# Supplementary appendix

# Table of contents

# Section 1: Search strategy and PICOs

## 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 oligoarthriti$.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.

17 Peficitinib.tw.

18 Decernotinib.tw.

19 (Ruxolitinib or jaka?i).tw.

20 or/10-19

21 randomized controlled trial.pt.

22 controlled clinical trial.pt.

23 randomized.ab.

24 placebo.ab.

25 drug therapy.fs.

26 randomly.ab.

27 trial.ab.

28 groups.ab.

29 or/21-28

30 exp animals/ not humans.sh.

31 29 not 30

32 (safe or safety).tw.

33 side effect$.tw.

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

35 exp product surveillance, postmarketing/

36 exp adverse drug reaction reporting systems/

37 clinical trials, phase iv/

38 Clinical Trials, Phase III/

39 exp poisoning/

40 exp substance-related disorders/

41 exp drug toxicity/

42 exp abnormalities, drug induced/

43 exp drug monitoring/

44 exp drug hypersensitivity/

45 (toxicity or complication$ or noxious or tolerability).tw.

46 exp Postoperative Complications/

47 exp Intraoperative Complications/

48 or/32-47

49 exp animals/ not humans.sh.

50 48 not 49

51 31 or 50

52 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?i: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. oligoarthriti*: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/j2 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?i).tw.

17 or/7-16

18 randomized controlled trial.pt.

19 controlled clinical trial.pt.

20 randomized.ab.

21 placebo.ab.

22 drug therapy.fs.

23 randomly.ab.

24 trial.ab.

25 groups.ab.

26 or/18-25

27 exp animals/ not humans.sh.

28 26 not 27 (3798143)

29 (safe or safety).tw.

30 side effect$.tw.

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

32 exp product surveillance, postmarketing/

33 exp adverse drug reaction reporting systems/

34 clinical trials, phase iv/

35 Clinical Trials, Phase III/

36 exp poisoning/

37 exp substance-related disorders/

38 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?i: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 Erythematosus] explode all trees

#2 “systemic lupus erythematosus”:ti,ab

#3 sle:ti,ab

#4 ((“libman sacks” OR libman sacks) NEXT disease):ti,ab

#5 (lupus NEXT (nephritis OR vasculitis)):ti,ab

#6 #1 OR #2 OR #3 OR #4 OR #5

#7 MeSH descriptor: [Janus Kinase Inhibitors] this term only

#8 "janus kinase inhibitor*":ti,ab

#9 "JAK inhibitor*":ti,ab

#10 Tofacitinib:ti,ab

#11 (Tofacitinib or xeljanz or tasocitinib):ti,ab

#12 (Baricitinib or olumiant):ti,ab

#13 (Filgotinib or cyclopropanecarboxamide):ti,ab

#14 Peficitinib:ti,ab

#15 Decernotinib:ti,ab

#16 (Ruxolitinib or jaka?i):ti,ab

#17 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16

#18 #9 AND #17

## 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)

5 (Crohn$ adj (disease or enteritis)).tw. (41405)

6 ulcerative colitis.tw. (35215)

7 psoriasis/ (32971)

8 Chronic plaque psoriasis.tw. (962)

9 ((atopic$ or disseminated) adj (dermatit$ or neurodermat$ or eczema)).tw. (20777)

10 Alopecia Areata/ (3021)

11 (alopecia adj (Areat$ or circumscripta or universalis)).tw. (3576)

12 or/1-11 (149579)

13 Janus Kinase Inhibitors/ (127)

14 janus kinase inhibitor$.tw. (429)

15 JAK inhibitor$.tw. (1131)

16 Tofacitinib.tw. (798)

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

18 (Baricitinib or olumiant).tw. (135)

19 (Filgotinib or cyclopropanecarboxamide).tw. (61)

20 Peficitinib.tw. (19)

21 Decernotinib.tw. (13)

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

23 or/13-21 (2055)

24 randomized controlled trial.pt. (477193)

25 controlled clinical trial.pt. (92945)

26 randomized.ab. (436251)

27 placebo.ab. (195836)

28 drug therapy.fs. (2088187)

29 randomly.ab. (306614)

30 trial.ab. (455752)

31 groups.ab. (1887119)

32 or/24-31 (4389362)

33 exp animals/ not humans.sh. (4554122)

34 32 not 33 (3795778)

35 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)

9 ((atopic$ or disseminated) adj (dermatit$ or neurodermat$ or eczema)).tw. (20777)

10 Alopecia Areata/ (3021)

11 (alopecia adj (Areat$ or circumscripta or universalis)).tw. (3576)

12 or/1-11 (149579)

13 Janus Kinase Inhibitors/ (127)

14 janus kinase inhibitor$.tw. (429)

15 JAK inhibitor$.tw. (1131)

16 Tofacitinib.tw. (798)

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

18 (Baricitinib or olumiant).tw. (135)

19 (Filgotinib or cyclopropanecarboxamide).tw. (61)

20 Peficitinib.tw. (19)

21 Decernotinib.tw. (13)

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

23 or/13-21 (2055)

24 (safe or safety).tw. (689909)

25 side effect$.tw. (228583)

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

27 exp product surveillance, postmarketing/ (14223)

28 exp adverse drug reaction reporting systems/ (7055)

29 clinical trials, phase iv/ (272)

30 Clinical Trials, Phase III/ (8565)

31 exp poisoning/ (151822)

32 exp substance-related disorders/ (264092)

33 exp drug toxicity/ (108814)

34 exp abnormalities, drug induced/ (14396)

35 exp drug monitoring/ (19339)

36 exp drug hypersensitivity/ (44141)

37 (toxicity or complication$ or noxious or tolerability).tw. (1205908)

38 exp Postoperative Complications/ (511878)

39 exp Intraoperative Complications/ (49901)

40 or/24-39 (2932032)

41 and/12,23,40 (151)

42 exp animals/ not humans.sh. (4554122)

43 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?i: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?i: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

### 1.3.5 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 cyclopropanecarboxamide):ti,ab

#21 Peficitinib:ti,ab

#22 Decernotinib:ti,ab

#23 (Ruxolitinib or jaka?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

#### 1.4.1.1.5 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

#### 1.4.1.1.6 Psoriasis (Pso)

- Outcome measures: Physician Global Assessment Score, PASI 75/90/100, BSA, NAPSI, DLQI

#### 1.4.1.1.7 Atopic dermatitis (AD)

- Outcome measures: Eczema Area and Severity Index (EASI), Physician Global Assessment Score, BSA

#### 1.4.1.1.8 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)? | See 1.4.1.1.1-1.4.1.1.8 | See 1.4.1.3 | See 1.4.1.4 | See 1.4.1.1.1-1.4.1.1.8 |
| 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 myocbacteria, 4) CMV, and 5) fungal infections of patients treated with JAKi as compared to bDMARDs? | See 1.4.1.1.1-1.4.1.1.8 | See 1.4.1.3 | See 1.4.1.4 | See 1.4.2 |
| 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 comedications (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 | | | | |

| | | | | | |
|---|---|---|---|---|---|
| | again? | | | | |
| 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 JAKi? | | | | |

# 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 |

| | | | |
|---|---|---|---|
| Genovese 2016b [15] | Upadacitinib | JAK-1/2 | MTX-IR |
| Genovese 2016c [16] | Decernotinib | JAK-3 | MTX-IR |
| Genovese 2016d [17] | Decernotinib | JAK-3 | 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 |
| Vanhoutte 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 |

| | | | |
|---|---|---|---|
| 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) [45] | 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 |

## Table S2.1.5: Psoriasis

| 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 |

| | | | |
|---|---|---|---|
| Papp 2018 [65] | BMS-986165 | TYK2 | 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 |

| | | | |
|---|---|---|---|
| | | | immunosuppressants |
| Nakagawa 2018 [71] | Topical JTE-052 | JAK-1-3 | Atopic dermatitis; Eczema Area Severity Index (EASI) score ≥ 10; Investigator's Global<br><br>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 |

## Table S2.1.8: Crohn's disease

| 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 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 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 | Low | Unclear | Unclear | protocol changes after study initiation and enrollment of 97 patients (excluding |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | treatment naïve patients) |
| Kivitz 2017 [25] | Unclear | Low | Low | Low | Low | Low | Unclear | Unclear | |
| Kavanaugh 2017 (DARWIN 2) [26] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Taylor 2017 (RA-BEAM) [27] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Vanhoutte 2017 [28] | Unclear | Unclear | Low | Low | Low | Low | Low | Unclear | |
| Westhovens 2017 (DARWIN 1) [29] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Burmester 2018 (SELECT-NEXT) [30] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Fleischmann 2018 (SELECT-COMPARE) [31, 32] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Genovese 2018 (SELECT-BEYOND) [33] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Kivitz ACR 2018 [34] | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | |
| Hu 2018 (RA-BALANCE) [35] | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | |
| Smolen 2018 (SELECT-MONOTHERAPY) | Low | Low | Low | Low | Low | Low | Low | Low | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [37, 38] | | | | | | | | | |
| Tanaka 2018a (SELECT-SUNRISE) [39, 40] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Tanaka & Takeuchi 2018 [41, 42] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Takeuchi 2018 [43, 44] | Low | Low | Low | Low | Low | Low | Low | Low | |
| van Vollenhoven ACR 2018 (SELECT-EARLY) [45] | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | Abstract | |
| Tanaka 2019 [48] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Takeuchi 2019 (RA-BEYOND) [47] | 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 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2018 [53] | | | | | | | | | |

## 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 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| [57] | | | | | | | | | |
| Bissonnette 2014 [58] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Papp 2015 [59] | Low | Low | Low | Low | Low | Low | Low | Low | |
| Papp 2015 [60] | 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 | |
| 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 | |
| Papp 2018 [65] | 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 |
|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 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 | |

## Table S2.2.8: Crohn's disease

| 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 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 S2.3: 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 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | TOFA 15mg BID | 57 | 53 | 8,7 | 5,46 | | 1,62 | |
| | ADA 40mg EOW | 53 | 54 | 7,7 | 5,35 | | 1,44 | |
| 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 | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | group) | | | | | | | |
| 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 | | | | 1.35 | | |
| | 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 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Lee 2014 [11] | MTX | 186 | 48.8 | 2.7 | 6.6 | | 1.5 | 16.1 |
| | TOFA 5mg BID | 373 | 50.3 | 2.9 | 6.6 | | 1.5 | 19.1 |
| | TOFA 10mg BID | 397 | 49.3 | 3.4 | 6.5 | | 1.5 | 17.9 |
| 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 [13] | Placebo | 41 | 54.9 | 10.6 | 6.0 | | 1.6 | |
| | 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 [14] | Placebo + csDMARD | 176 | 56 | 14 | 5.9 | 41 | 1.78 | |
| | BARI 2mg + csDMARD | 174 | 55 | 14 | 6 | 43 | 1.71 | |
| | BARI 4mg + csDMARD | 177 | 56 | 14 | 5.9 | 40 | 1.74 | |
| Genovese 2016b [15] | Placebo + MTX | 50 | 55 | 5.9 | 5.6 | 40 | 1.4 | |
| | 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 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | UPA 12mg BID + MTX | 50 | 56 | 9.3 | 5.6 | 39 | 1.5 | |
| | UPA 18mg BID + MTX | 50 | 55 | 7.3 | 5.7 | 40 | 1.6 | |
| | UPA 24mg QD + MTX | 49 | 56 | 8.3 | 5.7 | 41 | 1.5 | |
| 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 | 1,6 | |
| | UPA 3 mg + MTX | 55 | 57 | 11,8 | 5,7 | 40 | 1,5 | |
| | UPA 6 mg + MTX | 55 | 56 | 12,3 | 5,9 | 42 | 1,6 | |
| | UPA 12 mg + MTX | 55 | 59 | 12,2 | 5,7 | 40 | 1,6 | |
| | UPA 18 mg + MTX | 55 | 57 | 10,9 | 5,8 | 41 | 1,5 | |
| 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 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PEF 100mg OD | 55 | 52.1 | 12.1 | 5.34 | | 1.0 | |
| | PEF 150mg OD | 58 | 51.6 | 12.1 | 5.41 | | 1.0 | |
| Tanaka 2016 [20] | 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 | 1.6 | |
| 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 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PEF 150mg + HCQ/SZP | 64 | 54.4 | 10.5 | 5.9 | 41.6 | 1.5 | |
| Kivitz 2017 [25] | Placebo + MTX | 72 | 52.6 | 7.2 | 5.4 | 36 | 1.4 | |
| | PEF 25mg + MTX | 66 | 52.8 | 8.1 | 5.5 | 37.6 | 1.4 | |
| | PEF 50mg + MTX | 78 | 52.3 | 8 | 5.6 | 37.8 | 1.3 | |
| | PEF 100mg + MTX | 84 | 54.5 | 7.5 | 5.6 | 39.4 | 1.3 | |
| | PEF 150mg + MTX | 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 | |
| | FILGO 50mg OD | 72 | 52 | 9 | 6.03 | 41 | 1.8 | |
| | FILGO 100mg OD | 70 | 53 | 9 | 6.18 | 44 | 1.8 | |
| | FILGO 200mg OD | 69 | 52 | 9 | 6.09 | 42 | 1.8 | |
| Taylor 2017 (RA-BEAM) [27] | Placebo + MTX | 488 | 53 | 10 | 5.7 | 38 | 1.55 | 45 |
| | BARI 4mg + MTX | 487 | 54 | 10 | 5.8 | 38 | 1.57 | 43 |
| | ADA 40mg Q2W + MTX | 330 | 53 | 10 | 5.8 | 38 | 1.59 | 44 |
| Vanhoutte 2017 [28] | Study 1: Placebo + MTX | 12 | 47 | 5.6 | 6.3 | | 2.0 | |
| | Study 1: FILGO 200mg OD + MTX | 12 | 52 | 7.5 | 6.4 | | 2.1 | |
| | Study 1: FILGO 100mg BID + MTX | 12 | 53 | 9.7 | 6.6 | | 1.9 | |
| | Study 2: Placebo + MTX | 17 | 44 | 4.4 | 6.1 | | 1.7 | |
| | Study 2: FILGO 30mg OD + MTX | 17 | 52 | 8.0 | 5.7 | | 1.5 | |
| | Study 2: FILGO 75mg OD + MTX | 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 | 36 |
| | UPA 15mg OD + MTX | 651 | 54 | 8 | 5.8 | 40 | 1.6 | 34 |
| | ADA 40mg Q2W + MTX | 327 | 54 | 8 | 5.9 | 40 | 1.6 | 35 |
| 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 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 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 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 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 TJC 68 | 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 | |

## 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 | 73 |
| | BARI 2mg OD ± csDMARD | 105 | 43.2 | 11.8 | | 8.8 | 75 |
| | BARI 4mg OD ± csDMARD | 104 | 45.0 | 11.5 | | 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 | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Papp 2015 [60] | 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 |
| Bissonnette 2016 [61] | 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 |
| Papp 2016 [62] | 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 | |
| Papp 2016 [63] | 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 | 70 | 50.7 | | 9.9 | 7.8 | 32.9 | 67.1 | | 12.2 |
| | 1% TOFA OD | 74 | 47.8 | | 10.1 | 8.4 | 27.0 | 73.0 | | 10.9 |
| Zhang 2017 [64] | Placebo | 88 | 41.7 | 13.2 | 26.1 | 35.8 | | 76.1 | 23.9 | 12.3 |
| | TOFA 5mg BID | 88 | 40.7 | 15.6 | 25.3 | 37.4 | | 87.5 | 12.5 | 13.5 |
| | TOFA 10mg BID | 90 | 41.0 | 14.4 | 25.3 | 36.4 | | 85.6 | 14.4 | 14.1 |
| Papp 2018 [65] | Placebo | 45 | 46 | 18 | 19 | 24 | | | | 13 |
| | BMS-986165 3mg EOD | 44 | 41 | 18 | 17 | 20 | | | | 12 |
| | BMS-986165 3mg OD | 44 | 45 | 13 | 18 | 23 | | | | 12 |
| | BMS-986165 3mg BID | 45 | 46 | 13 | 19 | 24 | | | | 13 |
| | BMS-986165 6mg BID | 45 | 43 | 15 | 18 | 25 | | | | 11 |
| | BMS-986165 12mg OD | 44 | 47 | 20 | 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 | 5.6 |
| | Topical JTE-052 1% | 66 | 28.6 | 20.8 | 17.8 | 25.3 | | 85 | 15 | 5.0 |
| | Topical JTE-052 3% | 65 | 32.3 | 25.2 | 16.5 | 24.5 | | 86 | 14 | 4,9 |
| | Topical tacrolimus | 30 | 33.1 | 23.0 | 16.7 | 24.1 | | 87 | 13 | 4.7 |

## Table S2.3.7: Ulcerative Colitis

| 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 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | UPA 15mg OD | 49 | 47 | 4.58 | 8.7 | 9.7 | 1843 | 0 | 51.0 | 49.0 |
| | UPA 30mg OD | 52 | 42 | 6.06 | 6.7 | 9.0 | 1648 | 0 | 44.2 | 55.8 |
| | UPA 45mg OD | 56 | 37 | 6.46 | 6.3 | 9.0 | 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 Crohns 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 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sandborn 2017 / Panés 2018 [79-81] | Placebo | 37 | 40 | 8.7 | 7.0 | 276.0 | 896.0 | 24.3 | 16.2 | 59.5 | |
| | 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 | 6 | 29.2 | 2,6 | 1,3 | | | | -0.3 | |
| | TOFA 5mg BID | 61 | | 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 | 12 | 14.3 | 14.3 | 3.6 | | | | -0.05 | |
| | TOFA 1mg BID + MTX | 28 | | 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 | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | TOFA 3mg BID | 51 | | 45.1 | 25.49 | 11.76 | 5.9 | | | | |
| | TOFA 5mg BID | 49 | | 61.22 | 38.78 | 14.29 | 12.5 | | | -0.51 | |
| | TOFA 10mg BID | 61 | | 72.13 | 45.9 | 24.59 | 14.8 | | | -0.66 | |
| | TOFA 15mg BID | 57 | | 71.93 | 50.88 | 26.32 | 19.3 | | | -0.82 | |
| | ADA 40mg EOW | 53 | | 39.62 | 20.75 | 3.77 | 3.9 | | | -0.35 | |
| Fleischmann 2012 [4] | Placebo | 122 | 12 | 26.7 | 12.5 | 5.8 | 4.4 | | | -0.19 | |
| | TOFA 5mg BID | 243 | | 59.8 | 31.1 | 15.4 | 5.6 | | | -0.5 | |
| | TOFA 10mg BID | 245 | | 65.7 | 36.8 | 20.3 | 8.7 | | | -0.57 | |
| Kremer 2012 [5] | Placebo + MTX | 69 | 12 | 33.3 | | | 6.1 | | | -0.16 | |
| | TOFA 1mg BID + MTX | 70 | | 45.7 | | | | | | -0.34 | |
| | TOFA 3mg BID + MTX | 68 | | 52.9 | | | 23.1 | | | -0.48 | |
| | TOFA 5mg BID + MTX | 71 | | 50.7 | | | | | | -0.49 | |
| | TOFA 10mg BID + MTX | 74 | | 58.1 | | | 27.5 | | | -0.39 | |
| | TOFA 15mg BID + MTX | 75 | | 56.0 | | | 29.2 | | | -0.43 | |
| | TOFA 20mg | 80 | | 53.8 | | | 20.8 | | | -0.53 | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | BID + MTX | | | | | | | | | | |
| Van Vollenhoven 2012 [6] | TOFA 5mg BID + MTX | 204 | 24 | 51.53 | 36.73 | 19.9 | 6.21 | | | -0.55 | |
| | TOFA 10mg BID + MTX | 201 | | 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 | 12 | 24.4 | 8.4 | 1.5 | 1.7 | | 0 | -0.18 | |
| | TOFA 5mg BID + MTX | 133 | | 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 | 24 | 31.21 | 12.74 | 3.18 | 2.6 | | | -0.16 | |
| | TOFA 5mg BID + DMARD | 315 | | 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 | 24 | 25,32 | 8,44 | 1,3 | | | | | |
| | Placebo + | 81 | | | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 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 | | 51,46 | 32,36 | 14,56 | | | | | |
| | TOFA 10mg BID + DMARD | 316 | | 61,81 | 43,69 | 22,33 | | | | | |
| Lee 2014 [11] | MTX | 186 | 24 | 50.5 | 26.6 | 12 | 7.6 | | | -0.6 | 0.65 |
| | TOFA 5mg BID | 373 | | 71.3 | 46.6 | 25.5 | 14.6 | | | -0.8 | 0.2 |
| | TOFA 10mg BID | 397 | | 76.1 | 56.4 | 37.7 | 21.8 | | | -0.9 | 0.15 |
| Tanaka 2015 [12] | Placebo | 52 | 12 | 15.4 | 7.7 | 7.5 | | | | 0.18 | |
| | TOFA 1mg BID | 53 | | 37.7 | 13.2 | 13.2 | | | | -0.19 | |
| | TOFA 3mg BID | 53 | | 67.9 | 26.4 | 26.9 | | | | -0.38 | |
| | TOFA 5mg BID | 52 | | 73.1 | 46.1 | 49.1 | | | | -0.55 | |
| | TOFA 10mg | 53 | | 84.9 | 69.8 | 51.9 | | | | -0.67 | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | BID | | | | | | | | | | |
| | TOFA 15mg BID | 54 | | 90.7 | 72.2 | 1.9 | | | | -0.68 | |
| Fleischmann 2015 [13] | Placebo | 41 | 12 | 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 | 12 | 27 | 8 | 2 | 4 | 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 | 12 | 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 + MTX | 49 | | 76 | 39 | 22 | 22 | 6 | | -0.6 | |
| Genovese 2016c [16] | Placebo + MTX | 71 | 24 | 16.9 | 7 | 2.8 | 5.6 | | | -0.6 | |
| | DEC 100mg OD + MTX | 71 | | 60.6 | 38 | 16.9 | 21.1 | | | -0.62 | |
| | DEC 150mg 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 100mg BID + MTX | 72 | | 62.5 | 47.2 | 25 | 31.9 | | | -0.75 | |
| Genovese 2016d [17] | Placebo + csDMARD | 12 | 12 | 25 | 8.3 | 8.3 | | | | | |
| | DEC 100mg BID + csDMARD | 11 | | 63 | 27.3 | 18.2 | | | | | |
| | DEC 200mg BID + csDMARD | 10 | | 60 | 30 | 10 | | | | | |
| | DEC 300mg BID + csDMARD | 10 | | 60 | 60 | 20 | | | | | |
| Kremer 2016 [18] | Placebo | 56 | 12 | 34 | 16 | 4 | 13 | 7 | | -0,2 | |
| | UPA 3 mg + MTX | 55 | | 53 | 24 | 13 | 24 | 9 | | -0,3 | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | UPA 6 mg + MTX | 55 | | 58 | 36 | 26 | 26 | 11 | | -0,5 | |
| | UPA 12 mg + MTX | 55 | | 71 | 42 | 22 | 33 | 13 | | -0,5 | |
| | UPA 18 mg + MTX | 55 | | 67 | 38 | 22 | 27 | 16 | | -0,5 | |
| Takeuchi 2016 [19] | Placebo | 56 | 12 | 10.7 | 5.4 | 1.8 | 5.4 | | | 0.16 | |
| | PEF 25mg OD | 55 | | 23.6 | 7.3 | 0 | 0 | | | 0.14 | |
| | PEF 50mg OD | 57 | | 31.6 | 8.8 | 1.8 | 7 | | | 0.05 | |
| | PEF 100mg OD | 55 | | 54.5 | 30.9 | 16.4 | 27.3 | | | -0.17 | |
| | PEF 150mg OD | 58 | | 65.5 | 29.3 | 12.1 | 20.7 | | | -0.23 | |
| Tanaka 2016 [20] | Placebo + MTX | 49 | 12 | | | 0 | 22 | | | -0.08 | |
| | BARI 1mg OD + MTX | 24 | | | | 13 | 33 | | | -0.3 | |
| | BARI 2mg OD + MTX | 24 | | | | 29 | 33 | | | -0.40 | |
| | BARI 4mg OD + MTX | 24 | | | | 29 | 42 | | | -0.47 | |
| | BARI 8mg OD + MTX | 24 | | | | 21 | 50 | | | -0.42 | |
| Dougados 2017 [21] | Placebo + csDMARD | 228 | 12/24[a] | 39.47 | 12.72 | 3.07 | | | 0.44 | -0.3 | 0.70[a] |
| | BARI 2mg + csDMARD | 229 | | 65.94 | 33.62 | 17.9 | | | 6.99 | -0.52 | 0.33[a] |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | BARI 4mg + csDMARD | 227 | | 61.67 | 33.48 | 18.06 | | | 6.61 | -0.52 | 0.15[a] |
| Fleischmann 2017a [22] | TOFA 5mg BID + PLC | 384 | 24 | 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 | 24 | 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 + HCQ/SZP | 51 | 12 | 29.4 | 9.8 | 7.8 | 9.8 | | | | |
| | PEF 25mg + HCQ/SZP | 59 | | 22 | 15.3 | 6.8 | 6.8 | | | | |
| | PEF 50mg + HCQ/SZP | 57 | | 36.8 | 24.6 | 15.8 | 12.5 | | | | |
| | PEF 100mg + HCQ/SZP | 58 | | 48.3 | 27.6 | 19 | 22.8 | | | | |
| | PEF 150mg + HCQ/SZP | 64 | | 56.3 | 28.1 | 10.9 | 20.3 | | | | |
| Kivitz 2017 [25] | Placebo + MTX | 72 | 12 | 44.4 | 26.4 | 11.1 | | | | | |
| | PEF 25mg + | 66 | | 43.9 | 18.2 | 9.1 | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | MTX | | | | | | | | | | |
| | PEF 50mg + MTX | 78 | | 61.5 | 33.3 | 15.4 | | | | | |
| | PEF 100mg + MTX | 84 | | 46.4 | 33.3 | 16.7 | | | | | |
| | PEF 150mg + MTX | 78 | | 57.7 | 37.2 | 19.2 | | | | | |
| Kavanaugh 2017 (DARWIN 2) [26] | Placebo | 72 | 12 | 29.2 | 11.1 | 2.8 | 6.9 | 2.8 | 1.4 | -0.226 | |
| | FILGO 50mg OD | 72 | | 66.7 | 34.7 | 8.3 | 12.5 | 2.8 | 1.4 | -0.661 | |
| | FILGO 100mg OD | 70 | | 65.7 | 37.1 | 18.6 | 14.3 | 5.7 | 4.3 | -0.677 | |
| | FILGO 200mg OD | 69 | | 72.5 | 43.5 | 13 | 17.4 | 8.7 | 4.3 | -0.739 | |
| Taylor 2017 (RA-BEAM) [27] | Placebo + MTX | 488 | 12/24[a] | 40.2 | 16.8 | 4.7 | 4 | 2 | 1 | -0.34 | 0.9[a] |
| | BARI 4mg + MTX | 487 | | 69.6 | 45 | 18.9 | 24 | 8 | 7.2 | -0.66 | 0.41[a] |
| | ADA 40mg Q2W + MTX | 330 | | 61.2 | 34.8 | 12.7 | 19 | 7 | 5.2 | -0.56 | 0.33[a] |
| Vanhoutte 2017 [28] | Study 1: Placebo + MTX | 12 | 4 | 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 | 12 | 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 | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 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 | |
| Burmester 2018 (SELECT-NEXT) [30] | Placebo + csDMARD | 221 | 12 | 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 | 12/26[a] | 36.4 | 14.9 | 4.9 | 6.1 | 3.1 | 2 | -0.28 | 0.92[a] |
| | UPA 15mg OD + MTX | 651 | | 70.5 | 45.2 | 24.9 | 28.7 | 13.4 | 9.8 | -0.6 | 0.24[a] |
| | ADA 40mg Q2W + MTX | 327 | | 63 | 29.1 | 13.5 | 18 | 7.6 | 4 | -0.49 | 0.1[a] |
| Genovese 2018 (SELECT-BEYOND) [33] | Placebo + csDMARD | 169 | 12 | 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 | 12 | 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 | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | OD + MTX | | | | | | | | | | |
| Hu 2018 (RA-BALANCE) [35, 36] | Placebo + MTX | 145 | 12 | 28.3 | 8.3 | 1.4 | 2.8 | | | -0.35 | |
| | BARI 4mg + MTX | 145 | | 58.6 | 30.3 | 9.7 | 11.7 | | | -0.57 | |
| 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 | 12 | 42.9 | 16.3 | 2 | 6.1 | 2 | | -0.1 | |
| | UPA 7.5mg + csDMARDs | 49 | | 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 | 12 | 30.7 | 8.9 | 1.0 | 5 | 0 | | | |
| | PEF 100mg OD ± csDMARDs | 104 | | 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 | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Takeuchi 2018 [43, 44] | Placebo + MTXs | 170 | 12[b]/28[c] | 21.8[b] | 7.6[b] | 2.4[b] | 7.7[b] | 0.6 | 0.6 | 0.0 | 3.37[c] |
| | PEF 100mg OD + MTXs | 174 | | 58.6[b] | 29.9[b] | 12.1[b] | 31.4[b] | 4.7 | 5.8 | -0.25 | 1.62[c] |
| | PEF 150mg OD + MTXs | 174 | | 64.4[b] | 46[b] | 23.6[b] | 35.1[b] | 14.6 | 9.9 | -0.38 | 1.03[c] |
| van Vollenhoven ACR 2018 (SELECT-EARLY) [45] | Placebo + MTX | 314 | 12/24[d] | 54.1 | 28.3 | 14 | 18.5[d] | 6.4 | 6.4 | -0.49 | 0.67[d] |
| | UPA 15mg + MTX | 317 | | 75.7 | 52.1 | 32.5 | 48.3[d] | 16.1 | 12.9 | -0.83 | 0.14[d] |
| | UPA 30mg + MTX | 314 | | 77.1 | 56.4 | 36.9 | 50[d] | 21.3 | 15.3 | -0.86 | 0.07[d] |
| 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 [b,c] / 0.09 [b,d] | 32.8 | 21.5 |
| | TOFA 5mg BID ± csDMARD | 107 | | 50 | 28 | 17 | -1.3 | 26 | 43 | -0.35 | 0.01 [b] | 34.4 | 33.3 |
| | TOFA 10mg BID ± csDMARD | 104 | | 61 | 40 | 14 | -1.6 | 26 | 44 | -0.4 | -0.01 [b] | 60 | 40.6 |
| | ADA 40mg Q2W ± csDMARD | 106 | | 52 | 33 | 19 | -1.5 | 25 | 39 | -0.38 | -0.07 [b] | 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 | | | |

[a] week 24; [b] week 52; [c] Placebo advancing to TOFA 5mg BID; [d] 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 Arthrits; 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 (%) | ASDAS inactive disease (%) | 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 | 7.8 | -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 | -1.2 | -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 | -1.4 | -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 | -1.4 | -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 | ΔSLEDAI-2K | SRI-4 response | Resolution of arthritis/rash (SLEDAI-2K) | LLDAS | ΔCLASI | SLICC/ACR Damage Index score |
|---|---|---|---|---|---|---|---|---|---|---|
| Kahl 2016 [54] | Placebo ± csDMARD | 11 | 12 | -6.2 | | 0/5 | | | | |
| | Solcitinib 50mg BID ± csDMARD | 9 | | -3.6 | | 1/4 | | | | |
| | Solcitinib 100mg BID ± csDMARD | 10 | | | | 1/5 | | | | |
| | 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 |
|---|---|---|---|---|---|---|---|---|---|---|

| | | (n) | (weeks) | (%) | (%) | (%) | | | response | |
|---|---|---|---|---|---|---|---|---|---|---|
| Papp 2012 [56] | Placebo | 50 | 12 | 20.0 | 2.0 | 0 | | | 10.0 | |
| | TOFA 2mg BID | 49 | | 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 | 16 | | 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 | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Papp 2015 [60] | Study 1: Placebo | 177 | 16 | | 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 | |
| Bissonnette 2016 [61] | Placebo | 12 | 4 | 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 | |
| Papp 2016 [62] | Placebo | 34 | 12 | | 17.6 | | | | | |
| | BARI 2mg | 32 | | | 31.3 | | | | | |
| | BARI 4mg | 72 | | | 29.2 | | | | | |
| | BARI 8mg | 64 | | | 43.8 | | | | | |
| | BARI 10mg | 69 | | | 55.1 | | | | | |
| Papp 2016 [63] | Vehicle BID | 71 | 8 | | 8 | | | -23.5% | 25.2 | |
| | 2% TOFA BID | 71 | | | 15.2 | | | -31.8% | 41.8 | |
| | 1% TOFA BID | 70 | | | 9.1 | | | -26.7% | 20.9 | |
| | Vehicle OD | 74 | | | 8.3 | | | -19.1% | 13.8 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2% TOFA OD | 70 | | | 17.9 | | | -28.3% | 35.9 | |
| | 1% TOFA OD | 74 | | | 7.2 | | | -25.5% | 23.4 | |
| Zhang 2017 [64] | Placebo | 88 | | | 12.5 | 3.4 | | | 19.3 | |
| | TOFA 5mg BID | 88 | 16 | | 54.6 | 35.2 | | | 52.3 | |
| | TOFA 10mg BID | 90 | | | 81.1 | 60.0 | | | 75.6 | |
| Papp 2018 [65] | Placebo | 45 | | 31 | 7 | 2 | 0 | | 7 | |
| | BMS-986165 3mg EOD | 44 | | 43 | 9 | 7 | 2 | | 20 | |
| | BMS-986165 3mg OD | 44 | | 68 | 39 | 16 | 0 | | 39 | |
| | BMS-986165 3mg BID | 45 | 12 | 91 | 69 | 44 | 9 | | 76 | |
| | BMS-986165 6mg BID | 45 | | 78 | 67 | 44 | 18 | | 64 | |
| | BMS-986165 12mg OD | 44 | | 89 | 75 | 43 | 25 | | 75 | |

## 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) | | | 48 | 33.6 | | | | | |
| | PF-06700841 60mg OD (4 weeks) /30mg OD (20 weeks) | | | 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 | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | BARI 4mg OD + topical steroids | 38 | | | -66% | | 61 | | |
| Nakagawa 2018 [71] | 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 |

## 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 [72] | Placebo ± Mesalamine | 48 | 8 | 42 | 10 | 46 | 2 | 0.9 | -400 |
| | TOFA 0.5mg BID ± Mesalamine | 31 | | 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 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mesalamine | | | | | | | | |
| Sandborn 2017 [73] | OCTAVE Induction 1: Placebo | 122 | 8 | 32.8 | 8.2 | | 1.6 | | |
| | OCTAVE Induction 1: TOFA 10mg BID | 476 | | 59.9 | 18.5 | | 6.7 | | |
| | OCTAVE Induction 2: Placebo | 112 | | 28.6 | 3.6 | | 1.8 | | |
| | OCTAVE Induction 2: TOFA 10mg BID | 429 | | 55.0 | 16.6 | | 7.0 | | |
| | OCTAVE Sustain: Placebo | 198 | 52 | | 11.1 | | 13.1 | | |
| | OCTAVE Sustain: TOFA 5mg BID | 198 | | | 34.3 | | 37.4 | | |
| | OCTAVE Sustain: TOFA 10mg BID | 197 | | | 40.6 | | 45.7 | | |
| Sandborn 2018 [74, 75] | Placebo | 46 | 8 | 13.0 | 0 | 2.2 | 0 | 1.14 | 154 |
| | UPA 7.5mg OD | 47 | | 29.8 | 8.5 | 14.9 | 6.4 | -0.34 | -338 |
| | UPA 15mg OD | 49 | | 44.9 | 10.2 | 30.6 | 4.1 | -4.9 | -742 |
| | UPA 30mg OD | 52 | | 44.2 | 11.5 | 26.9 | 9.6 | -3.4 | -1093 |
| | UPA 45mg OD | 56 | | 50.0 | 19.6 | 35.7 | 17.9 | -4.4 | -720 |
| Sands 2018 [76] | Placebo | 43 | 8 | 39.5 | 7.0 | 18.6 | 2.3 | | |
| | Peficitinib 25mg OD | 44 | | 34.1 | 15.9 | 20.5 | 11.4 | | |
| | Peficitinib 75mg OD | 44 | | 54.5 | 15.9 | 29.5 | 15.9 | | |
| | Peficitinib 150mg OD | 44 | | 54.5 | 27.3 | 45.5 | 11.4 | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Peficitinib 75mg BID | 44 | | 54.5 | 15.9 | 36.4 | 22.7 | | |

## 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 (log) |
| | Maintenance: TOFA 5mg BID | 60 | | | 37.2 | 37.2 | -63.5 | | 0.57 (log) |
| | Maintenance: TOFA 10mg BID | 61 | | | 55.8 | 41.9 | -19.1 | | -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 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Induction: UPA 12mg BID | 36 | | 44.4 | | 39 | | -6.1 | -32.1 |
| | Induction: UPA 24mg BID | 36 | | 61.1 | | 31 | | -14.8 | -44.4 |
| | Induction: UPA 24mg OD | 35 | | 48.6 | | 20 | | -2.7 | -22.5 |
| | Maintenance: UPA 3mg BID | 20 | 52 | 55 | | 55 | | -4.3 | -51.9 |
| | Maintenance: UPA 6mg BID | 8 | | 75 | | 50 | | -7.0 | -524.1 |
| | Maintenance: UPA 12mg BID | 16 | | 75 | | 69 | | -20.4 | -3047.5 |
| | Maintenance: UPA 24mg OD | 10 | | 40 | | 40 | | -6.2 | -2371.8 |
| Vermeire 2017 [82] | Placebo | 44 | 10 | | 41 | 23 | | | |
| | FILGO 200mg OD | 130 | | | 59 | 47 | | | |

## 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 |

| | | | | |
|---|---|---|---|---|
| | | MACE | | |
| 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 |

| | | | | |
|---|---|---|---|---|
| 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 [88] | 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 |

## Table S4.1.5: Psoriasis

| 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 [79, 80] | 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 | |
| | 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 | |
| | TOFA 1mg BID + MTX | 28 | | | 3.6 | 10.7 | | | 0 | |
| | TOFA 3mg BID + MTX | 27 | | | 3.7 | 29.6 | | | 3.7 | |
| | TOFA 5mg BID + MTX | 27 | | | 3.7 | 11.1 | | | 0 | |
| | TOFA 10mg BID + MTX | 26 | | | 7.7 | 42.3 | | | 0 | |
| Fleischmann 2012 [3] | Placebo[a] | 34 | 12[b]/24 | | 5.9 | 17.6 | 2.9 | | 2.9 | |
| | TOFA 1mg BID[a] | 37 | | | 5.4 | 29.7 | 5.9 | | 5.4 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | TOFA 3mg BID[a] | 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[b] | 53 | | | 1.9 | 18.9 | 0 | | 0 | |
| Fleischmann 2012 [4] | Placebo | 122 | 12 | | 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 | 12/24 | | 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 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | TOFA 20mg BID + MTX | 80 | | | 3.0 | 19.4 | 1.5 | | 5.0 | |
| Van Vollenhoven 2012 [6] | Placebo + MTX (cross-over to TOFA 5mg BID + MTX after 3 months) | 56 | 24 | | | | | | | |
| | 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 | 0 |
| | TOFA 10mg BID + MTX | 201 | | | 5.0 | | 2.0 | 1 | 3.5 | 3.0 |
| | ADA 40mg EOW + MTX | 204 | | | 2.5 | | 0 | 0 | 3.4 | 0 |
| | Placebo + MTX (Combination group) | 106 | | | 1.9 | | 0.9 | 0 | 0.9 | 0 |
| Burmester 2013 [7] | Placebo + MTX | 132 | 12 | | 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 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Kremer 2013 [8] | Placebo + DMARD (Combination group) | 159 | 52 | 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) | 160 | 12 | | 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 | | | | 0 | |
| | TOFA 1mg BID | 53 | | | 0 | | | | 0 | |
| | TOFA 3mg BID | 53 | | | 5.7 | | | | 0 | |
| | TOFA 5mg BID | 52 | | | 3.9 | | | | 1.9 | 1.9 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | TOFA 10mg BID | 53 | | | 3.8 | | | | 5.7 | 5.7 |
| | TOFA 15mg BID | 54 | | | 1.9 | | | | 0 | 1.9 |
| Fleischmann 2015 [13] | Placebo | 41 | 12 | | 2.4 | 17.1 | | | | |
| | DEC 25mg BID | 41 | | | 0 | 12.2 | | | | |
| | DEC 50mg BID | 41 | | | 2.4 | 12.2 | | | | |
| | DEC 100mg BID | 40 | | | 12.5 | 25.0 | | | | |
| | DEC 150mg BID | 41 | | | 4.9 | 19.5 | | | | |
| Genovese 2016a [14] | Placebo + csDMARD | 176 | 24 | 65.8 | 7 | 31 | | | 5 | 1 |
| | BARI 2mg + csDMARD | 174 | | 69.9 | 4 | 44 | | | 9 | 1 |
| | BARI 4mg + csDMARD | 177 | | 73.3 | 10 | 40 | | | 6 | 4 |
| Genovese 2016b [15] | Placebo + MTX | 50 | 12 | | 0 | 14 | | | | 0 |
| | UPA 3mg BID + MTX | 50 | | | 0 | 20 | | | | 2 |
| | UPA 6mg BID + MTX | 50 | | | 4 | 14 | | | | 0 |
| | UPA 12mg BID + MTX | 50 | | | 2 | 24 | | | | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | UPA 18mg BID + MTX | 50 | | | 6 | 22 | | | | 0 |
| | UPA 24mg QD + MTX | 49 | | | 4 | 18 | | | | 4 |
| Genovese 2016c [16] | Placebo + MTX | 71 | 24 | | 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 | | | | |
| | DEC 100mg BID + MTX | 72 | | | 9.7 | 4.2 | | | | |
| Genovese 2016d [17] | Placebo + csDMARD | 12 | 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 | 12 | | 4 | 23 | 2 | | 1,79 | 4 |
| | UPA 3 mg + | 55 | | | 2 | 20 | 0 | | 3,64 | 2 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | MTX | | | | | | | | | |
| | UPA 6 mg + MTX | 55 | | | 4 | 22 | 0 | | 1,82 | 0 |
| | UPA 12 mg + MTX | 55 | | | 4 | 40 | 0 | | 7,27 | 2 |
| | UPA 18 mg + MTX | 55 | | | 2 | 38 | 0 | | 7,27 | 2 |
| Takeuchi 2016 [19] | Placebo | 56 | 12 | | 1.8 | 21.4 | | | | 0 |
| | PEF 25mg OD | 55 | | | 1.8 | 32.7 | | | | 3.6 |
| | PEF 50mg OD | 57 | | | 3.5 | 24.6 | | | | 0 |
| | PEF 100mg OD | 55 | | | 5.5 | 12.7 | | | | 3.6 |
| | PEF 150mg OD | 58 | | | 0 | 29.3 | | | | 0 |
| Tanaka 2016 [20] | Placebo + MTX | 49 | 12 | | 2 | 22 | 0 | 0 | 2.04 | 0 |
| | BARI 1mg OD + MTX | 24 | | | 0 | 25 | 0 | 0 | 4.17 | 0 |
| | BARI 2mg OD + MTX | 24 | | | 4 | 17 | 0 | 0 | 0 | 0 |
| | BARI 4mg OD + MTX | 24 | | | 0 | 29 | 0 | 0 | 0 | 0 |
| | BARI 8mg OD + MTX | 24 | | | 4 | 21 | 0 | 0 | 0 | 0 |
| Dougados 2017 (RA-BUILD) [21] | Placebo + csDMARD | 228 | 24 | 89.8 | 5 | 35 | | | 7.89 | 0 |
| | BARI 2mg + | 229 | | 97.7 | 3 | 31 | | | 6.11 | 2 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | csDMARD | | | | | | | | | |
| | BARI 4mg + csDMARD | 227 | | 96.4 | 5 | 42 | | | 10.57 | 1 |
| Fleischmann 2017a [22] | 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 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | PEF 25mg + MTX | 66 | | | 0 | | 0 | | 3.0 | 0 |
| | PEF 50mg + MTX | 78 | | | 0 | | 0 | | 3.8 | 0 |
| | PEF 100mg + MTX | 84 | | | 2.4 | | 1.2 | | 4.8 | 2.4 |
| | PEF 150mg + MTX | 78 | | | 1.3 | | 1.3 | | 3.8 | 1.3 |
| Kavanaugh 2017 (DARWIN 2) [26] | Placebo | 72 | 12 | | 1.4 | | 0 | 0 | | 0 |
| | FILGO 50mg OD | 72 | | | 1.4 | | 1.4 | 0 | | 0 |
| | FILGO 100mg OD | 70 | | | 0 | | 0 | 0 | | 0 |
| | FILGO 200mg OD | 69 | | | 4.3 | | 1.4 | 0 | | 0 |
| Taylor 2017 (RA-BEAM) [27] | Placebo + MTX | 488 | 24 | 197.7 | 5 | 27 | 1 | 0 | 2.87 | <1 |
| | BARI 4mg + MTX | 487 | | 215.0 | 5 | 36 | 1 | 0 | 3.08 | 1 |
| | ADA 40mg Q2W + MTX | 330 | | 141.9 | 5 | 33 | <1 | <1 | 3.94 | 1 |
| Vanhoutte 2017 [28] | Study 1: Placebo + MTX | 12 | 4 | | | 8.3 | | | | |
| | 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 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 | | | | |
| Westhovens 2017 (DARWIN 1) [29] | 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 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | FILGO 50mg BID + MTX | 85 | | | 0 | | 0 | 0 | | 0 |
| | FILGO 100mg BID + MTX | 84 | | | 3.6 | | 1.2 | 0 | | 2.24 |
| 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 | | | 0.5 |
| | UPA 15mg OD + MTX | 650 | | 289.6 | 3.7 | 34.8 | 1.8 | | | 0.8 |
| | ADA 40mg Q2W + MTX | 327 | | 137.6 | 4.3 | 29.1 | 1.5 | | | 0.3 |
| 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 + csDMARDs | 49 | 12 | | 0 | 22.4 | 0 | 0 | 0 | 2 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| [39, 40] | UPA 7.5mg + csDMARDs | 49 | | | 2 | 36.7 | 0 | 0 | 0 | 2 |
| | UPA 15mg + csDMARDs | 49 | | | 2 | 32.7 | 2 | 0 | 2.04 | 0 |
| | UPA 30mg + csDMARDs | 50 | | | 10 | 44.0 | 6 | 0 | 2 | 6 |
| Tanaka & Takeuchi 2018 [41, 42] | Placebo ± csDMARDs | 101 | 12/52* | 22.6 | 4 | | 0* | | 1.98 | 0/0 |
| | PEF 100mg OD ± csDMARDs | 104 | | 88.2 | 2.9 | | 1.1* | | 2.88 | 0.96/5.8* |
| | PEF 150mg OD ± csDMARDs | 102 | | 92.1 | 0 | | 2.2* | | 2.94 | 0/4.4* |
| | Open-label ETA 50mg QW ± csDMARDs | 200 | | 195.5 | 2 | | 1.7* | | 1.50 | 1.0/2.6* |
| Takeuchi 2018 [43, 44] | Placebo + MTXs | 170 | 12 | 62.9 | 2.4 | | 0/0* | | | 1.2/3.2* |
| | PEF 100mg OD + MTXs | 174 | | 159.5 | 2.9 | | 3.4/3.8* | | | 7.5/8.3* |
| | PEF 150mg OD + MTXs | 174 | | 160.8 | 1.7 | | 3.4/3.7* | | | 3.5/3.8* |
| van Vollenhoven ACR 2018 (SELECT-EARLY) [45] | Placebo + MTX | 314 | 12/24[a] | | 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); [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; [c] 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 | 12/54 | | 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 | | | 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 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | csDMARD | | | | | | | | | |
| Mease 2018 (EQUATOR) [51] | Placebo ± csDMARD | 66 | 16 | | 2 | 21 | 0 | 0 | 15 | 2 |
| | FILGO 200mg OD ± csDMARD | 65 | | | 2 | 22 | 2 | 0 | 15 | 0 |

## Table S4.2.3: Ankylosing spondylitis

| **Study** | **Group** | **No. of patients** | **Timepoint (weeks)** | **Exposure (Pat. Years)** | **SAE (%)** | **Infections (%)** | **Serious infection (%)** | **Tuberculosis (%)** | **URT Infection (%)** | **Herpes zoster (%)** |
|---|---|---|---|---|---|---|---|---|---|---|
| Van der Heijde 2017 [52] | 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 [53] | Placebo ± csDMARD | 58 | 12 | | 0 | | 0 | 0 | | |
| | FILGO 200mg OD ± | 58 | | | 2 | | 2 | 0 | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | csDMARD | | | | | | | | | |

## Table S4.2.4: Systemic Lupus Erythematosus

| Study | Group | No. of patients | Timepoint (weeks) | Exposure (Pat. Years) | SAE (%) | Infections (%) | Serious infection (%) | Tuberculosis (%) | URT Infection (%) | Herpes zoster (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Kahl 2016 [54] | Placebo ± csDMARD | 11 | 12 | | 0 | 27 | | | 0 | |
| | Solcitinib 50mg BID ± csDMARD | 9 | | | 11 | 67 | | | 0 | |
| | Solcitinib 100mg BID ± csDMARD | 10 | | | 20 | 40 | | | 10 | |
| | Solcitinib 200mg BID ± csDMARD | 10 | | | 40 | 30 | | | 0 | |
| | Solcitinib 400mg BID ± csDMARD | 10 | | | 10 | 40 | | | 20 | |
| Wallace 2018 [55] | Placebo ± csDMARD | 105 | 24 | | 5 | 39 | 1 | 0 | | 1 |
| | BARI 2mg OD ± csDMARD | 105 | | | 10 | 45 | 2 | 0 | | 0 |
| | BARI 4mg OD ± csDMARD | 104 | | | 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 | | | | 10.0 | |
| | TOFA 2mg BID | 49 | | | 4.1 | | | | 8.2 | |
| | TOFA 5mg BID | 49 | | | 2.0 | | | | 8.2 | |
| | TOFA 15mg BID | 49 | | | 0 | | | | 4.1 | |
| Bachelez 2015 [57] | Placebo | 107 | 12 | | 2 | 18.7 | 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 | | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | BID | | | | | | | | | |
| | PEF 50mg OD | 19 | | | 0 | | | | | |
| Papp 2015 [60] | Study 1: Placebo | 177 | 16 | | 2.2 | | 1.1 | | 4.7 | 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 | | 0 | | | |
| | Itacitinib 200mg BID | 9 | | | 0 | 23.7 | 0 | | | |
| | Itacitinib 600mg OD | 11 | | | 0 | | 0 | | | |
| Papp 2016 [62] | Placebo | 34 | 12 | | 2.9 | 26.5 | | | 2.9 | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | BARI 2mg | 32 | | | 3.1 | 18.8 | | | 3.1 | 0 |
| | BARI 4mg | 72 | | | 1.4 | 16.7 | | | 0 | 0 |
| | BARI 8mg | 64 | | | 1.6 | 23.4 | | | 1.6 | 1.6 |
| | BARI 10mg | 69 | | | 1.4 | 24.6 | | | 2.9 | 0 |
| Papp 2016 [63] | Vehicle BID | 71 | 8 | | 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 | 16 | | 0 | | 0 | | | 0 |
| | TOFA 5mg BID | 88 | | | 2.3 | | 1.1 | | | 2.3 |
| | TOFA 10mg BID | 90 | | | 0 | | 0 | | | 3.3 |
| Papp 2018 [65] | Placebo | 45 | 12 | | 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 12mg OD | 44 | | | 0 | | | | 2 | |

## Table S4.2.6: Alopecia & Atopic Dermatitis

| 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 | | | | | | | |
| | PF-06651600 200mg OD (4 weeks) / 50mg OD (20 weeks) | | | | | | | | | |
| | PF-06700841 60mg OD (4 weeks) /30mg OD (20 weeks) | | | | | | | | | |
| **Atopic dermatitis** | | | | | | | | | | |
| Bissonette 2016 [67] | Topical TOFA 2% BID | 35 | 4 | | 0 | 17.1 | | 0 | 0 | 0 |
| | Topical Vehicle BID | 34 | | | 0 | 8.8 | | 0 | 2.9 | 0 |
| De Bruin-Weller 2018 [68, 69] | Placebo | 41 | 16 | | 2.5 | 20 | 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 | | | | 2 | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 2018 [70] | steroids | | | | | | | | | |
| | BARI 2mg OD + topical steroids | 37 | | | 0 | | | | 0 | 0 |
| | BARI 4mg OD + topical steroids | 38 | | | 3 | | | | 5 | 0 |
| Nakagawa 2018 [71] | Vehicle | 31 | 4 | | 0 | | | | | |
| | 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 | | | | | |

## 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 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 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] | OCTAVE Induction 1: Placebo | 122 | 8 | | 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 | 52 | | 6.6 | 24.2 | 1.0 | 0 | | 0.5 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 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 | | | 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

| **Study** | **Group** | **No. of** | **Timepoint** | **Exposure (Pat.** | **SAE** | **Infections** | **Serious infection** | **Tuberculosis** | **URT Infection** | **Herpes zoster** |
|---|---|---|---|---|---|---|---|---|---|---|

| | | 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 | | 0 |
| | Induction: UPA 3mg BID | 39 | | | 12.8 | 41.0 | 7.7 | 0 | | 0 |
| | Induction: | 37 | | | 5.4 | 51.4 | 0 | 0 | | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | UPA 6mg BID | | | | | | | | | |
| | Induction: UPA 12mg BID | 36 | | | 27.8 | 44.4 | 8.3 | 0 | | 0 |
| | Induction: UPA 24mg BID | 36 | | | 8.3 | 55.6 | 2.8 | 0 | | 2.8 |
| | Induction: UPA 24mg OD | 35 | | | 20.0 | 34.3 | 5.7 | 0 | | 0 |
| | Maintenance: UPA 3mg BID | 20 | 52 | | 25.0 | 36.7 | 8.3 | 0 | | 0 |
| | Maintenance: UPA 6mg BID | 8 | | | 8.7 | 26.1 | 0 | 0 | | 0 |
| | Maintenance: UPA 12mg BID | 16 | | | 8.5 | 37.3 | 1.7 | 0 | | 1.7 |
| | Maintenance: UPA 24mg OD | 10 | | | 11.1 | 27.8 | 0 | 0 | | 2.8 |
| Vermeire 2017 [82] | Placebo | 44 | 0-20 | | 14 | 27 | | | | 0 |
| | Placebo | 22 | 0-10 | | 0 | 23 | | | | 0 |
| | Placebo to FILGO 100mg | 22 | 10-20 | | 5 | 27 | | | | 0 |
| | FILGO 200mg | 23 | 0-10 | | 0 | 30 | | | | 0 |
| | FILGO 200mg to Placebo | 23 | 10-20 | | 0 | 26 | | | | 0 |
| | FILGO 200 to | 30 | 0-20 | | 3 | 30 | | | | 3 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 100mg | | | | | | | | | |
| | FILGO 200mg | 77 | 0-20 | | 16 | 34 | | | | 0 |

## 4.3 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 (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | 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 | | |
| | TOFA 1mg BID + MTX | 28 | | | | | | | | | | 0 | 0 | | |
| | TOFA 3mg BID + MTX | 27 | | | | | | | | | | 0 | 0 | | |
| | TOFA 5mg BID + MTX | 27 | | | | | | | | | | 3.7 | 0 | | |
| | TOFA 10mg BID + MTX | 26 | | | | | | | | | | 0 | 3.9 | | |
| Fleischmann 2012 [3] | Placebo[a] | 34 | 12[b]/24 | | | 0 | | | 0 | | | 0 | | | |
| | TOFA 1mg BID[a] | 37 | | | | 0 | | | 0 | | | 0 | | | |
| | TOFA 3mg BID[a] | 34 | | | | 0 | | | 2.9 | | | 2.9 | | | |
| | TOFA 5mg BID | 49 | | | | 2.0 | | | 0 | | | 4.1 | | | |
| | TOFA 10mg BID | 61 | | | | 0 | | | 3.3 | | | 3.3 | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TOFA 15mg BID | 57 | | | | 0 | | | 0 | | | 1.8 | | | |
| | ADA 40mg EOW[b] | 53 | | | | 0 | | | 0 | | | 0 | | | |
| Fleischmann 2012 [4] | Placebo | 122 | 12 | | | 0 | | | 1.6 | | | 0 | | | |
| | TOFA 5mg BID | 243 | | | | 0.4 | | | 1.6 | | | 0.4 | | | |
| | TOFA 10mg BID | 245 | | | | 1.6 | | | 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 | 12 | | | | | | | | | 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 | | | 0 | | |
| | TOFA 10mg BID + MTX | 201 | | 2.0 | | | | | | 0.5 | | | 0 | | |
| | ADA 40mg EOW + MTX | 204 | | 0.5 | | | | | | 0 | | | 0.49 | | |
| | Placebo + MTX (Combination group) | 106 | | 0 | | | | | | 0 | | | 0 | | |
| Burmester | Placebo + MTX | 132 | 12 | 0 | 0 | | | | 0.8 | | 0 | | | 0 | 0 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2013 [7] | TOFA 5mg BID + MTX | 133 | | 0 | 0 | | | | 0 | | 0 | | | 0 | 0 |
| | TOFA 10mg BID + MTX | 134 | | 1.5 | 1.6 | | | | 0.7 | | 0[c] | | | 0 | 0 |
| Kremer 2013 [8] | Placebo + DMARD (Combination group) | 159 | 52 | <1/<1 | | 0* | | | 5.4* | | | 0* | | | |
| | TOFA 5mg BID + DMARD | 315 | | <1/1.9 | | 0* | | | 2.8* | | | 0* | | | |
| | TOFA 10mg BID + DMARD | 318 | | <1/<1 | | 6.9* | | | 1.6* | | | 4.2* | | | |
| Van der Heijde 2013 [9] | Placebo + DMARD (Combination group) | 160 | 12 | 1.9 | 0 | 0 | | | 0 | | | 0 | | | |
| | TOFA 5mg BID + DMARD | 321 | | <1.0 | 0 | 0 | | | 0 | | | 1.6 | | | |
| | TOFA 10mg BID + DMARD | 316 | | 1.9 | 0.9 | 0 | | | 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 | | | |
| | TOFA 1mg BID | 53 | | 1.9 | | | | | 0 | | | 0 | | | |
| | TOFA 3mg BID | 53 | | 1.9 | | | | | 0 | | | 3.8 | | | |
| | TOFA 5mg BID | 52 | | 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 | | | | | |
| | DEC 25mg BID | 41 | | 0/0 | | | | | | 0 | | | | | |
| | DEC 50mg BID | 41 | | 0/2.4 | | | | | | 0 | | | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DEC 100mg BID | 40 | | 2.5/5.0 | | | | | | 2.5 | | | | | |
| | DEC 150mg BID | 41 | | 0/2.4 | | | | | | 0 | | | | | |
| Genovese 2016a [14] | Placebo + csDMARD | 176 | 24 | | | | | | 1 | | | 1 | 0 | | |
| | BARI 2mg + csDMARD | 174 | | | | | | | 2 | | | <1 | 0 | | |
| | BARI 4mg + csDMARD | 177 | | | | | | | <1 | | | 4 | 1 | | |
| Genovese 2016b [15] | Placebo + MTX | 50 | 12 | | | 0 | | | | | | | 0 | | |
| | UPA 3mg BID + MTX | 50 | | | | 0 | | | | | | | 0 | | |
| | UPA 6mg BID + MTX | 50 | | | | 0 | | | | | | | 0 | | |
| | UPA 12mg BID + MTX | 50 | | | | 6 | | | | | | | 2 | | |
| | UPA 18mg BID + MTX | 50 | | | | 2 | | | | | | | 0 | | |
| | UPA 24mg QD + MTX | 49 | | | | 0 | | | | | | | 0 | | |
| Genovese 2016c [16] | 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 [17] | Placebo + csDMARD | 12 | 12 | | | | | | | | | | | | |
| | DEC 100mg BID + csDMARD | 11 | | | | | | | | | | | | | |
| | DEC 200mg BID + csDMARD | 10 | | | | | | | | | | | | | |
| | DEC 300mg BID + csDMARD | 10 | | | | | | | | | | | | | |
| Kremer 2016 [18] | Placebo | 56 | 12 | | | 0 | 0 | 16 | 0 | 0 | 0 | | | 0 | |
| | UPA 3 mg + MTX | 55 | | | | 0 | 0 | 15 | 0 | 0 | 0 | | | 0 | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | UPA 6 mg + MTX | 55 | | | | 0 | 0 | 15 | 7 | 1,82 | 1,82 | | | 2 | |
| | UPA 12 mg + MTX | 55 | | | | 5,45 | 4 | 20 | 4 | 0 | 0 | | | 0 | |
| | UPA 18 mg + MTX | 55 | | | | 1,82 | 2 | 16 | 4 | 0 | 0 | | | 0 | |
| 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 | 12 | | | 0 | | 2.04 | 0 | 0 | | 0 | | | |
| | BARI 1mg OD + MTX | 24 | | | | 0 | | 0 | 4.2 | 0 | | 0 | | | |
| | BARI 2mg OD + MTX | 24 | | | | 0 | | 4.17 | 0 | 0 | | 0 | | | |
| | BARI 4mg OD + MTX | 24 | | | | 0 | | 4.17 | 4.2 | 0 | | 4.17 | | | |
| | BARI 8mg OD + MTX | 24 | | | | 0 | | 4.17 | 4.2 | 0 | | 12.5 | | | |
| Dougados 2017 (RA-BUILD) [21] | Placebo + csDMARD | 228 | 24 | | | | | | 2.63 | | 0 | 0.88 | <1 | | |
| | BARI 2mg + csDMARD | 229 | | | | | | | 2.62 | | 0 | 2.18 | 0 | | |
| | BARI 4mg + csDMARD | 227 | | | | | | | 1.76 | | 0.44 | 3.96 | 0 | | |
| Fleischmann 2017a [22] | TOFA 5mg BID + PLC | 384 | 24 | <1/2 | | | | | | | 0.26 | | 0 | | |
| | TOFA 5mg BID + MTX | 376 | | 4/8 | | | | | | | 0 | | 0 | | |
| | ADA 40mg Q2W + MTX | 386 | | 4/7 | | | | | 0.95 | | 0.26 | | 1 | | |
| Fleischmann 2017b (RA-BEGIN) [23] | Placebo + MTX | 210 | 52 | | <1 | | | | 1.26 | | 0.48 | 1.43 | 2 | <1 | 1 |
| | BARI 4mg + Placebo | 159 | | | 3 | | | | 2.79 | | 0 | 2.52 | 1 | 0 | 0 |
| | BARI 4mg + MTX | 215 | | | 2 | | | | | | 0 | 1.86 | 0 | 0 | <1 |
| Genovese | Placebo + HCQ/SZP | 51 | 12 | 0 | | | 0 | 0 | | | | | | 0 | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2017 [24] | PEF 25mg + HCQ/SZP | 59 | | 0 | | | 0 | 0 | | | | | | 0 | |
| | PEF 50mg + HCQ/SZP | 57 | | 0 | | | 0 | 0 | | | | | | 0 | |
| | PEF 100mg + HCQ/SZP | 58 | | 0 | | | 0 | 0 | | | | | | 0 | |
| | PEF 150mg + HCQ/SZP | 64 | | 0 | | | 0 | 0 | | | | | | 0 | |
| Kivitz 2017 [25] | Placebo + MTX | 72 | 12 | 0 | | 0 | 0 | 0 | 2.8 | | | | | | |
| | PEF 25mg + MTX | 66 | | 0 | | 0 | 0 | 0 | 4.5 | | | | | | |
| | PEF 50mg + MTX | 78 | | 0 | | 1.3 | 0 | 0 | 0 | | | | | | |
| | PEF 100mg + MTX | 84 | | 0 | | 0 | 0 | 1.2 | 1.2 | | | | | | |
| | PEF 150mg + MTX | 78 | | 0 | | 0 | 0 | 0 | 0 | | | | | | |
| Kavanaugh 2017 (DARWIN 2) [26] | Placebo | 72 | 12 | | | | 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 | 24 | | | | | | | 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 | 0 |
| Vanhoutte 2017 [28] | Study 1: Placebo + MTX | 12 | 4 | | | | | | 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 | | | | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OD + MTX | | | | | | | | | | | | | | |
| | 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 | | | | | | |
| Westhovens 2017 (DARWIN 1) [29] | Placebo + MTX | 86 | 12 | | | | 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 | |
| Burmester 2018 (SELECT-NEXT) [30] | Placebo + csDMARD | 221 | 12 | 2 | 0 | | <1 | <1 | 1 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 15mg + csDMARD | 221 | | 2 | 2 | | 2 | <1 | 0 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 30mg + csDMARD | 219 | | 3 | 3 | | 4 | 2 | 1 | 0 | 0 | | <1 | <1 | <1 |
| Fleischmann 2018 (SELECT-COMPARE) [31, 32] | Placebo + MTX | 652 | 26 | 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 | |
| Hu 2018 (RA- | Placebo + MTX | 145 | 24 | | | 0 | | 1.38 | 9.66 | | | 2.76 | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | 0 |
| Tanaka 2018a (SELECT-SUNRISE) [39, 40] | Placebo + csDMARDs | 49 | 12 | 4.1 | 0 | 0 | 2 | 10.2 | 2 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 7.5mg + csDMARDs | 49 | | 0 | 0 | 0 | 2 | 20.4 | 0 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 15mg + csDMARDs | 49 | | 4.1 | 0 | 0 | 0 | 20.4 | 0 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 30mg + csDMARDs | 50 | | 2.0 | 6 | 4 | 2 | 38 | 10 | 0 | 0 | | 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[a] | | | | | | 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; [c] 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 S4.3.2: Psoriatic arthritis.

| Study | Group | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mease 2017 (OPAL Broaden) [49] | Placebo ± csDMARD | 105 | 12/54 | 0/NA | 1/NA | | 0/NA | 0/NA | | 0/NA | | | 0/NA | 0/NA | 0/NA |
| | Placebo to TOFA 5mg BID ± csDMARD | 52 | | NA/5.8 | NA/1.9 | | | | | NA/0 | | | NA/2 | 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 |
| | TOFA 5mg BID ± csDMARD | 107 | | 0.9/2.8 | 0.9/4.7 | | 0 | 0 | | 0/0 | | | 0/0 | 2/3 | 0/0 |
| | TOFA 10mg BID ± csDMARD | 104 | | 1.0/2.9 | 0/4.8 | | 0 | 0 | | 0/0 | | | 0/0 | 0/0 | 1/1 |
| | ADA 40mg Q2W ± csDMARD | 106 | | 3.8/7.5 | 1.9/2.8 | | 0 | 0 | | 0/0 | | | 0/2 | 0/0 | 0/0 |
| Gladman 2017 (OPAL Beyond) [50] | Placebo ± csDMARD | 131 | 24 | | | | | | | | | | 0 | 0 | 0 |
| | TOFA 5mg BID ± csDMARD | 131 | | | | | | | | | | | 0 | 0 | 0 |
| | TOFA 10mg BID ± csDMARD | 132 | | | | | | | | | | | 0 | 0 | 0 |
| Mease 2018 (EQUATOR) [51] | Placebo ± csDMARD | 66 | 16 | | 0 | | | 3 | | 0 | 0 | 8 | 2 | 0 | |
| | FILGO 200mg OD ± csDMARD | 65 | | | 2 | | | 0 | | 0 | 0 | 0 | 0 | 0 | |

## Table S4.3.3: Ankylosing spondylitis

| Study | Group | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Van der Heijde 2017 [52] | Placebo ± csDMARD | 51 | 12 | 2 | 4.0 | | 0 | 0 | | | | | 0 | 0 | 0 |
| | TOFA 2mg BID ± csDMARD | 52 | | 0 | 0 | | 0 | 0 | | | | | 0 | 0 | 0 |
| | TOFA 5mg BID ± csDMARD | 52 | | 3.8 | 3.8 | | 1.9 | 1.9 | | | | | 0 | 0 | 0 |
| | TOFA 10mg BID ± csDMARD | 52 | | 2.0 | 2.0 | | 2.0 | 0 | | | | | 2 | 0 | 0 |
| Van der Heijde 2018 [53] | Placebo ± csDMARD | 58 | 12 | | 5 | | | | | 0 | | | | 0 | |
| | FILGO 200mg OD ± csDMARD | 58 | | | 0 | | | | | 2 | | | | 0 | |

## Table S4.3.4: Systemic Lupus Erythematosus

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

## Table S4.3.5: Psoriasis

| Study | Group | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Papp 2012 [56] | Placebo | 50 | 12 | | | | | 0 | 0 | | | 0 | | | |
| | TOFA 2mg BID | 49 | | | | | | 0 | 2.04 | | | 2.04 | | | |
| | TOFA 5mg BID | 49 | | | | | | 2.04 | 0 | | | 0 | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TOFA 15mg BID | 49 | | | | | | 0 | 0 | | | 0 | | | |
| Bachelez 2015 [57] | Placebo | 107 | 12 | | 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 | 16 | 0.46/0.46 | | | 0 | | | | | 1.38 | | 0 | 0.6 |
| | TOFA 10mg BID | 335 | | 1.27/1.91 | | | 0 | | | | | 1.91 | | 0.9 | 0.6 |
| Papp 2015 [59] | Placebo | 29 | 6 | | | | | | | | | | | | |
| | PEF 10mg BID | 19 | | | | | | | | | | | | | |
| | PEF 25mg BID | 21 | | | | | | | | | | | | | |
| | PEF 60mg BID | 19 | | | | | | | | | | | | | |
| | PEF 100mg BID | 17 | | | | | | | | | | | | | |
| | PEF 50mg BID | 19 | | | | | | | | | | | | | |
| 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 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bissonnette 2016 [61] | Placebo | 12 | 4 | | | | | | | | | | | | |
| | Itacitinib 100mg OD | 9 | | | | | | | | | | | | | |
| | Itacitinib 200mg OD | 9 | | | | | | | | | | | | | |
| | Itacitinib 200mg BID | 9 | | | | | | | | | | | | | |
| | Itacitinib 600mg OD | 11 | | | | | | | | | | | | | |
| Papp 2016 [62] | Placebo | 34 | 12 | | | | 0 | 0 | 0 | | 0 | | | 0 | 0 |
| | BARI 2mg | 32 | | | | | 0 | 0 | 0 | | 0 | | | 0 | 0 |
| | BARI 4mg | 72 | | | | | 0 | 0 | 1.4 | | 0 | | | 1.39 | 0 |
| | BARI 8mg | 64 | | | | | 0 | 4.7 | 1.6 | | 0 | | | 0 | 1.56 |
| | BARI 10mg | 69 | | | | | 4.3 | 0 | 2.9 | | 0 | | | 0 | 0 |
| Papp 2016 [63] | Vehicle BID | 71 | 8 | 1.4 | 1.4 | | 0 | 0 | 0 | | | | | | |
| | 2% TOFA BID | 71 | | 0 | 0 | | 0 | 0 | 0 | | | | | | |
| | 1% TOFA BID | 70 | | 2.9 | 0 | | 0 | 0 | 0 | | | | | | |
| | Vehicle OD | 74 | | 0 | 0 | | 0 | 0 | 0 | | | | | | |
| | 2% TOFA OD | 70 | | 1.5 | 3.0 | | 1.5 | 0 | 0 | | | | | | |
| | 1% TOFA OD | 74 | | 0 | 0 | | 0 | 0 | 1.35 | | | | | | |
| Zhang 2017 [64] | Placebo | 88 | 16 | | | | 0 | 0 | 0 | | | | 0 | 0 | |
| | TOFA 5mg BID | 88 | | | | | 0 | 0 | 0 | | | | 0 | 1.1 | |
| | TOFA 10mg BID | 90 | | | | | 0 | 0 | 0 | | | | 0 | 0 | |
| Papp 2018 [65] | Placebo | 45 | 12 | | | | | | | | | | | | |
| | BMS-986165 3mg EOD | 44 | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 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 (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **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) | | | | | | | | | | | | | | |
| **Atopic dermatitis** | | | | | | | | | | | | | | | |
| Bissonette 2016 [67] | Topical TOFA 2% BID | 35 | 4 | | | | | | | | | | | 0 | 0 |
| | Topical Vehicle BID | 34 | | | | | | | | | | | | 0 | 0 |
| De Bruin-Weller 2018 [68, 69] | Placebo | 41 | 16 | | | | 0 | 0 | 0 | 0 | 0 | | | 0 | 0 |
| | UPA 7.5mg OD | 42 | | | | | 2.4 | 0 | 0 | 0 | 0 | | | 0 | 0 |
| | UPA 15mg OD | 42 | | | | | 4.8 | 2.4 | 0 | 0 | 0 | | | 0 | 0 |
| | UPA 30mg OD | 42 | | | | | 4.8 | 0 | 2.4 | 0 | 0 | | | 0 | 0 |
| Guttman-Yassky 2018 [70] | Placebo + topical steroids | 49 | 16 | | | 6.12 | | | | | | | | | |
| | BARI 2mg OD + topical steroids | 37 | | | | 0 | | | | | | | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | BARI 4mg OD + topical steroids | 38 | | | | 2.63 | | | | | | | | | |
| Nakagawa 2018 [71] | Vehicle | 31 | 4 | | | | | | | | | | | | |
| | Topical JTE-052 0.25% | 69 | | | | | | | | | | | | | |
| | Topical JTE-052 0.5% | 65 | | | | | | | | | | | | | |
| | Topical JTE-052 1% | 66 | | | | | | | | | | | | | |
| | Topical JTE-052 3% | 65 | | | | | | | | | | | | | |
| | Topical tacrolimus | 30 | | | | | | | | | | | | | |

## Table S4.3.7: Ulcerative Colitis

| Study | Group | No. of patients | Time-point (weeks) | AST and/or ALT ≥ 3x ULN (%) | CK ≥ 3x ULN (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sandborn 2012 [72] | Placebo ± Mesalamine | 48 | 8 | | | | 0 | | 0 | 2.08 | | | | | |
| | TOFA 0.5mg BID ± Mesalamine | 31 | | | | | 0 | | 0 | 0 | | | | | |
| | TOFA 3mg BID ± Mesalamine | 33 | | | | | 0 | | 3 | 0 | | | | | |
| | TOFA 10mg BID ± Mesalamine | 33 | | | | | 3 | | 0 | 0 | | | | | |
| | TOFA 15mg BID ± Mesalamine | 49 | | | | | 4.1 | | 2 | 0 | | | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sandborn 2017 [73] | OCTAVE Induction 1: Placebo | 122 | 8 | | | | | | 4.92 | | | 9 | 0 | 0 | 0 |
| | OCTAVE Induction 1: TOFA 10mg BID | 476 | | | | | | | 2.31 | | | 17 | <1 | 0 | <1 |
| | OCTAVE Induction 2: Placebo | 112 | | | | | | | 1.79 | | | 5.4 | 0 | 0 | 0 |
| | OCTAVE Induction 2: TOFA 10mg BID | 429 | | | | | | | 2.56 | | | 17.2 | <1 | 0 | <1 |
| | OCTAVE Sustain: Placebo | 198 | 52 | | | | | | | | | 8.1 | 0 | <1 | <1 |
| | OCTAVE Sustain: TOFA 5mg BID | 198 | | | | | | | | | | 27.3 | <1 | 0 | 0 |
| | OCTAVE Sustain: TOFA 10mg BID | 197 | | | | | | | | | | 22.6 | <1 | 0 | 1.5 |
| Sandborn 2018 [74, 75] | Placebo | 46 | 8 | 0 | 0 | | 0 | 0 | 6.5 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 7.5mg OD | 47 | | 0 | 0 | | 0 | 4.3 | 2.1 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 15mg OD | 49 | | 0 | 2.0 | | 2 | 2.0 | 8.2 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 30mg OD | 52 | | 0 | 1.9 | | 0 | 4.0 | 3.8 | 0 | 0 | | 0 | 0 | 0 |
| | UPA 45mg OD | 56 | | 1.8 | 3.6 | | 3.6 | 3.6 | 0 | 1.8 | 1.8 | | 1.8 | 0 | 0 |
| Sands 2018 [76] | Placebo | 43 | 8 | | | | | | 4.7 | | | | | 0 | 0 |
| | Peficitinib 25mg OD | 44 | | | | | | | 4.5 | | | | | 2.3 | 2.3 |
| | Peficitinib 75mg OD | 44 | | | | | | | 0 | | | | | 0 | 0 |
| | Peficitinib 150mg OD | 44 | | | | | | | 6.8 | | | | | 0 | 0 |
| | Peficitinib 75mg BID | 44 | | | | | | | 4.5 | | | | | 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 (%) | Leuko-penia (%) | Neutro-penia G3 or G4 (%) | Lympho-penia G3 or G4 (%) | Anemia (%) | Deep vein thrombosis (%) | Pulmonary embolism (%) | Hyper-cholesterol-aemia (%) | MACE (%) | Malignancy (%) | NMSC (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sandborn 2014 [77] | Placebo | 34 | 4 | | | | | | 0 | | | | | 2.94 | |
| | TOFA 1mg BID | 36 | | | | | | | 2.78 | | | | | 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 | |
| | Induction: TOFA 5mg BID | 86 | | | | | | | 4.65 | | | 1.2 | 0 | 0 | |
| | Induction: TOFA 10mg BID | 86 | | | | | | | 2.33 | | | 1.2 | 0 | 1.2 | |
| | Maintenance: Placebo | 59 | 26 | | | | | | 1.69 | | | 0 | 0 | 0 | |
| | Maintenance: TOFA 5mg BID | 60 | | | | | | | 5 | | | 0 | 0 | 0 | |
| | Maintenance: TOFA 10mg BID | 61 | | | | | | | 8.2 | | | 1.6 | 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 | 36 | | | | | | | | 0 | 0 | | 2.8 | 0 | 0 |
| | Induction: UPA 24mg BID | 36 | | | | | | | | 0 | 0 | | 0 | 0 | 2.8 |
| | Induction: UPA 24mg OD | 35 | | | | | | | | 0 | 0 | | 0 | 0 | 0 |
| | Maintenance: UPA 3mg BID | 20 | 52 | | | | | | | 0 | 0 | | 1.7 | 0 | 0 |
| | Maintenance: UPA 6mg BID | 8 | | | | | | | | 0 | 0 | | 0 | 0 | 0 |
| | Maintenance: UPA 12mg BID | 16 | | | | | | | | 0 | 0 | | 0 | 3.4 | 0 |
| | Maintenance: UPA 24mg OD | 10 | | | | | | | | 0 | 0 | | 0 | 0 | 0 |
| Vermeire 2017 [82] | Placebo | 44 | 0-20 | | | | | | | | | | | | |
| | Placebo | 22 | 0-10 | | | | | | | | | | | | |
| | Placebo to FILGO 100mg | 22 | 10-20 | | | | | | | | | | | | |
| | FILGO 200mg | 23 | 0-10 | | | | | | | | | | | | |
| | FILGO 200mg to Placebo | 23 | 10-20 | | | | | | | | | | | | |
| | FILGO 200 to 100mg | 30 | 0-20 | | | | | | | | | | | | |
| | FILGO 200mg | 77 | 0-20 | | | | | | | | | | | | |

# Section 5 References


1. Kremer JM, Bloom BJ, Breedveld FC, Coombs JH, Fletcher MP, Gruben D, et al. The safety and efficacy of a JAK inhibitor in patients with active rheumatoid arthritis: Results of a double-blind, placebo-controlled phase IIa trial of three dosage levels of CP-690,550 versus placebo. Arthritis & Rheumatism. 2009 Jul; 60(7):1895-1905.
2. Tanaka Y, Suzuki M, Nakamura H, Toyoizumi S, Zwillich SH, Tofacitinib Study I. Phase II study of tofacitinib (CP-690,550) combined with methotrexate in patients with rheumatoid arthritis and an inadequate response to methotrexate. Arthritis care & research. 2011 Aug; 63(8):1150-1158.
3. Fleischmann R, Cutolo M, Genovese MC, Lee EB, Kanik KS, Sadis S, et al. Phase IIb dose-ranging study of the oral JAK inhibitor tofacitinib (CP-690,550) or adalimumab monotherapy versus placebo in patients with active rheumatoid arthritis with an inadequate response to disease-modifying antirheumatic drugs. Arthritis & Rheumatism. 2012 Mar; 64(3):617-629.
4. Fleischmann R, Kremer J, Cush J, Schulze-Koops H, Connell CA, Bradley JD, et al. Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. New England Journal of Medicine. 2012 Aug 09; 367(6):495-507.
5. Kremer JM, Cohen S, Wilkinson BE, Connell CA, French JL, Gomez-Reino J, et al. A phase IIb dose-ranging study of the oral JAK inhibitor tofacitinib (CP-690,550) versus placebo in combination with background methotrexate in patients with active rheumatoid arthritis and an inadequate response to methotrexate alone. Arthritis & Rheumatism. 2012 Apr; 64(4):970-981.
6. van Vollenhoven RF, Fleischmann R, Cohen S, Lee EB, Garcia Meijide JA, Wagner S, et al. Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. New England Journal of Medicine. 2012 Aug 09; 367(6):508-519.
7. Burmester GR, Blanco R, Charles-Schoeman C, Wollenhaupt J, Zerbini C, Benda B, et al. Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. Lancet. 2013 Feb 09; 381(9865):451-460.
8. Kremer J, Li ZG, Hall S, Fleischmann R, Genovese M, Martin-Mola E, et al. Tofacitinib in combination with nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: a randomized trial. Annals of Internal Medicine. 2013 Aug 20; 159(4):253-261.
9. van der Heijde D, Tanaka Y, Fleischmann R, Keystone E, Kremer J, Zerbini C, et al. Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving methotrexate: twelve-month data from a twenty-four-month phase III randomized radiographic study. Arthritis & Rheumatism. 2013 Mar; 65(3):559-570.
10. van der Heijde D, Strand V, Tanaka Y, Keystone E, Kremer J, Zerbini CAF, et al. Tofacitinib in Combination with Methotrexate in Patients with Rheumatoid Arthritis: Clinical Efficacy, Radiographic and Safety Outcomes from the 24-Month Phase 3 ORAL Scan Study. Arthritis & Rheumatology. 2019 Jan 22; 22:22.
11. Lee EB, Fleischmann R, Hall S, Wilkinson B, Bradley JD, Gruben D, et al. Tofacitinib versus methotrexate in rheumatoid arthritis. New England Journal of Medicine. 2014 Jun 19; 370(25):2377-2386.
12. Tanaka Y, Takeuchi T, Yamanaka H, Nakamura H, Toyoizumi S, Zwillich S. Efficacy and safety of tofacitinib as monotherapy in Japanese patients with active rheumatoid arthritis: a 12-week, randomized, phase 2 study. Modern Rheumatology. 2015 Jul; 25(4):514-521.
13. Fleischmann RM, Damjanov NS, Kivitz AJ, Legedza A, Hoock T, Kinnman N. A randomized, double-blind, placebo-controlled, twelve-week, dose-ranging study of decernotinib, an oral selective JAK-3 inhibitor, as monotherapy in patients with active rheumatoid arthritis. Arthritis rheumatol. 2015 Feb; 67(2):334-343.
14. Genovese MC, Kremer J, Zamani O, Ludivico C, Krogulec M, Xie L, et al. Baricitinib in Patients with Refractory Rheumatoid Arthritis. New England Journal of Medicine. 2016 Mar 31; 374(13):1243-1252.

15. Genovese MC, Smolen JS, Weinblatt ME, Burmester GR, Meerwein S, Camp HS, et al. Efficacy and Safety of ABT-494, a Selective JAK-1 Inhibitor, in a Phase IIb Study in Patients With Rheumatoid Arthritis and an Inadequate Response to Methotrexate. Arthritis & Rheumatology. 2016 12; 68(12):2857-2866.
16. Genovese MC, van Vollenhoven RF, Pacheco-Tena C, Zhang Y, Kinnman N. VX-509 (Decernotinib), an Oral Selective JAK-3 Inhibitor, in Combination With Methotrexate in Patients With Rheumatoid Arthritis. Arthritis & Rheumatology. 2016 Jan; 68(1):46-55.
17. Genovese MC, Yang F, Ostergaard M, Kinnman N. Efficacy of VX-509 (decernotinib) in combination with a disease-modifying antirheumatic drug in patients with rheumatoid arthritis: clinical and MRI findings. Annals of the Rheumatic Diseases. 2016 Nov; 75(11):1979-1983.
18. Kremer JM, Emery P, Camp HS, Friedman A, Wang L, Othman AA, et al. A Phase IIb Study of ABT-494, a Selective JAK-1 Inhibitor, in Patients With Rheumatoid Arthritis and an Inadequate Response to Anti–Tumor Necrosis Factor Therapy. Arthritis and Rheumatology. 2016; 68(12):2867-2877.
19. Takeuchi T, Tanaka Y, Iwasaki M, Ishikura H, Saeki S, Kaneko Y. Efficacy and safety of the oral Janus kinase inhibitor peficitinib (ASP015K) monotherapy in patients with moderate to severe rheumatoid arthritis in Japan: a 12-week, randomised, double-blind, placebo-controlled phase IIb study. Annals of the Rheumatic Diseases. 2016 Jun; 75(6):1057-1064.
20. Tanaka Y, Emoto K, Cai Z, Aoki T, Schlichting D, Rooney T, et al. Efficacy and Safety of Baricitinib in Japanese Patients with Active Rheumatoid Arthritis Receiving Background Methotrexate Therapy: A 12-week, Double-blind, Randomized Placebo-controlled Study. Journal of Rheumatology. 2016 Mar; 43(3):504-511.
21. Dougados M, van der Heijde D, Chen YC, Greenwald M, Drescher E, Liu J, et al. Baricitinib in patients with inadequate response or intolerance to conventional synthetic DMARDs: results from the RA-BUILD study. Annals of the Rheumatic Diseases. 2017 Jan; 76(1):88-95.
22. Fleischmann R, Mysler E, Hall S, Kivitz AJ, Moots RJ, Luo Z, et al. Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. Lancet. 2017 07 29; 390(10093):457-468.
23. Fleischmann R, Schiff M, van der Heijde D, Ramos-Remus C, Spindler A, Stanislav M, et al. Baricitinib, Methotrexate, or Combination in Patients With Rheumatoid Arthritis and No or Limited Prior Disease-Modifying Antirheumatic Drug Treatment. Arthritis & Rheumatology. 2017 03; 69(3):506-517.
24. Genovese MC, Greenwald M, Codding C, Zubrzycka-Sienkiewicz A, Kivitz AJ, Wang A, et al. Peficitinib, a JAK Inhibitor, in Combination With Limited Conventional Synthetic Disease-Modifying Antirheumatic Drugs in the Treatment of Moderate-to-Severe Rheumatoid Arthritis. Arthritis & Rheumatology. 2017 05; 69(5):932-942.
25. Kivitz AJ, Gutierrez-Urena SR, Poiley J, Genovese MC, Kristy R, Shay K, et al. Peficitinib, a JAK Inhibitor, in the Treatment of Moderate-to-Severe Rheumatoid Arthritis in Patients With an Inadequate Response to Methotrexate. Arthritis & Rheumatology. 2017 04; 69(4):709-719.
26. Kavanaugh A, Kremer J, Ponce L, Cseuz R, Reshetko OV, Stanislavchuk M, et al. Filgotinib (GLPG0634/GS-6034), an oral selective JAK1 inhibitor, is effective as monotherapy in patients with active rheumatoid arthritis: results from a randomised, dose-finding study (DARWIN 2). Annals of the Rheumatic Diseases. 2017 Jun; 76(6):1009-1019.
27. Taylor PC, Keystone EC, van der Heijde D, Weinblatt ME, Del Carmen Morales L, Reyes Gonzaga J, et al. Baricitinib versus Placebo or Adalimumab in Rheumatoid Arthritis. New England Journal of Medicine. 2017 02 16; 376(7):652-662.
28. Vanhoutte F, Mazur M, Voloshyn O, Stanislavchuk M, Van der Aa A, Namour F, et al. Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Filgotinib, a Selective JAK-1 Inhibitor, After Short-Term Treatment of Rheumatoid Arthritis: Results of Two Randomized Phase IIa Trials. Arthritis & Rheumatology. 2017 10; 69(10):1949-1959.
29. Westhovens R, Taylor PC, Alten R, Pavlova D, Enriquez-Sosa F, Mazur M, et al. Filgotinib (GLPG0634/GS-6034), an oral JAK1 selective inhibitor, is effective in combination with methotrexate

(MTX) in patients with active rheumatoid arthritis and insufficient response to MTX: results from a randomised, dose-finding study (DARWIN 1). Annals of the Rheumatic Diseases. 2017 Jun; 76(6):998-1008.
30. Burmester GR, Kremer JM, Van den Bosch F, Kivitz A, Bessette L, Li Y, et al. Safety and efficacy of upadacitinib in patients with rheumatoid arthritis and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (SELECT-NEXT): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2018 06 23; 391(10139):2503-2512.
31. Fleischmann R, Pangan AL, Mysler E, Bessette L, Peterfy C, Durez P, et al. A phase 3, randomized, double-blind study comparing upadacitinib to placebo and to adalimumab, in patients with active rheumatoid arthritis with inadequate response to methotrexate. 2018 ACR/ARHP Annual Meeting Chicago, USA; 2018: Arthritis & Rheumatology; 2018.
32. Fleischmann R, Pangan AL, Song IH, Mysler E, Bessette L, Peterfy C, et al. Upadacitinib Versus Placebo or Adalimumab in Patients With Rheumatoid Arthritis and an Inadequate Response to Methotrexate: Results of a Phase III, Double-Blind, Randomized Controlled Trial. Arthritis Rheumatol. 2019 Nov; 71(11):1788-1800.
33. Genovese MC, Fleischmann R, Combe B, Hall S, Rubbert-Roth A, Zhang Y, et al. Safety and efficacy of upadacitinib in patients with active rheumatoid arthritis refractory to biologic disease-modifying anti-rheumatic drugs (SELECT-BEYOND): a double-blind, randomised controlled phase 3 trial. Lancet. 2018 06 23; 391(10139):2513-2524.
34. Kivitz A, Mehta D, Matzkies F, Mozaffarian A, Kunder R, Paolo JAD, et al. GS-9876, a Novel, Highly Selective, SYK Inhibitor in Patients with Active Rheumatoid Arthritis: Safety, Tolerability and Efficacy Results of a Phase 2 Study. *2018 ACR/ARHP Annual Meeting Chicago, USA*: Arthritis & Rheumatology 2018.
35. Hu J, Bao C, Li X, Spindler A, Zhang X, Xu J, et al. Efficacy and safety of baricitinib in MTX-IR patients with rheumatoid arthritis: 52 week results from a phase 3 study (RA-balance). Annals of the rheumatic diseases Conference: annual european congress of rheumatology, EULAR 2018 Netherlands. 2018; 77(Supplement 2):969-970.
36. Yue Y, Hu J, Bao C, Li X, Spindler AJ, Zhang X, et al. Patient-reported outcomes from a phase 3 study (RA-BALANCE) of baricitinib versus placebo in rheumatoid arthritis. International journal of rheumatic diseases Conference: 20th asia pacific league of associations for rheumatology congress, APLAR 2018 Taiwan (republic of china). 2018; 21(Supplement 1):40.
37. Smolen J, Cohen S, Emery P, Rigby W, Tanaka Y, Zhang Y, et al. Upadacitinib as monotherapy: a phase 3 randomised controlled double-blind study in patients with active rheumatoid arthritis and inadequate response to methotrexate. Annals of the rheumatic diseases Conference: annual european congress of rheumatology, EULAR 2018 Netherlands. 2018; 77(Supplement 2):67-68.
38. Smolen JS, Pangan AL, Emery P, Rigby W, Tanaka Y, Vargas JI, et al. Upadacitinib as monotherapy in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebo-controlled, double-blind phase 3 study. Lancet. 2019 Jun 8; 393(10188):2303-2311.
39. Tanaka Y, Takeuchi T, Yamaoka K, Oribe M, Kawano M, Zhou Y, et al. A phase 2b/3 randomised, placebo-controlled, double-blind study of upadacitinib, a selective jak1 inhibitor, in Japanese patients with active rheumatoid arthritis and inadequate response to conventional synthetic DMARDs. Annals of the rheumatic diseases Conference: annual european congress of rheumatology, EULAR 2018 Netherlands. 2018; 77(Supplement 2):991-992.
40. Kameda H, Takeuchi T, Yamaoka K, Oribe M, Kawano M, Zhou Y, et al. Efficacy and safety of upadacitinib in Japanese patients with rheumatoid arthritis (SELECT-SUNRISE): a placebo-controlled phase IIb/III study. Rheumatology (Oxford). 2020 Apr 11.
41. Tanaka Y, Takeuchi T, Tanaka S, Kawakami A, Iwasaki M, Song YW, et al. Efficacy and Safety of the Novel Oral Janus Kinase (JAK) Inhibitor, Peficitinib (ASP015K), in a Phase 3, Double-Blind, Placebo-Controlled, Randomized Study of Patients with RA Who Had an Inadequate Response to Dmards. 2018 ACR/ARHP Annual Meeting Chicago, USA; 2018: Arthritis & Rheumatology; 2018.
42. Tanaka Y, Takeuchi T, Tanaka S, Kawakami A, Iwasaki M, Song YW, et al. Efficacy and safety of peficitinib (ASP015K) in patients with rheumatoid arthritis and an inadequate response to

conventional DMARDs: a randomised, double-blind, placebo-controlled phase III trial (RAJ3). Ann Rheum Dis. 2019 Oct; 78(10):1320-1332.
43. Takeuchi T, Tanaka Y, Tanaka S, Kawakami A, Iwasaki M, Rokuda M, et al. Efficacy and safety of the novel oral Janus kinase (JAK) inhibitor, peficitinib (ASP015K), in a phase 3, double-blind, placebo-controlled, randomized study of patients with RA who had an inadequate response to methotrexate. 2018 ACR/ARHP Annual Meeting Chicago, USA; 2018: Arthritis & Rheumatology; 2018.
44. Takeuchi T, Tanaka Y, Tanaka S, Kawakami A, Iwasaki M, Katayama K, et al. Efficacy and safety of peficitinib (ASP015K) in patients with rheumatoid arthritis and an inadequate response to methotrexate: results of a phase III randomised, double-blind, placebo-controlled trial (RAJ4) in Japan. Ann Rheum Dis. 2019 Oct; 78(10):1305-1319.
45. van Vollenhoven R, Takeuchi T, Pangan AL, Friedman A, Mohamed M, Chen S, et al. A Phase 3, Randomized, Controlled Trial Comparing Upadacitinib Monotherapy to MTX Monotherapy in MTX-Naïve Patients with Active Rheumatoid Arthritis - ACR Meeting Abstracts. 2018 ACR/ARHP Annual Meeting Chicago, USA; 2018 2018: Arthritis Rheumatol.; 2018.
46. Takeuchi T, Genovese MC, Haraoui B, Li Z, Xie L, Klar R, et al. Dose reduction of baricitinib in patients with rheumatoid arthritis achieving sustained disease control: results of a prospective study. Annals of the rheumatic diseases. 2018.
47. Takeuchi T, Genovese MC, Haraoui B, Li Z, Xie L, Klar R, et al. Dose reduction of baricitinib in patients with rheumatoid arthritis achieving sustained disease control: results of a prospective study. Annals of the Rheumatic Diseases. 2019 Feb; 78(2):171-178.
48. Tanaka Y, Sugiyama N, Toyoizumi S, Lukic T, Lamba M, Zhang R, et al. Modified- versus immediate-release tofacitinib in Japanese rheumatoid arthritis patients: a randomized, phase III, non-inferiority study. Rheumatology. 2019 Jan 01; 58(1):70-79.
49. Mease P, Hall S, FitzGerald O, van der Heijde D, Merola JF, Avila-Zapata F, et al. Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis. New England Journal of Medicine. 2017 10 19; 377(16):1537-1550.
50. Gladman D, Rigby W, Azevedo VF, Behrens F, Blanco R, Kaszuba A, et al. Tofacitinib for Psoriatic Arthritis in Patients with an Inadequate Response to TNF Inhibitors. New England Journal of Medicine. 2017 10 19; 377(16):1525-1536.
51. Mease P, Coates LC, Helliwell PS, Stanislavchuk M, Rychlewska-Hanczewska A, Dudek A, et al. Efficacy and safety of filgotinib, a selective Janus kinase 1 inhibitor, in patients with active psoriatic arthritis (EQUATOR): results from a randomised, placebo-controlled, phase 2 trial. Lancet. 2018 12 01; 392(10162):2367-2377.
52. van der Heijde D, Deodhar A, Wei JC, Drescher E, Fleishaker D, Hendrikx T, et al. Tofacitinib in patients with ankylosing spondylitis: a phase II, 16-week, randomised, placebo-controlled, dose-ranging study. Annals of the Rheumatic Diseases. 2017 Aug; 76(8):1340-1347.
53. van der Heijde D, Baraliakos X, Gensler LS, Maksymowych WP, Tseluyko V, Nadashkevich O, et al. Efficacy and safety of filgotinib, a selective Janus kinase 1 inhibitor, in patients with active ankylosing spondylitis (TORTUGA): results from a randomised, placebo-controlled, phase 2 trial. Lancet. 2018 12 01; 392(10162):2378-2387.
54. Kahl L, Patel J, Layton M, Binks M, Hicks K, Leon G, et al. Safety, tolerability, efficacy and pharmacodynamics of the selective JAK1 inhibitor GSK2586184 in patients with systemic lupus erythematosus. Lupus. 2016; 25(13):1420-1430.
55. Wallace DJ, Furie RA, Tanaka Y, Kalunian KC, Mosca M, Petri MA, et al. Baricitinib for systemic lupus erythematosus: a double-blind, randomised, placebo-controlled, phase 2 trial. Lancet. 2018 07 21; 392(10143):222-231.
56. Papp KA, Menter A, Strober B, Langley RG, Buonanno M, Wolk R, et al. Efficacy and safety of tofacitinib, an oral Janus kinase inhibitor, in the treatment of psoriasis: a Phase 2b randomized placebo-controlled dose-ranging study. British Journal of Dermatology. 2012 Sep; 167(3):668-677.
57. Bachelez H, van de Kerkhof PC, Strohal R, Kubanov A, Valenzuela F, Lee JH, et al. Tofacitinib versus etanercept or placebo in moderate-to-severe chronic plaque psoriasis: a phase 3 randomised non-inferiority trial. Lancet. 2015 Aug 08; 386(9993):552-561.

58. Bissonnette R, Iversen L, Sofen H, Griffiths CE, Foley P, Romiti R, et al. Tofacitinib withdrawal and retreatment in moderate-to-severe chronic plaque psoriasis: a randomized controlled trial. British Journal of Dermatology. 2015; 172(5):1395-1406.
59. Papp K, Pariser D, Catlin M, Wierz G, Ball G, Akinlade B, et al. A phase 2a randomized, double-blind, placebo-controlled, sequential dose-escalation study to evaluate the efficacy and safety of ASP015K, a novel Janus kinase inhibitor, in patients with moderate-to-severe psoriasis. British Journal of Dermatology. 2015 Sep; 173(3):767-776.
60. Papp KA, Menter MA, Abe M, Elewski B, Feldman SR, Gottlieb AB, et al. Tofacitinib, an oral Janus kinase inhibitor, for the treatment of chronic plaque psoriasis: results from two randomized, placebo-controlled, phase III trials. British Journal of Dermatology. 2015 Oct; 173(4):949-961.
61. Bissonnette R, Luchi M, Fidelus-Gort R, Jackson S, Zhang H, Flores R, et al. A randomized, double-blind, placebo-controlled, dose-escalation study of the safety and efficacy of INCB039110, an oral janus kinase 1 inhibitor, in patients with stable, chronic plaque psoriasis. Journal of Dermatological Treatment. 2016; 27(4):332-338.
62. Papp KA, Menter MA, Raman M, Disch D, Schlichting DE, Gaich C, et al. A randomized phase 2b trial of baricitinib, an oral Janus kinase (JAK) 1/JAK2 inhibitor, in patients with moderate-to-severe psoriasis. British Journal of Dermatology. 2016 Jun; 174(6):1266-1276.
63. Papp KA, Bissonnette R, Gooderham M, Feldman SR, Iversen L, Soung J, et al. Treatment of plaque psoriasis with an ointment formulation of the Janus kinase inhibitor, tofacitinib: a Phase 2b randomized clinical trial. BMC Dermatology. 2016 10 03; 16(1):15.
64. Zhang J, Tsai TF, Lee MG, Zheng M, Wang G, Jin H, et al. The efficacy and safety of tofacitinib in Asian patients with moderate to severe chronic plaque psoriasis: A Phase 3, randomized, double-blind, placebo-controlled study. Journal of Dermatological Science. 2017 Oct; 88(1):36-45.
65. Papp K, Gordon K, Thaci D, Morita A, Gooderham M, Foley P, et al. Phase 2 Trial of Selective Tyrosine Kinase 2 Inhibition in Psoriasis. New England Journal of Medicine. 2018 10 04; 379(14):1313-1321.
66. Guttman-Yassky E, Page K, Pavel AB, Diaz A, Estrada Y, Banerjee A, et al. Selective oral JAK3 and TYK2/JAK1 kinase inhibitors both demonstrate significant hair-growth compared to placebo and improvement of hair-associated keratins in patients with moderate-to-severe Alopecia Areata. Experimental Dermatology. 2018; 27:52-53.
67. Bissonnette R, Papp KA, Poulin Y, Gooderham M, Raman M, Mallbris L, et al. Topical tofacitinib for atopic dermatitis: a phase IIa randomized trial. British Journal of Dermatology. 2016 Nov; 175(5):902-911.
68. De Bruin-Weller MS, Guttman-Yassky E, Forman SB, Bodhani A, Chen S, Pangan AL, et al. Effects of upadacitinib on atopic dermatitis signs, symptoms and patient-reported outcomes from a phase IIb randomized, placebo-controlled trial. British Journal of Dermatology. 2018; 179(1):e13.
69. Guttman-Yassky E, Thaci D, Pangan AL, Hong HC, Papp KA, Reich K, et al. Upadacitinib in adults with moderate to severe atopic dermatitis: 16-week results from a randomized, placebo-controlled trial. J Allergy Clin Immunol. 2020 Mar; 145(3):877-884.
70. Guttman-Yassky E, Silverberg JI, Nemoto O, Forman SB, Wilke A, Prescilla R, et al. Baricitinib in adult patients with moderate-to-severe atopic dermatitis: a phase 2 parallel, double-blinded, randomized placebo-controlled multiple-dose study. Journal of the American Academy of Dermatology. 2018 Feb 01; 01:01.
71. Nakagawa H, Nemoto O, Igarashi A, Nagata T. Efficacy and safety of topical JTE-052, a Janus kinase inhibitor, in Japanese adult patients with moderate-to-severe atopic dermatitis: a phase II, multicentre, randomized, vehicle-controlled clinical study. British Journal of Dermatology. 2018 02; 178(2):424-432.
72. Sandborn WJ, Ghosh S, Panes J, Vranic I, Su C, Rousell S, et al. Tofacitinib, an oral Janus kinase inhibitor, in active ulcerative colitis. New England Journal of Medicine. 2012 Aug 16; 367(7):616-624.
73. Sandborn WJ, Su C, Sands BE, D'Haens GR, Vermeire S, Schreiber S, et al. Tofacitinib as Induction and Maintenance Therapy for Ulcerative Colitis. New England Journal of Medicine. 2017 05 04; 376(18):1723-1736.

74. Sandborn WJ, Ghosh S, Panés J, Schreiber S, D'Haens G, Tanida S, et al. Efficacy and safety of upadacitinib as an induction therapy for patients with moderately-toseverely active ulcerative colitis: Data from the phase 2b study u-achieve. United European Gastroenterology Journal. 2018; 6(8):A74-A75.
75. Sandborn WJ, Ghosh S, Panes J, Schreiber S, D'Haens G, Tanida S, et al. Efficacy of Upadacitinib in a Randomized Trial of Patients With Active Ulcerative Colitis. Gastroenterology. 2020 Feb 22.
76. Sands BE, Sandborn WJ, Feagan BG, Lichtenstein GR, Zhang H, Strauss R, et al. Peficitinib, an Oral Janus Kinase Inhibitor, in Moderate-to-severe Ulcerative Colitis: Results From a Randomised, Phase 2 Study. Journal of Crohn's & colitis. 2018 Nov 09; 12(10):1158-1169.
77. Sandborn WJ, Ghosh S, Panes J, Vranic I, Wang W, Niezychowski W, et al. A phase 2 study of tofacitinib, an oral Janus kinase inhibitor, in patients with Crohn's disease. Clinical Gastroenterology & Hepatology. 2014 Sep; 12(9):1485-1493.e1482.
78. Panes J, Sandborn WJ, Schreiber S, Sands BE, Vermeire S, D'Haens G, et al. Tofacitinib for induction and maintenance therapy of Crohn's disease: results of two phase IIb randomised placebo-controlled trials. Gut. 2017; 16:16.
79. Sanborn WJ, Feagan B, Panes J, D'Haens G, Colombel J, Zhou Q, et al. Safety and efficacy of upadacitinib (ABT-494), an oral JAK1 inhibitor, as induction therapy in patients with crohn's disease: Results from celest. United European Gastroenterology Journal. 2017; 5(5):A3-A4.
80. Panes J, Sandborn WJ, Loftus EV, Van Assche G, Ghosh S, Zhou Q, et al. Efficacy and safety of upadacitinib maintenance treatment for moderate to severe Crohn's disease: Results from the CELEST study. Journal of Crohn's and Colitis. 2018; 12:S238-S239.
81. Sandborn WJ, Feagan BG, Loftus EV, Jr., Peyrin-Biroulet L, Van Assche G, D'Haens G, et al. Efficacy and Safety of Upadacitinib in a Randomized Trial of Patients With Crohn's Disease. Gastroenterology. 2020 Feb 8.
82. Vermeire S, Schreiber S, Petryka R, Kuehbacher T, Hebuterne X, Roblin X, et al. Clinical remission in patients with moderate-to-severe Crohn's disease treated with filgotinib (the FITZROY study): results from a phase 2, double-blind, randomised, placebo-controlled trial. Lancet. 2017 01 21; 389(10066):266-275.
83. Genovese M, Van Der Heijde D, Dougados M, Chen Y, Greenwald M, Drescher E, et al. Baricitinib inhibits radiographic progression of structural joint damage at 1 year in patients with rheumatoid arthritis (RA) and an inadequate response to conventional synthetic disease-modifying antirheumatic drugs (CSDMARDS). Internal medicine journal Conference: new zealand rheumatology association and australian rheumatology association with the rheumatology health professionals association joint annual scientific meeting New zealand. 2017; 47:32.
84. Tanaka Y, Takeuchi T, Yamanaka H, Suzuki M, Nakamura H, Toyoizumi S, et al. Tofacitinib (CP-690,550), an oral janus kinase inhibitor, as monotherapy in japanese patients with active rheumatoid arthritis: a 12-week phase 2b study. Arthritis and rheumatism. 2011; 63(10 SUPPL. 1).
85. Charles-Schoeman C, Wicker P, Gonzalez-Gay MA, Boy M, Zuckerman A, Soma K, et al. Cardiovascular safety findings in patients with rheumatoid arthritis treated with tofacitinib, an oral Janus kinase inhibitor. Seminars in Arthritis & Rheumatism. 2016 12; 46(3):261-271.
86. Clowse ME, Feldman SR, Isaacs JD, Kimball AB, Strand V, Warren RB, et al. Pregnancy Outcomes in the Tofacitinib Safety Databases for Rheumatoid Arthritis and Psoriasis. Drug Safety. 2016 08; 39(8):755-762.
87. Cohen SB, Tanaka Y, Mariette X, Curtis JR, Lee EB, Nash P, et al. Long-term safety of tofacitinib for the treatment of rheumatoid arthritis up to 8.5 years: integrated analysis of data from the global clinical trials. Annals of the Rheumatic Diseases. 2017 Jul; 76(7):1253-1262.
88. Smolen JS, Genovese MC, Takeuchi T, Hyslop DL, Macias WL, Rooney T, et al. Safety Profile of Baricitinib in Patients with Active Rheumatoid Arthritis with over 2 Years Median Time in Treatment. Journal of Rheumatology. 2019 Jan; 46(1):7-18.
89. Desai RJ, Pawar A, Weinblatt ME, Kim SC. Comparative Risk of Venous Thromboembolism in Rheumatoid Arthritis Patients Receiving Tofacitinib Versus Those Receiving Tumor Necrosis Factor Inhibitors: An Observational Cohort Study. Arthritis & Rheumatology. 2019; 71(6):892-900.

90. Wu JJ, Strober BE, Hansen PR, Ahlehoff O, Egeberg A, Qureshi AA, et al. Effects of tofacitinib on cardiovascular risk factors and cardiovascular outcomes based on phase III and long-term extension data in patients with plaque psoriasis. Journal of the American Academy of Dermatology. 2016 Nov; 75(5):897-905.
91. Winthrop KL, Lebwohl M, Cohen AD, Weinberg JM, Tyring SK, Rottinghaus ST, et al. Herpes zoster in psoriasis patients treated with tofacitinib. Journal of the American Academy of Dermatology. 2017; 77(2):302-309.
92. Strober BE, Gottlieb AB, van de Kerkhof PCM, Puig L, Bachelez H, Chouela E, et al. Benefit-risk profile of tofacitinib in patients with moderate-to-severe chronic plaque psoriasis: pooled analysis across six clinical trials. British Journal of Dermatology. 2019 Jan; 180(1):67-75.
93. Winthrop KL, Melmed GY, Vermeire S, Long MD, Chan G, Pedersen RD, et al. Herpes zoster infection in patients with ulcerative colitis receiving tofacitinib. American journal of gastroenterology Conference: 82nd annual scientific meeting of the american college of gastroenterology United states. 2017; 112(Supplement 1):S327-S328.
94. Winthrop KL, Melmed GY, Vermeire S, Long MD, Chan G, Pedersen RD, et al. Herpes zoster infection in patients with ulcerative colitis receiving tofacitinib. Journal of crohn's and colitis Conference: 13th congress of european crohn's and colitis organisation, ECCO 2018 Austria. 2018; 12(Supplement 1):S364.
95. Mahadevan U, Dubinsky MC, Su C, Lawendy N, Jones TV, Marren A, et al. Outcomes of Pregnancies With Maternal/Paternal Exposure in the Tofacitinib Safety Databases for Ulcerative Colitis. Inflammatory Bowel Diseases. 2018 Nov 29; 24(12):2494-2500.
96. Sandborn WJ, Panes J, D'Haens GR, Sands BE, Su C, Moscariello M, et al. Safety of Tofacitinib for Treatment of Ulcerative Colitis, Based on 4.4 Years of Data From Global Clinical Trials. Clinical Gastroenterology & Hepatology. 2018 Nov 23; 23:23.
97. Sands BE, Taub PR, Feagan BG, Armuzzi A, Friedman GS, Moscariello M, et al. The effect of tofacitinib on serum lipids and cardiovascular safety in patients with ulcerative colitis: Results from the tofacitinib ulcerative colitis clinical programme. Journal of Crohn's and Colitis. 2018; 12:S023.