Supplementary appendix

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table of contents

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Section 1: Search strategy and PICOs

Table S1.1: MEDLINE Search strategy: Efficacy

1	psoriatic arthritis/ (5297)
2	(psoria$ adj (arthriti$ or arthropath$)).tw. (6883)
3	((arthriti$ or arthropath$) adj psoria$).tw. (635)
4	oligoarthriti$.tw. (840)
5	or/1-4 (8793)
6	randomized controlled trial.pt. (471779)
7	controlled clinical trial.pt. (92751)
8	randomized.ab. (372150)
9	placebo.ab. (176049)
10	drug therapy.fs. (2065352)
11	randomly.ab. (258409)
12	trial.ab. (385998)
13	groups.ab. (1608724)
14	or/6-13 (3993642)
15	exp animals/ not humans.sh. (4519948)
16	14 not 15 (3407424)
17	5 and 16 (4109)
18	limit 17 to yr="2015 -Current" (995)

Table S1.2: EMBASE Search strategy: Efficacy

#18. #17 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND (2015:py 2016:py OR 2017:py OR 2018:py OR 2019:py)

#17. #3 AND #16

#16. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15

#15. random*:ab,ti

#14. 'randomized controlled trial'/exp

#13. trial:ti

#12. allocat*:ab,ti

#11. (doubl* NEAR/2 blind*):ab,ti

#10. placebo*:ab,ti

#9. crossover*:ab,ti OR 'cross over*':ab,ti

#8. 'single blind procedure'/de

#7. 'randomized controlled trial'/de

#6. 'double blind procedure'/de

#5. 'crossover procedure'/de

#4. #1 OR #2 OR #3

#3. oligoarthriti*:ab,ti

#2. (psoria* NEAR/2 (arthriti* OR arthropath*)):ab,ti

#1. 'psoriatic arthritis'/de

Table S1.3: Cochrane Library Search strategy: Efficacy

#1 MeSH descriptor: [Arthritis, Psoriatic] this term only

#2 (psoria* next (arthriti* or arthropath*)):ti,ab

#3 ((arthriti* or arthropath*) next psoria*):ti,ab

#4 oligoarthriti*:ti,ab

#5 #1 or #2 or #3 or #4 Publication Year from 2015 to 2018

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table S1.4: MEDLINE Search strategy: Safety

1. psoriatic arthritis/
2. (psoria$ adj (arthriti$ or arthropath$)).tw.
3. ((arthriti$ or arthropath$) adj psoria$).tw.
4. oligoarthriti$.tw.
5. or/1-4
6. (safe or safety).tw.
7. side effect$.tw.
8. ((adverse or undesirable or harms$ or serious or toxic) adj3 (effect$ or reaction$ or event$ or outcome$)).tw.
9. exp product surveillance, postmarketing/
10. exp adverse drug reaction reporting systems/
11. clinical trials, phase iv/
12. Clinical Trials, Phase III/
13. exp poisoning/
14. exp substance-related disorders/
15. exp drug toxicity/
16. exp abnormalities, drug induced/
17. exp drug monitoring/
18. exp drug hypersensitivity/
19. (toxicity or complication$ or noxious or tolerability).tw.
20. exp Postoperative Complications/
21. exp Intraoperative Complications/
22. exp INFECTION/
23. infection$.tw.
24. exp TUBERCULOSIS/
25. (Tuberculosis or tb).tw.
26. exp Neoplasms/
27. cancer$.tw.
28. neoplasm$.tw.
29. carcinoma$.tw.
30. lymphoma$.tw.
31. (leukaemia or leukemia).tw.
32. myeloma$.tw.
33. tumo?r$.tw.
34. melanoma$.tw.
35. melanoma$.tw.
36. Malignanc$.tw.
37. Dermatitis, Atopic/
38. (dermatitis or skin exacerbat$).tw.
39. exp Cardiovascular Diseases/
40. (cardiovasc$ or mace).tw.
41. exp Demyelinating Diseases/
42. demyelinat$.tw.
43. exp Herpes Zoster/
44. herpe$.tw.
45. Venous Thromboembolism/
46. (embolism$ or thromboembolism$).tw.
47. exp Gastrointestinal Diseases/
48. Gastrointestinal.tw.
49. exp depressive disorder/

50. depress$.tw.
51. exp Suicide/
52. suicid$.tw.
53. or/6-52
54. 5 and 53
55. exp animals/ not humans.sh.
56. 54 not 55
57. limit 56 to yr="2015 -Current"

Table S1.5: EMBASE Search strategy: Safety

#52. #51 AND (2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py)
#51. #4 AND #49 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim
#50. #4 AND #49
#49. #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #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 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48
#48. suicid*:ab,ti
#47. 'suicidal behavior'/exp OR 'suicide'/de
#46. depress*:ab,ti
#45. 'depression'/exp
#44. gastrointestinal:ab,ti
#43. 'gastrointestinal disease'/de
#42. embolism*:ab,ti OR thromboembolism*:ab,ti
#41. 'venous thromboembolism'/exp
#40. herpe*:ab,ti
#39. 'herpes zoster'/exp
#38. demyelinat*:ab,ti
#37. 'demyelinating disease'/exp
#36. cardiovasc*:ab,ti OR mace:ab,ti
#35. 'cardiovascular disease'/exp
#34. dermatitis:ab,ti OR 'skin exacerbat*':ab,ti
#33. 'atopic dermatitis'/de
#32. malignanc*.ab,ti
#31. melanoma*:ab,ti
#30. tumor*:ab,ti OR tumour*:ab,ti
#29. myeloma:ab,ti
#28. leukaemia:ab,ti OR leukemia:ab,ti
#27. lymphoma*:ab,ti
#26. carcinoma*:ab,ti
#25. neoplasm*:ab,ti
#24. cancer*:ab,ti
#23. 'neoplasm'/exp
#22. tuberculosis:ab,ti OR tb:ab,ti
#21. 'mycobacterium tuberculosis'/de
#20. infection*:ab,ti
#19. 'infection'/exp
#18. 'peroperative complication'/de
#17. 'postoperative complication'/exp
#16. toxicity:ab,ti OR complication*:ab,ti OR noxious:ab,ti OR tolerability:ab,ti
#15. 'drug hypersensitivity'/exp
#14. 'drug monitoring'/de
#13. 'congenital malformation'/exp
#12. 'drug toxicity'/exp
#11. 'intoxication'/exp
#10. 'phase 4 clinical trial (topic)'/de
#9. 'postmarketing surveillance'/exp
#8. ((adverse OR undesirable OR harms* OR serious OR toxic) NEAR/3 (effect* OR reaction* OR event* OR outcome*)):ab,ti
#7. 'side effect':ab,ti OR 'side effects':ab,ti

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

#6. safe:ab,ti OR safety:ab,ti
#5. 'adverse drug reaction'/lnk OR 'complication'/lnk OR 'side effect'/lnk
#4. #1 OR #2 OR #3
#3. oligoarthriti*:ab,ti
#2. (psoria* NEAR/2 (arthriti* OR arthropath*)):ab,ti
#1. 'psoriatic arthritis'/de

Table S1.6: Cochrane Libary Search strategy: Safety

#1	MeSH descriptor: [Arthritis, Psoriatic] this term only
#2	(psoria* next (arthriti* or arthropath*)):ti,ab
#3	((arthriti* or arthropath*) next psoria*):ti,ab
#4	oligoarthriti*:ti,ab
#5	#1 or #2 or #3 or #4 Publication Year from 2015 to 2018

Table S1.7: Pharmacologic interventions of interest

Biological disease modifying anti-rheumatic drugs (bDMARDs)	all formulations and duration (biosimilars included): anakinra (ANA), infliximab (INF), etanercept (ETN), adalimumab (ADA), golimumab (GOL), certolizumab pegol (CZP), rituximab (RTX), ofatumumab (OFA), abatacept (ABA), tocilizumab (TCZ), sarilumab (SAR), sirukumab (SKM), ocrelizumab (OKM), tabalumab (TBM), olokizumab (OLO), clazakizumab (CZK), pateclizumab (PZK), ixekizumab (IXE), brodalumab (BLM), guselkumab (GLM), ustekinumab (UKM), mavrilimumab (MAV)
Targeted synthetic DMARDs (tsDMARDs)	Tofacitinib (TOFA), baricitinib (BARI), peficitinib (PEF), filgotinib (FILGO), upadacitinib (UPA), fostamatinib (FOSTA)
Conventional synthetic DMARDs (csDMARDs)	Methotrexate (MTX), leflunomide (LEF), sulfasalazine (SZP), hydroxychloroquine (HCQ), injectable gold (GOLD), chloroquine (CQ)
Systemic glucocorticoids (GC)	
Any combination of the previous	

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table S1.8: Patient population, Intervention, Control (PICO) definition. See table S1.7 for specific definition of interventions.

#	Research question	Population	Intervention	Control	Outcome
1	What is the efficacy of pharmacological treatments in PsA?	Adult Patients with PsA	As described in table S1.7	○ Placebo ○ (Another) bDMARD ○ (Another) conventional synthetic DMARD ○ (Another) targeted synthetic DMARD ○ Steroid ○ NSAID ○ Combination therapy	▪ ACR 20/50/70 responses ▪ DAPSA / DAPSA remission and low disease activity ▪ Minimum disease activity/ very low disease activity ▪ EULAR responses (EULAR good or moderate response; EULAR moderate response) ▪ Psoriatic Arthritis Response Criteria (PsARC) ▪ Psoriasis Arthritis Impact of Disease Questionnaire (PSAID) ▪ PASI 75, PASI 90, PASI 100 ▪ Structural damage: PsA modified Sharp van der Heijde score
2	What is the safety of pharmacological treatments in PsA?	As in #1	As described in table S1.7	As described in #1 + None (if population-based incidence rates are reported)	▪ Serious adverse events (number and rate) ▪ Withdrawals due to AEs ▪ Serious infections ▪ Tuberculosis ▪ Malignancies (lymphoma, non-melanoma skin-cancer, melanoma, solid tumors, other haematological malignancies, unspecified) ▪ Skin exacerbation ▪ Major Adverse Cardiac Events (MACE) ▪ Demyelinating disease ▪ Herpes zoster ▪ Venous thromboembolic events ▪ Gastrointestinal adverse events / toxicities, including IBD ▪ Depression ▪ Suicide attempt / suicide

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Section 2: Efficacy study characteristics of articles and abstracts included.

Table S2.1: Efficacy: Details of articles and abstracts selected for inclusion.

PICO	Study	Treatment	Target	Population
1	Mease 2017a (ASTRAEA) [1]	Abatacept	CD80/CD86	Mixed csDMARD-IR / TNFi-IR
1	Mease 2018a (ABT-122 Phase 2) [2]	ABT-122	TNF/IL-17A	MTX-IR
1	Mease 2016 (Clazakizumab Phase 2) [3]	Clazakizumab	IL-6	csDMARD / NSAID-IR
1	Mease 2017b (SPIRIT-P1) [4, 5]	Ixekizumab	IL-17A	csDMARD-IR
1	Coates 2017 (SPIRIT-P1) [6]			
1	Nash 2017 (SPIRIT-P2) [7]	Ixekizumab	IL-17A	TNFi-IR
1	Nash 2018 (SPIRIT-P2) [8]			
1	van der Heijde 2016 (FUTURE-1) [9]	Secukinumab	IL-17A	
1	Kavanaugh 2016 (FUTURE-2) [10]			
1	Nash 2018 (FUTURE-3) [11]			Mixed NSAID / csDMARD / TNFi-IR
1	Kivitz PANLAR 2018 (FUTURE-4) [12]			NSAID-IR
1	Mease 2018c (FUTURE-5) [13]			Mixded csDMARD-iR / TNFi-IR
1	Deodhar 2018 (Guselkumab Phase 2) [14]	Guselkumab	IL-23p19	Mixed csDMARD /TNFi (≤20%) IR
1	Mease 2017/2018 [15, 34]	Risankizumab	Il-23p19	Mixed MTX / TNFi-IR
1	Araujo 2018 (ECLIPSA) [16]	Ustekinumab	IL-12/23	Active Enthesitis
1	Gladman 2018 (PALACE 1-3) [17]	Apremilast	PDE-4	csDMARD / TNF (≤10%) IR
1	Cutolo 2016 (PALACE-2) [18]			
1	Edwards 2016 (PALACE-3) [19]			
1	Wells 2018 (PALACE-4) [20]			csDMARD naïve
1	Nash 2018 (ACTIVE) [21]			bDMARD naïve

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

1	Mease 2018 ACR (SEAM-PsA) [22]	Etanercept	TNF	DMARD naïve
1	Kavanaugh 2017 (GO-VIBRANT) [23]	Golimumab	TNF	csDMARD / NSAID IR
1	Van Der Heijde 2017 EULAR (RAPID-PsA) [24]	Certolizumab pegol	TNF	
1	Mease 2018d (EQUATOR) [25]	Filgotinib	JAK	csDMARD-IR
1	Gladman 2017 (OPAL Beyond) [26]	Tofacitinib	JAK	TNFi-IR
1	Mease 2017c (OPAL Broaden) [27]	Tofacitinib / Adalimumab	JAK / TNF	csDMARD-IR
1	Araujo 2015 [28]	DMARD stopping		No MSK symptoms, minimal skin/nail disease for ≥6 months, MTX-IR
1	Moverley 2015 (RETREAT) [29]	csDMARD / TNFi tapering + stopping	TNFi	MDA + stable disease ≥6 months
1	Kristensen 2016 [30]	TNFi switching	TNFi	
1	Kivitz ACR 2016 [31]	CHS-0214 / Etanercept	TNFi	
1	Jorgensen 2017 (NOR-SWITCH) [32]	CT-P13 / Infliximab	TNFi	
1	Glintborg 2017 (DANBIO) [33]	CT-P13 / Infliximab	TNFi	

cs: conventional synthetic; DMARD: disease modifying anti-rheumatic drug; IL: interleukin; IR: insufficient responders; JAK: janus kinase; MDA: minimal disease activity; MSK: musculoskeletal; MTX: methotrexate; NSAID: non-steroidal anti-inflammatory drug; PDE: phosphodiesterase; TNF: tumor necrosis factor;

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table S2.2: Efficacy: Risk of bias analysis.

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 2017a (ASTRAEA) [1]	Low	Low	Low	Low	Low	Low	Low	Low	
Mease 2018a (ABT-122 Phase 2) [2]	Low	Low	Low	Low	Low	Low	Low	Low	
Mease 2016 (Clazakizumab Phase 2) [3]	Low	Low	Low	Low	Low	Low	Low	Low	
Mease 2017b (SPIRIT-P1) [4-6]	Low	Low	Low	Low	Low	Low	Low	Low	
Nash 2017 (SPIRIT-P2) [7, 8]	Low	Low	Low	Low	Low	Low	Low	Low	
van der Heijde 2016 (FUTURE-1) [9]	Low	Low	Low	Low	Low	Low	Low	Low	
Kavanaugh 2016 (FUTURE-2) [10]									Post-hoc
Nash 2018 (FUTURE-3) [11]	Low	Low	Low	Low	Low	Low	Low	Low	
Kivitz PANLAR 2018 (FUTURE-4) [12]	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	
Mease 2018c (FUTURE-5) [13]	Low	Low	Low	Low	Low	Low	Low	Low	

Deodhar 2018 (Guselkumab Phase 2) [14]	Low	Low	Low	Low	Low	Low	Low	Low	
Mease 2017/2018 [15, 34]	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	
Araujo 2018 (ECLIPSA) [16]	Low	Low	High	High	Low	Low	High	High	
Gladman 2018 (PALACE 1-3) [17]									Post-hoc
Cutolo 2016 (PALACE-2) [18]	Unclear	Low	Low	Low	Low	Low	Low	Unclear	
Edwards 2016 (PALACE-3) [19]	Low	Low	Low	Low	Low	Low	Low	Low	
Wells 2018 (PALACE-4) [20]	Unclear	Low	Low	Low	Low	Low	Low	Unclear	
Nash 2018 (ACTIVE) [21]	Unclear	Low	Low	Low	Low	Low	Low	Unclear	
Mease 2018 ACR (SEAM-PsA) [22]	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	
Kavanaugh 2017 (GO-VIBRANT) [23]	Low	Low	Low	Low	Low	Low	Low	Low	
Van Der Heijde 2017 EULAR (RAPID-PsA) [24]									Long-term extension
Mease 2018d (EQUATOR) [25]	Low	Low	Low	Low	Low	Low	Low	Low	
Gladman 2017 (OPAL Beyond) [26]	Low	Low	Low	Low	Low	Low	Low	Low	

Mease 2017c (OPAL Broaden) [27]	Low	Low	Low	Low	Low	Low	Low	Low	
Araujo 2015 [28]									Prospective observational study
Moverley 2015 (RETREAT) [29]	Low	Low	Low	Low	Low	Low	High	High	
Kristensen 2016 [30]									Cohort study
Kivitz ACR 2016 [31]	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	Abstract	
Jorgensen 2017 (NOR-SWITCH) [32]	Low	Low	Low	Low	Low	Low	Low	Low	
Glintborg 2017 (DANBIO) [33]	High	High	High	High	High	High	High	High	

Table S2.3: Baseline characteristics of efficacy studies: Demographics.

Study	Treatment	No. of patients (n)	Mean age (years)	Mean PsO disease duration (years)	Mean PsA disease duration (years)	Female (%)	BMI (kg/m²)
Mease 2017a (ASTRAEA) [1]	ABA ± MTX	213	51		8.3	56.8	30.7
	Placebo ± MTX	211	49.8		8.8	53.1	31.3
Mease 2018a (ABT-122 Phase 2) [2]	Placebo + MTX	24	47.7		7.6	50	26.8
	ADA 40mg Q2W + MTX	72	50.5		8.4	45.8	29.4
	ABT-122 120mg Q2W	71	51		5.9	52.1	29.6
	ABT-122 240mg Q2W	73	47.4		7.5	50.7	28.3
Mease 2016 (Clazakizumab Phase 2) [3]	Placebo ± MTX	41	48		8.5	56.1	
	CKM 25 mg ± MTX	41	49.8		9.6	56.1	
	CKM 100 mg ± MTX	42	49.3		5.6	47.6	
	CKM 200 mg ± MTX	41	44.7		4.7	48.8	
Mease 2017b (SPIRIT-P1) [4, 5]	Placebo ± csDMARD	106	50.6	16	6.3	54.7	29.2
	IXE 80mg Q4W ± csDMARD	107	49.1	16.5	6.2	57.9	30.2
	IXE 80mg Q2W ± csDMARD	103	49.8	17	7.2	53.4	28.6
	ADA 40mg Q2W ± csDMARD	101	48.6	15.7	6.9	49.5	32.1
Coates 2017 (SPIRIT-P1) [6]	Placebo + csDMARD	69	51		6.1	53.6	
	IXE 80mg Q4W + csDMARD	68	49.1		5.6	57.4	
	IXE 80mg Q2W + csDMARD	63	49.3		7.4	57.1	
	Placebo + MTX	59	51.3		6.1	57.6	
	IXE 80mg Q4W + MTX	57	49.9		5.1	57.9	
	IXE 80mg Q2W + MTX	53	50.1		7.8	56.6	
	Placebo	37	49.9		6.8	56.8	
	IXE 80mg Q4W	39	49.1		7.3	59	

	IXE 80mg Q2W	40	50.5		7	47.5	
Nash 2017 (SPIRIT-P2) [7]	Placebo ± csDMARD	118	51.5	15.3	9.2	52.5	31.6
	IXE 80mg Q4W ± csDMARD	122	52.6	15.7	11	48.4	30.9
	IXE 80mg Q2W ± csDMARD	123	51.7	16.5	9.9	59.3	30.1
Nash 2018 (SPIRIT-P2) [8]	Placebo + csDMARD	52	53.1		11.3	50	31.6
	IXE 80mg Q4W + csDMARD	60	52.3		11.9	48.3	32.5
	IXE 80mg Q2W + csDMARD	73	49.8		10.9	60.3	29.7
	Placebo + MTX	40	54.3		11.4	47.5	32
	IXE 80mg Q4W + MTX	48	53.3		12	47.9	32.6
	IXE 80mg Q2W + MTX	61	48.9		11	57.4	29.6
	Placebo	66	50.2		11.1	54.5	31.5
	IXE 80mg Q4W	62	52.9		15.7	48.4	29.4
	IXE 80mg Q2W	50	54.6		12.4	58	30.7
van der Heijde 2016 (FUTURE-1) [9]	SEC 10mg/kg iv -> SEC 150mg Q4W s.c. ± csDMARD	202	49.6			52.5	
	SEC 10mg/kg iv -> SEC 75mg Q4W s.c. ± csDMARD	202	48.8			58.4	
	Placebo ± csDMARD	202	48.5			52.5	
Kavanaugh 2016 (FUTURE-2) [10]	SEC pooled (TNFi-naïve) ± MTX	195	47.1			49.2	29.7
	Placebo (TNF-naïve) ± MTX	63	49.1			63.5	29.3
	SEC pooled (TNFi-exposed) ± MTX	104	47.7			48.1	31.3
	Placebo ± MTX	35	51.3			54.3	31.6
Nash 2018 (FUTURE-3) [11]	SEC 300mg ± MTX	139	49.3		8.3	51.8	
	SEC 150mg ± MTX	138	50.1		7.7	55.8	
	Placebo ± MTX	137	50.1		6.6	56.9	
Kivitz PANLAR 2018 (FUTURE-4) [12]	SEC 150mg with loading dose ± MTX	114					
	SEC 150mg no loading dose	113					

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

	± MTX						
	Placebo ± MTX	114					
Mease 2018c (FUTURE-5) [13]	SEC 300 mg with loading dose ± MTX	222	12.8		6.7	51.4	
	SEC 150 mg with loading dose ± MTX	220	12.9		6.7	49.5	
	SEC 150 mg without loading dose ± MTX	222	11.8		6.2	45.9	
	Placebo ± MTX	332	12.1		6.6	51.5	
Deodhar 2018 (Guselkumab Phase 2) [14]	Placebo ± MTX	49	44.2		6.9	51	
	GKM 100 mg ± MTX	100	47.4		7	48	
Mease 2017/2018 [15, 34]	RKM 150 mg Q4W ± MTX	42	51.8			50	
	RKM 150 mg wk 0, 4, 16 ± MTX	42	50.1			33.3	
	RKM 150 mg wk 0, 12 ± MTX	39	51.6			43.6	
	RKM 75 mg wk 0 ± MTX	20	53.8			50	
	Placebo ± MTX	42	49.0			42.9	
Araujo 2018 (ECLIPSA) [16]	UKM 45mg/90mg ± MTX	23	62		2	56	26
	TNFi ± MTX	24	58		3	25	25
Gladman 2018 (PALACE 1-3) [17]	Placebo (enthesitis at BL)	311	50.2	18	7.3	55.9	30.5
	APR 30 mg BID (enthesitis at BL)	327	50.8	17.6	7.4	59.9	30.1
	APR 20mg BID (enthesitis at BL)	307	49.7	17.9	7.1	57	30.4
	Placebo (dactylitis at BL)	205	49.2	17.1	7.2	51.7	30.6
	APR 30 mg BID (dactylitis at BL)	221	49.5	17.3	7.7	47.5	29.5
	APR 20mg BID (dactylitis at BL)	207	47.8	17.6	8	48.8	29.6
Cutolo 2016 (PALACE-2) [18]	Placebo ± csDMARD	159	51.2	17.8	7.8	53.5	29.5
	APR 20mg BID ± csDMARD	163	50.9	17.9	7.8	58.3	29.3

	APR 30mg BID ± csDMARD	162	50.5	18.7	6.8	58.6	29.2
Edwards 2016 (PALACE-3) [19]	Placebo ± csDMARD	169	49.5	17.8	6.8	53.8	29.5
	APR 20mg BID ± csDMARD	169	49.6	18.3	7.7	53.3	30.1
	APR 30mg BID ± csDMARD	167	49.9	17.1	7.5	52.7	29.2
Wells 2018 (PALACE-4) [20]	Placebo	176	50.5	16.8	3.4	48.9	28.7
	APR 20mg BID	175	49.2	15.3	3.2	54.3	29.8
	APR 30mg BID	176	48.4	15.4	3.6	54.5	29.7
Nash 2018 (ACTIVE) [21]	Placebo	109	48		3.6	59.6	31.8
	APR 30mg BID	110	50.7		4	52.7	32
Mease 2018 ACR (SEAM-PsA) [22]	Placebo + MTX	284	48.7		3.6	56.3	30.6
	ETA 50mg QW + Placebo	284	48.5		3.1	46.8	30.4
	ETA 50mg QW + MTX	283	48.1		3	49.1	30
Kavanaugh 2017 (GO-VIBRANT) [23]	Placebo i.v. ± MTX	239	46.7		5.3	49.4	
	GLM 2mg/kg i.v. ± MTX	241	45.7		6.2	46.9	
Van Der Heijde 2017 EULAR (RAPID-PsA) [24]	Placebo ± csDMARD	136	47.3		7.9	58.1	29.2
	CZP 200mg Q2W ± csDMARD	138	48.2		9.6	53.6	30.5
	CZP 400mg Q4W ± csDMARD	135	47.1		8.1	54.1	29.6
Mease 2018d (EQUATOR) [25]	Placebo ± csDMARD	66	50		7	45	30.1
	FILGO 200mg OD ± csDMARD	65	49		7	55	28.6
Gladman 2017 (OPAL Beyond) [26]	Placebo ± csDMARD	131	49		9.4	61	29.5
	TOFA 5mg BID ± csDMARD	131	49.5		9.6	49	30.5
	TOFA 10mg BID ± csDMARD	132	51.3		9.1	56	31
Mease 2017c (OPAL Broaden) [27]	Placebo ± csDMARD	105	47.7		6.4	53	28.8
	TOFA 5mg BID ± csDMARD	107	49.4		7.3	53	29
	TOFA 10mg BID ± csDMARD	104	46.9		5.4	60	29.3
	ADA 40mg Q2W ± csDMARD	106	47.4		5.3	47	28.8

ABA: abatacept; ADA: adalimumab; APR: apremilast; bDMARD: biological disease modifying drug; BID: twice daily; BMI: Body mass index; CKM: clazakizumab; csDMARD: conventional synthetic disease modifying drug; CZP: certolizumab pegol; ETA: etanercept; FILGO: filgotinib; GLM: golimumab; GKM: guselkumab; IXE: ixekizumab; mTSS: PsA modified total Sharp score; MTX: methotrexate; PASI: Psoriasis Area and Severity Index; QNW: every N weeks; Ref: reference arm; RKM: risankizumab; RoB: Risk of bias; SEC: secukinumab; TNF: Tumor necrosis factor; TOFA: tofacitinib; UKM: ustekinumab;

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table S2.4: Baseline characteristics of efficacy studies: Patient reported outcomes.

Study	Treatment	No. of patients (n)	Mean PGA	Mean Pain	Mean HAQ-DI	Mean SF36-PCS
Mease 2017a (ASTRAEA) [1]	ABA ± MTX	213	61.1	64.2	1.3	
	Placebo ± MTX	211	62.6	64.4	1.3	
Mease 2018a (ABT-122 Phase 2) [2]	Placebo + MTX	24			1.2	
	ADA 40mg Q2W + MTX	72			1.3	
	ABT-122 120mg Q2W	71			1.3	
	ABT-122 240mg Q2W	73			1.3	
Mease 2016 (Clazakizumab Phase 2) [3]	Placebo ± MTX	41	64.3	66.7	1.4	
	CKM 25 mg ± MTX	41	63.6	60.7	1.4	
	CKM 100 mg ± MTX	42	62.4	65	1.3	
	CKM 200 mg ± MTX	41	61	59.1	1.4	
Mease 2017b (SPIRIT-P1) [4, 5]	Placebo	106	61.1	58.5	1.2	34
	IXE 80mg Q4W ± csDMARD	107	62.7	60.1	1.2	32.4
	IXE 80mg Q2W ± csDMARD	103	62.5	58.4	1.2	34.2
	ADA 40mg Q2W ± csDMARD	101	59.1	58.7	1.1	33.9
Coates 2017 (SPIRIT-P1) [6]	Placebo + csDMARD	69			1.19	
	IXE 80mg Q4W + csDMARD	68			1.25	
	IXE 80mg Q2W + csDMARD	63			1.23	
	Placebo + MTX	59			1.21	
	IXE 80mg Q4W + MTX	57			1.21	
	IXE 80mg Q2W + MTX	53			1.25	
	Placebo	37			1.09	
	IXE 80mg Q4W	39			1.22	
	IXE 80mg Q2W	40			1.09	
Nash 2017 (SPIRIT-P2)	Placebo ± csDMARD	118	64.1	63.9	1.2	33.9

[7]	IXE 80mg Q4W ± csDMARD	122	66.4	63.9	1.2	34.8
	IXE 80mg Q2W ± csDMARD	123	66	62.7	1.2	34.3
Nash 2018 (SPIRIT-P2) [8]	Placebo + csDMARD	52			1.14	
	IXE 80mg Q4W + csDMARD	60			1.13	
	IXE 80mg Q2W + csDMARD	73			1.14	
	Placebo + MTX	40			1.26	
	IXE 80mg Q4W + MTX	48			1.11	
	IXE 80mg Q2W + MTX	61			1.1	
	Placebo	66			1.31	
	IXE 80mg Q4W	62			1.23	
	IXE 80mg Q2W	50			1.29	
Kavanaugh 2016 (FUTURE-2) [10]	SEC pooled (TNFi-naïve) ± MTX	195			1.2	
	Placebo (TNF-naïve) ± MTX	63			1.2	
	SEC pooled (TNFi-exposed) ± MTX	104			1.3	
	Placebo ± MTX	35			1.1	
Nash 2018 (FUTURE-3) [11]	SEC 300mg ± MTX	139	59.9	54.8	1.1	39.2
	SEC 150mg ± MTX	138	59.8	54.4	1.2	37.9
	Placebo ± MTX	137	60.6	53.3	1.2	37.4
Mease 2018c (FUTURE-5) [13]	SEC 300 mg with loading dose ± MTX	222	55	52.8	1.2	
	SEC 150 mg with loading dose ± MTX	220	53.9	56.5	1.3	
	SEC 150 mg without loading dose ± MTX	222	54.6	54.5	1.3	
	Placebo ± MTX	332	52.5	53.6	1.3	
Deodhar 2018 (Guselkumab Phase 2) [14]	Placebo ± MTX	49	64.7	61.9	1.3	34.4
	GKM 100 mg ± MTX	100	67	62.1	1.4	33.5
Araujo 2018 (ECLIPSA) [16]	UKM 45mg/90mg ± MTX	23	55	55	0.87	29.1
	TNFi ± MTX	24	62	67	1.17	29.5
Gladman 2018 (PALACE 1-3) [17]	PLC (enthesitis at BL)	311			1.3	
	APR 30 mg BID (enthesitis at BL)	327			1.3	

	APR 20mg BID (enthesitis at BL)	307			1.3	
	PLC (dactylitis at BL)	205			1.3	
	APR 30 mg BID (dactylitis at BL)	221			1.3	
	APR 20mg BID (dactylitis at BL)	207			1.2	
Cutolo 2016 (PALACE-2) [18]	Placebo ± csDMARD	159			1.2	
	APR 20mg BID ± csDMARD	163			1.1	
	APR 30mg BID ± csDMARD	162			1.2	
Edwards 2016 (PALACE-3) [19]	Placebo ± csDMARD	169	56.1		1.2	
	APR 20mg BID ± csDMARD	169	54.3		1.1	
	APR 30mg BID ± csDMARD	167	56.5		1.2	
Wells 2018 (PALACE-4) [20]	Placebo	176	54	52.8	1	36.1
	APR 20mg BID	175	52.3	54.5	1.1	35.2
	APR 30mg BID	176	53.6	52.6	1.1	35.7
Nash 2018 (ACTIVE) [21]	Placebo	109			1.2	
	APR 30mg BID	110			1.25	
Mease 2018 ACR (SEAM-PsA) [22]	Placebo + MTX	284			1.27	35.6
	ETA 50mg QW + Placebo	284			1.15	37.8
	ETA 50mg QW + MTX	283			1.15	37.4
Kavanaugh 2017 (GO-VIBRANT) [23]	Placebo i.v. ± MTX	239	63	64	1.3	34
	GLM 2mg/kg i.v. ± MTX	241	65	64	1.3	33.1
Van Der Heijde 2017 EULAR (RAPID-PsA) [24]	Placebo ± csDMARD	136	57	60	1.3	
	CZP 200mg Q2W ± csDMARD	138	60.2	59.7	1.3	
	CZP 400mg Q4W ± csDMARD	135	60.2	61.1	1.3	
Mease 2018d (EQUATOR) [25]	Placebo ± csDMARD	66	63.3		1.36	36.3
	FILGO 200mg OD ± csDMARD	65	61.8		1.43	35.2
Gladman 2017 (OPAL Beyond) [26]	Placebo ± csDMARD	131	55.8	54.9	1.3	34
	TOFA 5mg BID ± csDMARD	131	57.4	56.4	1.3	33.5
	TOFA 10mg BID ± csDMARD	132	58.5	59.5	1.4	32.1
Mease 2017c (OPAL	Placebo ± csDMARD	105	53.9	53.2	1.1	

Broaden) [27]	TOFA 5mg BID ± csDMARD	107	54.7	55.7	1.2	
	TOFA 10mg BID ± csDMARD	104	53.6	54.4	1.1	
	ADA 40mg Q2W ± csDMARD	106	50.6	50.7	1.1	

ABA: abatacept; ADA: adalimumab; APR: apremilast; bDMARD: biological disease modifying drug; BID: twice daily; BL: baseline; CKM: clazakizumab; csDMARD: conventional synthetic disease modifying drug; CZP: certolizumab pegol; ETA: etanercept; FILGO: filgotinib; GLM: golimumab; GKM: guselkumab; HAQ-DI: Health Assessment Questionnaire Disability Index; IXE: ixekizumab; NR: not reported; MTX: methotrexate; PGA: Patients Global Assessment of disease activity; QNW: every N weeks; RKM: risankizumab; SEC: secukinumab; SF-36 PCS: Short Form-36 Health Survey Physical Component Score; TNF: Tumor necrosis factor; TOFA: tofacitinib; UKM: ustekinumab;

Table S2.5: Baseline characteristics of efficacy studies: Arthritis / Extra-articular manifestations / X-Ray

Study	Treatment	No. of patients (n)	Mean SJC66	Mean TJC 68	Mean EGA	Mean CRP (mg/dL)	Mean DAPSA	Mean PASDAS	Mean DAS28-CRP	Dactylitis (%)	Enthesitis (%)	Skin disease (%)	PASI (mean)	Mean mTSS
Mease 2017a (ASTRAEA) [1]	ABA ± MTX	213	12.1	21	53.9	1.4			5	28.6	65.7	68.5	7.4	20
	Placebo ± MTX	211	11.1	19.3	55	1.43			4.9	23.7	62.6	70.1	7.2	17.7
Mease 2018a (ABT-122 Phase 2) [2]	Placebo + MTX	24	13.4	19					4.6	54.2	58.3	45.8	8.8	
	ADA 40mg Q2W + MTX	72	14	23.4					5.1	58.3	75	45.8	11.9	
	ABT-122 120mg Q2W	71	12.7	21.7					5	56.3	70.4	60.6	11.8	
	ABT-122 240mg Q2W	73	14.8	23.6					4.8	63	72.6	67.1	14.9	
Mease 2016 (CKM Phase 2) [3]	Placebo ± MTX	41	11.2	21.2	58.2	1.1		6.3	5	41.5	80.5	97.6	7.9	
	CKM 25 mg ± MTX	41	12.4	23	64	1.32		6.3	5.2	36.6	75.6	97.6	9.1	
	CKM 100 mg ± MTX	42	13.8	19	62.5	1.74		6.2	5.1	28.6	83.3	97.6	9.5	
	CKM 200 mg ± MTX	41	10.8	16.6	57.8	1.62		6.1	4.9	31.7	75.6	95.1	8.7	
Mease 2017b (SPIRIT-P1) [4, 5]	Placebo	106	10.6	19.2	55.9	1.51			4.9	36.8	53.8	63.2	6.2	17.6
	IXE 80mg Q4W ± csDMARD	107	11.4	20.5	57.6	1.28			5	50.5	65.4	68.2	6.9	19.2
	IXE 80mg Q2W ± csDMARD	103	12.1	21.5	58.5	1.51			5	39.8	57.3	57.3	6	15.2
	ADA 40mg Q2W ± csDMARD	101	9.9	19.3	55.4	1.32			4.9	22.8	55.4	67.3	5.5	15.9
Van der Heijde EULAR 2017 (SPIRIT-P1) [5]	PLC/IXE 80mg Q4W ± csDMARD	45	9.6	18.5										11.5
	PLC/IXE 80mg Q2W ± csDMARD	46	10.7	19.2										24.5
	ADA/IXE 80mg Q4W ± csDMARD	49	10.1	18.8										15.6

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

	ADA/IXE 80mg Q2W ± csDMARD	48	9.6	18.8										15.4
	IXE 80mg Q4W ± csDMARD	97	11.0	20.8										19.6
	IXE 80mg Q2W ± csDMARD	96	12.2	21.3										15.2
Coates 2017 (SPIRIT-P1) [6]	Placebo + csDMARD	69												18.9
	IXE 80mg Q4W + csDMARD	68												21.2
	IXE 80mg Q2W + csDMARD	63												17.3
	Placebo + MTX	59												17
	IXE 80mg Q4W + MTX	57												21
	IXE 80mg Q2W + MTX	53												19.2
	Placebo	37												15.3
	IXE 80mg Q4W	39												15.7
	IXE 80mg Q2W	40												11.9
Nash 2017 (SPIRIT-P2) [7]	Placebo ± csDMARD	118	10.3	23	58.9	1.21			5	11.9	58.5	56.8	5.2	
	IXE 80mg Q4W ± csDMARD	122	13.1	22	60.3	1.7			5.1	23	55.7	55.7	6.4	
	IXE 80mg Q2W ± csDMARD	123	13.5	25	64.6	1.35			5.1	16.3	68.3	55.3	6.2	
Nash 2018 (SPIRIT-P2) [8]	Placebo + csDMARD	52	10.3	21.9		1.3	46.2		4.87			86.5		
	IXE 80mg Q4W + csDMARD	60	13.7	20.8		1.6	49.6		5.01			95		
	IXE 80mg Q2W + csDMARD	73	13.1	23.8		1.12	50.9		5.05			90.4		
	Placebo + MTX	40	10.3	22.6		1.57	47.5		4.96			85		
	IXE 80mg Q4W + MTX	48	13.1	20.8		1.67	49.3		5.11			93.8		

	IXE 80mg Q2W + MTX	61	11.9	21		1.2	46.8		4.99			93.4		
	Placebo	66	10.2	23.8		1.14	48.3		5.09			95.5		
	IXE 80mg Q4W	62	12.4	23.2		1.79	51.1		5.19			98.4		
	IXE 80mg Q2W	50	14.1	26.8		1.7	57.1		5.26			94		
van der Heijde 2016 (FUTURE-1) [9]	SEC 10mg/kg iv -> SEC 150mg Q4W s.c. ± csDMARD	202				1.32			4.8					21.9
	SEC 10mg/kg iv -> SEC 75mg Q4W s.c. ± csDMARD	202				1.38			4.9					20
	Placebo ± csDMARD	202				1.48			4.9					28.1
Kavanaugh 2016 (FUTURE-2) [10]	SEC pooled (TNFi-naïve) ± MTX	195	10.8	20.3					4.7	40	61	50.8		
	Placebo (TNF-naïve) ± MTX	63	10.6	21.9					4.6	27	66.7	49.2		
	SEC pooled (TNFi-exposed) ± MTX	104	12.4	25.6					5	31.7	66.3	48.1		
	Placebo ± MTX	35	14.7	26.1					4.9	28.6	65.7	34.3		
Nash 2018 (FUTURE-3) [11]	SEC 300mg ± MTX	139	8.9	19.7	51.8				4.5	33.1	63.3	44.6	10.1	
	SEC 150mg ± MTX	138	11.2	23.3	55.2				4.6	26.1	68.8	49.3	8.8	
	Placebo ± MTX	137	10.3	21.9	54.8				4.7	26.3	71.5	43.1	10.4	
Mease 2018c (FUTURE-5) [13]	SEC 300 mg with loading dose ± MTX	222	10	19.8	55.4				4.5	36.9	63.1	49.5		12.9
	SEC 150 mg with loading dose ± MTX	220	12.1	21.2	57.7				4.7	36.4	64.1	56.8		13.6
	SEC 150 mg without loading dose ± MTX	222	11.9	21.8	57.3				4.6	46.4	58.1	52.7		15.3
	Placebo ± MTX	332	11.7	21.2	54.3				4.6	37.3	57.8	48.8		15
Deodhar 2018	Placebo ± MTX	49	10.6	20.1	61.9	0.9				47	63	13.6	9.9	

(GKM Phase 2) [14]	GKM 100 mg ± MTX	100	11.9	20.7	63.2	0.9				58	76	17.2	12	
Araujo 2018 (ECLIPSA) [16]	UKM 45mg/90mg ± MTX	23	4	4		3.5	20.5		4				3	
	TNFi ± MTX	24	5	5.5		2.7	23.6		4.4				2.8	
Gladman 2018 (PALACE 1-3) [17]	PLC (enthesitis at BL)	311	11.6	22.6		1.1			4.8				8.8	
	APR 30 mg BID (enthesitis at BL)	327	12.3	25.1		1			4.9				8.4	
	APR 20mg BID (enthesitis at BL)	307	12.4	24.9		0.94			4.8				7.5	
	PLC (dactylitis at BL)	205	13.3	22.4		1.17			4.8				8.1	
	APR 30 mg BID (dactylitis at BL)	221	14.2	23.9		1.21			4.9				8.5	
	APR 20mg BID (dactylitis at BL)	207	14	24.7		1.05			4.7				7.8	
Cutolo 2016 (PALACE-2) [18]	Placebo ± csDMARD	159	9.2	18					4.5	65.4	41.5	45.3	8.6	
	APR 20mg BID ± csDMARD	163	10.4	20.3					4.6	65.6	47.2	49.1	7.4	
	APR 30mg BID ± csDMARD	162	10.3	21.8					4.7	62.3	45.1	44.4	7.8	
Edwards 2016 (PALACE-3) [19]	Placebo ± csDMARD	169	11.1	18.3	52.8				4.5	42	64.5	55.6	7.6	
	APR 20mg BID ± csDMARD	169	11.4	20.8	55.2				4.6	42	57.4	55	7.6	
	APR 30mg BID ± csDMARD	167	11.6	20.9	56.1				4.6	47.9	67.1	55.1	7.9	
Wells 2018 (PALACE-4) [20]	Placebo	176	11.3	13.7	54.3	1.1		6.6	4.6	51.1	65.3	52.8	6.6	
	APR 20mg BID	175	11.3	15.1	54.1	0.9		8.3	4.7	50.9	66.9	59.4	8.3	
	APR 30mg BID	176	10.9	14.4	51.7	0.8		6.6	4.5	47.7	63.1	61.9	6.6	
Nash 2018 (ACTIVE) [21]	Placebo	109	10	18.4		1.25					46.8			
	APR 30mg BID	110	9	17.2		1.44					50.9			

Mease 2018 ACR (SEAM-PsA) [22]	Placebo + MTX	284	12.9	20.9							67.3	67.6		2.76
	ETA 50mg QW + Placebo	284	11.5	18.8							66.5	63		2.97
	ETA 50mg QW + MTX	283	11.2	20							69.3	62.5		2.7
Kavanaugh 2017 (GO-VIBRANT) [23]	Placebo i.v. ± MTX	239	14.1	26.1	64	2				51.9	75.7	82.8	8.9	34.5
	GLM 2mg/kg i.v. ± MTX	241	14	25.1	62	1.9				55.6	76.8	81.3	11	35.5
Van Der Heijde 2017 EULAR (RAPID-PsA) [24]	Placebo ± csDMARD	136	10.4	19.9	58.7	2				25.7	66.9	63.2	7.1	24.4
	CZP 200mg Q2W ± csDMARD	138	11	21.5	56.8	2				25.4	63.8	65.2	7	18
	CZP 400mg Q4W ± csDMARD	135	10.5	19.6	58.2	1				28.1	62.2	56.3	8.1	22.8
Mease 2018d (EQUATOR) [25]	Placebo ± csDMARD	66	12.7	21.6	66	10.9	6.2	47.8				61	6.9	
	FILGO 200mg OD ± csDMARD	65	11.6	18.3	66.1	13.9	6.1	44				65	6.5	
Gladman 2017 (OPAL Beyond) [26]	Placebo ± csDMARD	131	10.5	19.8	53.7	0.44			4.4	48	71	66	7.1	
	TOFA 5mg BID ± csDMARD	131	12.1	20.5	53.5	0.57			4.5	50	63	61	7.6	
	TOFA 10mg BID ± csDMARD	132	12.8	25.5	55.8	0.49			4.7	49	75	61	8.8	
Mease 2017c (OPAL Broaden) [27]	Placebo ± csDMARD	105	11.5	20.6	53.8				4.5	55	62	78	6.6	17.6
	TOFA 5mg BID ± csDMARD	107	12.9	20.5	54.6				4.6	57	70	77	5.6	17.1
	TOFA 10mg BID ± csDMARD	104	11.7	20.3	55.2				4.5	58	62	67	7.8	10.4
	ADA 40mg Q2W ± csDMARD	106	9.8	12.9	50.5				4.4	55	72	74	7	14.4

ABA: abatacept; 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; EGA: evaluators global assessment of disease activity; ETA: etanercept; FILGO: filgotinib; GLM: golimumab; GKM: guselkumab; IXE:

ixekizumab; mTSS: PsA modified total Sharp score; NR: not reported; MTX: methotrexate; PASDAS: Psoriatic Arthritis Disease Activity Score; PASI: Psoriasis Area and Severity Index; QNW: every N weeks; Ref: reference arm; RKM: risankizumab; SEC: secukinumab; SJC: swollen joint count; TJC: tender joint count; TNF: Tumor necrosis factor; TOFA: tofacitinib; UKM: ustekinumab;

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Section 3: Efficacy outcomes

Table S3.1: Efficacy outcomes: Arthritis and composite measures, PROs, Structural damage.

Study	Treatment	No. of patients (n)	Timepoint (weeks)	ACR20 (%)	ACR50 (%)	ACR70 (%)	ΔDAPSA (%)	DAS28-CRP<2.6	ΔHAQ-DI	ΔSF36-PCS	MDA (%)	ΔmTSS
Mease 2017a (ASTRAEA) [1]	ABA ± MTX	213	24	39.4	19.2	10.3	-18.75		-0.33	5.11	11.7	0.3
	Placebo ± MTX	211		22.3	12.3	6.6	-13		-0.2	3.69	8.1	0.35
Mease 2018a (ABT-122 Phase 2) [2]	Placebo + MTX	24	12	25	12.5	4.2	16.7		-0.28			
	ADA 40mg Q2W + MTX	72		68.1	37.5	15.3	40		-0.58			
	ABT-122 120mg Q2W	71		64.8	36.6	22.5	45.1		-0.55			
	ABT-122 240mg Q2W	73		75.3	53.4	31.5	52.1		-0.56			
Mease 2016 (Clazakizumab Phase 2) [3]	Placebo ± MTX	41	16	29.3	7.3	0.1		12.2	-0.27	1.4		
	CKM 25 mg ± MTX	41		46.3	29.3	28.6		36.6	-0.44	1.2		
	CKM 100 mg ± MTX	42		52.4	35.7	24.9		47.6	-0.4	3.7		
	CKM 200 mg ± MTX	41		39	17.1	16.5		26.8	-0.26	1.1		
Mease 2017b (SPIRIT-P1) [4]	Placebo	106	24	30.2	15.1	5.7			-0.18			0.49
	IXE 80mg Q4W ± csDMARD	107		57.9	40.2	23.4			-0.44			0.17
	IXE 80mg Q2W ± csDMARD	103		62.1	46.6	34			-0.5			0.08
	ADA 40mg Q2W ± csDMARD	101		57.4	38.6	25.7			-0.37			0.1
Van der Heijde EULAR 2017 (SPIRIT-P1) [5]	PLC/IXE 80mg Q4W ± csDMARD	45	52									0.27
	PLC/IXE 80mg Q2W ± csDMARD	46										0.41
	ADA/IXE 80mg Q4W ± csDMARD	49										0.32
	ADA/IXE 80mg Q2W ± csDMARD	48										-0.03
	IXE 80mg Q4W ± csDMARD	97										0.54

	IXE 80mg Q2W ± csDMARD	96										0.09
Coates 2017 (SPIRIT-P1) [6]	Placebo + csDMARD	69	24									0.44
	IXE 80mg Q4W + csDMARD	68										0.11
	IXE 80mg Q2W + csDMARD	63										0.11
	Placebo + MTX	59										0.52
	IXE 80mg Q4W + MTX	57										0.13
	IXE 80mg Q2W + MTX	53										0.14
	Placebo	37										0.57
	IXE 80mg Q4W	39										0.25
	IXE 80mg Q2W	40										0.03
Nash 2017 (SPIRIT-P2) [7]	Placebo ± csDMARD	118	24	19.5	5.1	0			-0.2	3.3	3.4	
	IXE 80mg Q4W ± csDMARD	122		53.3	35.2	22.1			-0.6	8.9	27.9	
	IXE 80mg Q2W ± csDMARD	123		48	33.3	12.2			-0.4	8.2	23.6	
van der Heijde 2016 (FUTURE-1) [9]	SEC 10mg/kg iv -> SEC 150mg Q4W s.c. ± csDMARD	202	24/52									0.13/0.23
	SEC 10mg/kg iv -> SEC 75mg Q4W s.c. ± csDMARD	202										0.02/0.20
	Placebo ± csDMARD	202										0.57/-0.03
Kavanaugh 2016 (FUTURE-2) [10]	SEC 300mg (TNF-naïve) ± MTX	67	24	58.2	38.8	22.4		-1.76	-0.59	8.05		
	SEC 150mg (TNF-naïve) ± MTX	63		63.5	44.4	27.0		-1.69	-0.55	7.91		
	SEC 75mg (TNF-naïve) ± MTX	65		36.9	24.6	6.2		-1.27	-0.37	5.37		
	Placebo (TNF-naïve) ± MTX	63		15.9		1.6		-1.11	-0.35	2.08		
	SEC 300mg (TNF-exposed) ± MTX	33		45.5	27.3	15.2		-1.39	-0.53	6.56		
	SEC 150mg (TNF-exposed) ± MTX	37		29.7	18.9	10.8		-1.45	-0.35	4.21		
	SEC 75mg (TNF-exposed) ± MTX	34		14.7	5.9	5.9		-0.89	-0.23	3.15		

	Placebo (TNF-exposed) ± MTX	35		14.3	8.6	0		-0.69	-0.23	2.65		
Nash 2018 (FUTURE-3) [11]	SEC 300mg ± MTX	139	24	48.2	34.5				-0.38			
	SEC 150mg ± MTX	138		42	18.8				-0.27			
	Placebo ± MTX	137		16.1	8.8				-0.17			
Kivitz PANLAR 2018 (FUTURE-4) [12]	SEC 150mg with loading dose ± MTX	114	16	41.2	22.8			-0.98		3.42		
	SEC 150mg no loading dose ± MTX	113		39.8	16.8			-0.84		3.44		
	Placebo ± MTX	114		18.4	6.1			-0.21		0.63		
Mease 2018c (FUTURE-5) [13]	SEC 300 mg with loading dose ± MTX	222	16	62.6	39.6	20.3	−1.49		-0.55			0.08
	SEC 150 mg with loading dose ± MTX	220		55.5	35.9	18.2	−1.29		-0.44			0.17
	SEC 150 mg without loading dose ± MTX	222		59.5	32	14.9	−1.29		-0.45			-0.09
	Placebo ± MTX	332		27.4	8.1	4.2	−0.63		-0.21			0.5
Deodhar 2018 (Guselkumab Phase 2) [14]	Placebo ± MTX	49	24	18	10	2			-0.06	0.46		
	Guselkumab 100 mg ± MTX	100		58	34	14			-0.42	6.59		
Mease 2017/2018 [15, 34]	RKM 150 mg Q4W ± MTX	42	16	57.1	23.8	14.3			-0.18		28.6	-0.3[a]
	RKM 150 mg wk 0, 4, 16 ± MTX	42		61.9	23.8	7.1			-0.16		28.6	0.2[a]
	RKM 150 mg wk 0, 12 ± MTX	39		59.0	38.5	25.6			-0.25		33.3	-0.5[a]
	RKM 75 mg wk 0 ± MTX	20		65.0	25.0	15.0			-0.16		35.0	-0.2[a]
	Placebo ± MTX	42		35.7	11.9	0			-0.09		7.1	0.6[a]
Araujo 2018 (ECLIPSA) [16]	UKM 45mg/90mg ± MTX	23	24								77	
	TNFi ± MTX	24									45	
Gladman 2018 (PALACE 1-3) [17]	PLC (enthesitis at BL)	311	24									
	APR 30 mg BID (enthesitis at BL)	327										
	APR 20mg BID (enthesitis at BL)	307										

	PLC (dactylitis at BL)	205										
	APR 30 mg BID (dactylitis at BL)	221										
	APR 20mg BID (dactylitis at BL)	207										
Cutolo 2016 (PALACE-2) [18]	Placebo ± csDMARD	159	16	18.9	5	0.6		8.2	-0.07	1.1		
	APR 20mg BID ± csDMARD	163		37.4	14.7	3.7		17.8	-0.17	2.5		
	APR 30mg BID ± csDMARD	162		32.1	10.5	1.2		11.7	-0.23	3.5		
Edwards 2016 (PALACE-3) [19]	Placebo ± csDMARD	169	16	18.3	8.3	2.4		8	-0.07			
	APR 20mg BID ± csDMARD	169		28.4	12.4	4.7		17	-0.13			
	APR 30mg BID ± csDMARD	167		40.7	15	3.6		18	-0.2			
Wells 2018 (PALACE-4) [20]	Placebo	176	16	15.9	4.5	1.1	8.5		0.03			
	APR 20mg BID	175		28	11.4	4	13.1		-0.17			
	APR 30mg BID	176		30.7	11.4	4	9.7		-0.21			
Nash 2018 (ACTIVE) [21]	Placebo	109	16	20.2	4.6	0	-0.39		-0.06	-0.31		
	APR 30mg BID	110		38.2	18.2	6.4	-1.07		-0.21	4.03		
Mease 2018 ACR (SEAM-PsA) [22]	Placebo + MTX	284	24	50.7	30.6	13.8		-22.6	-0.41	9.2	22.9	0.08
	ETA 50mg QW + Placebo	284		60.9	44.4	29.2		-25	-0.44	10.6	35.9	-0.04
	ETA 50mg QW + MTX	283		64	45.7	27.7		-24.9	-0.47	11.3	35.7	-0.01
Kavanaugh 2017 (GO-VIBRANT) [23]	Placebo i.v. ± MTX	239	14	21.8	6.3	2.1			-0.12	1	4.2	2[a]
	GLM 2mg/kg i.v. ± MTX	241		75.1	43.6	24.5			-0.6	5.3	27	-0.4[a]
Van Der Heijde 2017 EULAR (RAPID-PsA) [24]	Placebo ± csDMARD	136	216									
	CZP 200mg Q2W ± csDMARD	138										0.7
	CZP 400mg Q4W ± csDMARD	135										0.7
Mease 2018d (EQUATOR) [25]	Placebo ± csDMARD	66	16	33.3	15.2	6.1		-27.9	-0.28			
	FILGO 200mg OD ± csDMARD	65		80	47.7	23.1		-18.1	-0.57			
Gladman 2017 (OPAL Beyond) [26]	Placebo ± csDMARD	131	24	24	15	10			-0.14		14.5	
	TOFA 5mg BID ± csDMARD	131		50	30	17			-0.39		22.9	

	TOFA 10mg BID ± csDMARD	132		47	28	14			-0.35		21.2	
Mease 2017c (OPAL Broaden) [27]	Placebo ± csDMARD	105	12	33	10	5	-0.8		-0.18	2.1	7	0.00 [b,c] / 0.09 [b,d]
	TOFA 5mg BID ± csDMARD	107		50	28	17	-1.3		-0.35	5.2	26	0.01 [b]
	TOFA 10mg BID ± csDMARD	104		61	40	14	-1.6		-0.4	5.2	26	-0.01 [b]
	ADA 40mg Q2W ± csDMARD	106		52	33	19	-1.5		-0.38	5.2	25	-0.07 [b]

[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 S3.2: Efficacy outcomes: Extra-articular efficacy outcomes of trials investigating bDMARDs.

Study	Treatment	No. of patients (n)	Timepoint (weeks)	PASI 50 (%)	PASI 75 (%)	PASI 90 (%)	PASI 100 (%)	ΔPASI	Resolution of dactylitis (%)	Resolution of enthesitis (%)
Mease 2017a (ASTRAEA) [1]	ABA +- MTX	213	24	26.7	16.4				44.3	32.9
	Placebo +- MTX	211		19.6	10.1				34	21.2
Mease 2018a (ABT-122 Phase 2) [2]	Placebo + MTX	24	12		27	18				
	ADA 40mg Q2W + MTX	72			57.6	46				
	ABT-122 120mg Q2W	71			74.4	49				
	ABT-122 240mg Q2W	73			77.6	47				
Mease 2016 (Clazakizumab Phase 2) [3]	Placebo ± MTX	41	16	36.6	14.6					
	CKM 25 mg ± MTX	41		34.1	12.2					
	CKM 100 mg ± MTX	42		31	16.7					
	CKM 200 mg ± MTX	41		19.5	4.9					
Mease 2017b (SPIRIT-P1) [4]	Placebo ± csDMARD	106	24		10.4	6	3		25	19.3
	IXE 80mg Q4W ± csDMARD	107			71.2	56.2	42.5		79.5	42.6
	IXE 80mg Q2W ± csDMARD	103			79.7	67.8	52.5		76.9	38.6
	ADA 40mg Q2W ± csDMARD	101			54.4	36.8	23.5		77.8	33.3
Nash 2017 (SPIRIT-P2) [7]	Placebo ± csDMARD	118	24		8.5	6.8	2.5		2.5	12.7
	IXE 80mg Q4W ± csDMARD	122			31.1	24.6	19.7		17.2	19.7
	IXE 80mg Q2W ± csDMARD	123			33.3	27.6	15.4		8.1	21.1
Kavanaugh 2016 (FUTURE-2) [10]	SEC 300mg (TNF-naïve) ± MTX	67	24		63.3	53.3			54.8	45.9
	SEC 150mg (TNF-naïve) ± MTX	63			55.6	38.9			57.1	45.9
	SEC 75mg (TNF-naïve) ± MTX	65			30.3	12.1			30.8	35.6
	Placebo (TNF-naïve) ± MTX	63			19.4	9.7			17.6	28.6

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

	SEC 300mg (TNF-exposed) ± MTX	33			63.6	36.4			60.0	52.6
	SEC 150mg (TNF-exposed) ± MTX	37			36.4	22.7			36.4	37.0
	SEC 75mg (TNF-exposed) ± MTX	34			23.5	11.8			28.6	26.1
	Placebo (TNF-exposed) ± MTX	35			8.3	8.3			10.0	8.7
Nash 2018 (FUTURE-3) [11]	SEC 300mg ± MTX	139	24		46.8	33.9			47.8	39.8
	SEC 150mg ± MTX	138			50	36.8			38.9	36.8
	Placebo ± MTX	137			10.2	6.8			13.9	15.3
Kivitz PANLAR 2018 (FUTURE-4) [12]	SEC 150mg with loading dose ± MTX	114	16		52.7					
	SEC 150mg no loading dose ± MTX	113			50					
	Placebo ± MTX	114			8.1					
Mease 2018c (FUTURE-5) [13]	SEC 300 mg with loading dose ± MTX	222	16		70	53.6			65.9	55.7
	SEC 150 mg with loading dose ± MTX	220			60	36.8			57.5	54.6
	SEC 150 mg without loading dose ± MTX	222			58.1	31.6			56.3	41.9
	Placebo ± MTX	332			12.3	9.3			32.3	35.4
Deodhar 2018 (Guselkumab Phase 2) [14]	Placebo ± MTX	49	24	29	13	6	6		17	29
	GKM 100 mg ± MTX	100		87	79	66	40		55	57
Mease 2017/2018 [15, 34]	RKM 150 mg Q4W ± MTX	42	16		75.0	58.3	33.3			
	RKM 150 mg wk 0, 4, 16 ± MTX	42			70.0	66.7	52.2			
	RKM 150 mg wk 0, 12 ± MTX	39			73.9	52.2	34.8			
	RKM 75 mg wk 0 ± MTX	20			66.7	55.6	55.6			
	Placebo ± MTX	42			9.5	9.5	9.5			
Araujo 2018	UKM 45mg/90mg ± MTX	23	24			86	59			77

(ECLIPSA) [16]	TNFi ± MTX	24				29	29			29
Gladman 2018 (PALACE 1-3) [17]	PLC (enthesitis at BL)	311	24							22.5
	APR 30 mg BID (enthesitis at BL)	327								27.5
	APR 20mg BID (enthesitis at BL)	307								27.4
	PLC (dactylitis at BL)	205							39	
	APR 30 mg BID (dactylitis at BL)	221							46.2	
	APR 20mg BID (dactylitis at BL)	207							45.9	
Cutolo 2016 (PALACE-2) [18]	Placebo ± csDMARD	159	16	13.5	2.7					
	APR 20mg BID ± csDMARD	163		33.8	18.8					
	APR 20mg BID ± csDMARD	162		41.6	22.1					
Edwards 2016 (PALACE-3) [19]	Placebo ± csDMARD	169	16	24	8					
	APR 20mg BID ± csDMARD	169		33	20					
	APR 20mg BID ± csDMARD	167		41	21					
Wells 2018 (PALACE-4) [20]	Placebo	176	16	19.4	10.8				31.1	19.1
	APR 20mg BID	175		44.2	17.3				40.4	21.4
	APR 30mg BID	176		45.9	25.7				40.5	35.1
Nash 2018 (ACTIVE) [21]	Placebo	109								33.3
	APR 30mg BID	110								46.4
Mease 2018 ACR (SEAM-PsA) [22]	Placebo + MTX	284	24						65.2	43.1
	ETA 50mg QW + Placebo	284							76.4	52.6
	ETA 50mg QW + MTX	283							79.3	47.5
Kavanaugh 2017 (GO-VIBRANT) [23]	Placebo i.v. ± MTX	239	14		13.6	6.6	4.5			
	GLM 2mg/kg i.v. ± MTX	241			59.2	39.3	16.8			
Mease 2018d (EQUATOR) [25]	Placebo ± csDMARD	66	16		15					
	FILGO 200mg OD ± csDMARD	65			45.2					
Gladman 2017	Placebo ± csDMARD	131	24		14				28.6	21.5

(OPAL Beyond) [26]	TOFA 5mg BID ± csDMARD	131			21				51.5	39.8
	TOFA 10mg BID ± csDMARD	132			43				50.8	32.3
Mease 2017c (OPAL Broaden) [27]	Placebo ± csDMARD	105	12		15				32.8	21.5
	TOFA 5mg BID ± csDMARD	107			43				34.4	33.3
	TOFA 10mg BID ± csDMARD	104			44				60	40.6
	ADA 40mg Q2W ± csDMARD	106			39				46.6	47.4

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; ETA: etanercept; FILGO: filgotinib; GLM: golimumab; GKM: guselkumab; IXE: ixekizumab; MTX: methotrexate; PASI: Psoriasis Area and Severity Index; QNW: every N weeks; RKM: risankizumab; SEC: secukinumab; TOFA: tofacitinib; UKM: ustekinumab;

Section 4: Safety study characteristics of articles and abstracts included.

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table S4.1: Safety: Details of articles and abstracts selected for inclusion.

Study	Type	Outcome	Exposure	Control
Choquette 2015	Cohort study	Infusion reactions	Infliximab + premedication	Infliximab without premedication
Li 2015	Case-control study	Cardiovascular events	DMARDs therapy / steroids	No DMARD
Ogdie 2015	Cohort study	Cardiovascular events	DMARD	No DMARD
Polachek 2015	Cohort study	Vaccination	Biologic DMARD therapy	csDMARD therapy
Costa 2016	Cohort study	Malignancies	Biologic DMARD therapy	csDMARD therapy
Eder 2016	Cohort study	Cardiovascular events	TNF inhibitor / MTX / other DMARDs / steroids	No DMARD
Haddad 2016	Cohort study	Infections	Biologic DMARD therapy	Non biologic DMARD therapy
Dreyer 2016	Cohort study	Multiple sclerosis	TNF inhibitor	Not receiving TNF inhibitor
Zisman 2016	Cohort study	Herpes zoster	TNF inhibitors / csDMARDs / steroids	Not receiving csDMARD / TNF inhibitor
Hellgren 2017	Cohort study	Malignancies	TNF inhibitors	TNF naïve
Mariette 2015	Long term extension	Tuberculosis	Certolizumab pegol	None
Kavanaugh 2015	Long term extension	Clinical trial safety	Apremilast	None
Kavanaugh 2015	Long term extension	Clinical trial safety	Ustekinumab	None
Mease 2018	Long term extension	Clinical trial safety	Secukinumab	None
van der Heijde 2018	Long term extension	Clinical trial safety	Certolizumab	None
Walsh 2018	Long term extension	Clinical trial safety	Certolizumab	None
Genovese 2015	Long term extension	Clinical trial safety	Brodalumab	None
McInnes 2017	Long term extension	Clinical trial safety	Secukinumab	None
Chandran 2018	Long term extension	Clinical trial safety	Ixekizumab	None
Orbai ACR 2018	Long term extension	Clinical trial safety	Ixekizumab	None
Mease EULAR 2018	Long term extension	Clinical trial safety	Tofacitinib	None
Burmester EULAR 2018	Long term extension	Clinical trial safety	Tofacitinib	None
Kavanaugh 2019	Long term extension	Clinical trial safety	Apremilast	None
Cs: conventional synthetic; DMARD: disease modifying anti-rheumatic drug; MTX: methotrexate; TNF: Tumor necrosis factor;				

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table S4.2: Safety: Risk of Bias analysis

Table 4.2.1: Newcastle Ottawa scale for cohort studies

Type of bias	**Category**	**Assessment**
Selection bias	Representativeness of the exposed cohort	representative* / selected group / no description
	Selection of the non-exposed cohort	same cohort as exposed* / different source / no description
	Ascertainment of exposure	secure record* / structured interview* / written self-report / no description
	Demonstration that outcome of interest was not present at start of study	yes* / no
Comparability of cohorts (design/analysis)	Study controls for most important factor	yes* / no
	Study controls for any additional factor	yes* / no
Outcome	Assessment of outcome	blinded* / record linkage* / self-report / not described
	Follow up long enough for outcomes to occur	yes* / no
	Adequacy of follow up of cohorts	complete* / lost to follow up / not stated
Each category can be rated with a star (*), based on the respective assessment. This leads to a possible maximum of 4 stars for selection, 2 stars for comparability and 3 stars for outcome.		

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table 4.2.2: Newcastle Ottawa scale for case-control studies

Type of bias	**Category**	**Assessment**
Selection bias	Case definition adequate?	Yes, with independent validation * / yes (record linkage, self-reports) / no description
	Representativeness of the cases	Consecutive and representative series of cases * / potential selection bias / not stated
	Selection of controls	Community controls * / hospital controls / no description
	Definition of controls	No history of endpoint * / no description
Comparability of cases and controls (design/analysis)	Study controls for most important factor	yes* / no
	Study controls for any additional factor	yes* / no
Exposure	Ascertainment of exposure	Secure record * / structured blinded interview * / non-blinded interview / written self report or medical record only / no description
	Same method of ascertainment for cases and controls	yes* / no
	Non-response rate	Same rate for both groups * / non respondents described / rate different and no designation
Each category can be rated with a star (*), based on the respective assessment. This leads to a possible maximum of 4 stars for selection, 2 stars for comparability and 3 stars for exposure.		

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table 4.2.3: Risk of bias analysis of cohort studies

Study	Selection bias				Comparability of cohorts (design/analysis)		Outcome		
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Study controls for most important factor	Study controls for any additional factor	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Choquette 2015	*	*	*	*	*	*	*	*	*
Ogdie 2015	*	*		*	*	*	*	*	*
Polachek 2015	*		*	*	*	*	*	*	*
Costa 2016	*	*	*	*	*	*		*	
Eder 2016	*	*	*	*	*	*	*	*	
Haddad 2016	*	*	*		*	*	*		*
Dreyer 2016	*	*	*	*	*		*	*	*
Zisman 2016	*	*			*	*	*	*	*
Hellgren 2017	*	*	*	*	*		*	*	*
Each category can be rated with a star (*), based on the respective assessment. This leads to a possible maximum of 4 stars for selection, 2 stars for comparability and 3 stars for exposure.									

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Table 4.2.4: Risk of bias analysis of case-control studies

Study	Selection bias				Comparability of cases and controls (design/analysis)		Exposure		
	Case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls	Study controls for most important factor	Study controls for any additional factor	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate
Li 2015		*	*	*	*	*		*	
Each category can be rated with a star (*), based on the respective assessment. This leads to a possible maximum of 4 stars for selection, 2 stars for comparability and 3 stars for exposure.									

Table S4.3: Safety: Baseline characteristics of cohort and case control studies.

Study	Cohort	No. of patients (n)	Mean age (years)	Mean PsO disease duration (years)	Mean PsA disease duration (years)	Female (%)	BMI (kg/m²)
Choquette 2015	Overall	89	49.0			46.1	
Ogdie 2015	No DMARD	4174	51.63		5.75		
	DMARD	4532	49.80		4.39		
Polachek 2015	PsA patients	67	50.0	14.5	8		
	Control	30	43.3				
Costa 2016	DMARD	322	57.2			62	
	TNF inhibitor	296	47.5			60	
Eder 2016	Overall	1091	43.8	15.17	5.65	43.9	
Haddad 2016	Overall	695	49.5	21.5	12.5	42	29.3
Dreyer 2016	TNF inhibitor experienced	1603				53	
	TNF inhibitor naïve	2286				57	
Zisman 2016	Overall	3128	50.26			53.8	
Hellgren 2017	TNF inhibitor	3833					
	TNF naïve	15908					
Li 2015	PsA (CVD)	7982	46.1		7.7	50.68	
	PsA (MACE)	8454	47.0		7.6	50.63	

BMI: body mass index; CVD: cardiovascular disease; DMARD: disease modifying anti-rheumatic drug; MACE: major adverse cardiovascular events; PsA: psoriasis arthritis; Pso: psoriasis; TNF: tumor necrosis factor;

Kerschbaumer A, *et al. Ann Rheum Dis* 2020; 79:778–786. doi: 10.1136/annrheumdis-2020-217163

Section 4: References

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