Long-term Efficacy and Safety of Bimekizumab and Other Biologics in Moderate to Severe Plaque Psoriasis: Updated Systematic Literature Review and Network Meta-Analysis

Richard B. Warren,[1] Kerry Donnelly,[2] Sandeep Kiri,[2] Vanessa Taieb,[3] Mahmoud Slim,[4,5] Kyle Fahrbach,[6] Binod Neupane,[4] Marissa Betts,[6] April Armstrong[7]

[1] Dermatology Centre, Northern Care Alliance NHS Foundation Trust, Manchester, UK; 2 NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK
[2] UCB Pharma, Slough, UK
[3] UCB Pharma, Colombes, France
[4] Evidera Inc, St-Laurent, Canada
[5] Institute of Neurosciences "Federico Olóriz", University of Granada, Granada, Spain
[6] Evidera Inc, Waltham, Massachusetts USA
[7] University of California Los Angeles (UCLA), Los Angeles, California USA

Corresponding Author:
April Armstrong, MD MPH
Professor and Chief
Division of Dermatology
University of California Los Angeles (UCLA), Los Angeles, California, USA
E-mail: aprilarmstrong@post.harvard.edu

Supplementary Materials

Supplementary Tables

Supplementary Table 1. SLR Search Strategy Embase via Ovid

#	Search Strings
1	exp psoriasis/
2	(psoria$ or palmoplantar$ pustulosis or pustulosis palmaris et plantaris).ti,ab
3	or/1-2
4	exp methotrexate/
5	(methotrexate$ or amethopterin or mtx or mexate).ti,ab.
6	exp cyclosporine/
7	(Ciclosporin or cyclosporine or cyclosporin).ti,ab.
8	exp etretin/
9	(acitretin or soriatane or neotigason).ti,ab.
10	exp certolizumab pegol/
11	(certolizumab pegol or cimzia or CDP870 or CDP 870).ti,ab.
12	exp adalimumab/
13	(adalimumab$ or humira or d2e7).ti,ab.
14	exp etanercept/
15	(etanercept$ or enbrel or embrel or benepali).ti,ab.
16	exp brodalumab/
17	(brodalumab or siliq or kyntheum or KHK4827 or KHK 4827 or AMG 827 or AMG827).ti,ab.
18	exp ixekizumab/
19	(ixekizumab or taltz or ly2439821 or ly 2439821).ti,ab.
20	exp secukinumab/
21	(secukinumab or cosentyx or ain457 or ain 457).ti,ab.
22	exp guselkumab/
23	(guselkumab or tremfya or cnto 1959 or cnto1959).ti,ab.
24	exp ustekinumab/
25	(ustekinumab or stelara or cnto 1275 or cnto1275).ti,ab.
26	exp tildrakizumab/
27	(tildrakizumab or Ilumya or Ilumetri or mk 3222 or mk3222 or sch 900222 or sch900222).ti,ab.
38	exp risankizumab/
29	(risankizumab or bi 655066 or bi655066 or "abbv 066" or abbv066).ti,ab.
30	exp bimekizumab/
31	(bimekizumab or UCB4940 or UCB 4940).ti,ab.
32	exp infliximab/
33	(infliximab or remicade or renflexis or inflectra or ca2).ti,ab.
34	(apremilast or otezla or cc-10004 or cc 10004 or cc10004).ti,ab.
35	exp fumaric acid dimethyl ester/
36	(dimethyl fumarate or dimethylfumarate or bg 0012 or bg00012 or bg-00012 or tecfidera or fag201 or fag 201 or fag-201 or fumaderm or bg12 or bg-12).ti,ab.
37	exp interleukin 23p19/
38	(interleukin 23p19 or interleukin23p19 or interleukin-23p19 or IL-23p19 or IL-23 p19).ti,ab.

#	Search Strings
39	or/4-38
40*	exp randomized controlled trial/
41	exp RANDOMIZATION/
42*	random*.ti,ab.
43	'rct'.ti,ab.
44	'controlled trial'.ti,ab.
45*	'clinical trial'.ti,ab.
46*	'trial'.ti,ab.
47*	exp Single Blind Procedure/
48*	exp Double Blind Procedure/
49*	exp Crossover Procedure/
50*	'cross over'.ti,ab.
51*	'crossover'.ti,ab.
52*	exp PLACEBO/
53*	'placebo'.ti,ab.
54	(doubl* and blind*).ti,ab.
55	(singl* and blind*).ti,ab.
56	('open' and label*).ti,ab.
57*	factorial*.ti,ab.
58*	assign*.ti,ab.
59*	allocate*.ti,ab.
60*	volunteer*.ti,ab.
61	'controlled study'.ti,ab.
62	'major clinical study'.ti,ab.
63	'clinical article'.ti,ab.
64	or/40-63
65	3 and 39 and 64
66*	animal/ not human/
67	nonhuman/
68	exp animal experiment/
69	exp experimental animal/
70	animal model/
71	exp rodent/
72	(rat or rats or mouse or mice).ti.
73	or/66-72
74	65 not 73
75	limit 74 to english language
76	limit 75 to abstracts
77	'conference abstract'.pt.
78	limit 77 to yr="1966 - 2019"
79	76 not 78

*Search strategy adapted based on Cochrane Handbook for maximising search sensitivity and precision for interventions [40].

Supplementary Table 2. SLR Search Strategy MEDLINE and MEDLINE In-process via Ovid

#	Search Strings
1	exp Psoriasis/
2	(psoria$ or palmoplantar$ pustulosis or pustulosis palmaris et plantaris).ti,ab.
3	or/1-2
4	exp Methotrexate/
5	(methotrexate$ or amethopterin or mtx or mexate).ti,ab.
6	exp Cyclosporine/
7	(Ciclosporin or cyclosporine or cyclosporin).ti,ab.
8	exp Acitretin/
9	(acitretin or soriatane or neotigason).ti,ab.
10	exp Certolizumab pegol/
11	(certolizumab pegol or cimzia or CDP870 or CDP 870).ti,ab.
12	exp Adalimumab/
13	(adalimumab$ or humira or d2e7).ti,ab.
14	exp Etanercept/
15	(etanercept$ or enbrel or embrel or benepali).ti,ab.
16	(brodalumab or siliq or kyntheum or KHK4827 or KHK 4827 or AMG 827 or AMG827).ti,ab.
17	(ixekizumab or taltz or ly2439821 or ly 2439821).ti,ab.
18	(secukinumab or cosentyx or ain457 or ain 457).ti,ab.
19	(guselkumab or tremfya or cnto 1959 or cnto1959).ti,ab.
20	exp ustekinumab/
21	(ustekinumab or stelara or cnto 1275 or cnto1275).ti,ab.
22	(tildrakizumab or Ilumya or Ilumetri or mk 3222 or mk3222 or sch 900222 or sch900222).ti,ab.
23	(risankizumab or bi 655066 or bi655066 or "abbv 066" or abbv066).ti,ab.
24	(bimekizumab or UCB4940 or UCB 4940).ti,ab.
25	exp infliximab/
26	(infliximab or remicade or renflexis or inflectra or ca2).ti,ab.
27	(apremilast or otezla or cc-10004 or cc 10004 or cc10004).ti,ab.
28	exp dimethyl fumarate/
29	(dimethyl fumarate or dimethylfumarate or bg 0012 or bg00012 or bg-00012 or tecfidera or fag201 or fag 201 or fag-201 or fumaderm or bg12 or bg-12).ti,ab.
30	exp Interleukin-23 Subunit p19/
31	(interleukin 23p19 or interleukin23p19 or interleukin-23p19 or IL-23p19 or IL-23 p19).ti,ab.
32	or/4-31
33	exp random allocation/
34*	exp Randomized Controlled Trial/
35*	random*.ti,ab.
36	'rct'.ti,ab.
37*	'controlled trial'.ti,ab.
38*	'clinical trial'.ti,ab.
39*	'trial'.ti,ab.
40	exp Single-Blind Method/
41	exp Double-Blind Method/
42	'cross over'.ti,ab.
43	'crossover'.ti,ab.

#	Search Strings
44*	exp PLACEBOS/
45	exp placebo effect/
46*	'placebo'.ti,ab.
47	(doubl* and blind*).ti,ab.
48	(singl* and blind*).ti,ab.
49	('open' and label*).ti,ab.
50	factorial*.ti,ab.
51	assign*.ti,ab.
52	allocate*.ti,ab.
53	volunteer*.ti,ab.
54	'controlled study'.ti,ab.
55	'major clinical study'.ti,ab.
56	'clinical article'.ti,ab.
57	or/33-56
58	3 and 32 and 57
59*	animals/ not humans/
60	exp animals, laboratory/
61	exp animal experimentation/
62	exp models, animal/
63	exp rodentia/
64	(rat or rats or mouse or mice).ti.
65	or/59-64
66	58 not 65
67	limit 66 to english language
68	limit 67 to abstracts
69	congress.pt.
70	clinical conference.pt.
71	or/69-70
72	limit 71 to yr="1966 - 2019"
73	68 not 72

*Search strategy adapted based on Cochrane Handbook for maximising search sensitivity and precision for interventions [40].

Supplementary Table 3. SLR Search Strategy CDSR via Ovid

#	Search Strings
1	[exp Psoriasis/]
2	(psoria$ or palmoplantar$ pustulosis or pustulosis palmaris et plantaris).ti,ab.
3	or/1-2
4	[exp Methotrexate/]
5	(methotrexate$ or amethopterin or mtx or mexate).ti,ab.
6	[exp Cyclosporine/]
7	(Ciclosporin or cyclosporine or cyclosporin).ti,ab.
8	[exp Acitretin/]
9	(acitretin or soriatane or neotigason).ti,ab.
10	[exp Certolizumab pegol/]
11	(certolizumab pegol or cimzia or CDP870 or CDP 870).ti,ab.
12	[exp Adalimumab/]
13	(adalimumab$ or humira or d2e7).ti,ab.
14	[exp Etanercept/]
15	(etanercept$ or enbrel or embrel or benepali).ti,ab.
16	(brodalumab or siliq or kyntheum or KHK4827 or KHK 4827 or AMG 827 or AMG827).ti,ab.
17	(ixekizumab or taltz or ly2439821 or ly 2439821).ti,ab.
18	(secukinumab or cosentyx or ain457 or ain 457).ti,ab.
19	(guselkumab or tremfya or cnto 1959 or cnto1959).ti,ab.
20	[exp ustekinumab/]
21	(ustekinumab or stelara or cnto 1275 or cnto1275).ti,ab.
22	(tildrakizumab or Ilumya or Ilumetri or mk 3222 or mk3222 or sch 900222 or sch900222).ti,ab.
23	(risankizumab or bi 655066 or bi655066 or "abbv 066" or abbv066).ti,ab.
24	(bimekizumab or UCB4940 or UCB 4940).ti,ab.
25	[exp infliximab/]
26	(infliximab or remicade or renflexis or inflectra or ca2).ti,ab.
27	(apremilast or otezla or cc-10004 or cc 10004 or cc10004).ti,ab.
28	[exp dimethyl fumarate/]
29	(dimethyl fumarate or dimethylfumarate or "bg 0012" or bg00012 or bg-00012 or tecfidera or fag201 or fag 201 or fag-201 or fumaderm or bg12 or bg-12).ti,ab.
30	[exp Interleukin-23 Subunit p19/]
31	(interleukin 23p19 or interleukin23p19 or interleukin-23p19 or IL-23p19 or IL-23 p19).ti,ab.
32	or/4-31
33	[exp random allocation/]
34	[exp Randomized Controlled Trial/]
35	random*.ti,ab.
36	'rct'.ti,ab.
37	'controlled trial'.ti,ab.
38	'clinical trial'.ti,ab.
39	'trial'.ti,ab.
40	[exp Single-Blind Method/]
41	[exp Double-Blind Method/]
42	'cross over'.ti,ab.

#	Search Strings
43	'crossover'.ti,ab.
44	[exp PLACEBOS/]
45	[exp placebo effect/]
46	'placebo'.ti,ab.
47	(doubl* and blind*).ti,ab.
48	(singl* and blind*).ti,ab.
49	('open' and label*).ti,ab.
50	factorial*.ti,ab.
51	assign*.ti,ab.
52	allocate*.ti,ab.
53	volunteer*.ti,ab.
54	'controlled study'.ti,ab.
55	'major clinical study'.ti,ab.
56	'clinical article'.ti,ab.
57	or/33-56
58	3 and 32 and 57
59	[animals/ not humans/]
60	[exp animals, laboratory/]
61	[exp animal experimentation/]
62	[exp models, animal/]
63	[exp rodentia/]
64	(rat or rats or mouse or mice).ti.
65	or/59-64
66	58 not 65
67	limit 66 to english language [Limit not valid; records were retained]
68	limit 67 to abstracts [Limit not valid; records were retained]
69	congress.pt.
70	clinical conference.pt.
71	or/69-70
72	limit 71 to yr="1966 - 2019"
73	68 not 72

*Search strategy adapted based on Cochrane Handbook for maximising search sensitivity and precision for interventions [40].

Supplementary Table 4. Search Strategy CENTRAL via Ovid

#	Search Strings
1	[exp Psoriasis/]
2	(psoria$ or palmoplantar$ pustulosis or pustulosis palmaris et plantaris).ti,ab.
3	or/1-2
4	[exp Methotrexate/]
5	(methotrexate$ or amethopterin or mtx or mexate).ti,ab.
6	[exp Cyclosporine/]
7	(Ciclosporin or cyclosporine or cyclosporin).ti,ab.
8	[exp Acitretin/]
9	(acitretin or soriatane or neotigason).ti,ab.
10	[exp Certolizumab pegol/]
11	(certolizumab pegol or cimzia or CDP870 or CDP 870).ti,ab.
12	[exp Adalimumab/]
13	(adalimumab$ or humira or d2e7).ti,ab.
14	[exp Etanercept/]
15	(etanercept$ or enbrel or embrel or benepali).ti,ab.
16	(brodalumab or siliq or kyntheum or KHK4827 or KHK 4827 or AMG 827 or AMG827).ti,ab.
17	(ixekizumab or taltz or ly2439821 or ly 2439821).ti,ab.
18	(secukinumab or cosentyx or ain457 or ain 457).ti,ab.
19	(guselkumab or tremfya or cnto 1959 or cnto1959).ti,ab.
20	[exp ustekinumab/]
21	(ustekinumab or stelara or cnto 1275 or cnto1275).ti,ab.
22	(tildrakizumab or Ilumya or Ilumetri or mk 3222 or mk3222 or sch 900222 or sch900222).ti,ab.
23	(risankizumab or bi 655066 or bi655066 or "abbv 066" or abbv066).ti,ab.
24	(bimekizumab or UCB4940 or UCB 4940).ti,ab.
25	[exp infliximab/]
26	(infliximab or remicade or renflexis or inflectra or ca2).ti,ab.
27	(apremilast or otezla or cc-10004 or cc 10004 or cc10004).ti,ab.
28	[exp dimethyl fumarate/]
29	(dimethyl fumarate or dimethylfumarate or "bg 0012" or bg00012 or bg-00012 or tecfidera or fag201 or fag 201 or fag-201 or fumaderm or bg12 or bg-12).ti,ab.
30	[exp Interleukin-23 Subunit p19/]
31	(interleukin 23p19 or interleukin23p19 or interleukin-23p19 or IL-23p19 or IL-23 p19).ti,ab.
32	or/4-31
33	[exp random allocation/]
34	[exp Randomized Controlled Trial/]
35	random*.ti,ab.
36	'rct'.ti,ab.
37	'controlled trial'.ti,ab.
38	'clinical trial'.ti,ab.
39	'trial'.ti,ab.
40	[exp Single-Blind Method/]
41	[exp Double-Blind Method/]
42	'cross over'.ti,ab.

#	Search Strings
43	'crossover'.ti,ab.
44	[exp PLACEBOS/]
45	[exp placebo effect/]
46	'placebo'.ti,ab.
47	(doubl* and blind*).ti,ab.
48	(singl* and blind*).ti,ab.
49	('open' and label*).ti,ab.
50	factorial*.ti,ab.
51	assign*.ti,ab.
52	allocate*.ti,ab.
53	volunteer*.ti,ab.
54	'controlled study'.ti,ab.
55	'major clinical study'.ti,ab.
56	'clinical article'.ti,ab.
57	or/33-56
58	3 and 32 and 57
59	[animals/ not humans/]
60	[exp animals, laboratory/]
61	[exp animal experimentation/]
62	[exp models, animal/]
63	[exp rodentia/]
64	(rat or rats or mouse or mice).ti.
65	or/59-64
66	58 not 65
67	limit 66 to english language [Limit not valid; records were retained]
68	limit 67 to abstracts [Limit not valid; records were retained]
69	congress.pt.
70	clinical conference.pt.
71	or/69-70
72	limit 71 to yr="1966 - 2019"
73	68 not 72

*Search strategy adapted based on Cochrane Handbook for maximising search sensitivity and precision for interventions [40].

Supplementary Table 5. Selection Criteria for SLR

Category	Inclusion Criteria*	Exclusion Criteria
Population	Adult (≥18 years) patients with moderate to severe or very severe chronic psoriasis who were candidates for systemic psoriasis therapy	• Studies on patients with other than moderate to severe forms of chronic psoriasis • Studies primarily focused on the treatment of PsA • Studies on paediatric patients
Interventions	Systemic biologics: • Adalimumab 80 mg at Week 0 and 40 mg Q2W • Brodalumab 210 mg Weeks 0 and 1, and 2 then Q2W • Bimekizumab** (64 mg Q4W, 160 mg Q4W with 320 mg loading dose, 320 mg Q4W, 320 mg Q8W, and 480 mg Q4W) • Certolizumab pegol, a loading dose of 400 mg at Weeks 0, 2 and 4, followed by 200 mg Q2W • Certolizumab pegol, a loading dose of 400 mg at Weeks 0, 2 and 4, followed by 400 mg Q2W • Etanercept 50 mg twice weekly for three months then once weekly for maintenance • Etanercept 25 mg twice weekly • Guselkumab 100 mg at Weeks 0 and 4 then Q8W • Infliximab 5 mg/kg Weeks 0, 2, and 6 then Q8W • IL-31 100 mg • Ixekizumab 160 mg Week 0 followed by 80 mg Q2W from Weeks 2–12 then Q4W • Risankizumab 150 mg at Week 0 and 4 then Q12W • Secukinumab 150 mg or 300 mg Weeks 0, 1, 2, and 3, followed by maintenance dosing at Week 4 Q4W • Tildrakizumab 100 mg at Weeks 0 and 4 and then Q12W thereafter (In patients with certain characteristics [for example, high disease burden, body weight of 90 kg or more] a 200 mg dose may provide greater efficacy) • Ustekinumab 45 mg or 90 mg both at Weeks 0, 4, then Q12W Systemic non-biologics:*** • Apremilast • Methotrexate • Cyclosporine • Dimethyl fumarate • Acitretin	Studies that did not include a treatment arm with any of the selected comparators of interest
Comparisons	Placebo; any of the above therapies	Comparisons of different dosages of the same intervention
Outcomes****	• PASI 50, 75, 90, 100 • Adverse effects of treatment (including discontinuation due to adverse effects)	Publications that did not report data on relevant outcomes
Study designs	RCTs, phase II, III, IV, including follow-up studies of RCTs	Observational/real-world evidence studies; single-arm trials
Subgroups	• Previous use of phototherapy and systemic non-biological therapy • Previous use of biological therapy • Severity of psoriasis	NA

Category	Inclusion Criteria*	Exclusion Criteria
Publication types	NA	Publications of the following types: • Narrative publications • Non-systematic reviews • Phase I studies • Case studies • Case reports • Editorials
Limits	Only English-language articles/conference abstracts were included	Journal articles and conference abstracts not available in English
	No limitation for peer reviewed publications; conference abstracts were restricted to 2016–current	Studies published outside the time frame of interest

*Studies/treatment arms only evaluating ustekinumab 45 mg have been excluded from the SLR and NMA, as the ustekinumab 45 mg body weight requirement results in limited available data, comparability to the population for other treatments, and generalisability of the findings.

**Only the approved dose of bimekizumab (i.e., 320 mg) was included in the quantitative synthesis.

***Any dose of systemic non-biologic treatments have been included, as doses are often modified or titrated.

****All variations in outcome endpoints were extracted as reported.

Abbreviations: IL = interleukin; NA = not applicable; PASI = Psoriasis Area and Severity Index; PsA = psoriatic arthritis; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks; Q12W = every 12 weeks; RCT = randomised controlled trials SLR = systematic literature review.

Supplementary Table 6. Study and Patient Characteristics of Studies Included in the Efficacy and/or Safety NMA

Study (Phase)	Severity Definition	Intervention(s) and Comparators	Age in Years: Mean (SD)	Male (%)	PsA (%)	Disease Duration (Years)	% with Prior Therapy: Biologic/Non-Biologic	PASI Base Case	PASI SA	SAE NMA
ALLURE [41] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Secukinumab 300 mg Q4W (single 300 mg/2 mL pre-filled syringe)	43 (14)	61	19	19	NR/NR	✓		
		Secukinumab 300 mg Q4W (two 150 mg/1 mL pre-filled syringes)	46 (14)	61	23	15	NR/NR			
		Placebo	41 (13)	65	17	18	NR/NR			
AMAGINE 2 [42] **(Phase 3)**	PASI ≥12 BSA ≥10% PGA ≥3	Ustekinumab 45 or 90 mg Q12W	45 (13)	68	17	19	28/NR	✓	✓	
		Brodalumab 210 mg Q2W	45 (13)	69	19	19	29/NR			
		Placebo	44 (13)	71	17	18	29/NR			
AMAGINE 3 [42] **(Phase 3)**	PASI ≥12 BSA ≥10% PGA ≥3	Placebo	44 (13)	66	19	18	24/NR	✓	✓	
		Ustekinumab 45 or 90 mg Q12W	45 (13)	68	20	18	24/NR			
		Brodalumab 210 mg Q2W	45 (13)	69	20	18	25/NR			
BE RADIANT [18] **(Phase 3b)**	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	NR	NR	NR	NR	NR/ NR	✓	✓	✓
		Secukinumab 300 mg Q4W	NR	NR	NR	NR	NR/ NR			
BE SURE [19] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	44.6 (13.3)	67.1	NR	18.8	31.3/71.5	✓	✓	
		Adalimumab 40 mg Q2W	45.5 (14.3)	71.7	NR	16.2	33.3/69.2			
BE VIVID [9] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	45.2 (14)	71.3	NR	16	38.9/83.2	✓	✓	✓
		Ustekinumab 45 or 90 mg Q12W	46 (13.6)	71.8	NR	17.8	38.7/81			
		Placebo	49.7 (13.6)	72.3	NR	19.7	39.8/77.1			
CAIN457A2318 [43] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Secukinumab 150 mg Q4W	41 (11.39)	72.8	NR	NR	NR	✓	✓	✓
		Secukinumab 300 mg Q4W	39.9 (12.35)	75.4	NR	NR	NR			
		Placebo	40.1 (11.01)	80.0	NR	NR	NR			
CARIMA [33]	PASI ≥10	Secukinumab 150 mg Q4W	46 (14.4)	57.4	27.8	20.8	31.1/89.6	✓		

Study (Phase)	Severity Definition	Intervention(s) and Comparators	Age in Years: Mean (SD)	Male (%)	PsA (%)	Disease Duration (Years)	% with Prior Therapy: Biologic/Non-Biologic	PASI Base Case	PASI SA	SAE NMA
(Phase 3)		Secukinumab 300 mg Q4W	44.2 (12.9)	77.1	25	20.6	37/85.2			
		Placebo to Secukinumab 150 mg*	46.8 (13.1)	69.6	17.4	20.3	39.1/69.6			
		Placebo to Secukinumab 300 mg*	43.7 (11.4)	69.2	15.4	18.9	30.8/92.3			
CLARITY [44] **(Phase 3)**	PASI ≥12 BSA ≥10% Modified IGA 2011 ≥3	Secukinumab 300 mg Q4W	45.4 (14.1)	64.7	NR	16.8	20/NR	✓	✓	✓
		Ustekinumab 45 or 90 mg Q12W	45.3 (14.2)	68.1	NR	17.3	23.6/NR			
CLEAR [45] **(Phase 3)**	PASI ≥12 BSA ≥10% Modified IGA 2011 ≥3	Secukinumab 300 mg Q4W	45.2 (14)	68	20.5	19.7	14.2/NR	✓	✓	✓
		Ustekinumab 45 or 90 mg Q12W	44.6 (13.7)	74.3	15.9	16.1	13/NR			
ECLIPSE [26] **(Phase 3)**	NR	Guselkumab 100 mg Q8W	NR	NR	NR	NR	NR/NR	✓	✓	✓
		Secukinumab 300 mg Q4W	NR	NR	NR	NR	NR/NR			
ERASURE [46] **(Phase 3)**	PASI ≥12 BSA ≥10% PGA ≥3	Secukinumab 300 mg Q4W	44.9 (13.5)	69	23.3	17.4	28.6/NR	✓	✓	
		Secukinumab 150 mg Q4W	44.9 (13.3)	68.6	18.8	17.5	29.8/NR			
		Placebo	45.4 (12.6)	69.4	27.4	17.3	29.4/NR			
EXPRESS [47] **(Phase 3)**	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg Q8W	42.6 (11.7)	68.8	NR	19.1	0**/NR	✓		
		Placebo	43.8 (12.6)	79.2	NR	17.3	0**/NR			
EXPRESS II [48] **(Phase 3)**	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg Q8W	44.5 (13)	65	28.3	19.1	14.3/NR	✓		
		Placebo	44.4 (12.5)	69.2	26	17.8	13/NR			
FEATURE [49, 50] **(Phase 3)**	PASI ≥12 BSA ≥10% Modified IGA 2011 ≥3	Secukinumab 300 mg Q4W	45.1 (12.6)	64.4	NR	18	39/NR	✓	✓	
		Secukinumab 150 mg Q4W	46 (15.1)	67.8	NR	20.4	47.5/NR			
		Placebo	46.5 (14.1)	66.1	NR	20.2	44.1/NR			
FIXTURE [46]	PASI ≥12	Secukinumab 300 mg Q4W	44.5 (13.2)	68.5	15.3	15.8	11.6/NR	✓	✓	

Study (Phase)	Severity Definition	Intervention(s) and Comparators	Age in Years: Mean (SD)	Male (%)	PsA (%)	Disease Duration (Years)	% with Prior Therapy: Biologic/Non-Biologic	PASI Base Case	PASI SA	SAE NMA
(Phase 3)	BSA ≥10% PGA ≥3	Secukinumab 150 mg Q4W	45.4 (12.9)	72.2	15	17.3	13.8/NR			
		Etanercept 50 mg BIW	43.8 (13)	71.2	13.5	16.4	13.8/NR			
		Placebo	44.1 (12.6)	72.7	15	16.6	10.7/NR			
Igarashi, 2012 [51] **(Phase 2/3)**	PASI ≥12 BSA ≥10%	Ustekinumab 45 mg Q12W	Median: 45	82.8	9.4	15.8	1.6/0	✓		
		Ustekinumab 90 mg Q12W	Median: 44	75.8	11.3	17.3	0/0			
		Placebo	Median: 49.0	83.9	3.1	16	0/0			
IMMerge [52] **(Phase 3)**	PASI ≥12 BSA ≥10% Static PGA ≥3	Risankizumab 150 mg Q12W	47.3	68.3	NR	18.6	37.8/NR	✓	✓	✓
		Secukinumab 300 mg Q4W	46.8	62	NR	17.4	35.6/NR			
IXORA-S [53] **(Phase 3)**	PASI ≥10	Ustekinumab 45 mg or 90 mg Q12W	44 (13.3)	67.5	NR	18.2	15.1/NR	✓	✓	✓
		Ixekizumab 80 mg Q2W	42.7 (12.7)	66.2	NR	18	13.2/NR			
JUNCTURE [54] **(Phase 3)**	PASI ≥12 BSA ≥10% PGA ≥3	Secukinumab 300 mg	46.6 (14.2)	76.7	23.3	21	25/NR	✓	✓	
		Secukinumab 150 mg	43.9 (14.4)	67.2	26.2	20.6	24.6/NR			
		Placebo	43.7 (12.7)	62.3	19.7	19.9	21.3/NR			
LIBERATE [55] **(Phase 3)**	PASI ≥12 BSA ≥10% PGA ≥3	Etanercept 50 mg QW	47 (14.1)	59	NR	18.1	0**/NR	✓		
		Placebo	43.4 (14.9)	70.2	NR	16.6	0**/NR			
		Apremilast 30 mg BID	46 (13.6)	59	NR	19.7	0**/NR			
M02-528 [56] **(Phase 2)**	BSA ≥5% Psoriasis ≥1 year	Adalimumab 40mg Q2W	46	71	33	21	0**/NR	✓		
		Placebo	43	65	31	19	0**/NR			
MATURE [57] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Secukinumab 300 mg Q4W	44.7 (12.79)	70.7	19.5	19.6	12.2/NR	✓		
		Placebo	43.6 (14.08)	70.0	12.5	17.6	17.5/NR			
Nakagawa, 2016 [58] **(Phase 3)**	PASI ≥12 BSA ≥10%	Brodalumab 210 mg Q2W	46.4 (11.8)	78.4	13.5	14.97	13.5/NR	✓		
		Placebo	46.6 (10.8)	71.1	18.4	16.86	7.9/NR			

Study (Phase)	Severity Definition	Intervention(s) and Comparators	Age in Years: Mean (SD)	Male (%)	PsA (%)	Disease Duration (Years)	% with Prior Therapy: Biologic/Non-Biologic	PASI Base Case	PASI SA	SAE NMA
OASIS-2 [59] **(Phase 3)**	NR	Secukinumab 300 mg Q4W	NR	NR	NR	NR	NR	✓		
		Placebo	NR	NR	NR	NR	NR			
Obe-Pso-S [34] **(Phase 4)**	PASI ≥12 BSA ≥10% IGA ≥3	Secukinumab 300 mg Q4W	41.5 (15.2)	59.3	NR	NR	NR	✓		
		Placebo	50.4 (13.1)	71.4	NR	NR	NR			
Ohtsuki, 2017 [60] **(Phase 2)**	PASI ≥12 BSA ≥10%	Apremilast 30 mg BID	51.7 (12.7)	83.5	NR	13.9	2.4/NR	✓		
		Placebo	48.3 (12)	73.8	NR	12.4	4.8/NR			
Ohtsuki, 2018 [61] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Guselkumab 100 mg Q8W	47.8 (11.1)	74.6	15.9	14.4	17.5/NR	✓		
		Placebo	48.3 (10.6)	84.4	15.6	13.7	15.6/NR			
Papp-2021 [62] **(Phase 2)**	PASI ≥12 BSA ≥10% IGA ≥3	Secukinumab 300 mg Q4W	47.5 (13.8)	71.7	3.8	20.2	13.2/NR	✓		
		Placebo	45.9 (12.9)	75	5.8	16.3	15.4/NR			
Seo 2021 [63] **(Phase 3)**	PASI ≥12 BSA ≥10% Static PGA ≥3	Brodalumab 210 mg Q2W	43.5 (14.3)	57.5	NR	10.9 years	10/NR	✓		
		Placebo	43.7 (15.8)	68.2	NR	13.6 years	36.4/NR			
SustaIMM [64] **(Phase 2/3)**	PASI ≥12 BSA ≥10% Static PGA ≥3	Risankizumab 150 mg Q12W	53.3 (11.9)	91	9	NR	29/NR	✓		
		Placebo	50.9 (11.2)	78	12	NR	24/NR			
TRANSFIGURE [65] **(Phase 3)**	PASI ≥12 BSA ≥10% NAPSI ≥16 at least 4 fingernails	Secukinumab 300 mg Q4W	45.1 (12.9)	80	26	18	24/NR	✓	✓	
		Secukinumab 150 mg Q4W	43.5 (10.9)	82	24	20	22/NR			
		Placebo	43.6 (11.2)	80	28	17.4	23/NR			
Tyring, 2006 [66]	PASI ≥12	Etanercept 50 mg BIW	45.8 (12.8)	65	35	20.1	0**/NR	✓		

Study (Phase)	Severity Definition	Intervention(s) and Comparators	Age in Years: Mean (SD)	Male (%)	PsA (%)	Disease Duration (Years)	% with Prior Therapy: Biologic/Non-Biologic	PASI Base Case	PASI SA	SAE NMA
(Phase 3)	BSA ≥10%	Placebo	45.6 (12.1)	70	33	19.7	0**/NR			
UltIMMa-1 [67] **(Phase 3)**	PASI ≥12 BSA ≥10% Static PGA ≥3	Risankizumab 150 mg Q12W	48.3 (13.4)	70	28	NR	34/NR	✓	✓	
		Ustekinumab 45 or 90 mg Q12W	46.5 (13.4)	70	23	NR	30/NR			
		Placebo	49.3 (13.6)	77	35	NR	39/NR			
UltIMMa-2 [67] **(Phase 3)**	PASI ≥12 BSA ≥10% Static PGA ≥3	Risankizumab 150 mg Q12W	46.2 (13.7)	69	25	NR	40/NR	✓	✓	
		Ustekinumab 45 or 90 mg Q12W	48.6 (14.8)	67	27	NR	43/NR			
		Placebo	46.3 (13.3)	68	33	NR	43/NR			
UNCOVER 3 [68] **(Phase 3)**	PASI ≥12 BSA ≥10% Static PGA ≥3	Ixekizumab 80 mg Q4W	46 (13)	67	NR	18	15/NR	✓		
		Etanercept 50 mg BIW	46 (14)	70	NR	18	15.7/NR			
		Placebo	46 (12)	71	NR	18	17.1/NR			
UNVEIL [69] **(Phase 4)**	BSA 5%-10% Static PGA=3	Apremilast 30 mg BID	48.6 (15.4)	50	NR	17.5	0**/NR	✓		
		Placebo	51.1 (13.7)	56.2	NR	13.9	0**/NR			
VOYAGE 1 [27] **(Phase 3)**	PASI ≥12 BSA ≥10% IGA ≥3	Guselkumab 100 mg Q8W	43.9 (12.7)	72.9	19.5	17.9	21.6/NR	✓	✓	✓
		Adalimumab 40 mg Q2W	42.9 (12.6)	74.6	18.6	17	21/NR			
		Placebo	44.9 (12.9)	68.4	17.2	17.6	19.5/NR			

* The CARIMA trial included two placebo arms, each subsequently switched to secukinumab 300 mg or 150 mg at Week 12. Pooled results of the placebo groups were included in the NMA.

** Assumed based on enrolment criteria (i.e., inclusion, exclusion criteria) regarding prior systemic therapies (e.g., anti-TNF).

Abbreviations: BID = twice daily; BIW = twice per week; BSA = body surface area; IGA = Investigator's Global Assessment; NAPSI = Nail Psoriasis Severity Index; NMA = network meta-analysis; NR = not reported; PASI = Psoriasis Area and Severity Index; PGA = Physician Global Assessment; PsA = psoriatic arthritis; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks; Q12W = every 12 weeks; QW = weekly; SAE = serious adverse event; SD = standard deviation; TNF = tumour necrosis factor.

Supplementary Table 7. Risk of Bias Assessment of Randomised Controlled Trials (Cochrane v.2.0)

Trial	Randomisation Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Bias
ALLURE	Low	Low	Low	Low	Low	Low
AMAGINE 2	Low	Low	Low	Low	Low	Low
AMAGINE 3	Low	Low	Low	Low	Low	Low
BE RADIANT	Low	Low	Low	Low	Low	Low
BE SURE	Low	Low	Low	Low	Low	Low
BE VIVID	Low	Low	Low	Low	Low	Low
CAIN457A2223	Low	Low	Low	Low	Low	Low
CARIMA	Low	Low	High	Low	Low	High
CLARITY	Low	Low	Low	Low	Low	Low
CLEAR	Low	Low	Low	Low	Low	Low
ECLIPSE	Some concerns	Low	High	Low	Some concerns	High
ERASURE	Low	Low	Low	Low	Low	Low
EXPRESS	Low	Low	Some concerns	Low	Low	Some concerns
EXPRESS-II	Low	Low	Some concerns	Low	Low	Some concerns
FEATURE	Low	Low	Low	Low	Low	Low
FIXTURE	Low	Low	Low	Low	Low	Low
Igarashi, 2012	Low	Low	Some concerns	Low	Low	Some concerns
IMMerge	Low	Low	Low	Low	Low	Low
IXORA-S	Low	Low	Low	Low	Low	Low
JUNCTURE	Low	Low	Low	Low	Low	Low
LIBERATE	Low	Low	Low	Low	Low	Low
M02-528	Low	Low	Low	Low	Low	Low
MATURE	Low	Low	Low	Low	Low	Low
Nakagawa, 2016	Low	Low	Low	Low	Low	Low
Ohtsuki, 2017	Low	Low	Low	Low	Low	Low
Ohtsuki, 2018	Low	Low	Low	Low	Low	Low
Papp, 2021	Low	Low	Low	Low	Low	Low
Seo, 2021	Low	Low	Low	Some concerns	Low	Some concerns
SustalMM	Some concerns	Low	Low	Low	Low	Some concerns
TRANSFIGURE	Low	Low	Low	Low	Low	Low
Tyring, 2006	Low	Low	Low	Low	Low	Low
UltIMMA-1	Low	Low	Low	Low	Low	Low
UltIMMA-2	Low	Low	Low	Low	Low	Low
UNCOVER 3	Low	Low	Low	Low	Low	Low
UNVEIL	Low	Low	Some concerns	Low	Low	Some concerns
VOYAGE 1	Low	Low	Low	Low	Low	Low

Supplementary Table 8. Multinomial NMA for Achieving PASI 100 at Weeks 44–60 (Base-case, Active Treatment Only)

Treatment	Risk Ratio (95% CrI) for BKZ 320 mg Q4W/Q8W versus Comparators	Risk Ratio (95% CrI) for BKZ 320 mg Q4W/Q4W versus Comparators
Bimekizumab 320 mg Q4W/Q8W*	Reference	1.09 (0.95, 1.28)
Bimekizumab 320 mg Q4W/Q4W	0.92 (0.78, 1.06)	Reference
Brodalumab 210 mg	0.97 (0.79, 1.18)	1.06 (0.90, 1.25)
Risankizumab 150 mg	0.90 (0.73, 1.07)	0.97 (0.83, 1.14)
Ixekizumab 80 mg	1.26 (0.93, 1.81)	1.38 (1.03, 1.95)
Guselkumab 100 mg	1.15 (0.90, 1.39)	1.25 (1.03, 1.49)
Secukinumab 300 mg	1.52 (1.27, 1.83)	1.66 (1.42, 1.98)
Ustekinumab 45 or 90 mg	1.99 (1.56, 2.55)	2.17 (1.75, 2.74)
Secukinumab 150 mg	2.52 (1.92, 3.42)	2.74 (2.11, 3.75)
Adalimumab 40 mg	2.34 (1.66, 3.14)	2.55 (1.89, 3.35)
Etanercept 50 mg	5.09 (3.19, 8.94)	5.56 (3.50, 9.83)

Model: Random effects, REZ, multinomial NMA

*Bimekizumab-treated patients were dosed 320 mg every 4 weeks through Week 16 and then switched to every 8 weeks maintenance dosing (Q4W/Q8W).

Abbreviations: BKZ = bimekizumab; CrI = credible interval; NMA = network meta-analysis; PASI 100 = achievement of 100% improvement from baseline in Psoriasis Area and Severity Index; Q4W = every 4 weeks; Q8W = every 8 weeks; REZ = random effects model combined with the parameter.

Supplementary Table 9. Multinomial NMA at Weeks 44–60 – Probabilities of Achieving PASI Outcomes, Sensitivity Analysis (Treat-though, with Placebo)

Treatment	PASI 100 (95% CrI)
Bimekizumab 320 mg Q4W/Q8W*	0.591 (0.476, 0.697)
Bimekizumab 320 mg Q4W/Q4W	0.643 (0.555, 0.720)
Brodalumab 210 mg	0.599 (0.537, 0.665)
Risankizumab 150 mg	0.599 (0.534, 0.663)
Ixekizumab 80 mg	0.529 (0.431, 0.624)
Guselkumab 100 mg	0.491 (0.413, 0.567)
Secukinumab 300 mg	0.400 (0.362, 0.438)
Ustekinumab 90 mg	0.357 (0.179, 0.576)
Ustekinumab 45 or 90 mg	0.298 (0.258, 0.343)
Secukinumab 150 mg	0.250 (0.204, 0.299)
Adalimumab 40 mg	0.221 (0.154, 0.302)
Infliximab 5 mg/kg	0.188 (0.091, 0.328)
Etanercept 50 mg	0.111 (0.071, 0.164)
Apremilast 30 mg	0.080 (0.025, 0.199)
Placebo	0.004 (0.002, 0.008)

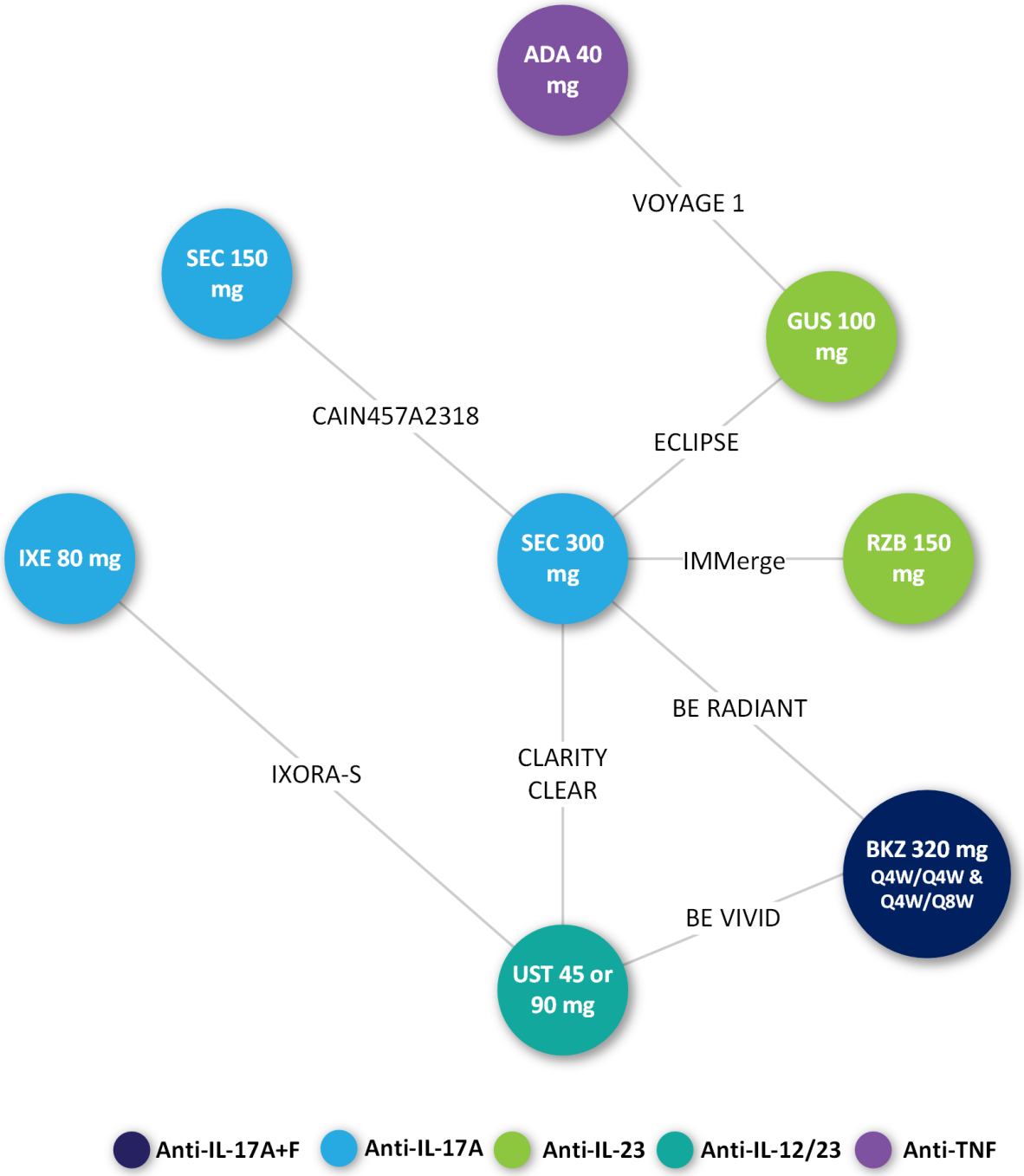
Model: Base case (treat-through, with placebo); random effects, baseline-adjusted, REZ, multinomial NMA.

*Bimekizumab-treated patients were dosed 320 mg every 4 weeks through Week 16 and then switched to every 8 weeks dosing (Q4W/Q8W).

Abbreviations: CrI = credible interval; NMA = network meta-analysis; PASI 100 = achievement of 100% improvement from baseline in Psoriasis Area and Severity Index; Q4W = every 4 weeks; Q8W = every 8 weeks; REZ = random effects model combined with the parameter.

Supplementary Figures

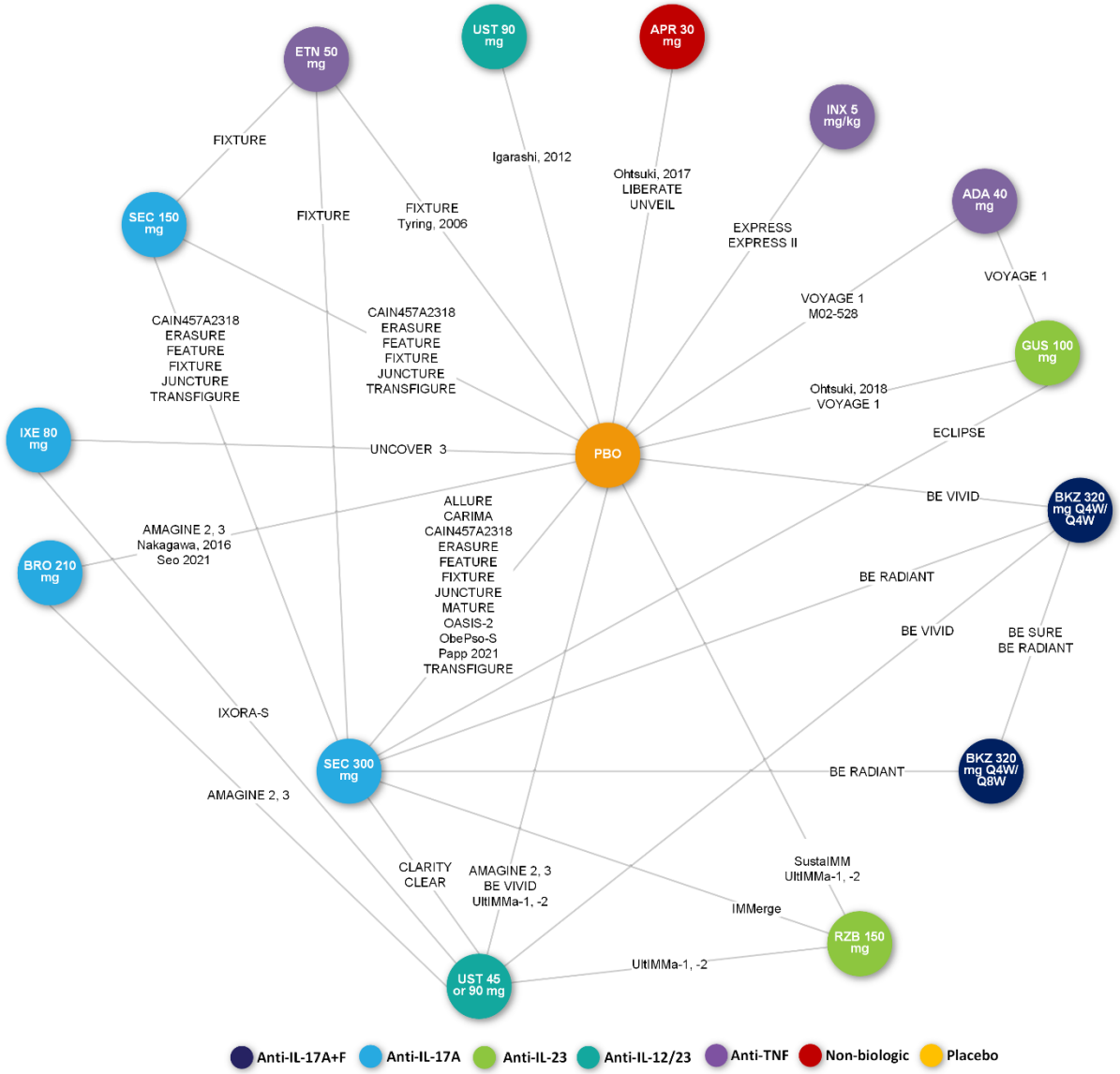
Supplementary Figure 1. Network Diagram for Trials Reporting SAEs



Number of studies included = 9.

Abbreviations: ADA = adalimumab; BKZ = bimekizumab; GUS = guselkumab; IL = interleukin; IXE = ixekizumab; Q4W = every 4 weeks; Q8W = every 8 weeks; RZB = risankizumab; SAE = serious adverse event; SEC = secukinumab; TNF = tumour necrosis factor; UST = ustekinumab.

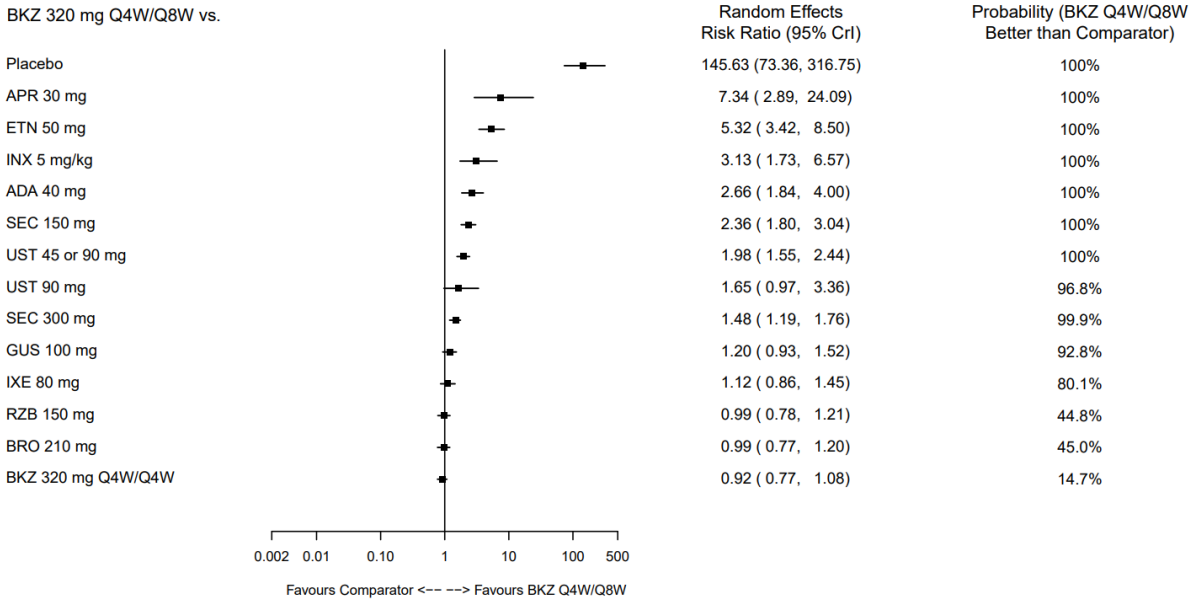
Supplementary Figure 2. Network Diagram for Trials Reporting PASI Outcomes (Sensitivity Analysis: Treat-though with Placebo)



Number of studies included = 38.

Abbreviations: ADA = adalimumab; APR = apremilast; BKZ = bimekizumab; BRO = brodalumab; ETN = etanercept; GUS = guselkumab; IL = interleukin; INX = infliximab; IXE = ixekizumab; PASI = Psoriasis Area and Severity Index; PBO = placebo; Q4W = every 4 weeks; Q8W = every 8 weeks; RZB = risankizumab; SEC = secukinumab; TNF = tumour necrosis factor; UST = ustekinumab.

Supplementary Figure 3. Multinomial NMA at Weeks 44–60 – Risk Ratios of Achieving PASI 100 (Sensitivity Analysis: Treat-though, with Placebo) between Bimekizumab 320 mg Q4W/Q8W* and Other Treatments



Model: Treat-through, with placebo; random effects, baseline-adjusted, REZ, multinomial NMA.

*Bimekizumab-treated patients were dosed 320 mg every 4 weeks through Week 16 and then switched to every 8 weeks dosing (Q4W/Q8W).

Abbreviations: ADA = adalimumab; APR = apremilast; BKZ = bimekizumab; BRO = brodalumab; CrI = credible interval; ETN = etanercept; GUS = guselkumab; INX = infliximab; IXE = ixekizumab; NMA = network meta-analysis; PASI 100 = achievement of 100% improvement from baseline in Psoriasis Area and Severity Index; Q4W = every 4 weeks; Q8W = every 8 weeks; REZ = random effects model combined with the parameter z; RZB = risankizumab; SEC = secukinumab; UST = ustekinumab.