 5mg BID | | 52 | | 3.9 | | 1.9 |
| Drug                  | Placebo | DEC 25mg BID | DEC 50mg BID | DEC 100mg BID | DEC 150mg BID |
|----------------------|---------|--------------|--------------|--------------|--------------|
| TOFA 10mg BID        | 53      |              |              |              |              |
| TOFA 15mg BID        | 54      | 1.9          |              |              | 0            |

Fleischmann 2015 [13]

| Drug                  | Placebo | DEC 25mg BID | DEC 50mg BID | DEC 100mg BID | DEC 150mg BID |
|----------------------|---------|--------------|--------------|--------------|--------------|
| Placebo              | 41      | 2.4          |              | 12.5         | 4.9          |
| DEC 25mg BID         | 41      |              | 0            | 12.2         | 2.4          |
| DEC 50mg BID         | 41      |              |              | 12.2         |              |
| DEC 100mg BID        | 40      |              |              |              |              |
| DEC 150mg BID        | 41      |              |              |              |              |

Genovese 2016a [14]

| Drug                  | Placebo + csDMARD | BARI 2mg + csDMARD | BARI 4mg + csDMARD |
|----------------------|-------------------|--------------------|--------------------|
| Placebo + csDMARD    | 176               | 65.8               | 69.9               |
| BARI 2mg + csDMARD   | 174               | 7                  | 4                  |
| BARI 4mg + csDMARD   | 177               | 31                 | 44                 |

Genovese 2016b [15]

| Drug                  | Placebo + MTX | UPA 3mg BID + MTX | UPA 6mg BID + MTX | UPA 12mg BID + MTX |
|----------------------|---------------|-------------------|-------------------|-------------------|
| Placebo + MTX        | 50            | 0                 | 4                 | 2                 |
| UPA 3mg BID + MTX    | 50            | 0                 | 4                 | 0                 |
| UPA 6mg BID + MTX    | 50            | 0                 | 4                 | 0                 |
| UPA 12mg BID + MTX   | 50            | 2                 | 4                 | 0                 |
| Study                | Group Description                  | N  | 6 | 22 | 4 | 18 | 4 | 0 |
|----------------------|-----------------------------------|----|---|----|---|----|---|---|
| Genovese 2016c [16]  | UPA 18mg BID + MTX                | 50 |   | 6  | 22|    |   | 0 |
|                      | UPA 24mg QD + MTX                 | 49 |   | 4  | 18|    |   | 4 |
|                      | Placebo + MTX                     | 71 |   | 5.6| 2.8|    |   |   |
|                      | DEC 100mg OD + MTX                | 71 |   | 4.2| 4.2|    |   |   |
|                      | DEC 150mg OD + MTX                | 72 |   | 8.3| 1.4|    |   |   |
|                      | DEC 200mg OD + MTX                | 72 |   | 6.9| 4.2|    |   |   |
| Genovese 2016d [17]  | Placebo + csDMARD                 | 12 |   | 0  |    |    |   |   |
|                      | DEC 100mg BID + csDMARD           | 11 |   | 9.1|    |    |   |   |
|                      | DEC 200mg BID + csDMARD           | 10 |   | 10.0|   |    |   |   |
|                      | DEC 300mg BID + csDMARD           | 10 |   | 0  |    |    |   |   |
| Kremer 2016 [18]     | Placebo                           | 56 |   | 4  | 23| 2  | 1,79| 4 |
|                      | UPA 3 mg +                         | 55 |   | 2  | 20| 0  | 3,64| 2 |
|                | MTX          | UPA 6 mg + MTX | UPA 12 mg + MTX | UPA 18 mg + MTX | Placebo      | PEF 25mg OD | PEF 50mg OD | PEF 100mg OD | PEF 150mg OD | Placebo + MTX | BARI 1mg OD + MTX | BARI 2mg OD + MTX | BARI 4mg OD + MTX | BARI 8mg OD + MTX | Placebo + csDMARD | BARI 2mg + csDMARD |
|----------------|--------------|----------------|----------------|----------------|--------------|-------------|-------------|-------------|-------------|--------------|-------------------|-------------------|-------------------|-------------------|---------------------|-------------------|
| Takeuchi 2016  |              |                |                |                | Placebo      | 1.8         | 3.5         | 5.5         | 0           | Placebo      | 2                 | 4                 | 0                 | 0                 | 89.8               | 97.7               |
|                |              | UPA 6 mg + MTX | 55             | 4              | 22            | 0           | 1.82        | 0           | 0           | 1.8          | 32.7              | 2                 | 0                 | 0                 | 0                   | 0                  |
|                |              | UPA 12 mg + MTX| 55             | 4              | 40            | 0           | 7.27        | 2           | 0           | 3.5          | 24.6              | 0                 | 0                 | 0                 | 0                   | 0                  |
|                |              | UPA 18 mg + MTX| 55             | 2              | 38            | 0           | 7.27        | 2           | 0           | 5.5          | 12.7              | 3.6               | 0                 | 0                 | 0                   | 0                  |
| Tanaka 2016    |              |                |                |                | Placebo + MTX| 2           | 22          | 0           | 0           | 2.04         | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
|                |              | BARI 1mg OD + MTX| 24             | 0              | 25            | 0           | 4.17        | 0           | 0           | 0           | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
|                |              | BARI 2mg OD + MTX| 24             | 4              | 17            | 0           | 0           | 0           | 0           | 0           | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
|                |              | BARI 4mg OD + MTX| 24             | 0              | 29            | 0           | 0           | 0           | 0           | 0           | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
|                |              | BARI 8mg OD + MTX| 24             | 4              | 21            | 0           | 0           | 0           | 0           | 0           | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
| Dougados 2017 (RA-BUILD) | | Placebo + csDMARD | 228          | 89.8           | 5             | 35          | 7.89        | 0           | 0           | 0           | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
|                |              | BARI 2mg + csDMARD | 229          | 97.7           | 3             | 31          | 6.11        | 2           | 0           | 0           | 0                 | 0                 | 0                 | 0                 | 0                   | 0                  |
| Study | Treatment | N  | AI  | DMARD | N  | AI  | DMARD |
|-------|-----------|----|-----|--------|----|-----|--------|
| Fleischmann 2017a [22] | BARI 4mg + csDMARD | 227 | 96.4 | 5 | 42 | 10.57 | 1 |
| | TOFA 5mg BID + PLC | 384 | 24 | 9 | 2 | 0 | 7 | 1 |
| | TOFA 5mg BID + MTX | 376 | 7 | 3 | 1 | 10 | 2 |
| | ADA 40mg Q2W + MTX | 386 | 6 | 2 | 0 | 8 | 2 |
| Fleischmann 2017b (RA-BEGIN) [23] | Placebo + MTX | 210 | 52 | 10 | 38 | 7.14 | <1 |
| | BARI 4mg + Placebo | 159 | 8 | 43 | 7.55 | 2 |
| | BARI 4mg + MTX | 215 | 8 | 50 | 7.44 | 1 |
| Genovese 2017 [24] | Placebo + HCQ/SZP | 51 | 12 | 3.9 | 0 | 2.0 |
| | PEF 25mg + HCQ/SZP | 59 | 3.4 | 1.7 | 0 |
| | PEF 50mg + HCQ/SZP | 57 | 3.5 | 0 | 0 |
| | PEF 100mg + HCQ/SZP | 58 | 6.9 | 0 | 0 |
| | PEF 150mg + HCQ/SZP | 64 | 3.1 | 0 | 0 |
| Kivitz 2017 [25] | Placebo + MTX | 72 | 12 | 0 | 0 | 5.6 | 0 |
| Treatment | Patients | Month | PEF 25mg + MTX | PEF 50mg + MTX | PEF 100mg + MTX | PEF 150mg + MTX | Placebo | FILGO 50mg OD | FILGO 100mg OD | FILGO 200mg OD | Placebo + MTX | BARI 4mg + MTX | ADA 40mg Q2W + MTX | Study 1: Placebo + MTX | Study 1: FILGO 200mg OD + MTX |
|-----------|----------|-------|----------------|----------------|----------------|----------------|--------|----------------|----------------|----------------|----------------|----------------|----------------|----------------------|--------------------------|--------------------------|
|           |          |       | 66             | 78             | 84             | 78             | 72     | 72             | 70             | 69             | 488            | 487            | 330                 | 12                      | 12                      |
|           |          |       | 0              | 0              | 2.4            | 1.3            | 1.4    | 1.4            | 0              | 4.3            | 197.7          | 215.0          | 141.9               | 8.3                     | 0                      |
|           |          |       | 0              | 0              | 1.2            | 1.3            | 0      | 0              | 0              | 1.4            | 27             | 36             | 33                  | <1                      | <1                      |
|           |          |       | 3.0            | 3.8            | 4.8            | 3.8            | 0      | 0              | 0              | 0              | 2.87           | 3.08           | 3.94                | 0.0                     | 0                      |
|           |          |       | 0              | 0              | 2.4            | 1.3            | 0      | 0              | 0              | 0              | <1             | 1              | 1                   | 8.3                     | 0                      |

Kavanaugh 2017 (DARWIN 2) [26]

Taylor 2017 (RA-BEAM) [27]

Vanhoultte 2017 [28]
| Study 1: FILGO 100mg BID + MTX | 12 | | | 0 |
| Study 2: Placebo + MTX | 17 | | | 0 |
| Study 2: FILGO 30mg OD + MTX | 17 | | | 5.9 |
| Study 2: FILGO 75mg OD + MTX | 22 | | | 0 |
| Study 2: FILGO 150mg OD + MTX | 15 | | | 0 |
| Study 2: FILGO 300mg OD + MTX | 20 | | | 0 |
| Placebo + MTX | 86 | 12 | 7.1 | 1.8 | 0 | 1.12 |
| FILGO 50mg OD + MTX | 82 | | 0 | 0 | 0 | 0 |
| FILGO 100mg OD + MTX | 85 | | 4.7 | 3.5 | 0 | 0 |
| FILGO 200mg OD + MTX | 86 | | 2.3 | 1.2 | 0 | 1.12 |
| FILGO 25mg BID + MTX | 86 | | 1.4 | 0 | 0 | 1.12 |

Westhovens 2017 (DARWIN 1) [29]
| Study                                      | Placebo + csDMARD | Placebo + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX | csDMARD + MTX |
|-------------------------------------------|-------------------|---------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Burmester 2018 (SELECT-NEXT) [30]         | Placebo + csDMARD | 221           | 12             | 2              | 21             | <1             | 0              | 4.07           | <1             |
|                                           | UPA 15mg + csDMARD| 221           |                | 4              | 29             | <1             | 0              | 5.43           | <1             |
|                                           | UPA 30mg + csDMARD| 219           |                | 3              | 32             | 1              | 0              | 5.94           | 1              |
| Fleischmann 2018 (SELECT-COMPARE) [31, 32]| Placebo + MTX    | 652           | 26             | 250.3          | 2.9            | 23.6           | 0.8            | 0              | 0              |
|                                           | UPA 15mg OD + MTX| 650           | 24             | 289.6          | 3.7            | 34.8           | 1.8            | 0              | 0.8            |
|                                           | ADA 40mg Q2W + MTX| 327           |                | 137.6          | 4.3            | 29.1           | 1.5            | 0.3            | 0              |
| Hu 2018 (RA-BALANCE) [35, 36]            | Placebo + MTX    | 145           | 24             | 2.76           |                | 15.17          | 0              |                |                |
|                                           | BARI 4mg + MTX   | 145           |                | 2.76           |                | 19.31          | 0.69           |                |                |
| Smolen 2018 (SELECT-MONOTHERAPY) [37, 38] | Continued MTX   | 216           | 14             | 3              | 26             | <1             | 0              |                | <1             |
|                                           | UPA 15mg OD      | 217           |                | 5              | 19             | <1             | 0              |                | 1              |
|                                           | UPA 30mg OD      | 215           |                | 3              | 25             | 0              | 0              |                | 3              |
| Tanaka 2018a (SELECT-SUNRISE)            | Placebo + csDMARD| 49            | 12             | 0              | 22.4           | 0              | 0              | 0              | 2              |
| Study                          | Treatment                        | n   | 12   | ACR20 |
|-------------------------------|----------------------------------|-----|------|-------|
| [39, 40]  | UPA 7.5mg + csDMARDs           | 49  | 2    | 36.7  |
|                  | UPA 15mg + csDMARDs            | 49  | 2    | 32.7  |
|                  | UPA 30mg + csDMARDs            | 50  | 10   | 44.0  |
| Tanaka & Takeuchi 2018 [41, 42] | Placebo ± csDMARDs             | 101 | 22.6 | 0*    |
|                  | PEF 100mg OD ± csDMARDs        | 104 | 88.2 | 2.9   |
|                  | PEF 150mg OD ± csDMARDs        | 102 | 92.1 | 0     |
|                  | Open-label ETA 50mg QW ± csDMARDs | 200 | 195.5 | 2   |
| Takeuchi 2018 [43, 44]       | Placebo + MTXs                 | 170 | 62.9 | 0/0*  |
|                  | PEF 100mg OD + MTXs            | 174 | 159.5 | 2.9 |
|                  | PEF 150mg OD + MTXs            | 174 | 160.8 | 1.7 |
| van Vollenhoven ACR 2018 (SELECT-EARLY) [45] | Placebo + MTX             | 314 | 4.14 | 4.14 |
|                  | UPA 15mg + MTX                 | 317 | 4.73 | 6.31 |
|                  | UPA 30mg + MTX                 | 314 | 6.37 | 7.01 |
* reported as incidence rate (95% confidence intervals); * patients with insufficient response were re-assigned to TOFA 5mg BID at week 12, data shown here for patients not reassigned; * all patients in ADA 40mg EOW re-assigned to TOFA 5mg, therefore data at week 12 shown for this treatment arm; * Two events (2/200; 1%) of pulmonary embolism in the TOFA 10mg BID arm were reported between month 3 and month 6; NR: not reported;
Table S4.2.2: Psoriatic Arthritis

| Study                                      | Group                        | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|--------------------------------------------|------------------------------|-----------------|-------------------|-----------------------|---------|----------------|-----------------------|------------------|-----------------|------------------|
| Mease 2017 (OPAL Broaden) [49]             | Placebo ± csDMARD           | 105             |                   | 1/NA                  | 0/NA    | 0/0            | 4.8/NA               | 0/NA             |                 |                  |
|                                            | Placebo to TOFA 5mg BID ± csDMARD | 52             |                   | NA/6                  | NA/4    | 0/0            | NA/9.6               | NA/0             |                 |                  |
|                                            | Placebo to TOFA 10mg BID ± csDMARD | 53             | 12/54             | NA/8                  | NA/0    | 0/0            | NA/9.4               | NA/0             |                 |                  |
|                                            | TOFA 5mg BID ± csDMARD       | 107             |                   | 3/8                   | 0/0     | 0/0            | 1.9/9.3              | 1/2              |                 |                  |
|                                            | TOFA 10mg BID ± csDMARD      | 104             |                   | 1/4                   | 0/1     | 0/0            | 4.8/10.6             | 0/2              |                 |                  |
|                                            | ADA 40mg Q2W ± csDMARD       | 106             |                   | 1/8                   | 0/1     | 0/0            | 2.8/7.5              | 0/0              |                 |                  |
| Gladman 2017 (OPAL Beyond) [50]           | Placebo ± csDMARD           | 131             | 24                | 2                     | 0       | 0              | 4.6                  | 0                |                 |                  |
|                                            | TOFA 5mg BID ± csDMARD       | 131             |                   | 1                     | 0       | 0              | 7.6                  | 1                |                 |                  |
|                                            | TOFA 10mg BID ±              | 132             |                   | 2                     | 2       | 0              | 4.5                  | 1                |                 |                  |
| Study                           | Group                           | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|--------------------------------|---------------------------------|-----------------|-------------------|-----------------------|---------|----------------|-----------------------|-----------------|------------------|------------------|
| Mease 2018                     | Placebo ± csDMARD               | 66              |                   |                        | 2       | 21             | 0                     | 0               | 15               | 2                |
|                                | FILGO 200mg OD ± csDMARD        | 65              | 16                |                        | 2       | 22             | 2                     | 0               | 15               | 0                |
| Van der Heijde 2017            | Placebo ± csDMARD               | 51              | 12                |                        | 3.9     | 23.5           | 0                     | 0               | 2.0              | 0                |
|                                | TOFA 2mg BID ± csDMARD          | 52              |                   |                        | 0       | 23.1           | 0                     | 0               | 7.7              | 2                |
|                                | TOFA 5mg BID ± csDMARD          | 52              |                   |                        | 1.9     | 21.2           | 0                     | 0               | 0                | 0                |
|                                | TOFA 10mg BID ± csDMARD         | 52              |                   |                        | 1.9     | 17.3           | 0                     | 0               | 5.8              | 2                |
| Van der Heijde 2018            | Placebo ± csDMARD               | 58              | 12                |                        | 0       | 0              | 0                     | 0               |                  |                  |
|                                | FILGO 200mg OD ±                | 58              |                   |                        | 2       | 2              | 0                     |                  |                  |                  |

Table S4.2.3: Ankylosing spondylitis
| csDMARD |   |   |   |   |   |   |   |
| Study         | Group                                      | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|--------------|--------------------------------------------|-----------------|-------------------|-----------------------|---------|----------------|------------------------|-----------------|-------------------|-------------------|
|              | Placebo ± csDMARD                          | 11              |                   |                       | 0       | 27             |                        | 0               |                   |                   |
|              | Solcitinib 50mg BID ± csDMARD               | 9               | 12                |                       | 0       | 11             | 67                     | 0               |                   |                   |
| Kahl 2016 [54] | Solcitinib 100mg BID ± csDMARD              | 10              |                   |                       | 0       | 20             | 40                     | 0               | 10                |                   |
|              | Solcitinib 200mg BID ± csDMARD              | 10              |                   |                       | 0       | 40             | 30                     | 0               |                   |                   |
|              | Solcitinib 400mg BID ± csDMARD              | 10              |                   |                       | 0       | 10             | 40                     | 0               | 20                |                   |
|              | Placebo ± csDMARD                          | 105             |                   |                       | 0       | 5              | 39                     | 1               | 0                 | 1                 |
| Wallace 2018 [55] | BARI 2mg OD ± csDMARD                      | 105             |                   |                       | 0       | 10             | 45                     | 2               | 0                 | 0                 |
|              | BARI 4mg OD ± csDMARD                       | 104             |                   |                       | 0       | 10             | 45                     | 6               | 0                 | 1                 |
### Table S4.2.5: Psoriasis

| Study               | Group                      | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|---------------------|----------------------------|-----------------|-------------------|-----------------------|---------|----------------|----------------------|------------------|------------------|-------------------|
| Papp 2012 [56]      | Placebo                    | 50              | 12                | 0                     | 0       | 18.7           | 0                    | 10.0             |                  |                   |
|                     | TOFA 2mg BID               | 49              |                   | 4.1                   |         |                |                      |                  |                  |                   |
|                     | TOFA 5mg BID               | 49              |                   | 2.0                   |         |                |                      |                  |                  |                   |
|                     | TOFA 15mg BID              | 49              |                   | 0                     |         |                |                      |                  |                  | 4.1               |
| Bachelez 2015 [57]  | Placebo                    | 107             | 12                | 2                     | 18.7    | 0              | 0                    | 0                | 0                | 0                 |
|                     | TOFA 5mg BID               | 329             |                   | 2                     | 19.1    | 0.6            | 1.8                  | 0.3              |                  |                   |
|                     | TOFA 10mg BID              | 330             |                   | 2                     | 21.5    | 0.6            | 1.2                  | 0.6              |                  |                   |
|                     | ETA 50mg twice weekly      | 335             |                   | 2                     | 23.3    | 0.6            | 2.1                  | 0.6              |                  |                   |
| Bissonnette 2014 [58]| TOFA 5mg BID              | 331             | 16                | 1.8                   |         |                |                      | 5.4              |                  | 0                 |
|                     | TOFA 10mg BID              | 335             |                   | 3.3                   |         |                |                      | 6.0              |                  | 0.6               |
| Papp 2015 [59]      | Placebo                    | 29              | 6                 | 0                     |         |                |                      |                  |                  |                   |
|                     | PEF 10mg BID               | 19              |                   | 0                     |         |                |                      |                  |                  |                   |
|                     | PEF 25mg BID               | 21              |                   | 0                     |         |                |                      |                  |                  |                   |
|                     | PEF 60mg BID               | 19              |                   | 0                     |         |                |                      |                  |                  |                   |
|                     | PEF 100mg                  | 17              |                   | 0                     |         |                |                      |                  |                  |                   |
| Study  | Group          | N  | No. | Mean | SE  | Median | SE  |
|--------|----------------|----|-----|------|-----|--------|-----|
|        |                |    |     |      |     |        |     |
| Papp 2015 [60] |                |    |     |      |     |        |     |
| Study 1: Placebo | PEF 50mg OD | 19 | 0   |      |     |        |     |
| Study 1: TOFA 5mg BID | 363   | 2.8 | 0   | 6.7 | 0.8 |
| Study 1: TOFA 10mg BID | 360   | 2.8 | 0.6 | 2.8 | 1.4 |
| Study 2: Placebo | 196   | 2.9 | 0   | 4.7 | 0   |
| Study 2: TOFA 5mg BID | 382   | 1.3 | 0.8 | 5.5 | 0.8 |
| Study 2: TOFA 10mg BID | 381   | 1.0 | 0   | 3.1 | 0.3 |
| Bissonnette 2016 [61] | Placebo | 12 | 4   | 0   | 8.3 | 0     |
| Itacitinib 100mg OD | 9     | 0   |     | 0   |
| Itacitinib 200mg OD | 9     | 0   |     | 23.7|
| Itacitinib 200mg BID | 9     | 0   |     | 0   |
| Itacitinib 600mg OD | 11    | 0   |     | 0   |
| Papp 2016 [62] | Placebo | 34 | 12  | 2.9 | 26.5| 2.9   |


| Treatment                  | N  | PBO | BMS-986165 |
|---------------------------|----|-----|------------|
| **BARI 2mg**              | 32 | 3.1 | 18.8       |
| **BARI 4mg**              | 72 | 1.4 | 16.7       |
| **BARI 8mg**              | 64 | 1.6 | 23.4       |
| **BARI 10mg**             | 69 | 1.4 | 24.6       |
| **Papp 2016 [63]**        |    |     |            |
| Vehicle BID               | 71 | 2.8 | 8.45       |
| 2% TOFA BID               | 71 | 0   | 2.82       |
| 1% TOFA BID               | 70 | 7.1 | 14.29      |
| Vehicle OD                | 74 | 1.4 | 1.35       |
| 2% TOFA OD                | 70 | 0   | 2.86       |
| 1% TOFA OD                | 74 | 2.7 | 0          |
| **Zhang 2017 [64]**       |    |     |            |
| Placebo                   | 88 | 0   | 0          |
| TOFA 5mg BID              | 88 | 2.3 | 1.1        |
| TOFA 10mg BID             | 90 | 0   | 3.3        |
| **Papp 2018 [65]**        |    |     |            |
| Placebo                   | 45 | 2   | 0          |
| BMS-986165 3mg EOD        | 44 | 2   | 2          |
| BMS-986165 3mg OD         | 44 | 2   | 7          |
| BMS-986165 3mg BID        | 45 | 2   | 2          |
| BMS-986165                | 45 | 0   | 9          |
| 6mg BID    |        |        |        |        |        |
|-----------|--------|--------|--------|--------|--------|
| BMS-986165| 44     | 0      |        |        | 2      |
| 12mg OD   |        |        |        |        |        |
| Study                        | Group                     | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|------------------------------|---------------------------|-----------------|-------------------|-----------------------|---------|----------------|------------------------|----------------|------------------|------------------|
| Alopecia areata              |                           |                 |                   |                       |         |                |                        |                |                  |                  |
| Guttman-Yassky 2018 [66]     | Placebo                   | 142             | 24                |                       | 0       | 17.1           | 0                      | 0               | 0                | 0                |
|                             | PF-06651600               |                 |                   | 200mg OD (4 weeks) / 50mg OD (20 weeks) | 0       |                |                        | 0               |                  | 0                |
|                             | PF-06700841               |                 |                   | 60mg OD (4 weeks) /30mg OD (20 weeks) | 0       |                |                        | 0               |                  | 0                |
| Atopic dermatitis            |                           |                 |                   |                       |         |                |                        |                |                  |                  |
| Bissonette 2016 [67]         | Topical TOFA 2% BID       | 35              | 4                 |                       | 0       | 17.1           | 0                      | 0               | 0                | 0                |
|                             | Topical Vehicle BID       | 34              |                   |                       | 0       | 8.8            | 0                      | 2.9             | 0                | 2.9              |
| De Bruin-Weller 2018 [68, 69] | Placebo                   | 41              | 16                |                       | 2.5     | 20             | 0                      | 0               | 0                | 10               |
|                             | UPA 7.5mg OD              | 42              |                   |                       | 4.8     | 52             | 4.8                    | 0               | 17               |                  |
|                             | UPA 15mg OD               | 42              |                   |                       | 2.4     | 43             | 2.4                    | 0               | 12               |                  |
|                             | UPA 30mg OD               | 42              |                   |                       | 0       | 41             | 0                      | 0               | 12               |                  |
| Guttman-Yassky               | Placebo + topical         | 49              | 16                |                       | 0       |                |                        | 0               | 2                | 0                |
### Table S4.2.7: Ulcerative Colitis

| Study           | Group                  | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|-----------------|------------------------|-----------------|-------------------|-----------------------|---------|----------------|-----------------------|-----------------|-----------------|------------------|
| Sandborn 2012 [72] | Placebo ± Mesalamine  | 48              | 8                 |                       | 8       | 15             | 0                     | 0               | 0               | 0                |

| 2018 [70] | steroids |
|-----------|----------|
| BARI 2mg OD + topical steroids | 37 | 0 | 0 |
| BARI 4mg OD + topical steroids | 38 | 3 | 5 |

| Nakagawa 2018 [71] | Vehicle |
|-------------------|---------|
| Topical JTE-052 0.25% | 69 | 0 |
| Topical JTE-052 0.5%  | 65 | 0 |
| Topical JTE-052 1% | 66 | 0 |
| Topical JTE-052 3% | 65 | 0 |
| Topical tacrolimus | 30 | 0 |
| Dose Level                  | Patients | Remission Rate | Low (0-1.5) | Moderate (1.6-4) | Severe (4+) | NAC (mg) | NAC (mg) |
|-----------------------------|----------|----------------|-------------|------------------|-------------|----------|----------|
| TOFA 0.5mg BID ± Mesalamine | 31       | 3              | 26          | 0                | 3.23        | 3.23     |
| TOFA 3mg BID ± Mesalamine  | 33       | 3              | 9           | 0                | 3.03        | 0        |
| TOFA 10mg BID ± Mesalamine | 33       | 6              | 27          | 6                | 3           | 3.03     |
| TOFA 15mg BID ± Mesalamine | 49       | 4              | 6           | 0                | 0           | 0        |
| Sandborn 2017 [73]ÓCTAVE Induction 1: Placebo | 122 | 4.1           | 15.6        | 0                | 0           | 0.82     | 0.8      |
| OCTAVE Induction 1: TOFA 10mg BID | 476 | 3.4           | 23.3        | 1.3              | 0           | 3.15     | 0.6      |
| OCTAVE Induction 2: Placebo | 112 | 8.0           | 15.2        | 0                | 0           | 0        |
| OCTAVE Induction 2: TOFA 10mg BID | 429 | 4.2           | 18.2        | 0.2              | 0           | 0.5      |
| OCTAVE Sustain: Placebo    | 198 | 6.6           | 24.2        | 1.0              | 0           | 0.5      |
| Study | Group | No. of | Timepoint | Exposure (Pat.) | SAE | Infections | Serious infection | Tuberculosis | URT Infection | Herpes zoster |
|-------|-------|-------|-----------|-----------------|-----|------------|------------------|--------------|----------------|---------------|
| OCTAVE Sustain: TOFA 5mg BID | 198 | | | | 5.1 | 35.9 | 1.0 | 0 | 1.5 |
| OCTAVE Sustain: TOFA 10mg BID | 197 | | | | 5.6 | 39.8 | 0.5 | 0 | 5.1 |
| Sandborn 2018 [74, 75] | Placebo | 46 | 8 | | 10.9 | 34.8 | 4.3 | 0 | |
| | UPA 7.5mg OD | 47 | | | 0 | 19.1 | 0 | 0 | |
| | UPA 15mg OD | 49 | | | 4.1 | 20.4 | 2.0 | 0 | |
| | UPA 30mg OD | 52 | | | 5.8 | 11.5 | 0 | 0 | |
| | UPA 45mg OD | 56 | | | 5.4 | 23.2 | 3.6 | 1.8 | |
| Sands 2018 [76] | Placebo | 43 | 8 | | 4.7 | 14 | 2.3 | 0 | 0 |
| | Peficitinib 25mg OD | 44 | 8 | | 4.5 | 4.5 | 0 | 0 | 0 |
| | Peficitinib 75mg OD | 44 | | | 0 | 11.4 | 0 | 0 | 0 |
| | Peficitinib 150mg OD | 44 | | | 2.3 | 11.4 | 0 | 0 | 0 |
| | Peficitinib 75mg BID | 44 | | | 6.8 | 22.7 | 2.3 | 0 | 0 |

Table S4.2.8: Crohn’s Disease
|                | patients | (weeks) | Years | (%) | (%) | (%) | (%) |
|----------------|----------|---------|-------|-----|-----|-----|-----|
| **Sandborn 2014 [77]** |          |         |       |     |     |     |     |
| Placebo        | 34       | 4       |       | 14.7| 23.5| 2.94|     |
| TOFA 1mg BID   | 36       |         |       | 11.1| 13.9| 0   |     |
| TOFA 5mg BID   | 34       |         |       | 11.8| 23.5| 0   |     |
| TOFA 15mg BID  | 35       |         |       | 2.9 | 14.3| 2.86|     |
| **Panés 2017 [78]** |          |         |       |     |     |     |     |
| Induction: Placebo | 91     | 8       |       | 13.08| 3.3 | 2   | 0   |
| Induction: TOFA 5mg BID | 86  |         |       | 12.95| 3.5 | 2   | 0   |
| Induction: TOFA 10mg BID | 86 |         |       | 12.43| 11.6| 2   | 0   |
| Maintenance: Placebo | 59     | 26      |       | 20.17| 11.9| 0   | 3.39| 0   |
| Maintenance: TOFA 5mg BID | 60 |         |       | 22.87| 10.0| 5   | 1.67| 0   |
| Maintenance: TOFA 10mg BID | 61 |         |       | 23.55| 13.1| 3.2 | 1.64| 2.3 |
| **Sandborn 2017 / Panés 2018 [79-81]** |          |         |       |     |     |     |     |
| Induction: Placebo | 37     | 16      |       | 5.4 | 32.4| 0   | 0   |
| Induction: UPA 3mg BID | 39   |         |       | 12.8| 41.0| 7.7 | 0   |
| Induction:     | 37       |         |       | 5.4 | 51.4| 0   | 0   |
|                  | **UPA 6mg BID** | **UPA 12mg BID** | **UPA 24mg BID** | **UPA 24mg OD** | **UPA 24mg OD** | **UPA 24mg OD** | **UPA 24mg OD** | **UPA 24mg OD** |
|-----------------|----------------|------------------|------------------|----------------|----------------|----------------|----------------|----------------|
| **Induction:**  |                |                  |                  |                |                |                |                |                |
| **UPA 6mg BID** | 27.8          | 44.4             | 8.3              | 0              | 0              | 0              | 0              | 0              |
| **Induction:**  |                |                  |                  |                |                |                |                |                |
| **UPA 24mg BID**| 8.3           | 55.6             | 2.8              | 0              | 2.8            | 2.8            | 2.8            | 2.8            |
| **Induction:**  |                |                  |                  |                |                |                |                |                |
| **UPA 24mg OD** | 20.0          | 34.3             | 5.7              | 0              | 0              | 0              | 0              | 0              |
| **Maintenance:**|                |                  |                  |                |                |                |                |                |
| **UPA 3mg BID** | 25.0          | 36.7             | 8.3              | 0              | 0              | 0              | 0              | 0              |
| **Maintenance:**|                |                  |                  |                |                |                |                |                |
| **UPA 6mg BID** | 8.7           | 26.1             | 0                | 0              | 0              | 0              | 0              | 0              |
| **Maintenance:**|                |                  |                  |                |                |                |                |                |
| **UPA 12mg BID**| 8.5           | 37.3             | 1.7              | 0              | 1.7            | 1.7            | 1.7            | 1.7            |
| **Maintenance:**|                |                  |                  |                |                |                |                |                |
| **UPA 24mg OD** | 11.1          | 27.8             | 0                | 0              | 2.8            | 2.8            | 2.8            | 2.8            |

**Vermeire 2017 [82]**

|                  | **Placebo** | **Placebo** | **Placebo** | **Placebo** | **Placebo** | **Placebo** | **Placebo** | **Placebo** |
|------------------|------------|------------|------------|------------|------------|------------|------------|------------|
| **Placebo**      | 44         | 0-20       | 14         | 27         | 0          | 0          | 0          | 0          |
| **Placebo**      | 22         | 0-10       | 0          | 23         | 0          | 0          | 0          | 0          |
| **Placebo to FILGO 100mg** | 22 | 10-20 | 5 | 27 | 0 | 0 | 0 | 0 |
| **FILGO 200mg**  | 23         | 0-10       | 0          | 30         | 0          | 0          | 0          | 0          |
| **FILGO 200mg to Placebo** | 23 | 10-20 | 0 | 26 | 0 | 0 | 0 | 0 |
| **FILGO 200 to** | 30         | 0-20       | 3          | 30         | 3          | 3          | 3          | 3          |
### Safety outcomes (adverse events of special interest) of randomized controlled trials

**Table S4.3.1: Rheumatoid Arthritis**

| Study                  | Group                          | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolaemia (%) | MACE (%) | Malignancy (%) | Malignancy (%) | NMSC (%) |
|------------------------|--------------------------------|-----------------|-------------------|-----------------------------|----------------|----------------|--------------------------|--------------------------|-------------|--------------------------|--------------------------|--------------------------|-----------|---------------|---------------|---------|
| Kremer 2009 [1]        | Placebo                       | 65              | 6                 | 1.5                         | 4.6            | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 5mg BID                   | 61              |                   | 3.3                         | 1.6            | 3.3            |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 15mg BID                  | 69              |                   | 2.9                         | 2.9            | 5.8            |                          |                          | 1.45        |                          |                          |                          |           |               |               |         |
|                        | TOFA 30mg BID                  | 69              |                   | 10.1                        | 5.8            | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
| Tanaka 2011a [2]       | Placebo + MTX                 | 28              | 12                |                             | 0              | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 1mg BID + MTX             | 28              |                   |                             | 0              | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 3mg BID + MTX             | 27              |                   |                             | 0              | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 5mg BID + MTX             | 27              |                   |                             | 3.7            | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 10mg BID + MTX            | 26              |                   |                             | 0              | 3.9            |                          |                          |             |                          |                          |                          |           |               |               |         |
| Fleischmann 2012 [3]   | Placebo²                      | 34              | 12²/24            |                             | 0              | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 1mg BID¹                  | 37              |                   |                             | 0              | 0              |                          |                          | 0           |                          |                          |                          |           |               |               |         |
|                        | TOFA 3mg BID¹                  | 34              |                   |                             | 0              | 2.9            |                          |                          | 2.9         |                          |                          |                          |           |               |               |         |
|                        | TOFA 5mg BID                   | 49              |                   |                             | 2.0            | 0              |                          |                          | 4.1         |                          |                          |                          |           |               |               |         |
|                        | TOFA 10mg BID                  | 61              |                   |                             | 0              | 3.3            |                          |                          | 3.3         |                          |                          |                          |           |               |               |         |
| Study                        | Treatment                                      | n  | Duration | ESR | CRP |
|------------------------------|------------------------------------------------|----|----------|-----|-----|
| Fleischmann 2012 [4]        | Placebo                                        | 122| 12       | 1.6 | 0   |
| TOFA 5mg BID                 | 243                                            |    |          | 1.6 | 0.4 |
| TOFA 10mg BID                | 245                                            |    |          | 2.4 | 1.2 |
| Kremer 2012 [5]              | Placebo + MTX                                  | 69 |          |     | 0   |
| TOFA 1mg BID + MTX           | 70                                             |    |          |     | 2.9 |
| TOFA 3mg BID + MTX           | 68                                             |    |          |     | 1.5 |
| TOFA 5mg BID + MTX           | 71                                             |    |          |     | 0   |
| TOFA 10mg BID + MTX          | 74                                             |    |          |     | 0   |
| TOFA 15mg BID + MTX          | 75                                             |    |          |     | 5.3 |
| TOFA 20mg BID + MTX          | 80                                             |    |          |     | 2.5 |
| Van Vollenhoven 2012 [6]     | Placebo + MTX (cross-over to TOFA 5mg BID + MTX after 3 months) | 56 | 12       |     |     |
| Placebo + MTX (cross-over to TOFA 10mg BID + MTX after 3 months) | 52 |     |     |     |
| TOFA 5mg BID + MTX           | 204                                            |    |          | 1.5 | 0   |
| TOFA 10mg BID + MTX          | 201                                            |    |          | 2.0 | 0.5 |
| ADA 40mg EOW + MTX           | 204                                            |    |          | 0.5 | 0   |
| Placebo + MTX (Combination group) | 106                                          |    |          | 0   | 0.8 |
| Burmester                   | Placebo + MTX                                  | 132| 12       |     |     |
|                             |                                                |    |          |     |     |
|                             |                                                |    |          | 0.8 | 0   |
|                             |                                                |    |          | 0   | 0   |
| Year     | Treatment                        | n  | ACR50 | ACR20 | Complete | EULAR | PASI 75 |
|----------|----------------------------------|----|-------|-------|----------|-------|---------|
| 2013 [7] | TOFA 5mg BID + MTX              | 133| 0     | 0     | 0        | 0     | 0       |
|          | TOFA 10mg BID + MTX             | 134| 1.5   | 1.6   | 0.7      | 0     | 0       |
|          | Kremer 2013                      |    |       |       |          |       |         |
|          | Placebo + DMARD (Combination group) | 159| 52    | <1/1.9| 0*       | 6.9*  | 4.2*    |
|          | TOFA 5mg BID + DMARD             | 315|       | 0*    | 2.8*     |       |         |
|          | TOFA 10mg BID + DMARD            | 318|       | <1/1   | 6.9*     | 1.6*  |         |
|          | Van der Heijde 2013              |    |       |       |          |       |         |
|          | Placebo + DMARD (Combination group) | 160| 12    | 1.9   | 0        | 0     | 0       |
|          | TOFA 5mg BID + DMARD             | 321|       | <1.0  | 0        | 0     | 1.6     |
|          | TOFA 10mg BID + DMARD            | 316|       | 1.9   | 0.9      | 0.3   | 1.9     |
|          | Lee 2014 [11]                    |    |       |       |          |       |         |
|          | MTX                              | 186| 288   | 3.3/7.1| 3.8      | 0.1   | 0.5     |
|          | TOFA 5mg BID                     | 373|       | 1.6/3.0| 4.0      | 0     | 2.4     |
|          | TOFA 10mg BID                    | 397|       | 1.5/3.0| 3.0      | 0.002 | 3.8     |
|          | Tanaka 2015 [12]                 |    |       |       |          |       |         |
|          | Placebo                          | 52 | 12    | 3.8   | 0        | 0     | 0       |
|          | TOFA 1mg BID                     | 53 |       | 1.9   | 0        | 0     | 0       |
|          | TOFA 3mg BID                     | 53 |       | 1.9   | 0        | 0     | 3.8     |
|          | TOFA 5mg BID                     | 52 |       | 0     | 0        | 0     | 0       |
|          | TOFA 10mg BID                    | 53 |       | 0     | 0        | 5.7   |         |
|          | TOFA 15mg BID                    | 54 |       | 1.9   | 0        | 0     |         |
|          | Fleischmann 2015 [13]            |    |       |       |          |       |         |
|          | Placebo                          | 41 | 12    | 0/0   | 0        | 0     | 0       |
|          | DEC 25mg BID                     | 41 |       | 0/0   | 0        | 0     | 0       |
|          | DEC 50mg BID                     | 41 |       | 0/2.4 | 0        | 0     |         |
| Study                | Treatment                                           | N  | Median (IQR) | Mean (IQR) | Median (IQR) | Mean (IQR) | Median (IQR) | Mean (IQR) |
|---------------------|-----------------------------------------------------|----|--------------|------------|--------------|------------|--------------|------------|
| Genovese 2016a      | DEC 100mg BID                                       | 40 | 2.5/5.0      |            |              |            |              |            |
|                     | DEC 150mg BID                                       | 41 | 0/2.4        |            |              |            |              |            |
|                     | Placebo + csDMARD                                   | 176| 24           | 1          | 1            | 0          |              |            |
|                     | BARI 2mg + csDMARD                                 | 174|              | 2          |              | <1         |              | 0          |
|                     | BARI 4mg + csDMARD                                 | 177|              | <1         |              | 4          |              | 1          |
| Genovese 2016b      | Placebo + MTX                                      | 50 | 12           | 0          |              |            |              |            |
|                     | UPA 3mg BID + MTX                                 | 50 |              | 0          |              |            |              |            |
|                     | UPA 6mg BID + MTX                                 | 50 |              | 0          |              |            |              |            |
|                     | UPA 12mg BID + MTX                                | 50 |              | 6          |              | 2          |              |            |
|                     | UPA 18mg BID + MTX                                | 50 |              | 2          |              |            |              |            |
|                     | UPA 24mg QD + MTX                                 | 49 |              | 0          |              |            |              |            |
| Genovese 2016c      | Placebo + MTX                                      | 71 | 24           | 0          | 7            | 1.4        |              |            |
|                     | DEC 100mg OD + MTX                                | 71 |              | 2.8        | 2.8          | 4.2        |              |            |
|                     | DEC 150mg OD + MTX                                | 72 |              | 1.4        | 2.8          | 6.9        |              |            |
|                     | DEC 200mg OD + MTX                                | 72 |              | 2.8        | 8.3          | 4.2        |              |            |
|                     | DEC 100mg BID + MTX                               | 72 |              | 1.4        | 5.6          | 5.6        |              |            |
| Genovese 2016d      | Placebo + csDMARD                                  | 12 |              |            |              |            |              |            |
|                     | DEC 100mg BID + csDMARD                           | 11 |              |            |              |            |              |            |
|                     | DEC 200mg BID + csDMARD                           | 10 |              |            |              |            |              |            |
|                     | DEC 300mg BID + csDMARD                           | 10 |              |            |              |            |              |            |
| Kremer 2016         | Placebo                                            | 56 | 12           | 0          | 0            | 16         | 0            | 0          |
|                     | UPA 3 mg + MTX                                     | 55 |              | 0          | 0            | 15         | 0            | 0          |
| Study                          | Treatment                  | Placebo (%) | ESR (mm/h) | CRP (mg/L) | RF (%) | EULAR DAS28 (CRP) (Revised) |
|-------------------------------|----------------------------|-------------|------------|------------|--------|---------------------------|
| Takeuchi 2016 [19]           | Placebo                    | 56          | 12         | NR/1.8     |        |                           |
|                               | PEF 25mg OD                | 55          |            | NR/0       |        |                           |
|                               | PEF 50mg OD                | 57          |            | NR/0       |        |                           |
|                               | PEF 100mg OD               | 55          |            | NR/0       |        |                           |
|                               | PEF 150mg OD               | 58          |            | NR/0       |        |                           |
| Tanaka 2016 [20]              | Placebo + MTX              | 49          |            | 2.04       | 0      | 0                         |
|                               | BARI 1mg OD + MTX          | 24          |            | 0          | 0      | 0                         |
|                               | BARI 2mg OD + MTX          | 24          |            | 4.17       | 0      | 0                         |
|                               | BARI 4mg OD + MTX          | 24          |            | 4.17       | 4.2    | 0                         |
|                               | BARI 8mg OD + MTX          | 24          |            | 4.17       | 4.2    | 12.5                      |
| Dougados 2017 (RA-BUILD) [21]| Placebo + csDMARD          | 228         |            | 2.63       | 0      | 0.88                      |
|                               | BARI 2mg + csDMARD         | 229         |            | 2.62       | 0      | 2.18                      |
|                               | BARI 4mg + csDMARD         | 227         |            | 1.76       | 0.44   | 3.96                      |
| Fleischmann 2017a [22]       | TOFA 5mg BID + PLC         | 384         |            | <1/2       | 0.26   | 0                         |
|                               | TOFA 5mg BID + MTX         | 376         |            | 4/8        | 0      | 0                         |
|                               | ADA 40mg Q2W + MTX         | 386         |            | 0.95       | 0.26   | 1                         |
| Fleischmann 2017b (RA-BEGIN) [23]| Placebo + MTX         | 210         |            | <1         | 1.26   | 0.48                      |
|                               | BARI 4mg + Placebo         | 159         |            | 3          | 2.79   | 0                         |
|                               | BARI 4mg + MTX             | 215         |            | 2          | 1.86   | 0                         |
| Genovese                      | Placebo + HCQ/SZP          | 51          |            | 0          | 0      | 0                         |

Legend:
- ESR: Erythrocyte Sedimentation Rate
- CRP: C-reactive protein
- RF: Rheumatoid factor
- EULAR DAS28 (CRP) (Revised): European League Against Rheumatism Disease Activity Score 28 (CRP) (Revised)
| Study | Treatment | N  | 0  | 0  | 0  | 0  | 0  | 0  |
|-------|-----------|----|----|----|----|----|----|----|
| 2017 [24] | PEF 25mg + HCQ/SZP | 59 | 0  | 0  | 0  | 0  | 0  | 0  |
|       | PEF 50mg + HCQ/SZP | 57 | 0  | 0  | 0  | 0  | 0  | 0  |
|       | PEF 100mg + HCQ/SZP | 58 | 0  | 0  | 0  | 0  | 0  | 0  |
|       | PEF 150mg + HCQ/SZP | 64 | 0  | 0  | 0  | 0  | 0  | 0  |
| Kivitz 2017 [25] | Placebo + MTX | 72 | 0  | 0  | 0  | 0  | 0  | 2.8 |
|       | PEF 25mg + MTX | 66 | 0  | 0  | 0  | 0  | 0  | 4.5 |
|       | PEF 50mg + MTX | 78 | 0  | 1.3| 0  | 0  | 0  | 0  |
|       | PEF 100mg + MTX | 84 | 0  | 0  | 0  | 1.2| 1.2| 0  |
|       | PEF 150mg + MTX | 78 | 0  | 0  | 0  | 0  | 0  | 0  |
| Kavanaugh 2017 (DARWIN 2) [26] | Placebo | 72 | 0  | 0  | 0  | 25 | 0  |
|       | FILGO 50mg OD | 72 | 0  | 1.4| 20.8| 0  |
|       | FILGO 100mg OD | 70 | 1.4| 0  | 10  | 0  |
|       | FILGO 200mg OD | 69 | 1.4| 0  | 8.7 | 0  |
| Taylor 2017 (RA-BEAM) [27] | Placebo + MTX | 488| 0  | 0  | 0  | <1 | <1|
|       | BARI 4mg + MTX | 487| 0.2| 0.2| <1 | <1 | 0  |
|       | ADA 40mg Q2W + MTX | 330| 0  | 0  | 0  | 0  |
| Vanhoutte 2017 [28] | Study 1: Placebo + MTX | 12| 0  |
|       | Study 1: FILGO 200mg OD + MTX | 12| 0  |
|       | Study 1: FILGO 100mg BID + MTX | 12| 0  |
|       | Study 2: Placebo + MTX | 17| 0  |
|       | Study 2: FILGO 30mg | 17| 0  |
| Study 2: FILGO 75mg OD + MTX | 22 | | | | | 4.5 |
| Study 2: FILGO 150mg OD + MTX | 15 | | | | | 0 |
| Study 2: FILGO 300mg OD + MTX | 20 | | | | | 0 |
| Placebo + MTX | 86 | 0 | 1.8 | 0 |
| FILGO 50mg OD + MTX | 82 | 0 | 1.6 | 0 |
| FILGO 100mg OD + MTX | 85 | 1.2 | 2.4 | 0 |
| FILGO 200mg OD + MTX | 86 | 1.2 | 0 | 0 |
| FILGO 25mg BID + MTX | 86 | 0 | 1.4 | 0 |
| FILGO 50mg BID + MTX | 85 | 0 | 1.2 | 0 |
| FILGO 100mg BID + MTX | 84 | 1.2 | 0 | 0 |
| Placebo + csDMARD | 221 | 2 | 0 | <1 | <1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| UPA 15mg + csDMARD | 221 | 2 | 2 | <1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| UPA 30mg + csDMARD | 219 | 3 | 3 | 4 | 2 | 1 | 0 | 0 | <1 | <1 | <1 |
| Placebo + MTX | 652 | 4.9 | 0.5 | 0.2 | 14.6 | 0 | 0.2 | 0.5 | 0.3 |
| UPA 15mg OD + MTX | 650 | 6.6 | 0.8 | 0.6 | 17.8 | 0.2 | 0.2 | 0 | 0 |
| ADA 40mg Q2W + MTX | 327 | 3.7 | 0.3 | 0.3 | 5.5 | 0 | 0.9 | 0.6 | 0.3 |
| Placebo + MTX | 145 | 0 | 1.38 | 9.66 | 2.76 |

**Westhovens 2017 (DARWIN 1) [29]**

**Burmester 2018 (SELECT-NEXT) [30]**

**Fleischmann 2018 (SELECT-COMPARE) [31, 32]**

**Hu 2018 (RA-Pla)**
| Study & Year | Group Description | N  | Week(s) | ACR 20 | ACR 50 | ACR 70 | ACR 90 |
|-------------|-------------------|----|---------|--------|--------|--------|--------|
| Balance [35, 36] | BARI 4mg + MTX | 145 | 0 | 2.07 | 8.28 | 3.45 |
| Smolen 2018 [SELECT-MONOTHERAPY] [37, 38] | Continued MTX | 216 | 14 | 2 | 0 | <1 | <1 | 0 | 0 | <1 | <1 |
| | UPA 15mg OD | 217 | | 2 | 1 | 1 | 1 | <1 | <1 | 1 | 0 |
| | UPA 30mg OD | 215 | | 2 | 1 | 0 | 0 | 0 | 1 | 0 |
| Tanaka 2018a [SELECT-SUNRISE] [39, 40] | Placebo + csDMARDs | 49 | 12 | 4.1 | 0 | 0 | 2 | 10.2 | 2 | 0 | 0 | 0 |
| | UPA 7.5mg + csDMARDs | 49 | | 0 | 0 | 0 | 2 | 20.4 | 0 | 0 | 0 | 0 |
| | UPA 15mg + csDMARDs | 49 | | 4.1 | 0 | 0 | 0 | 20.4 | 0 | 0 | 0 | 0 |
| | UPA 30mg + csDMARDs | 50 | | 2.0 | 6 | 4 | 2 | 38 | 10 | 0 | 0 | 0 |
| Tanaka & Takeuchi 2018 [41, 42] | Placebo ± csDMARDs | 101 | 12/52* | 0 | 0 | 0.0* | 0 |
| | PEF 100mg OD ± csDMARDs | 104 | | 0 | 0 | 2.3* | 0 |
| | PEF 150mg OD ± csDMARDs | 102 | | 0 | 0 | 0.0* | 0 |
| | Open-label ETA 50mg QW ± csDMARDs | 200 | | 0 | 0 | 0.5* | 0 |
| Takeuchi 2018 [43, 44] | Placebo + MTXs | 170 | 12 | 0 | 0 | 0.5/1.6* |
| | PEF 100mg OD + MTXs | 174 | | 0 | 0 | 0.6/0.6* |
| | PEF 150mg OD + MTXs | 174 | | 0 | 0 | 0/0* |
| van Vollenhoven ACR 2018 [SELECT-EARLY] [45] | Placebo + MTX | 314 | 12/24* | 1.59 | 0.32 |
| | UPA 15mg + MTX | 317 | | 1.89 | 0 |
| | UPA 30mg + MTX | 314 | | 2.87 | 0 |

* reported as incidence rate (95% confidence intervals); ¶ not shown in original report/supplement/clinicaltrials.gov, source: FDA Briefing Document Arthritis Advisory Committee Meeting, April 23, 2018, pp. 54-55 (Table 25); a patients with insufficient response were re-assigned to TOFA 5mg BID at week 12, data shown here for patients not reassigned; b all patients in ADA 40mg EOW re-assigned to TOFA 5mg, therefore data at week 12
shown for this treatment arm;  Two events (2/200; 1%) of pulmonary embolism in the TOFA 10mg BID arm were reported between month 3 and month 6; NR: not reported;
| Study | Group                                      | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolaemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|-------|-------------------------------------------|-----------------|-------------------|----------------------------|-----------------|---------------|--------------------------|--------------------------|-------------|------------------------|------------------------|--------------------------|----------|---------------|--------|
|       | Placebo ± csDMARD                          | 105             |                    |                            | 0/NA            | 1/NA          | 0/NA                     | 0/NA                     | 0/NA        | 0/NA                  | 0/NA                  | 0/NA                   | 0/NA     | 0/NA          | 0/NA   |
| Mease 2017 (OPAL Broaden) [49] | Placebo to TOFA 5mg BID ± csDMARD          | 52              | 12/54             |                            | NA/5.8          | NA/1.9        |                          | NA/0                      | NA/2        | NA/0                  | NA/0                  | NA/0                    | NA/0     | NA/0          | NA/0   |
|       | Placebo to TOFA 10mg BID ± csDMARD         | 53              |                   |                            | NA/1.9          | NA/9.4        |                          | NA/2                      | NA/0        | NA/0                  | NA/0                  | NA/0                    | NA/0     | NA/0          | NA/0   |
|       | TOFA 5mg BID ± csDMARD                      | 107             |                   |                            | 0.9/2.8         | 0.9/4.7       | 0                         | 0/0                      | 0/0         | 0/0                   | 0/0                   | 2/3                     | 0/0      | 0/0           | 0/0    |
|       | TOFA 10mg BID ± csDMARD                     | 104             |                   |                            | 1.0/2.9         | 0/4.8         | 0                         | 0/0                      | 0/0         | 0/0                   | 0/0                   | 0/0                     | 1/1      | 0/0           | 0/0    |
|       | ADA 40mg Q2W ± csDMARD                      | 106             |                   |                            | 3.8/7.5         | 1.9/2.8       | 0                         | 0/0                      | 0/0         | 0/0                   | 0/0                   | 0/2                     | 0/0      | 0/0           | 0/0    |
|       | Placebo ± csDMARD                           | 131             | 24                |                            |                 |               |                          |                          |             |                       |                       |                          |          |               |        |
| Gladman 2017 (OPAL Beyond) [50] | TOFA 5mg BID ± csDMARD                      | 131             |                   |                            |                 |               |                          |                          |             |                       |                       |                          |          |               |        |
|       | TOFA 10mg BID ± csDMARD                     | 132             |                   |                            |                 |               |                          |                          |             |                       |                       |                          |          |               |        |
|       | Placebo ± csDMARD                           | 66              | 16                |                            | 0               | 3             | 0                         | 0/0                      | 8           | 2                     |                       |                          |          |               |        |
| Mease 2018 (EQUATOR) [51] | FILGO 200mg OD ± csDMARD                    | 65              |                   |                            | 2               | 0             | 0                         | 0/0                      | 0/0         | 0/0                   | 0/0                   | 0/0                     | 0/0      | 0/0           | 0/0    |
| Study             | Group                        | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolaemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|------------------|------------------------------|-----------------|--------------------|-------------------------------|----------------|-------------------------|--------------------------|--------------|---------------------------|-------------------------|---------------------------|-----------|----------------|---------|
| Van der Heijde 2017 [52] | Placebo ± csDMARD          | 51              | 12                 | 2                             | 4.0            | 0                       | 0                        | 0            | 0                          | 0                       | 0                          | 0         | 0              | 0       |
|                  | TOFA 2mg BID ± csDMARD      | 52              |                    | 0                             | 0              | 0                       | 0                        | 0            | 0                          | 0                       | 0                          | 0         | 0              | 0       |
|                  | TOFA 5mg BID ± csDMARD      | 52              |                    | 3.8                           | 3.8            | 1.9                     | 1.9                      | 0            | 0                          | 0                       | 0                          | 0         | 0              | 0       |
|                  | TOFA 10mg BID ± csDMARD     | 52              |                    | 2.0                           | 2.0            | 2.0                     | 0                        | 2            | 0                          | 0                       | 0                          | 0         | 0              | 0       |
| Van der Heijde 2018 [53] | Placebo ± csDMARD          | 58              | 12                 | 5                             |                | 0                       |                          | 0            |                          |                          |                           |           |                |         |
|                  | FILGO 200mg OD ± csDMARD    | 58              |                    | 0                             |                |                          |                          | 2            |                           |                          |                           |           |                |         |
### Table S4.3.4: Systemic Lupus Erythematosus

| Study   | Group                          | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolaemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---------|-------------------------------|-----------------|--------------------|-----------------------------|-----------------|-----------------|--------------------------|--------------------------|-------------|-------------------------|------------------------|--------------------------|----------|--------------|---------|
| Kahl 2016 [54] | Placebo ± csDMARD           | 11              | 12                 | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | Solcitinib 50mg BID ± csDMARD | 9               |                    | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | Solcitinib 100mg BID ± csDMARD | 10              |                    | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | Solcitinib 200mg BID ± csDMARD | 10              |                    | 20                          | 10              | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | Solcitinib 400mg BID ± csDMARD | 10              |                    | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
| Wallace 2018 [55] | Placebo ± csDMARD     | 105             | 24                 | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | BARI 2mg OD ± csDMARD             | 105             |                    | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | BARI 4mg OD ± csDMARD             | 104             |                    | 1                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |

### Table S4.3.5: Psoriasis

| Study   | Group      | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolaemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---------|------------|-----------------|--------------------|-----------------------------|-----------------|-----------------|--------------------------|--------------------------|-------------|-------------------------|------------------------|--------------------------|----------|--------------|---------|
| Papp 2012 [56] | Placebo   | 50              | 12                 | 0                           | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
|         | TOFA 2mg BID | 49              |                    | 0                           | 0               | 2.04            | 0                        | 0                        | 0           | 2.04                    | 0                      | 0                        | 0        | 0            | 0       |
|         | TOFA 5mg BID | 49              |                    | 2.04                        | 0               | 0               | 0                        | 0                        | 0           | 0                       | 0                      | 0                        | 0        | 0            | 0       |
| Study | Intervention | N  | %  | 0  | 0  | 0  |
|-------|--------------|----|----|----|----|----|
| Bachelez 2015 [57] | Placebo | 107 | 12 | 0 | 0 | 1.9 | 0 | 0 |
| | TOFA 5mg BID | 329 | 4.56 | 3.3 | 0 | 0.3 |
| | TOFA 10mg BID | 330 | 4.85 | 4.2 | 0.3 | 0.3 |
| | ETA 50mg twice weekly | 335 | 2.99 | 1.5 | 0.3 | 0.6 |
| Bissonnette 2014 [58] | TOFA 5mg BID | 331 | 0.46/0.46 | 0 | 1.38 | 0 | 0.6 |
| | TOFA 10mg BID | 335 | 1.27/1.9 | 0 | 1.91 | 0.9 | 0.6 |
| Papp 2015 [59] | Placebo | 29 | 6 | 0/0 | 0 | 0 | 0 |
| | PEF 10mg BID | 19 | 0 | 0 | 0 |
| | PEF 25mg BID | 21 | 0 | 0 | 0 |
| | PEF 60mg BID | 19 | 0 | 0 | 0 |
| | PEF 100mg BID | 17 | 0 | 0 | 0 |
| | PEF 50mg BID | 19 | 0 | 0 | 0 |
| Papp 2015 [60] | Study 1: Placebo | 177 | 16 | 0/0 | 0 | 0 | 0 |
| | Study 1: TOFA 5mg BID | 363 | 0.3/0.3 | 0 | 0.8 | 0 |
| | Study 1: TOFA 10mg BID | 360 | 0.3/1.7 | 0.3 | 0.3 | 0 |
| | Study 2: Placebo | 196 | 0.5/0.5 | 0 | 0 | 0 |
| | Study 2: TOFA 5mg BID | 382 | 0.8/1.1 | 0.5 | 0 | 0 |
| | Study 2: TOFA 10mg BID | 381 | 0.8/2.4 | 0 | 0 | 0.5 |
| Study             | Treatment          | N  | Week 1 | Week 2 | Week 3 | Week 4 |
|-------------------|--------------------|----|--------|--------|--------|--------|
| Bissonnette 2016  | Placebo            | 12 | 0      | 0      | 0      | 0      |
|                   | Itacitinib 100mg OD| 9  | 0      | 0      | 0      | 0      |
|                   | Itacitinib 200mg OD| 9  | 0      | 0      | 0      | 0      |
|                   | Itacitinib 200mg BID| 9  | 0      | 0      | 0      | 0      |
|                   | Itacitinib 600mg OD| 11 | 0      | 0      | 0      | 0      |
| Papp 2016 [62]    | Placebo            | 34 | 0      | 0      | 0      | 0      |
|                   | BARI 2mg           | 32 | 0      | 0      | 0      | 0      |
|                   | BARI 4mg           | 72 | 0      | 0      | 1.4    | 0      |
|                   | BARI 8mg           | 64 | 0      | 4.7    | 1.6    | 0      |
|                   | BARI 10mg          | 69 | 4.3    | 0      | 2.9    | 0      |
| Papp 2016 [63]    | Vehicle BID        | 71 | 1.4    | 1.4    | 0      | 0      |
|                   | 2% TOFA BID        | 71 | 0      | 0      | 0      | 0      |
|                   | 1% TOFA BID        | 70 | 2.9    | 0      | 0      | 0      |
|                   | Vehicle OD         | 74 | 0      | 0      | 0      | 0      |
|                   | 2% TOFA OD         | 70 | 1.5    | 3.0    | 1.5    | 0      |
|                   | 1% TOFA OD         | 74 | 0      | 0      | 0      | 1.35   |
| Zhang 2017 [64]   | Placebo            | 88 | 0      | 0      | 0      | 0      |
|                   | TOFA 5mg BID       | 88 | 0      | 0      | 0      | 1.1    |
|                   | TOFA 10mg BID      | 90 | 0      | 0      | 0      | 0      |
| Papp 2018 [65]    | Placebo            | 45 | 0      | 0      | 0      | 0      |
|                   | BMS-986165 3mg EOD | 44 | 0      | 0      | 0      | 0      |
| Drug                | Dose | Days |
|---------------------|------|------|
| BMS-986165 3mg OD   | 44   |      |
| BMS-986165 3mg BID  | 45   |      |
| BMS-986165 6mg BID  | 45   |      |
| BMS-986165 12mg OD  | 44   |      |
## Table S4.3.6: Alopecia & Atopic Dermatitis

| Study                  | Group                                         | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|------------------------|-----------------------------------------------|-----------------|-------------------|-----------------------------|----------------|----------------|------------------------|--------------------------|-------------|--------------------------|--------------------------|--------------------------|----------|---------------|---------|
| Guttman-Yassky 2018 [66] | Placebo                                       | 142             | 24                |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | PF-06651600 200mg OD (4 weeks) / 50mg OD (20 weeks) |                 |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | PF-06700841 60mg OD (4 weeks) / 30mg OD (20 weeks) |                 |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | Alopecia areata                                |                 |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
| Bissonette 2016 [67]   | Topical TOFA 2% BID                            | 35              | 4                 |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | Topical Vehicle BID                            | 34              |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
| De Bruin-Weller 2018 [68, 69] | Placebo                                       | 41              | 16                |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | UPA 7.5mg OD                                   | 42              |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | UPA 15mg OD                                    | 42              |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | UPA 30mg OD                                    | 42              |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
| Guttman-Yassky 2018 [70] | Placebo + topical steroids                     | 49              | 16                |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |
|                        | BARI 2mg OD + topical steroids                 | 37              |                   |                             |                |               |                        |                          |             |                          |                          |                          |          |               |         |

### Atopic dermatitis

- **Placebo:** 142 patients, Time-point: 24 weeks
- **PF-06651600 200mg OD (4 weeks) / 50mg OD (20 weeks):**
- **PF-06700841 60mg OD (4 weeks) / 30mg OD (20 weeks):**
- **Topical TOFA 2% BID:** 35 patients, Time-point: 4 weeks
- **Topical Vehicle BID:** 34 patients, Time-point: 4 weeks
- **Placebo, UPA 7.5mg OD, UPA 15mg OD, UPA 30mg OD:**
- **Placebo + topical steroids:** 49 patients, Time-point: 16 weeks
- **BARI 2mg OD + topical steroids:** 37 patients, Time-point: 16 weeks
| Study          | Group                     | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hypercholesterolaemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---------------|---------------------------|-----------------|-------------------|-----------------------------|----------------|----------------|-------------------------|--------------------------|-------------|-------------------------|------------------------|----------------------------|----------|--------------|---------|
| Nakagawa 2018 | Vehicle                   | 31              |                   | 4                           | 0              | 0             | 2.08                    |                          |             |                         |                        |                             |          |              |         |
|               | Topical JTE-052 0.25%     | 69              |                   |                             |                |               |                         |                          |             |                         |                        |                             |          |              |         |
|               | Topical JTE-052 0.5%      | 65              |                   |                             | 0              | 0             | 0                       |                          |             |                         |                        |                             |          |              |         |
|               | Topical JTE-052 1%        | 66              |                   |                             |                |               |                         |                          |             |                         |                        |                             |          |              |         |
|               | Topical JTE-052 3%        | 65              |                   |                             |                |               |                         |                          |             |                         |                        |                             |          |              |         |
|               | Topical tacrolimus       | 30              |                   |                             |                |               |                         |                          |             |                         |                        |                             |          |              |         |

Table S4.3.7: Ulcerative Colitis
|               | OCTAVE Induction 1: Placebo | OCTAVE Induction 1: TOFA 10mg BID | OCTAVE Induction 2: Placebo | OCTAVE Induction 2: TOFA 10mg BID | OCTAVE Sustain: Placebo | OCTAVE Sustain: TOFA 5mg BID | OCTAVE Sustain: TOFA 10mg BID |
|---------------|----------------------------|----------------------------------|-----------------------------|----------------------------------|-------------------------|-----------------------------|-------------------------------|
| Sandborn 2017 [73] | 122                        | 476                              | 112                         | 429                              | 198                     | 198                         | 197                           |
|               | 8                          |                                  | 1.79                        | 2.56                             | 52                      | 8                           | 52                            |
|               |                            |                                  | 4.92                        | 2.31                             | 17                      | <1                          | <1                            |
|                |                            |                                  |                             |                                  |                         |                             |                               |
| Sandborn 2018 [74,75] | Placebo                  | UPA 7.5mg OD                     | UPA 15mg OD                 | UPA 30mg OD                      | UPA 45mg OD             | Placebo                     | Peficitinib 25mg OD           |
|               | 46                        | 47                               | 49                          | 52                               | 56                      | 43                          | 44                            |
|               | 8                          |                                  |                              |                                  |                          | 4.7                         | 4.7                           |
|                |                            |                                  | 6.5                         | 4.3                              | 2.1                     | 0                           | 0                             |
|                |                            |                                  |                             |                                  |                         |                             |                               |
| Sands 2018 [76] | Placebo                   | Peficitinib 25mg OD              | Peficitinib 75mg OD         | Peficitinib 150mg OD             | Placebo                 | Peficitinib 75mg BID        |                               |
|               | 43                        | 44                               | 44                          | 44                               | 44                      | 44                          | 44                            |
|               | 8                          |                                  | 4.5                         | 4.5                              | 2.3                     | 2.3                         | 2.3                           |
|                |                            |                                  |                             |                                  |                         | 0                           | 0                             |
|                |                            |                                  |                             |                                  |                         |                             |                               |
### Table S4.3.8: Crohn’s Disease

| Study                      | Group        | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leukopenia G3 or G4 (%) | Neutropenia G3 or G4 (%) | Lymphopenia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterolemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|----------------------------|--------------|-----------------|-------------------|-----------------------------|---------------|------------------------|--------------------------|---------------------------|-------------|--------------------------|--------------------------|--------------------------|-----------|--------------|---------|
| Sandborn 2014 [77]         | Placebo      | 34              | 4                 |                             |               |                        |                          |                           | 0           |                         |                          |                          | 2.94      |              |         |
|                            | TOFA 1mg BID  | 36              |                   |                             |               |                        |                          |                           | 0           |                         |                          |                          | 0         |              |         |
|                            | TOFA 5mg BID  | 34              |                   |                             |               |                        |                          |                           | 0           |                         |                          |                          | 0         |              |         |
|                            | TOFA 15mg BID | 35              |                   |                             |               |                        |                          |                           | 0           |                         |                          |                          | 0         |              |         |
| Panés 2017 [78]            | Induction: Placebo | 91              | 8                 |                             |               |                        |                          |                           | 1.1         | 0                        | 0                        | 0                        | 0         |              |         |
|                            | Induction: TOFA 5mg BID | 86              |                   |                             |               |                        |                          |                           | 4.65        | 1.2                      | 0                        | 0                        | 0         |              |         |
|                            | Induction: TOFA 10mg BID | 86              |                   |                             |               |                        |                          |                           | 2.33        | 1.2                      | 0                        | 1.2                      | 0         |              |         |
|                            | Maintenance: Placebo | 59              | 26                |                             |               |                        |                          |                           | 1.69        | 0                        | 0                        | 0                        | 0         |              |         |
|                            | Maintenance: TOFA 5mg BID | 60              |                   |                             |               |                        |                          |                           | 5           | 0                        | 0                        | 0                        | 0         |              |         |
|                            | Maintenance: TOFA 10mg BID | 61              |                   |                             |               |                        |                          |                           | 8.2         | 1.6                      | 0                        | 0                        | 0         |              |         |
| Sandborn 2017 / Panés 2018 [79-81] | Induction: Placebo | 37              | 16                |                             |               |                        |                          |                           | 0           | 0                        | 0                        | 0                        | 0         |              |         |
|                            | Induction: UPA 3mg BID | 39              |                   |                             |               |                        |                          |                           | 0           | 0                        | 0                        | 0                        | 0         |              |         |
|                            | Induction: UPA | 37              |                   |                             |               |                        |                          |                           | 0           | 0                        | 0                        | 0                        | 0         |              |         |
|                | 6mg BID | Induction: UPA 12mg BID | Induction: UPA 24mg BID | Induction: UPA 24mg OD | Maintenance: UPA 3mg BID | Maintenance: UPA 6mg BID | Maintenance: UPA 12mg BID | Maintenance: UPA 24mg OD | Vermeire 2017 [82] |
|----------------|---------|-----------------------|------------------------|-----------------------|--------------------------|--------------------------|--------------------------|--------------------------|----------------------|
|                | 36      | 0 0 2.8 0 0           | 0 0 0 0 2.8            | 0 0 0 0 0             | 0 0 1.7 0 0             | 0 0 0 0 0               | 0 0 0 3.4 0             | 0 0 0 0 0             | Placebo 44 0-20      |
|                | 36      | 0 0 0 0 2.8           |                        |                       |                          |                          |                          |                          | Placebo 22 0-10      |
|                | 35      | 0 0 0 0 0             |                        |                       |                          |                          |                          |                          | Placebo to FILGO 100mg 22 10-20 |
|                | 20      | 0 0 1.7 0 0           |                        |                       |                          |                          |                          |                          | FILGO 200mg 23 0-10  |
|                | 8       | 0 0 0 0 0             |                        |                       |                          |                          |                          |                          | FILGO 200mg to Placebo 23 10-20 |
|                | 16      | 0 0 0 3.4 0           |                        |                       |                          |                          |                          |                          | FILGO 200 to 100mg 30 0-20 |
|                | 10      | 0 0 0 0 0             |                        |                       |                          |                          |                          |                          | FILGO 200mg 77 0-20  |
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