Efficacy of Bimekizumab and Other Biologics in Moderate to Severe Plaque Psoriasis: A Systematic Literature Review and a Network Meta-analysis

Authors:

April Armstrong,[1] Kyle Fahrbach,[2*] Craig Leonardi,[3] Matthias Augustin,[4] Binod Neupane,[5] Paulina Kazmierska,[6] Marissa Betts,[2] Andreas Freitag,[6] Sandeep Kiri,[7] Vanessa Taieb,[8] Mahmoud Slim,[5] Natalie Nunez Gomez,[9] Richard B. Warren[10]

[1]*Keck School of Medicine of USC, Dermatology, Los Angeles, CA, USA*

[2]*Evidera (Evidence Synthesis), Waltham, MA, USA*

[3]*Central Dermatology and Saint Louis University School of Medicine, St. Louis, Missouri, USA*

[4]*Institute for Health Services Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany*

[5]*Evidera (Evidence Synthesis), St-Laurent, Canada*

[6]*Evidera (Evidence Synthesis), London, UK*

[7]*UCB Pharma, Slough, UK*

[8]*UCB Pharma, Colombes, France*

[9]*UCB Pharma, Monheim, Germany*

[10]*Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, The University of Manchester, Manchester, UK*

* Corresponding Author:
Kyle Fahrbach, PhD
Evidera, Inc.
140 Kendrick St, 3rd floor
Needham MA 02494
Phone: +1 781 960 0245 | Email: kyle.fahrbach@evidera.com

Supplementary Materials

Statistical Methods

In the Bayesian NMAs, non-informative normal priors were used for all basic effect parameters (i.e. probit differences) and baseline effect regression parameters (i.e. coefficient for placebo effect in network meta-regression) in the baseline effect adjusted model. A Uniform(0,1) prior was used for τ, the square root of the between-study variance of probit differences (i.e. the heterogeneity standard deviation [SD]) in the RE model, and a Uniform(0, 0.5) prior was used for σ_z (the SD around the value between probit cut-offs) in the REZ model. To examine the impact of prior distributions for different SDs, we conducted sensitivity analyses around the prior values used in our Bayesian NMAs (using Uniform(0,0.5) and Uniform(0,2) for τ, and Uniform(0,0.25) and Uniform(0,1) for σ_z). No differences were found in the final estimates of these SD parameters, which was likely due to the relatively large size of the dataset.

Markov chain Monte Carlo simulations, with 50,000 discarded burn-in iterations followed by 50,000 iterations for parameter estimation were used for all Bayesian analyses. Convergence was confirmed by evaluating the three-chain, Brooks-Gelman-Rubin plots [1, 2] and values of $\hat{R}$ (potential scale reduction factor [1], considered converged if $\hat{R}$ <1.05 for all parameters being estimated), as well as the ratios of Monte Carlo error to the SDs of the posteriors.

The most recent, robust PASI data were used in a separate natural history model [3]; these data included placebo arms with n ≥50 patients in studies published from 2013 onward. The inclusion of these data ensured that extrapolated response proportions reflected current practice estimates of an 'anchor' placebo rate for PASI 50 of 16.4%; PASI probabilities for each treatment for each PASI level were estimated relative to this anchor in the models.

Bayesian Model Code for REZ, Baseline-adjusted, Random-effect Analysis

```
###! Binomial likelihood, probit link (different categories)
###! Random effects model for multi-arm trials

model{                          #! PROGRAM STARTS
 dummyvar<-nclass[1]+posttreat[1]+poststudy[1]
 for(i in 1:86){
       #! LOOP THROUGH STUDIES
       w[i,1] <- 0              #! adjustment for multi-arm trials for control arm
       delta[i,1] <- 0          #! treatment effect is zero for control arm
       mu[i] ~ dnorm(0,0.001) #! vague priors for all trial baselines
       for (k in 1:na[i]) {   #! LOOP THROUGH ARMS
         p[i,k,1] <- 1        #! Pr(PASI >0)
         for (j in 1:(nc[i]-1)) { #! LOOP THROUGH CATEGORIES
        r[i,k,j] ~ dbin(q[i,k,j],n[i,k,j]) #! binomial likelihood
        q[i,k,j] <- 1-(p[i,k,C[i,(j+1)]]/p[i,k,C[i,j]]) #! conditional probabilities
        theta[i,k,j] <- mu[i] + delta[i,k] + z[ntreat[i,k],C[i,(j+1)]-1] +
                      (BetaP[ntreat[i,k]]-BetaP[ntreat[i,1]]) * (mu[i]-Mmu)
        rhattreat[i,k,j] <- q[i,k,j] * n[i,k,j] #! predicted number events
        dv[i,k,j] <- 2 * (r[i,k,j]*(log(r[i,k,j])-log(rhattreat[i,k,j])) +(n[i,k,j]-r[i,k,j])
                     *(log(n[i,k,j]-r[i,k,j]) - log(n[i,k,j]-rhattreat[i,k,j]))) #! Deviance
       }
       dev[i,k] <- sum(dv[i,k,(1:(nc[i]-1))]) #! deviance contribution of each arm
       avgdev[i,k] <- dev[i,k]/(nc[i]-1) #! Average deviance contribution of each arm
       for (j in 2:nc[i]) { #! LOOP THROUGH CATEGORIES
         p[i,k,C[i,j]] <- 1 - phi.adj[i,k,j] #! link function
         phi.adj[i,k,j] <- step(8+theta[i,k,(j-1)]) * (step(theta[i,k,(j-1)]-8) +
                           step(8-theta[i,k,(j-1)])*phi(theta[i,k,(j-1)]) )
         }
       }
       for (k in 2:na[i]) { #! LOOP THROUGH ARMS
         delta[i,k] ~ dnorm(md[i,k],taud[i,k])
         md[i,k] <- dd[ntreat[i,k]] - dd[ntreat[i,1]] + sw[i,k] #! mean
         taud[i,k] <- prec*2*(k-1)/k
         #! prec of LHR dist (with multi-arm trial correction)
         w[i,k] <- (delta[i,k] - dd[ntreat[i,k]] + dd[ntreat[i,1]]) #! multi-arm adjustment
         sw[i,k] <- sum(w[i,(1:(k-1))])/(k-1) #! cumulative adjustment for multi-arm trials
       }
  resdev[i] <- sum(dev[i,1:na[i]])
  }
totresdev <- sum(resdev[]) #! Total Residual Deviance

for (i in 1:23) {                  #! LOOP THROUGH TREATMENTS
  z[i,1] <- 0
  for (j in 2:(Cmax-1)) {          #! LOOP THROUGH RESPONSE CATEGORIES
       z[i,j] <- z[i,(j-1)] + z.aux[i,j]  #! ensures z[j]~Uniform(z[j-1], z[j-1]+5)
       z.aux[i,j] ~ dnorm(MeanZ[j],precz)
```

```
  }
}

for (j in 2:(Cmax-1)) {
  MeanZ[j] ~ dunif(0,5)
}
precz <-1/(sdz*sdz)
sdz ~ dunif(0.001,0.5) # Prior for standard deviation of z's

###calculate prob of achieving threshold - on treat k
A ~ dnorm(0.977, 330.578512396694) # Distribution of placebo PASI50 response in probit term

for (k in 1:23) {
  for (j in 1: (Cmax-1)) {
    TThresh[j,k] <- 1 - phi(A + dd[k] + z[k,j] + (BetaP[k])*(A-Mmu)) # Probabilities
  }
}

dd[1] <- 0                    #! treatment effect is zero for placebo, reference treatment
BetaP[1]<- 0                  # Baseline (placebo) effect parameter for placebo
BetaPlac ~ dnorm(0,0.01)      #! vague prior for placebo effect on probit values
for (k in 2:23){
  dd[k] ~ dnorm(0,0.001)      #! vague priors for treatment effects
  BetaP[k]<-BetaPlac          #! Common baseline effect size for all active treatments vs placebo
}
sd ~ dunif(0.001,1)           #! U(0,1) prior for between-trial SD
tau<-sd
prec<- pow(tau,-2)            #! between-trial precision
tau2<-1/prec

for (index in 1:23){
  for (i in 1:(Cmax-1)) {
         Thresh[i,pretreat[index]]<-TThresh[i,index]
  }
  d[pretreat[index]]<-dd[index]
  rk[pretreat[index]]<-rkk[index]
  bestt[index]<-step(1.1 - rkk[index])
  for (j in 1:23) {
       preeffect[j,index]<- equals(index,rkk[j])
  }
}

rkk<- rank(dd[])       # Used when best = lowest
                       # but 1-p is modeled in probit anlaysis, so higher dd[] is better
                       # ranks changed during post-processing

for (index in 1:86){                        #! LOOP THORUGH STUDIES
       study[prestudy[index]]<-mu[index]    # baseline effect in each study
```

```
}

###! All pairwise comparisons of differences in probit
for (c in 1:(23-1)){
  for (k in (c+1):23){
  Pbitdiff[pretreat[c],pretreat[k]] <- dd[c] - dd[k] #! probit differences
  Pbitdiffprob[pretreat[c],pretreat[k]] <- step(Pbitdiff[pretreat[c],pretreat[k]])
  }
 }
}
```

Data

- nt = 23, number of treatments
- prettreat, original treatment IDs (analysis is run after recoding treatments to 1,2, …,nt)
- ns = 86, number of studies
- prestudy, original studies IDs (analysis is run after recoding study ids to 1,2, …,ns)
- Mmu = 0.977, centering value in probit scale for baseline effect adjustment
- na is a 86 (=ns) long vector of number of treatment arms (a study with 3-treatment arms will have na=3).
- ntreat is a 86 (=ns) x 4 (maximum number of arms) matrix of treatment IDs
- nc is a 86 (=ns) long vector of number of response categories (a study with PASI50,75,90 response data will have nc=4 response categories PASI 0 to <50, PASI 50 to <75, PASI 75 to <90, PASI 90 to <100).
- Cmax = 5, maximum number of response categories
- n is a 86 (=ns) x 4 (maximum number of arms) x 4 (= Cmax -1) array of matrices of number of subjects evaluated in response categories (original arm size is the n for PASI 0 to <50 category)
- r is a 86 (=ns) x 4 (maximum number of arms) x 4 (= Cmax -1) array of matrices of number of responders in response categories
- C is a 86 (=ns) x 5 (=Cmax) matrix of response categories IDs (a study with PASI50,75,90 response data will have 1,2,3,4, NA ids of the response categories PASI 0 to <50, PASI 50 to <75, PASI 75 to <90, PASI 90 to <100, PASI 100, respectively)

Initials for parameters

Initials for the following parameters in the first chain are provided below, where they were sufficiently different but in the same format other two chains.

- mu <- c(0, 0, …, 0) # 86 (number of studies)-element vector
- dd <- c(NA, 0, 0, …, 0) # 23 (number of treatment)-element vector, NA for placebo, ref treatment
- sd <- 1 # standard deviation of the same probit differences across studies (assumed common)
- sdz <- 1 # standard deviations of z's
- BetaPlac <- -0.2 # baseline (placebo) effect parameter

- delta is a 86 (number of studies) by 4 (maximum number of treatments) of probit differences in studies (first column for the baseline treatments in all studies are NAs)
- z.aux is a 23 (number of treatments) by 4 (maximum number of probit jumps from one response category to next higher category when number of categories, Cmax = 5) of probit differences in studies (first column for all the baseline treatments in all studies are NAs)

Supplementary Tables

Table S1. Search Strategy in Embase via Ovid 8
Table S2. Search Strategy in MEDLINE and MEDLINE In-process via Ovid 10
Table S3. Search Strategy in CDSR via Ovid 12
Table S4. Search Strategy in CENTRAL via Ovid 14
Table S5. Inclusion and Exclusion Criteria for the Systematic Literature Review 16
Table S6. Study and Patient Characteristics of Studies Included in the Efficacy and/or Safety NMAs 18
Table S7. Risk of Bias Assessment of RCTs (Cochrane v.2.0) 30
Table S8. Baseline Risk Slopes, Heterogeneity, and Fit Statistics for All Multinomial Ordered Probit Models 33
Table S9. Probit Probabilities (95% CrI) of Achieving PASI Outcomes Treatments (REZ, Adjusted, Random-effects Multinomial Model) 34
Table S10. Number Needed to Treat (95% CrI) for Treatments versus Placebo for Achieving PASI Outcomes (REZ, Adjusted, Random-effects Multinomial Model) 35
Table S11. Probit Probabilities (95% CrI) of Achieving PASI Outcomes (REZ, Unadjusted, Fixed-effects Multinomial Model) 36

Supplementary Figures

Figure S1. 10–16-week Response Rate (%) Using the PASI 75 in Placebo Group by Trial 37
Figure S2. Risk Ratios of Achieving (a) PASI 75, (b) PASI 90 and (c) PASI 100 across Biologic and Non-biologic Treatments (REZ, Adjusted, Random-effects Multinomial model) 38
Figure S3. Odds Ratios* of Achieving (a) PASI 75 and (b) PASI 90 across Biologic and Non-biologic Treatments (Random-effects Binomial Model) 41

Table S1. Search Strategy in Embase via Ovid

#	Searches
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/

#	Searches
38	(interleukin 23p19 or interleukin23p19 or interleukin-23p19 or IL-23p19 or IL-23 p19).ti,ab.
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.

#	Searches
78	limit 77 to yr="1966 - 2016"
79	76 not 78

Table S2. Search Strategy in MEDLINE and MEDLINE In-process via Ovid

#	Searches
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/

#	Searches
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.
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.

#	Searches
70	clinical conference.pt.
71	or/69-70
72	limit 71 to yr="1966 - 2016"
73	68 not 72

Table S3. Search Strategy in CDSR via Ovid

#	Searches
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

#	Searches
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.
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 - 2016"

#	Searches
73	68 not 72

Table S4. Search Strategy in CENTRAL via Ovid

#	Searches
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. (66)
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. (9)
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/]

#	Searches
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.
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]

#	Searches
69	congress.pt.
70	clinical conference.pt.
71	or/69-70
72	limit 71 to yr="1966 - 2016"
73	68 not 72

Table S5. Inclusion and Exclusion Criteria for the Systematic Literature Review

Category	Inclusion Criteria*	Exclusion Criteria
Population	Adult (≥18 years) patients with moderate to severe or very severe chronic PSO who are candidates for systemic PSO therapy	• Studies on patients with other than moderate to severe forms of chronic PSO • Studies primarily focused on the treatment of PsA • Studies on paediatric patients
Interventions	Systemic biologics: • Adalimumab 80 mg at week 0 and 40 mg EOW • Brodalumab 210 mg weeks 0, 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)** • Cimzia®, a loading dose of 400 mg at Weeks 0, 2 and 4, followed by 200 mg Q2W • Cimzia®, 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 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	Studies that do not include a treatment arm with any of the selected comparators of interest

Category	Inclusion Criteria*	Exclusion Criteria
	• Dimethyl fumarate • Acitretin	
Comparisons	Placebo; any of the above therapies	Comparisons of different dosages of the same intervention
Outcomes****	• PASI 50, 75, 90, 100	Publications that do not report data on relevant outcomes
Study designs	RCTs (phase 2, 3, 4) (including follow-up studies of RCTs)	Observational/real-world evidence studies; single-arm trials
Publication Types	NA	Publications of the following types: • Narrative publications • Non-systematic reviews • Phase 1 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: BSA = body surface area; DLQI = Dermatology Life Quality Index; EOW = every other week; IL = interleukin; NA = not applicable; PASI = Psoriasis Area and Severity Index; PGA = physician global assessment; PsA = psoriatic arthritis; PSO = plaque psoriasis; Q2W = every two weeks; Q4W = every four weeks; Q8W = every eight weeks; Q12W = every 12 weeks; RCT = randomised controlled trial

Table S6. Study and Patient Characteristics of Studies Included in the Efficacy and/or Safety NMAs

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
ACCEPT [4] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Etanercept 50 mg BIW	45.7 (13.4)	70.9	27.4	18.8	11.8/NR
			Ustekinumab 45 mg at wk 0 and 4	45.1 (12.6)	63.6	29.7	18.9	12.4/NR
			Ustekinumab 90 mg at wk 0 and 4	44.8 (12.3)	67.4	27.4	18.7	10.4/NR
AMAGINE 1 [5] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Brodalumab 210 mg at wk 0, 1 and 2 then Q2W	46 (12)	73	26	20	46/NR
			Placebo	47 (13)	73	29	21	45/NR
AMAGINE 2 [6] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	45 (13)	68	17	19	28/NR
			Brodalumab 210 mg at wk 0, 1 and 2 then Q2W	45 (13)	69	19	19	29/NR
			Placebo	44 (13)	71	17	18	29/NR
AMAGINE 3 [6] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Placebo	44 (13)	66	19	18	24/NR
			Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	45 (13)	68	20	18	24/NR
			Brodalumab 210 mg at wk 0, 1 and 2 then Q2W	45 (13)	69	20	18	25/NR
Antiga, 2010 [7] (NR)	12	PASI ≥10 BSA ≥10%	Etanercept 50 mg BIW	31-63	40	NR	NR	NR/NR
			Acitretin 0.4 mg/kg/day	27-58	50	NR	NR	NR/NR
Asahina, 2010 [8] (Phase 2/3)	16	PASI ≥12 BSA ≥10%	Adalimumab 80 mg at wk 0 then 40 mg Q2W	44.2 (14.3)	81.4	18.6 (Moderate PGA) to 55.8 (Severe PGA)	14	0*/NR
			Placebo	43.9 (10.8)	89.1	17.4 (Very Severe PGA) to 54.3 (Severe)	15.5	0*/NR
Bagel, 2012 [9] (NR)	12	PASI ≥10 BSA ≥10%	Etanercept 50 mg BIW	39	53.2	NR	17.5	NR/NR
			Placebo	42	58.1	NR	11.9	NR/NR
BE ABLE 1 [10]	12	PASI ≥12	Bimekizumab 320 mg Q4W	42.6 (13.6)	65.1	NR	15.9	23.3/53.5

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
(Phase 2)		BSA ≥10% IGA ≥3	Placebo	46.7 (12.3)	59.5	NR	15	23.8/33.3
BE RADIANT [11] (Phase 3b)	16	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	45.9 (14.2)	67.3	NR	18.4	33.5/ NR
			Secukinumab 300 mg QW to wk 4 then Q4W	44 (14.7)	63.5	NR	17.2	32.2/ NR
BE READY [12] (Phase 3)	16	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	44.5 (12.9)	73.1	NR	19.6	44.4/NR
			Placebo	43.5 (13.1)	67.4	NR	19.1	43/NR
BE SURE [13] (Phase 3)	16	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	44.6 (13.3)	67.1	NR	18.8	31.3/NR
			Adalimumab 80 mg at wk 0 then 40 mg Q2W	45.5 (14.3)	71.7	NR	16.2	33.3/NR
BE VIVID [14] (Phase 3)	16	PASI ≥12 BSA ≥10% IGA ≥3	Bimekizumab 320 mg Q4W	45.2 (14)	71.3	NR	16	38.9/NR
			Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	46 (13.6)	71.8	NR	17.8	38.7/NR
			Placebo	49.7 (13.6)	72.3	NR	19.7	39.8/NR
BRIDGE [15] (Phase 3)	16	PASI ≥10 BSA ≥10% PGA ≥3	Dimethyl fumarate up to 720 mg	45 (13.8)	65.4	NR	NR	NR/NR
			Placebo	44 (14.3)	67.9	NR	NR	NR/NR
Cai, 2017 [16] (Phase 3)	12	NR	Adalimumab 80 mg at wk 0 then 40 mg Q2W	43.1 (11.9)	75.1	12.7	14.8	0*/NR
			Placebo	43.8 (12.5)	66.7	11.5	15.8	0*/NR
CAIN457A2223 [17] (Phase 2)	12	PASI ≥ 12 BSA ≥ 10%	Secukinumab 300 mg QW to wk 4 then Q4W	47.5	71	NR	NR	NR/NR
			Placebo	50.3	50	NR	NR	NR/NR
Caproni, 2009 [18] (NR)	12	PASI ≥10 BSA ≥10%	Etanercept 50 mg BIW	28-67	43.3	NR	NR	NR/NR
			Acitretin 0.4 mg/kg/day	31-65	36.7	NR	NR	NR/NR
CARIMA [19] (Phase 3)	12	PASI ≥10	Secukinumab 300 mg QW to wk 4 then Q4W	44.2 (12.9)	77.1	25	20.6	37/85.2

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
			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
CHAMPION [20, 21] (Phase 3)	16	PASI ≥10 BSA ≥10%	Adalimumab 80 mg at wk 0 then 40 mg Q2W	42.9 (12.6)	64.8	21.3	17.9	0*/NR
			Methotrexate 7.5 mg – 25 mg QW	41.6 (12)	66.4	17.3	18.9	0*/NR
			Placebo	40.7 (11.4)	66	20.8	18.8	0*/NR
Chaudhari, 2001 [22] (NR)	10	BSA ≥5%	Infliximab 5 mg/kg at wk 0, 2, and 6	51 (14)	63.6	NR	NR	0*/NR
			Placebo	45 (12)	72.7	NR	NR	0*/NR
CIMPACT [23] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Certolizumab pegol 400 mg at wk 0, 2, and 4 then 200 mg Q2W	46.7 (13.5)	68.5	16.4	19.5	26.7/NR
			Certolizumab pegol 400 mg Q2W	45.4 (12.4)	64.1	14.4	17.8	28.7/NR
			Etanercept 50 mg BIW	44.6 (14.1)	74.7	15.9	17.4	30/NR
			Placebo	46.5 (12.5)	59.6	21.2	18.9	19.3/NR
CIMPASI-1 [24] (Phase 3)	16	PASI ≥12 BSA ≥10% PGA ≥3	Certolizumab pegol at wk 0, 2, and 4 then 200 mg Q2W	44.5 (13.1)	70.5	10.5	16.6	31.6/69.5
			Certolizumab pegol 400 mg Q2W	43.6 (12.1)	68.2	17.0	18.4	33/69.3
			Placebo	47.9 (12.8)	68.6	7.8	18.5	29.4/70.6
CIMPASI-2 [24] (Phase 3)	16	PASI ≥12 BSA ≥10% PGA ≥3	Certolizumab pegol 400 mg at wk 0, 2, and 4 then 200 mg Q2W	46.7 (13.3)	63.7	24.2	18.8	35.2/71.4
			Certolizumab pegol 400 mg Q2W	46.4 (13.5)	49.4	29.9	18.6	34.5/72.4
			Placebo	43.3 (14.5)	53.1	18.4	15.4	28.6/73.5
CLARITY [25] (Phase III)	12	PASI ≥12 BSA ≥10% mIGA 2011 ≥3	Secukinumab 300 mg QW to wk 4 then Q4W	45.4 (14.1)	64.7	NR	16.8	20/NR
			Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	45.3 (14.2)	68.1	NR	17.3	23.6/NR
CLEAR [26]	16	PASI ≥12	Secukinumab 300 mg QW to wk 4 then Q4W	45.2 (14)	68	20.5	19.7	14.2/NR

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
(Phase 3)		BSA ≥10% mIGA ≥3	Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	44.6 (13.7)	74.3	15.9	16.1	13/NR
ECLIPSE [27] (Phase 3)	12	NR	Guselkumab 100 mg at wk 0, 4, and 8 then Q8W	46.3 (13.7)	68	18	18.5	29/52
			Secukinumab 300 mg QW to wk 4 then Q4W	45.3 (13.6)	67	15	18.3	29/56
ERASURE [28] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Secukinumab 300 mg QW to wk 4 then Q4W	44.9 (13.5)	69	23.3	17.4	28.6/NR
			Secukinumab 150 mg QW to wk 4 then 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
ESTEEM 1 [29] (Phase 3)	16	PASI ≥12 BSA ≥10% PGA ≥3	Apremilast 30 mg BID	45.8 (13.1)	67	NR	19.8	28.8/NR
			Placebo	46.5 (12.7)	69	NR	18.7	28.4/NR
ESTEEM 2 [30] (Phase 3)	16	PASI ≥12 BSA ≥10% PGA ≥3	Apremilast 30 mg BID	45.3 (13.1)	64	NR	17.9	33.6/NR
			Placebo	45.7 (13.4)	73	NR	18.7	32.1/NR
EXPRESS [31] (Phase 3)	10	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg at wk 0, 2, and 6 then 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 [32] (Phase 3)	14	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg at wk 0, 2, and 6	44.5 (13)	65	28.3	19.1	14.3/NR
			Placebo	44.4 (12.5)	69.2	26	17.8	13/NR
FEATURE [33, 34] (Phase 3)	12	PASI ≥12 BSA ≥10% mIGA 2011 ≥3	Secukinumab 300 mg QW to wk 4 then Q4W	45.1 (12.6)	64.4	NR	18	39/NR
			Secukinumab 150 mg QW to wk 4 then 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 [28]	12	PASI ≥12	Secukinumab 300 mg QW to wk 4 then Q4W	44.5 (13.2)	68.5	15.3	15.8	11.6/NR

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
(Phase 3)		BSA ≥10% PGA ≥3	Secukinumab 150 mg QW to wk 4 then 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
Flystrom, 2008 [35] (NR)	12	NR	Methotrexate 7.5–15 mg QW	48	75.7	NR	NR	0*/NR
			Ciclosporin 3–5 mg/kg QD	45	87.1	NR	NR	0*/NR
Gisondi, 2008 [36] (NR)	24^	NR	Etanercept 25 mg BIW	55.3 (10.9)	54.6	NR	23.5	0*/NR
			Acitretin 0.4 mg/kg QD	55 (11.3)	60	NR	18.8	0*/NR
Goldminz, 2015 [37] (NR)	16	PGA≥3	Adalimumab 80 mg at wk 0 then 40 mg Q2W	50.5 (NR)	73.3	13.3	17.3	NR/NR
			Methotrexate 7.5-25 mg QW	50.3 (NR)	86.7	20.0	21.5	NR/NR
Gottlieb, 2003 [38] (Phase 2)	12	BSA ≥10%, active, stable plaque	Etanercept 25 mg BIW	48.2	58	28	23	0*/NR
			Placebo	46.5	67	35	20	0*/NR
Heydendael, 2003 [39] (NR)	16	PASI ≥8	Methotrexate 15 mg-22.5 QW	41.6 (13)	65.1	7	NR	0*/NR
			Cyclosporine 3 to 5 mg/kg/day	38.3 (12.4)	69	2.4	NR	0*/NR
Igarashi, 2012 [40] (Phase 2/3)	12	PASI ≥12 BSA ≥10%	Ustekinumab 45 mg at wk 0 and 4 then Q12W	Median: 45	82.8	9.4	15.8	1.6/0
			Ustekinumab 90 mg at wk 0 and 4 then Q12W	Median: 44	75.8	11.3	17.3	0/0
			Placebo	Median: 49.0	83.9	3.1	16	0/0
IMMerge [41] (Phase 3)	16	PASI ≥12 BSA ≥10% sPGA ≥3	Risankizumab 150 mg at wk 0 and 4 then Q12W	47.3	68.3	NR	18.6	37.8/NR
			Secukinumab 300 mg QW to wk 4 then Q4W	46.8	62	NR	17.4	35.6/NR

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
IMMhance [42] (Phase 3)	16	PASI ≥12 BSA ≥10% sPGA ≥3	Risankizumab 150 mg at wk 0 and 4 then Q12W	Median: 51	69.5	NR	NR	56.5/46.9
			Placebo	Median: 48	73	NR	NR	51/42
IMMvent [43] (Phase 3)	16	PASI ≥12 BSA ≥10% sPGA ≥3	Risankizumab 150 mg at wk 0 and 4 then Q12W	45.3	70	7.6	NR	39/NR
			Adalimumab 80 mg at wk 0 then 40 mg Q2W	47	70	12.2	NR	37/NR
IXORA-S [44] (Phase 3)	12	PASI ≥10	Ustekinumab 45 mg or 90 mg at wk 0 and 4 then Q12W	44 (13.3)	67.5	NR	18.2	15.1/NR
			Ixekizumab 160 mg at wk 0 then 80 mg Q2W	42.7 (12.7)	66.2	NR	18	13.2/NR
JUNCTURE [45] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Secukinumab 300 mg QW to wk 4 then Q4W	46.6 (14.2)	76.7	23.3	21	25/NR
			Secukinumab 150 mg QW to wk 4 then Q4W	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
Leonardi, 2003 [46] (Phase 3)	12	PASI ≥10 BSA ≥10%	Etanercept 25 mg BIW	45.4 (1)	67	NR	18.5	0*/NR
			Etanercept 50 mg BIW	44.8 (0.8)	65	NR	18.6	0*/NR
			Placebo	45.6 (1)	63	NR	18.4	0*/NR
LIBERATE [47] (Phase 3)	16	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 [48] (Phase 2)	12	BSA ≥5% PSO ≥1 year	Adalimumab 80 mg at wk 0 then 40 mg Q2W	46	71	33	21	0*/NR
			Placebo	43	65	31	19	0*/NR
M10-315 [49] (NR)	12	PASI ≥12 mIGA 2011≥3 BSA ≥10%	Etanercept 50 mg BIW	45.2 (14.8)	61.2	33.1	15.2	7.9/27.8
			Placebo	45.0 (13.9)	63.9	20.8	15.5	4.2/27.8

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
Meffert, 1997 [50] (NR)	10	PASI 8-25	Cyclosporin A 2.5 mg/kg/day	NR	NR	NR	NR	0*/NR
			Placebo	NR	NR	NR	NR	0*/NR
Nakagawa, 2016 [51] (Phase 3)	12	PASI ≥12 BSA ≥10%	Brodalumab 210 mg at wk 0, 1 and 2 then 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
Ohtsuki, 2017 [52] (Phase 2)	16	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 [53] (Phase 3)	16	PASI ≥12 BSA ≥10% IGA ≥3	Guselkumab 100 mg at wk 0 and 4 then 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
OPT Compare Study [54] (Phase 3)	12	PASI ≥12 BSA ≥10%	Etanercept 50 mg BIW	42	70	21	18	11/NR
			Placebo	46	66	24	17	11/NR
ORION [55] (Phase 3)	16	PASI ≥12 BSA≥10% IGA ≥3	Guselkumab 100 mg at wk 0 and 4 then Q8W	46.2 (12.92)	66.1	NR	19.1	NR/NR
			Placebo	45.4 (15.70)	75	NR	17.4	NR/NR
Papp, 2005 [56] (NR)	12	PASI ≥10 BSA ≥10%	Etanercept 50 mg BIW	44.5	67	26	18.1	0*/NR
			Etanercept 25mg BIW	46	65	28	21.5	0*/NR
			Placebo	44	64	26	17.5	0*/NR
Papp, 2012a [57, 58] (Phase 3)	12	NR	Brodalumab 210 mg at wk 0, 1 and 2 then Q2W	42.1 (12.2)	62	30	17.1	NR/NR
			Placebo	41.8 (14.4)	58	18	18.3	NR/NR
Papp, 2012b [59] (Phase 2)	16	PASI ≥12 BSA ≥10%	Apremilast 30 mg BID	44.1 (14.7)	57	24	19.2	NR/NR
			Placebo	44.1 (13.7)	60	19	19.6	NR/NR
Papp, 2015 [60]	16	PASI ≥12	Tildrakizumab 100 mg at wk 0 and 4 then Q12W	45.5 (12.8)	85	17	NR	NR/NR

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
(Phase 2)		BSA ≥10%	Tildrakizumab 200 mg at wk 0 and 4 then Q12W	43.2 (12.6)	76	17	NR	NR/NR
			Placebo	45.9 (11.7)	83	24	NR	NR/NR
PHOENIX 1 [61] (Phase 3)	12	PASI ≥12 BSA ≥10%	Ustekinumab 45 mg at wk 0 and 4 then Q12W	44.8 (12.5)	68.6	29	19.7	52.5/NR
			Ustekinumab 90 mg at wk 0 and 4 then Q12W	46.2 (11.3)	67.6	36.7	19.6	50.8/NR
			Placebo	44.8 (11.3)	71.8	35.3	20.4	50.2/NR
PHOENIX 2[62] (Phase 3)	12	PASI ≥12 BSA ≥10%	Ustekinumab 45 mg at wk 0 and 4 then Q12W	45.1 (12.1)	69.2	26.2	11.7	38.4/NR
			Ustekinumab 90 mg at wk 0 and 4 then Q12W	46.6 (12.1)	66.7	22.9	12.3	36.5/NR
			Placebo	47 (12.5)	69	25.6	12.2	38.8/NR
PIECE [63] (NR)	12	PASI ≥10 and/or BSA ≥ 10 and/or PASI≥ 8 Skindex-29 score ≥35	Etanercept 50 mg BIW	42.4 (13.2)	56	13	17.9	NR/NR
			Infliximab 5 mg/kg at wk 0, 2, and 6 then Q8W	45.9 (13.9)	72	8	21.5	NR/NR
Reich, 2012 [64] (Phase 2)	12	PASI ≥12 BSA ≥10%	Certolizumab pegol 400 mg at wk 0 then 200 mg Q2W	43.3 (10.1)	75	NR	21	22/NR
			Certolizumab pegol 400 mg Q2W	43.6 (12.4)	72	NR	19.6	24/NR
			Placebo	43.3 (12.8)	63	NR	19.7	24/NR
Reich, 2020 [65] (Phase 3b)	16	NR	Ixekizumab 160 mg at wk 0 then 80 mg Q2W	44.3 (13.8)	78	NR	13.9	0*/52
			Methotrexate 7.5–25 mg QW	38.7 (12.9)	67	NR	12.9	0*/24
RESTORE1 [66] (Phase 3)	16	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg at wk 0, 2 and 6 then Q8W	44.1	67	NR	18.8	8.3/61.1
			Methotrexate 15-20 mg QW	41.9	69	NR	17	8.4/64.7

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
RESURFACE 1 [67] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Tildrakizumab 200 mg at wk 0 and 4 then Q12W	46.9 (13.2)	73	NR	NR	23/NR
			Tildrakizumab 100 mg at wk 0 and 4 then Q12W	46.4 (13.3)	67	NR	NR	23/NR
			Placebo	47.9 (13.5)	65	NR	NR	23/NR
RESURFACE 2 [67] (Phase 3)	12	PASI ≥12 BSA ≥10% PGA ≥3	Tildrakizumab 200 mg at wk 0 and 4 then Q12W	44.6 (13.6)	72	NR	NR	12/NR
			Tildrakizumab 100 mg at wk 0 and 4 then Q12W	44.6 (13.6)	72	NR	NR	13/NR
			Etanercept 50 mg BIW	45.8 (14)	71	NR	NR	12/NR
			Placebo	46.4 (12.2)	72	NR	NR	13/NR
REVEAL [68, 69] (Phase 3)	16	PASI ≥12 BSA ≥10% PGA ≥ moderate	Adalimumab 80 mg at wk 0 then 40 mg Q2W	44.1 (13.2)	67.1	27.5	18.1	11.9/NR
			Placebo	45.4 (13.4)	64.6	28.4	18.4	13.3/NR
Rich, 2013 [70] (Phase 2)	12	NR	Secukinumab 150 mg Q4W	44.2 (13.0)	75.4	32.6	16.9	29.7/NR
			Placebo	44.2 (12.6)	65.7	17.9	15.4	25.4/NR
SPIRIT [71] (NR)	10	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg at wk 0, 2, and 6	Median (IQR): 44 (34 to 53)	73.7	29.3	NR	33.3/NR
			Placebo	Median (IQR): 45 (30 to 52)	60.8	33.3	NR	31.4/NR
SustaIMM [72] (Phase 2/3)	16	PASI ≥12 BSA ≥10% sPGA ≥3	Risankizumab 150 mg at wk 0 and 4 then Q12W	53.3 (11.9)	91	9	NR	29/NR
			Placebo	50.9 (11.2)	78	12	NR	24/NR
Torii, 2010 [73] (Phase 3)	10	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg at wk 0, 2, and 6 then Q8W	46.9 (13)	62.9	28.6	14.2	0*/NR
			Placebo	43.3 (12.3)	73.7	36.8	11.1	0*/NR

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
TRANSFIGURE [74] (Phase 3)	16	PASI ≥12 BSA ≥10% NAPSI ≥16 at least 4 fingernails	Secukinumab 300 mg QW to wk 4 then Q4W	45.1 (12.9)	80	26	18	24/NR
			Secukinumab 150 mg QW to wk 4 then Q4W	43.5 (10.9)	82	24	20	22/NR
			Placebo	43.6 (11.2)	80	28	17.4	23/NR
Tyring, 2006 [75] (Phase 3)	12	PASI ≥12 BSA ≥10%	Etanercept 50 mg BIW	45.8 (12.8)	65	35	20.1	0*/NR
			Placebo	45.6 (12.1)	70	33	19.7	0*/NR
UltIMMa 1 [76] (Phase 3)	16	PASI ≥12 BSA ≥10% sPGA ≥3	Risankizumab 150 mg at wk 0 and 4 then Q12W	48.3 (13.4)	70	28	NR	34/NR
			Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	46.5 (13.4)	70	23	NR	30/NR
			Placebo	49.3 (13.6)	77	35	NR	39/NR
UltIMMa 2 [76] (Phase 3)	16	PASI ≥12 BSA ≥10% sPGA ≥3	Risankizumab 150 mg at wk 0 and 4 then Q12W	46.2 (13.7)	69	25	NR	40/NR
			Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	48.6 (14.8)	67	27	NR	43/NR
			Placebo	46.3 (13.3)	68	33	NR	43/NR
UNCOVER 1 [77] (Phase 3)	12	PASI ≥12 BSA ≥10% sPGA ≥3	Ixekizumab 160 mg at wk 0 then 80 mg Q2W	45 (12)	67.2	NR	20	40/57
			Placebo	46 (13)	70.3	NR	20	42/52
UNCOVER 2 [77-80] (Phase 3)	12	PASI ≥12 BSA ≥10% sPGA ≥3	Ixekizumab 160 mg at wk 0 then 80 mg Q2W	45 (13)	63	NR	18	23.9/50.7
			Etanercept 50 mg BIW	45 (13)	66	NR	19	21.2/47.5
			Placebo	45 (12)	71.4	NR	19	25.6/47.6
UNCOVER 3 [77-80] (Phase 3)	12	PASI ≥12 BSA ≥10% sPGA ≥3	Ixekizumab 160 mg at wk 0 then 80 mg Q2W	46 (13)	66	NR	18	15.1/44.2
			Etanercept 50 mg BIW	46 (14)	70.4	NR	18	15.7/47.6
			Placebo	46 (12)	71	NR	18	17.1/42.5

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
UNVEIL [81] (Phase 4)	16	BSA 5%-10% sPGA=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
Van de Kerkhof, 2008 [82] (Phase 3)	12	PASI ≥10 BSA ≥10%	Etanercept 50 mg QW	45.9 (12.8)	61.5	15.6	19.3	0*/NR
			Placebo	43.6 (12.6)	54.4	10.9	17.3	0*/NR
VIP [83] (Phase 4)	12	PASI ≥12 BSA ≥10	Adalimumab 80 mg at wk 0 then 40 mg Q2W	44.1 (14)	72.7	12.1	14.9	NR/NR
			Placebo	44.3 (14.5)	64.5	6.5	19.3	NR/NR
VIP-S [84] (NR)	12	PASI ≥ 12 BSA ≥ 10% mIGA 2011 ≥3	Secukinumab 300 mg QW to wk 4 then Q4W	47.9 (12.7)	71.7	13	16.3	43.5/28.3
			Placebo	47.0 (14.7)	62.2	24.4	15.4	35.6/31.1
VIP-U [85] (NR)	12	PASI ≥ 12, BSA ≥ 10%	Ustekinumab 45 or 90 mg at wk 0 and 4 then Q12W	39.45 (13.6)	72.7	4.6	16.5	45.5/27.3
			Placebo	45.33 (12.76)	66.7	28.6	20.3	42.9/9.5
VOYAGE 1 [86] (Phase 3)	16	PASI ≥12 BSA ≥10% IGA ≥3	Guselkumab 100 mg at wk 0 and 4 then Q8W	43.9 (12.7)	72.9	19.5	17.9	21.6/NR
			Adalimumab 80 mg at wk 0 then 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
VOYAGE 2 [87] (Phase 3)	16	PASI ≥12 BSA ≥10% IGA ≥3	Guselkumab 100 at wk 0 and 4 then mg Q8W	43.7 (12.2)	70.4	17.9	17.9	20.4/NR
			Adalimumab 80 mg at wk 0 then 40 mg Q2W	43.2 (11.9)	68.5	17.7	17.6	19.8/NR
			Placebo	43.3 (12.4)	69.8	18.5	17.9	21.8/NR
X-PLORE [88] (Phase 2)	16	PASI ≥12 BSA ≥10% PGA ≥3	Guselkumab 100 mg Q8W	44	72	25	18.5	NR/NR
			Adalimumab 80 mg at wk 0 then 40 mg Q2W	50	70	26	19.3	60/NR
			Placebo	46.5	67	29	18	36/NR

Study (Phase)	Primary Endpoint (weeks)	Severity Definition	Intervention(s) and Comparators	Age in Years, Mean (SD)	Male (%)	PsA (%)	Mean Disease Duration (years)	% with Prior Therapy Biologic/Non-biologic
Yang, 2012 [89] (Phase 3)	10	PASI ≥12 BSA ≥10%	Infliximab 5 mg/kg at wk 0, 2, and 6 then Q8W	39.4 (12.3)	71.4	NR	16	NR/100
			Placebo	40.1 (11.1)	77.8	NR	16	NR/NR

*Assumed based on enrolment criteria (i.e. inclusion, exclusion criteria) regarding prior systemic therapies (e.g. anti-TNF).‡The CARIMA trial included two placebo arms, each subsequently switched to secukinumab 300 mg or 150 mg at week 12. Pooled efficacy results of the placebo groups were included in the NMA.
^PASI results at week 12 were included in the NMA
Abbreviations: BID = twice daily; BIW = twice per week; BSA = body surface area; IGA = investigator's global assessment; IQR = interquartile range; mIGA = modified 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; PSO = plaque psoriasis; QW = every week; Q2W = every two weeks; Q4W = every four weeks; Q8W = every eight weeks; Q12W = every 12 weeks; QD = daily; QW = weekly; SD = standard deviation; sPGA = static physician's global assessment; TNF = tumour necrosis factor; wk = week

Table S7. Risk of Bias Assessment of RCTs (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
ACCEPT	Low	Low	Low	Some concerns	Low	Some concerns
AMAGINE 1	Low	Low	Low	Low	Low	Low
AMAGINE 2	Low	Low	Low	Low	Low	Low
AMAGINE 3	Low	Low	Low	Low	Low	Low
Antiga, 2010	Low	Low	Some concerns	Low	Low	Some concerns
Asahina, 2010	Low	Low	Low	Low	Low	Low
Bagel, 2012	Low	Low	Low	Low	Low	Low
BE ABLE 1	Low	Low	Low	Low	Low	Low
BE RADIANT	Low	Low	Low	Low	Low	Low
BE READY	Low	Low	Low	Low	Low	Low
BE SURE	Low	Low	Low	Low	Low	Low
BE VIVID	Low	Low	Low	Low	Low	Low
BRIDGE	Low	Low	Low	Low	Low	Low
Cai, 2017	Low	Low	Low	Low	Low	Low
CAIN457A2223	Low	Low	Low	Low	Low	Low
Caproni, 2009	Low	Low	Low	Low	Some concerns	Some concerns
CARIMA	Low	Low	High	Low	Low	High
CHAMPION	Low	Low	Low	Low	Low	Low
Chaudhari, 2001	Low	Low	Low	Low	Low	Low
CIMPACT	Low	Low	Low	Low	Low	Low
CIMPASI-1	Low	Low	Low	Low	Low	Low
CIMPASI-2	Low	Low	Low	Low	Low	Low
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
ESTEEM 1	Low	Low	Low	Low	Low	Low
ESTEEM 2	Low	Low	Low	Low	Low	Low
EXPRESS	Low	Low	Some concerns	Low	Low	Some concerns
EXPRESS-II (Menter, 2007)	Low	Low	Some concerns	Low	Low	Some concerns
FEATURE	Low	Low	Low	Low	Low	Low
FIXTURE	Low	Low	Low	Low	Low	Low
Flystrom, 2008	Low	Low	Low	Low	Low	Low

Trial	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Gisondi, 2008	Low	Low	Low	Low	Low	Low
Goldminz, 2015	Low	Low	Low	Low	Low	Low
Gottlieb, 2003a	Low	Low	Low	Low	Low	Low
Heydendael, 2003	Low	Low	Low	Low	Low	Low
Igarashi, 2012	Low	Low	Some concerns	Low	Low	Some concerns
IMMerge	Low	Low	Low	Low	Low	Low
IMMhance	Low	Low	Low	Low	Low	Low
IMMvent	Low	Low	Low	Low	Low	Low
IXORA-S	Low	Low	Low	Low	Low	Low
JUNCTURE	Low	Low	Low	Low	Low	Low
Leonardi, 2003	Low	Low	Low	Low	Low	Low
LIBERATE	Low	Low	Low	Low	Low	Low
M02-528	Low	Low	Low	Low	Low	Low
M10-114	Low	Low	Low	Low	Low	Low
Meffert, 1997	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
OPT Compare Study	Low	Low	Low	Low	Low	Low
ORION	Low	Low	High	Low	Low	High
Papp, 2005	Low	Low	Low	Low	Low	Low
Papp, 2012	Low	Low	Low	Low	Low	Low
Papp, 2015	Low	Low	Low	Low	Low	Low
Papp, 2015a	Low	Low	Low	Low	Low	Low
PHOENIX 1	Low	Low	Low	Low	Low	Low
PHOENIX 2	Low	Low	Low	Low	Low	Low
PIECE	Low	Low	Low	Low	Low	Low
Reich, 2012	Low	Low	Low	Low	Low	Low
Reich, 2020	Some concerns	Low	Low	Some concerns	Low	Some concerns
RESTORE1	High	High	Low	Low	Low	High
reSURFACE 1	Low	Low	Low	Low	Low	Low
reSURFACE 2	Low	Low	Low	Low	Low	Low
REVEAL	Low	Low	Low	Low	Low	Low
Rich, 2013	Low	Low	Some concerns	Low	Low	Some concerns
SPIRIT	Low	Low	Some concerns	Low	Low	Some concerns

Trial	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
SustalMM	Some concerns	Low	Low	Low	Low	Some concerns
Torii, 2010	Low	Low	Low	Low	Low	Low
TRANSFIGURE	Low	Low	Low	Low	Low	Low
Tyring, 2006	Low	Low	Low	Low	Low	Low
UltiMMA 2	Low	Low	Low	Low	Low	Low
UltiMMA1	Low	Low	Low	Low	Low	Low
UNCOVER 1	Low	Low	Low	Low	Low	Low
UNCOVER 2	Low	Low	Low	Low	Low	Low
UNCOVER 3	Low	Low	Low	Low	Low	Low
UNVEIL	Low	Low	Some concerns	Low	Low	Some concerns
Van de Kerkhof, 2008	Low	Low	Low	Low	Low	Low
VIP	Low	Low	Low	Low	Low	Low
VIP-S	Some concerns	Low	Low	Low	Low	Some concerns
VIP-U	Some concerns	High	High	Low	Low	High
VOYAGE 1	Low	Low	Low	Low	Low	Low
VOYAGE 2	Low	Low	Some concerns	Low	Low	Some concerns
X-PLORE	Some concerns	Low	Some concerns	Low	Low	Some concerns
Yang, 2012	Low	Low	Low	Low	Low	Low

Table S8. Baseline Risk Slopes, Heterogeneity, and Fit Statistics for All Multinomial Ordered Probit Models

Model	β_{BL} (95% CrI)	$\hat{\sigma}_z$ (95% CrI)	$\hat{\tau}$ (95% CrI)	$\bar{D}$*	DIC
REZ, adjusted, fixed-effects model	-0.550 (-0.667, -0.408)	0.111 (0.087, 0.143)	-	840.3	1043.6
REZ, adjusted, random-effects model	-1.001 (-1.051, -0.672)	0.112 (0.088, 0.144)	0.143 (0.102, 0.183)	751.3	1017.5
REZ, unadjusted, fixed-effects model	-	0.113 (0.089, 0.146)	-	810.3	971.4
REZ, unadjusted, random-effects model	-	0.113 (0.089, 0.147)	0.127 (0.080, 0.180)	751.4	982.0
Standard, adjusted, fixed-effects model	-0.572 (-0.684, -0.438)	-	-	1100.0	1244.5
Standard, adjusted, random-effects model	-1.005 (-1.051, -0.719)	-	0.140 (0.103, 0.179)	1009.7	1216.6
Standard, unadjusted, fixed-effects model	-	-	-	1071.8	1185.1
Standard, unadjusted, random-effects model	-	-	0.129 (0.081, 0.184)	1011.6	1201.4

Notations and abbreviations: $\hat{\sigma}_z$, the estimate of σ_z, the between-treatment SD of each of z1, z2, z3 (PASI thresholds); $\hat{\tau}$, the estimate of τ, the between-study standard deviation on the probit differences for the entire network; $\bar{D}$, the mean deviance at residual; DIC, the deviance information criteria at residual.

*The total number of data points was 626 from 169 treatment arms from 71 studies. A treatment arm in a study with PASI 50, PASI 75, PASI 90, PASI 100 data contributes five data points as model needs to be fitted on 0% to <50%, 50% to <75%, 75% to <90%, 90% to <100% and 100% responses.

Abbreviations: CrI = credible interval; DIC = deviance information criteria

Table S9. Probit Probabilities (95% CrI) of Achieving PASI Outcomes Treatments (REZ, Adjusted, Random-effects Multinomial Model)

Treatment	PASI 75	PASI 90	PASI 100
Bimekizumab 320 mg	0.923 [0.893, 0.945]	0.840 [0.796, 0.877]	0.578 [0.514, 0.637]
Risankizumab 150 mg	0.899 [0.869, 0.923]	0.732 [0.684, 0.777]	0.445 [0.389, 0.500]
Ixekizumab 80 mg	0.891 [0.855, 0.918]	0.708 [0.651, 0.759]	0.381 [0.323, 0.441]
Brodalumab 210 mg	0.870 [0.835, 0.901]	0.722 [0.670, 0.773]	0.438 [0.381, 0.499]
Guselkumab 100 mg	0.865 [0.829, 0.896]	0.674 [0.618, 0.724]	0.328 [0.275, 0.383]
Secukinumab 300 mg	0.837 [0.802, 0.870]	0.634 [0.584, 0.685]	0.324 [0.279, 0.375]
Infliximab 5 mg/kg	0.794 [0.747, 0.836]	0.542 [0.483, 0.603]	0.237 [0.161, 0.326]
Certolizumab pegol 400 mg	0.771 [0.709, 0.824]	0.485 [0.412, 0.558]	0.171 [0.119, 0.233]
Ustekinumab 45 or 90 mg	0.713 [0.674, 0.749]	0.452 [0.409, 0.494]	0.178 [0.151, 0.208]
Certolizumab pegol 200 mg	0.711 [0.643, 0.771]	0.417 [0.346, 0.490]	0.142 [0.097, 0.198]
Ustekinumab 90 mg	0.701 [0.604, 0.788]	0.419 [0.321, 0.525]	0.157 [0.088, 0.257]
Adalimumab 40 mg	0.699 [0.660, 0.737]	0.454 [0.410, 0.497]	0.176 [0.148, 0.207]
Secukinumab 150 mg	0.685 [0.626, 0.752]	0.411 [0.350, 0.487]	0.141 [0.106, 0.191]
Tildrakizumab 200 mg	0.668 [0.598, 0.734]	0.398 [0.328, 0.472]	0.147 [0.105, 0.199]
Tildrakizumab 100 mg	0.630 [0.557, 0.698]	0.375 [0.306, 0.448]	0.135 [0.096, 0.183]
Etanercept 50 mg	0.510 [0.472, 0.549]	0.235 [0.205, 0.266]	0.063 [0.048, 0.079]
Cyclosporine 2.5 to 5 mg/kg	0.416 [0.293, 0.548]	0.168 [0.094, 0.272]	0.039 [0.014, 0.089]
Etanercept 25 mg	0.377 [0.317, 0.438]	0.139 [0.104, 0.181]	0.030 [0.015, 0.055]
Dimethyl fumarate up to 720 mg	0.366 [0.250, 0.496]	0.170 [0.098, 0.270]	0.040 [0.015, 0.090]
Methotrexate 7.5 to 25 mg	0.360 [0.285, 0.441]	0.154 [0.107, 0.212]	0.044 [0.024, 0.077]
Apremilast 30 mg	0.306 [0.258, 0.361]	0.104 [0.076, 0.139]	0.020 [0.010, 0.036]
Acitretin 0.4 mg/kg/day	0.227 [0.110, 0.390]	0.077 [0.025, 0.184]	0.013 [0.003, 0.049]
Placebo	0.057 [0.044, 0.073]	0.018 [0.012, 0.024]	0.003 [0.002, 0.005]

Treatments are sorted by the highest to lowest probabilities of reaching PASI 75. Green = highest probability in each category.
Abbreviation: CrI = credible interval; PASI = Psoriasis Area and Severity Index

Table S10. Number Needed to Treat (95% CrI) for Treatments versus Placebo for Achieving PASI Outcomes (REZ, Adjusted, Random-effects Multinomial Model)

Treatment	PASI 75	PASI 90	PASI 100
Bimekizumab 320 mg	1.16 (1.12, 1.20)	1.22 (1.16, 1.29)	1.74 (1.58, 1.96)
Risankizumab 150 mg	1.19 (1.15, 1.24)	1.40 (1.32, 1.50)	2.26 (2.01, 2.59)
Ixekizumab 80 mg	1.20 (1.16, 1.26)	1.45 (1.35, 1.58)	2.65 (2.28, 3.13)
Brodalumab 210 mg	1.23 (1.18, 1.29)	1.42 (1.32, 1.53)	2.30 (2.02, 2.65)
Guselkumab 100 mg	1.24 (1.19, 1.30)	1.52 (1.42, 1.67)	3.08 (2.63, 3.67)
Secukinumab 300 mg	1.28 (1.23, 1.35)	1.62 (1.50, 1.77)	3.11 (2.69, 3.63)
Infliximab 5 mg/kg	1.36 (1.28, 1.46)	1.91 (1.71, 2.15)	4.27 (3.10, 6.33)
Certolizumab pegol 400 mg	1.40 (1.30, 1.54)	2.14 (1.85, 2.53)	5.98 (4.36, 8.63)
Ustekinumab 45 or 90 mg	1.52 (1.44, 1.63)	2.30 (2.10, 2.56)	5.72 (4.88, 6.79)
Certolizumab pegol 200 mg	1.53 (1.40, 1.71)	2.50 (2.12, 3.04)	7.19 (5.12, 10.60)
Ustekinumab 90 mg	1.55 (1.37, 1.84)	2.49 (1.97, 3.30)	6.48 (3.94, 11.80)
Adalimumab 40 mg	1.56 (1.47, 1.67)	2.29 (2.08, 2.55)	5.78 (4.90, 6.92)
Secukinumab 150 mg	1.59 (1.44, 1.77)	2.54 (2.13, 3.01)	7.24 (5.34, 9.72)
Tildrakizumab 200 mg	1.64 (1.47, 1.86)	2.63 (2.20, 3.22)	6.96 (5.09, 9.78)
Tildrakizumab 100 mg	1.75 (1.56, 2.00)	2.80 (2.33, 3.47)	7.61 (5.55, 10.80)
Etanercept 50 mg	2.21 (2.04, 2.43)	4.61 (4.03, 5.35)	16.77 (13.10, 22.11)
Cyclosporine 2.5 to 5 mg/kg	2.79 (2.04, 4.26)	6.64 (3.92, 13.24)	27.83 (11.64, 91.26)
Etanercept 25 mg	3.13 (2.62, 3.89)	8.26 (6.13, 11.69)	37.62 (19.18, 87.24)
Dimethyl fumarate up to 720 mg	3.25 (2.28, 5.24)	6.58 (3.96, 12.46)	27.45 (11.58, 82.08)
Methotrexate 7.5 to 25 mg	3.31 (2.60, 4.42)	7.34 (5.15, 11.18)	24.43 (13.61, 49.04)
Apremilast 30 mg	4.03 (3.29, 5.05)	11.59 (8.24, 17.23)	60.82 (30.35, 157.90)
Acitretin 0.4 mg/kg/day	5.89 (3.01, 19.70)	16.77 (6.00, 140.91)	100.59 (-1094.80, 21.93)

Treatments are sorted by the lowest to highest numbers needed to treat to achieve PASI 75. Green = lowest number to treat in each threshold.

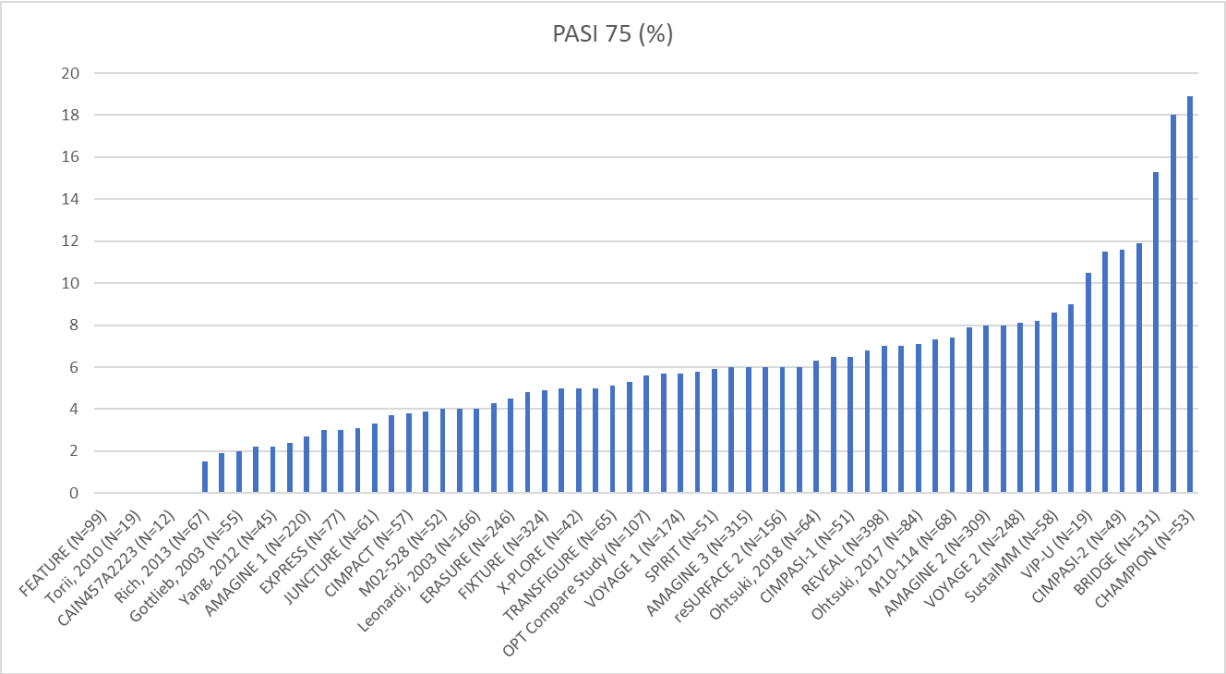
Abbreviations: CrI = credible interval; PASI = Psoriasis Area and Severity Index; REZ = random effects model combined with the parameter z

Table S11. Probit Probabilities (95% CrI) of Achieving PASI Outcomes (REZ, Unadjusted, Fixed-effects Multinomial Model)

Treatment	PASI 75	PASI 90	PASI 100
Bimekizumab 320 mg	0.925 [0.897, 0.948]	0.845 [0.802, 0.883]	0.586 [0.522, 0.648]
Ixekizumab 80 mg	0.917 [0.888, 0.939]	0.758 [0.707, 0.804]	0.441 [0.380, 0.503]
Risankizumab 150 mg	0.903 [0.870, 0.929]	0.740 [0.683, 0.791]	0.454 [0.391, 0.519]
Secukinumab 300 mg	0.875 [0.842, 0.902]	0.695 [0.644, 0.743]	0.386 [0.332, 0.441]
Brodalumab 210 mg	0.872 [0.835, 0.903]	0.725 [0.669, 0.776]	0.441 [0.379, 0.503]
Guselkumab 100 mg	0.863 [0.823, 0.895]	0.669 [0.610, 0.724]	0.325 [0.269, 0.384]
Infliximab 5 mg/kg	0.821 [0.766, 0.867]	0.581 [0.507, 0.655]	0.269 [0.182, 0.373]
Secukinumab 150 mg	0.783 [0.731, 0.830]	0.527 [0.461, 0.592]	0.214 [0.166, 0.269]
Certolizumab pegol 400 mg	0.775 [0.703, 0.836]	0.490 [0.404, 0.576]	0.170 [0.114, 0.240]
Ustekinumab 45 or 90 mg	0.749 [0.702, 0.792]	0.495 [0.440, 0.550]	0.207 [0.170, 0.250]
Ustekinumab 90 mg	0.740 [0.664, 0.807]	0.465 [0.380, 0.552]	0.186 [0.113, 0.282]
Certolizumab pegol 200 mg	0.714 [0.635, 0.784]	0.420 [0.338, 0.506]	0.143 [0.093, 0.208]
Adalimumab 40 mg	0.702 [0.648, 0.750]	0.455 [0.396, 0.513]	0.176 [0.140, 0.218]
Tildrakizumab 200 mg	0.695 [0.624, 0.760]	0.427 [0.354, 0.505]	0.165 [0.118, 0.221]
Tildrakizumab 100 mg	0.670 [0.597, 0.737]	0.416 [0.343, 0.493]	0.160 [0.115, 0.216]
Etanercept 50 mg	0.554 [0.501, 0.607]	0.270 [0.227, 0.317]	0.078 [0.058, 0.104]
Etanercept 25 mg	0.408 [0.342, 0.476]	0.156 [0.116, 0.205]	0.035 [0.017, 0.065]
Placebo	0.062 [0.049, 0.078]	0.020 [0.014, 0.027]	0.004 [0.002, 0.006]

Treatments are sorted by the highest to lowest probabilities of reaching PASI 75.
Green = highest probability in each category.
Abbreviation: CrI = credible interval; NMA = network meta-analysis; PASI = Psoriasis Area and Severity Index; REZ = random effects model combined with the parameter z

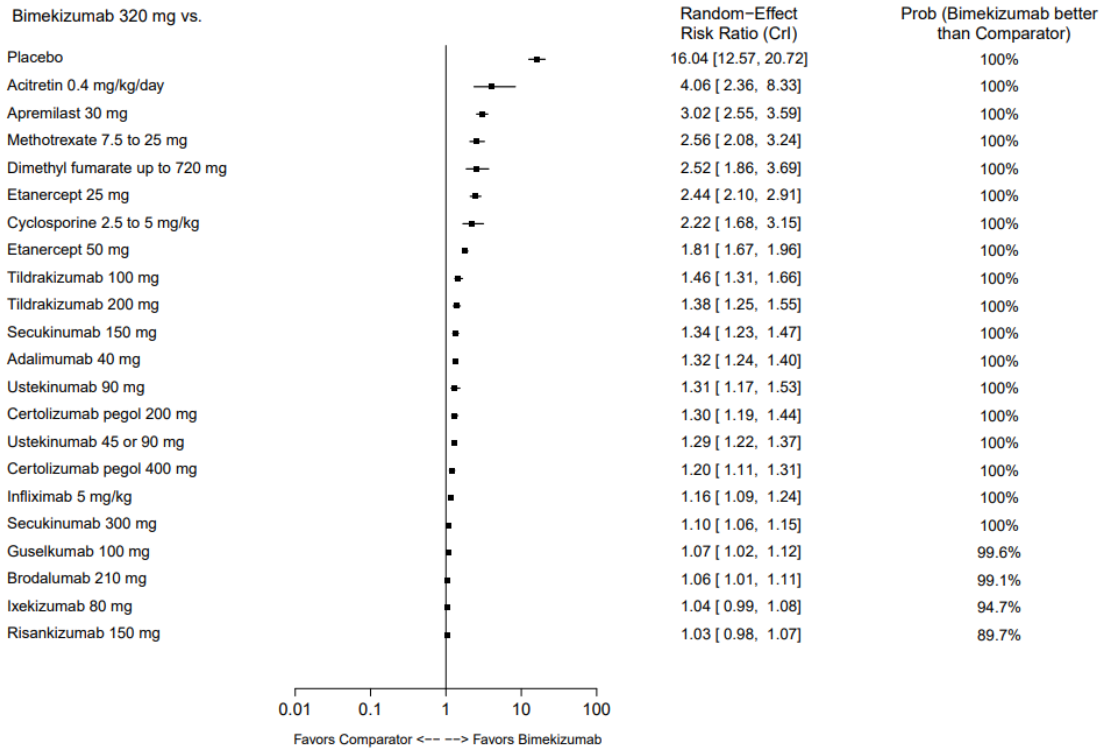
Figure S1. 10–16-week Response Rate (%) Using the PASI 75 in Placebo Group by Trial



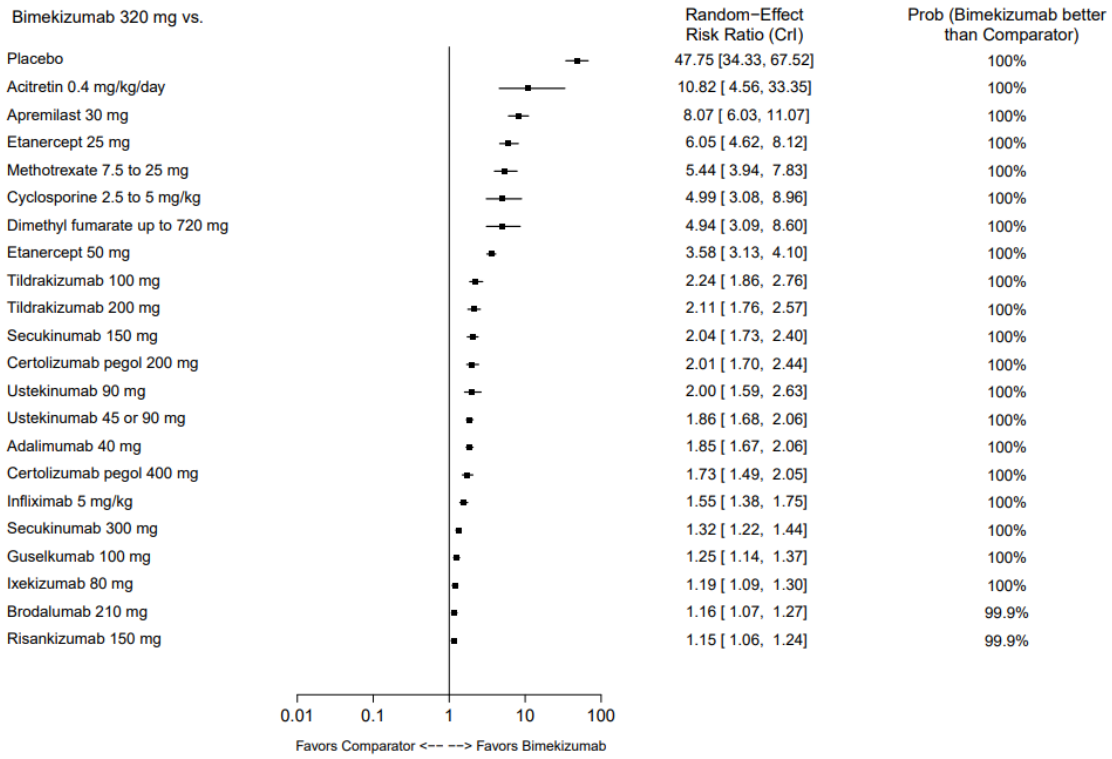
Note: None of the patients who were randomised to the placebo arm in the FEATURE, Torii 2020, and CAIN457A2223 trials achieved PASI 75 response. Sixty-five trials were included in this figure.
Abbreviation: PASI = Psoriasis Area and Severity Index

Figure S2. Risk Ratios of Achieving (a) PASI 75, (b) PASI 90 and (c) PASI 100 across Biologic and Non-biologic Treatments (REZ, Adjusted, Random-effects Multinomial model)

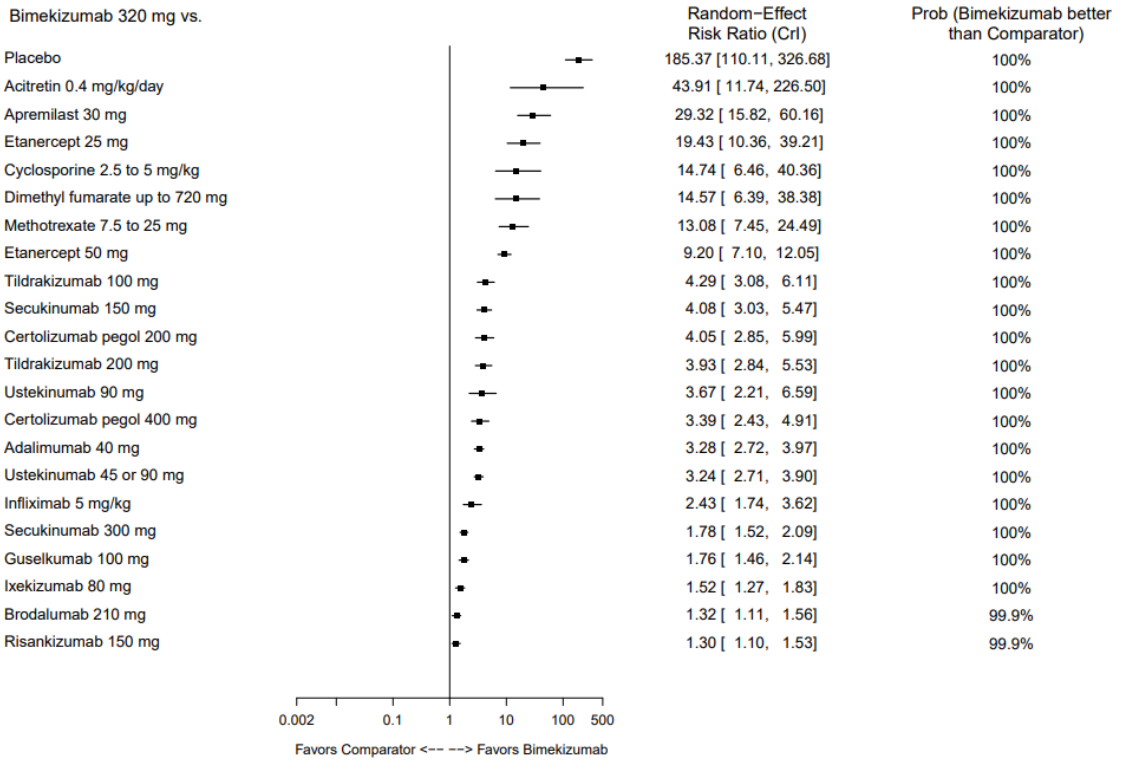
(a)



(b)


Bimekizumab 320 mg vs.
Random−Effect Risk Ratio (CrI)
Prob (Bimekizumab better than Comparator)
Placebo 47.75 [34.33, 67.52] 100%
Acitretin 0.4 mg/kg/day 10.82 [4.56, 33.35] 100%
Apremilast 30 mg 8.07 [6.03, 11.07] 100%
Etanercept 25 mg 6.05 [4.62, 8.12] 100%
Methotrexate 7.5 to 25 mg 5.44 [3.94, 7.83] 100%
Cyclosporine 2.5 to 5 mg/kg 4.99 [3.08, 8.96] 100%
Dimethyl fumarate up to 720 mg 4.94 [3.09, 8.60] 100%
Etanercept 50 mg 3.58 [3.13, 4.10] 100%
Tildrakizumab 100 mg 2.24 [1.86, 2.76] 100%
Tildrakizumab 200 mg 2.11 [1.76, 2.57] 100%
Secukinumab 150 mg 2.04 [1.73, 2.40] 100%
Certolizumab pegol 200 mg 2.01 [1.70, 2.44] 100%
Ustekinumab 90 mg 2.00 [1.59, 2.63] 100%
Ustekinumab 45 or 90 mg 1.86 [1.68, 2.06] 100%
Adalimumab 40 mg 1.85 [1.67, 2.06] 100%
Certolizumab pegol 400 mg 1.73 [1.49, 2.05] 100%
Infliximab 5 mg/kg 1.55 [1.38, 1.75] 100%
Secukinumab 300 mg 1.32 [1.22, 1.44] 100%
Guselkumab 100 mg 1.25 [1.14, 1.37] 100%
Ixekizumab 80 mg 1.19 [1.09, 1.30] 100%
Brodalumab 210 mg 1.16 [1.07, 1.27] 99.9%
Risankizumab 150 mg 1.15 [1.06, 1.24] 99.9%
0.01
0.1
1
10
100
Favors Comparator <-- --> Favors Bimekizumab

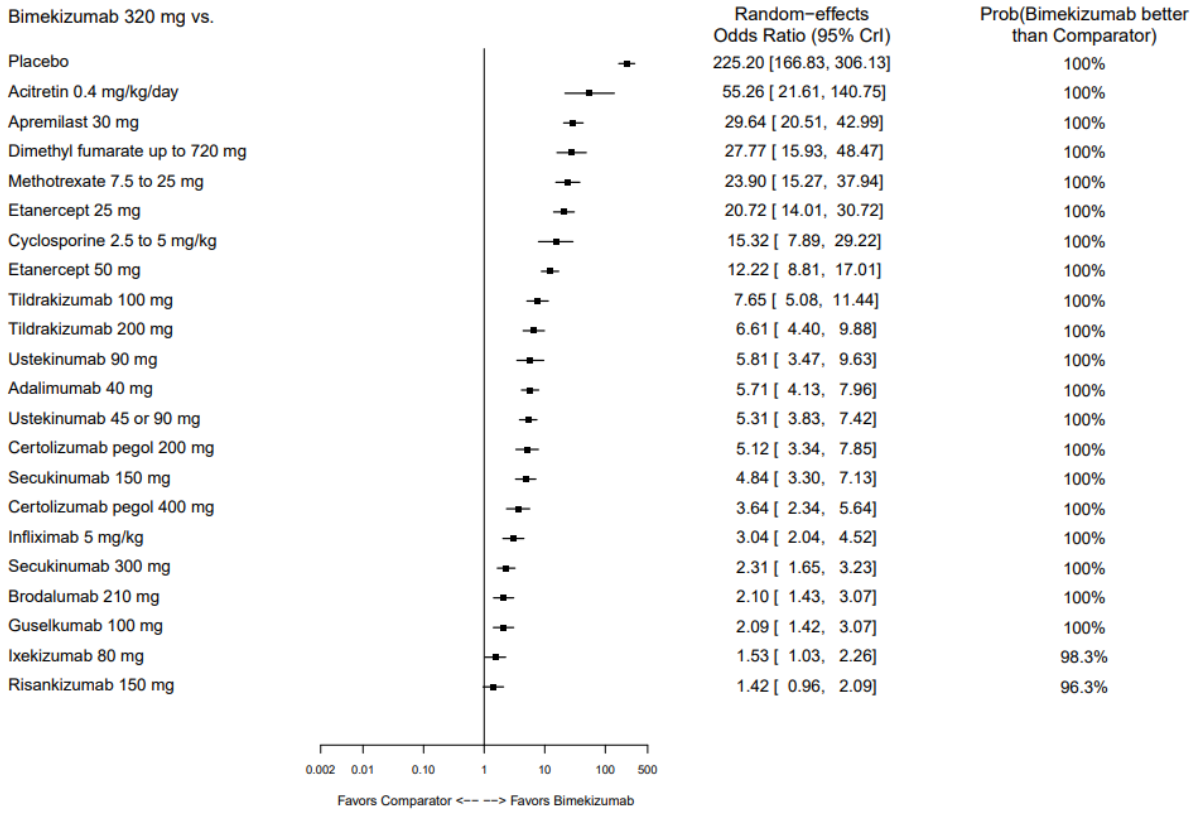
(c)



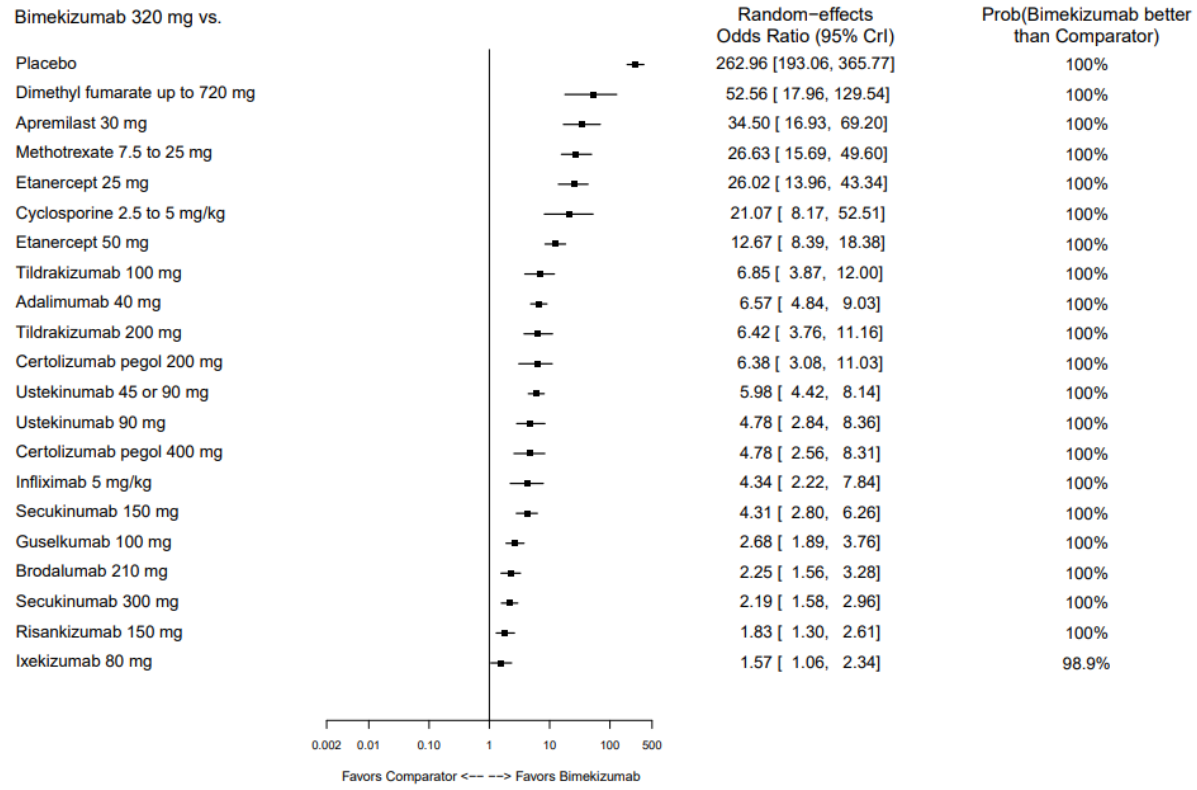
Abbreviations: CrI = credible interval; NMA = network meta-analysis; REZ = random effects model combined with the parameter z

Figure S3. Odds Ratios* of Achieving (a) PASI 75 and (b) PASI 90 across Biologic and Non-biologic Treatments (Random-effects Binomial Model)

(a)



(b)



* The rarity of events and sparseness of reported data precluded running binomial analyses for PASI 100.
Abbreviation: CrI = credible interval

Bibliography

1. Brooks SP, Gelman A. General methods for monitoring convergence of iterative simulations. Journal of Computational and Graphical Statistics. 1998;7(4):434-55.

2. Gilks WR RS, Spiegelhalter D (ed),. Markov Chain Monte Carlo in Practice. US: Chapman & Hall/CRC Interdisciplinary Statistics; 1996.

3. Dias S, Sutton A, Welton N, Ades AE. NICE DSU Technical Support Document 5: Evidence Synthesis in the Baseline Natural History Model 2012 [updated April 2012. Available from: http://nicedsu.org.uk/wp-content/uploads/2016/03/TSD5-Baseline.final-report.08.05.12.pdf.

4. Griffiths CE, Strober BE, van de Kerkhof P, et al. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. N Engl J Med. 2010;362(2):118-28.

5. Papp KA, Reich K, Paul C, et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2016;175(2):273-86.

6. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. New England Journal of Medicine. 2015;373(14):1318-28.

7. Antiga E, Volpi W, Chiarini C, et al. The role of etanercept on the expression of markers of T helper 17 cells and their precursors in skin lesions of patients with psoriasis vulgaris. Int J Immunopathol Pharmacol. 2010;23(3):767-74.

8. Asahina A, Nakagawa H, Etoh T, Ohtsuki M, Adalimumab MSG. Adalimumab in Japanese patients with moderate to severe chronic plaque psoriasis: efficacy and safety results from a Phase II/III randomized controlled study. J Dermatol. 2010;37(4):299-310.

9. Bagel J, Lynde C, Tyring S, Kricorian G, Shi Y, Klekotka P. Moderate to severe plaque psoriasis with scalp involvement: a randomized, double-blind, placebo-controlled study of etanercept. J Am Acad Dermatol. 2012;67(1):86-92.

10. Papp KA, Merola JF, Gottlieb AB, et al. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: Results from BE ABLE 1, a 12-week randomized, double-blinded, placebo-controlled phase 2b trial. J Am Acad Dermatol. 2018;79(2):277-86 e10.

11. Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus Secukinumab in Plaque Psoriasis. N Engl J Med. 2021;385(2):142-52.

12. UCB. Protocol PS0013 Amendment 3: A phase 3, multicenter, double-blind, placebo-controlled study with an initial treatment period followed by a randomizedwithdrawal period to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque psoriasis phase 3. 2019.

13. UCB. Protocol PS0008 Amendment 2: A phase 3, multicenter, randomized, double-blind study with an active-controlled initial treatment period followed by a dose-blind maintenance treatment period to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque psoriasis phase 3. 2018.

14. UCB. Protocol PS0009 Amendment 4: A phase 3, multicenter, randomized, double-blind, placebo- and active comparator-controlled, parallel-group study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque psoriasis phase 3. 2019.

15. Mrowietz U, Szepietowski JC, Loewe R, et al. Efficacy and safety of LAS41008 (dimethyl fumarate) in adults with moderate-to-severe chronic plaque psoriasis: a randomized, double-blind, Fumaderm((R)) - and placebo-controlled trial (BRIDGE). Br J Dermatol. 2017;176(3):615-23.

16. Cai L, Gu J, Zheng J, et al. Efficacy and safety of adalimumab in Chinese patients with moderate-to-severe plaque psoriasis: results from a phase 3, randomized, placebo-controlled, double-blind study. J Eur Acad Dermatol Venereol. 2017;31(1):89-95.

17. Krueger JG, Wharton KA, Jr., Schlitt T, et al. IL-17A inhibition by secukinumab induces early clinical, histopathologic, and molecular resolution of psoriasis. J Allergy Clin Immunol. 2019;144(3):750-63.

18. Caproni M, Antiga E, Melani L, Volpi W, Del Bianco E, Fabbri P. Serum levels of IL-17 and IL-22 are reduced by etanercept, but not by acitretin, in patients with psoriasis: a randomized-controlled trial. J Clin Immunol. 2009;29(2):210-4.

19. von Stebut E, Reich K, Thaci D, et al. Impact of Secukinumab on Endothelial Dysfunction and Other Cardiovascular Disease Parameters in Psoriasis Patients over 52 Weeks. J Invest Dermatol. 2019;139(5):1054-62.

20. Saurat JH, Stingl G, Dubertret L, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol. 2008;158(3):558-66.

21. Mrowietz U, Kragballe K, Reich K, et al. An assessment of adalimumab efficacy in three Phase III clinical trials using the European Consensus Programme criteria for psoriasis treatment goals. Br J Dermatol. 2013;168(2):374-80.

22. Chaudhari U, Romano P, Mulcahy LD, Dooley LT, Baker DG, Gottlieb AB. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial. Lancet. 2001;357(9271):1842-7.

23. Lebwohl M, Blauvelt A, Paul C, et al. Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT). J Am Acad Dermatol. 2018;79(2):266-76 e5.

24. Gottlieb AB, Blauvelt A, Thaci D, et al. Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). J Am Acad Dermatol. 2018;79(2):302-14 e6.

25. Bagel J, Nia J, Hashim PW, et al. Secukinumab is Superior to Ustekinumab in Clearing Skin in Patients with Moderate to Severe Plaque Psoriasis (16-Week CLARITY Results). Dermatol Ther (Heidelb). 2018;8(4):571-9.

26. Thaci D, Blauvelt A, Reich K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. J Am Acad Dermatol. 2015;73(3):400-9.

27. Reich K, Armstrong AW, Langley RG, et al. Guselkumab versus secukinumab for the treatment of moderate-to-severe psoriasis (ECLIPSE): results from a phase 3, randomised controlled trial. Lancet. 2019;394(10201):831-9.

28. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis--results of two phase 3 trials. N Engl J Med. 2014;371(4):326-38.

29. Papp K, Reich K, Leonardi CL, et al. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, in patients with moderate to severe plaque psoriasis: Results of a phase III, randomized, controlled trial (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis [ESTEEM] 1). J Am Acad Dermatol. 2015;73(1):37-49.

30. Paul C, Cather J, Gooderham M, et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate-to-severe plaque psoriasis over 52 weeks: a phase III, randomized controlled trial (ESTEEM 2). Br J Dermatol. 2015;173(6):1387-99.

31. Reich K, Nestle FO, Papp K, et al. Improvement in quality of life with infliximab induction and maintenance therapy in patients with moderate-to-severe psoriasis: a randomized controlled trial. Br J Dermatol. 2006;154(6):1161-8.

32. Menter A, Feldman SR, Weinstein GD, et al. A randomized comparison of continuous vs. intermittent infliximab maintenance regimens over 1 year in the treatment of moderate-to-severe plaque psoriasis. J Am Acad Dermatol. 2007;56(1):31 e1-15.

33. Blauvelt A, Prinz JC, Gottlieb AB, et al. Secukinumab administration by pre-filled syringe: efficacy, safety and usability results from a randomized controlled trial in psoriasis (FEATURE). Br J Dermatol. 2015;172(2):484-93.

34. Gottlieb AB, Blauvelt A, Prinz JC, et al. Secukinumab Self-Administration by Prefilled Syringe Maintains Reduction of Plaque Psoriasis Severity Over 52 Weeks: Results of the FEATURE Trial. J Drugs Dermatol. 2016;15(10):1226-34.

35. Flytstrom I, Stenberg B, Svensson A, Bergbrant IM. Methotrexate vs. ciclosporin in psoriasis: effectiveness, quality of life and safety. A randomized controlled trial. Br J Dermatol. 2008;158(1):116-21.

36. Gisondi P, Del Giglio M, Cotena C, Girolomoni G. Combining etanercept and acitretin in the therapy of chronic plaque psoriasis: a 24-week, randomized, controlled, investigator-blinded pilot trial. Br J Dermatol. 2008;158(6):1345-9.

37. Goldminz AM, Suarez-Farinas M, Wang AC, Dumont N, Krueger JG, Gottlieb AB. CCL20 and IL22 Messenger RNA Expression After Adalimumab vs Methotrexate Treatment of Psoriasis: A Randomized Clinical Trial. JAMA Dermatol. 2015;151(8):837-46.

38. Gottlieb AB, Matheson RT, Lowe N, et al. A randomized trial of etanercept as monotherapy for psoriasis. Arch Dermatol. 2003;139(12):1627-32; discussion 32.

39. Heydendael VM, Spuls PI, Opmeer BC, et al. Methotrexate versus cyclosporine in moderate-to-severe chronic plaque psoriasis. N Engl J Med. 2003;349(7):658-65.

40. Igarashi A, Kato T, Kato M, Song M, Nakagawa H, Japanese Ustekinumab Study G. Efficacy and safety of ustekinumab in Japanese patients with moderate-to-severe plaque-type psoriasis: long-term results from a phase 2/3 clinical trial. J Dermatol. 2012;39(3):242-52.

41. Warren RB, Blauvelt A, Poulin Y, et al. Efficacy and safety of risankizumab vs. secukinumab in patients with moderate-to-severe plaque psoriasis (IMMerge): results from a phase III, randomized, open-label, efficacy-assessor-blinded clinical trial. Br J Dermatol. 2021;184(1):50-9.

42. Blauvelt A, Leonardi CL, Gooderham M, et al. Efficacy and Safety of Continuous Risankizumab Therapy vs Treatment Withdrawal in Patients With Moderate to Severe Plaque Psoriasis: A Phase 3 Randomized Clinical Trial. JAMA Dermatol. 2020;156(6):649-58.

43. Reich K, Gooderham M, Thaci D, et al. Risankizumab compared with adalimumab in patients with moderate-to-severe plaque psoriasis (IMMvent): a randomised, double-blind, active-comparator-controlled phase 3 trial. Lancet. 2019;394(10198):576-86.

44. Reich K, Pinter A, Lacour JP, et al. Comparison of ixekizumab with ustekinumab in moderate-to-severe psoriasis: 24-week results from IXORA-S, a phase III study. Br J Dermatol. 2017;177(4):1014-23.

45. Paul C, Lacour JP, Tedremets L, et al. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). J Eur Acad Dermatol Venereol. 2015;29(6):1082-90.

46. Leonardi CL, Powers JL, Matheson RT, et al. Etanercept as monotherapy in patients with psoriasis. N Engl J Med. 2003;349(21):2014-22.

47. Reich K, Gooderham M, Green L, et al. The efficacy and safety of apremilast, etanercept and placebo in patients with moderate-to-severe plaque psoriasis: 52-week results from a phase IIIb, randomized, placebo-controlled trial (LIBERATE). J Eur Acad Dermatol Venereol. 2017;31(3):507-17.

48. Gordon KB, Langley RG, Leonardi C, et al. Clinical response to adalimumab treatment in patients with moderate to severe psoriasis: double-blind, randomized controlled trial and open-label extension study. J Am Acad Dermatol. 2006;55(4):598-606.

49. Strober BE, Crowley JJ, Yamauchi PS, Olds M, Williams DA. Efficacy and safety results from a phase III, randomized controlled trial comparing the safety and efficacy of briakinumab with etanercept and placebo in patients with moderate to severe chronic plaque psoriasis. Br J Dermatol. 2011;165(3):661-8.

50. Meffert H, Brautigam M, Farber L, Weidinger G. Low-dose (1.25 mg/kg) cyclosporin A: treatment of psoriasis and investigation of the influence on lipid profile. Acta Derm Venereol. 1997;77(2):137-41.

51. Nakagawa H, Niiro H, Ootaki K, Japanese brodalumab study g. Brodalumab, a human anti-interleukin-17-receptor antibody in the treatment of Japanese patients with moderate-to-severe plaque psoriasis: Efficacy and safety results from a phase II randomized controlled study. J Dermatol Sci. 2016;81(1):44-52.

52. Ohtsuki M, Okubo Y, Komine M, et al. Apremilast, an oral phosphodiesterase 4 inhibitor, in the treatment of Japanese patients with moderate to severe plaque psoriasis: Efficacy, safety and tolerability results from a phase 2b randomized controlled trial. J Dermatol. 2017;44(8):873-84.

53. Ohtsuki M, Kubo H, Morishima H, Goto R, Zheng R, Nakagawa H. Guselkumab, an anti-interleukin-23 monoclonal antibody, for the treatment of moderate to severe plaque-type psoriasis in Japanese patients: Efficacy and safety results from a phase 3, randomized, double-blind, placebo-controlled study. J Dermatol. 2018;45(9):1053-62.

54. Bachelez H, van de Kerkhof PC, Strohal R, et al. Tofacitinib versus etanercept or placebo in moderate-to-severe chronic plaque psoriasis: a phase 3 randomised non-inferiority trial. Lancet. 2015;386(9993):552-61.

55. Ferris LK, Ott E, Jiang J, et al. Efficacy and safety of guselkumab, administered with a novel patient-controlled injector (One-Press), for moderate-to-severe psoriasis: results from the phase 3 ORION study. J Dermatolog Treat. 2020;31(2):152-9.

56. Papp KA, Tyring S, Lahfa M, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol. 2005;152(6):1304-12.

57. Papp KA, Leonardi C, Menter A, et al. Brodalumab, an anti–interleukin-17–receptor antibody for psoriasis. New England Journal of Medicine. 2012;366(13):1181-9.

58. Papp K, Menter A, Strober B, et al. Efficacy and safety of brodalumab in subpopulations of patients with difficult-to-treat moderate-to-severe plaque psoriasis. J Am Acad Dermatol. 2015;72(3):436-9 e1.

59. Papp K, Cather JC, Rosoph L, et al. Efficacy of apremilast in the treatment of moderate to severe psoriasis: a randomised controlled trial. Lancet. 2012;380(9843):738-46.

60. Papp K, Thaci D, Reich K, et al. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. Br J Dermatol. 2015;173(4):930-9.

61. Leonardi CL, Kimball AB, Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). Lancet. 2008;371(9625):1665-74.

62. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). Lancet. 2008;371(9625):1675-84.

63. de Vries AC, Thio HB, de Kort WJ, et al. A prospective randomized controlled trial comparing infliximab and etanercept in patients with moderate-to-severe chronic plaque-type psoriasis: the Psoriasis Infliximab vs. Etanercept Comparison Evaluation (PIECE) study. Br J Dermatol. 2017;176(3):624-33.

64. Reich K, Ortonne JP, Gottlieb AB, et al. Successful treatment of moderate to severe plaque psoriasis with the PEGylated Fab' certolizumab pegol: results of a phase II randomized, placebo-controlled trial with a re-treatment extension. Br J Dermatol. 2012;167(1):180-90.

65. Reich K, Augustin M, Thaci D, et al. A 24-week multicentre, randomized, open-label, parallel-group study comparing the efficacy and safety of ixekizumab vs. fumaric acid esters and methotrexate in patients with moderate-to-severe plaque psoriasis naive to systemic treatment. Br J Dermatol. 2020;182(4):869-79.

66. Barker J, Hoffmann M, Wozel G, et al. Efficacy and safety of infliximab vs. methotrexate in patients with moderate-to-severe plaque psoriasis: results of an open-label, active-controlled, randomized trial (RESTORE1). Br J Dermatol. 2011;165(5):1109-17.

67. Reich K, Papp KA, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet. 2017;390(10091):276-88.

68. Menter A, Gordon KB, Leonardi CL, Gu Y, Goldblum OM. Efficacy and safety of adalimumab across subgroups of patients with moderate to severe psoriasis. J Am Acad Dermatol. 2010;63(3):448-56.

69. Menter A, Tyring SK, Gordon K, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. J Am Acad Dermatol. 2008;58(1):106-15.

70. Rich P, Sigurgeirsson B, Thaci D, et al. Secukinumab induction and maintenance therapy in moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled, phase II regimen-finding study. Br J Dermatol. 2013;168(2):402-11.

71. Gottlieb AB, Evans R, Li S, et al. Infliximab induction therapy for patients with severe plaque-type psoriasis: a randomized, double-blind, placebo-controlled trial. J Am Acad Dermatol. 2004;51(4):534-42.

72. Ohtsuki M, Fujita H, Watanabe M, et al. Efficacy and safety of risankizumab in Japanese patients with moderate to severe plaque psoriasis: Results from the SustaIMM phase 2/3 trial. J Dermatol. 2019;46(8):686-94.

73. Torii H, Nakagawa H, Japanese Infliximab Study i. Infliximab monotherapy in Japanese patients with moderate-to-severe plaque psoriasis and psoriatic arthritis. A randomized, double-blind, placebo-controlled multicenter trial. J Dermatol Sci. 2010;59(1):40-9.

74. Reich K, Sullivan J, Arenberger P, et al. Effect of secukinumab on the clinical activity and disease burden of nail psoriasis: 32-week results from the randomized placebo-controlled TRANSFIGURE trial. Br J Dermatol. 2019;181(5):954-66.

75. Tyring S, Gottlieb A, Papp K, et al. Etanercept and clinical outcomes, fatigue, and depression in psoriasis: double-blind placebo-controlled randomised phase III trial. Lancet. 2006;367(9504):29-35.

76. Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. Lancet. 2018;392(10148):650-61.

77. Gordon KB, Blauvelt A, Papp KA, et al. Phase 3 Trials of Ixekizumab in Moderate-to-Severe Plaque Psoriasis. N Engl J Med. 2016;375(4):345-56.

78. Gottlieb AB, Lacour JP, Korman N, et al. Treatment outcomes with ixekizumab in patients with moderate-to-severe psoriasis who have or have not received prior biological therapies: an integrated analysis of two Phase III randomized studies. J Eur Acad Dermatol Venereol. 2017;31(4):679-85.

79. Griffiths CE, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet. 2015;386(9993):541-51.

80. Kemeny L, Berggren L, Dossenbach M, Dutronc Y, Paul C. Efficacy and safety of ixekizumab in patients with plaque psoriasis across different degrees of disease severity: results from UNCOVER-2 and UNCOVER-3. J Dermatolog Treat. 2019;30(1):19-26.

81. Stein Gold L, Bagel J, Lebwohl M, et al. Efficacy and Safety of Apremilast in Systemic- and Biologic-Naive Patients with Moderate Plaque Psoriasis: 52-Week Results of UNVEIL. J Drugs Dermatol. 2018;17(2):221-8.

82. van de Kerkhof PC, Segaert S, Lahfa M, et al. Once weekly administration of etanercept 50 mg is efficacious and well tolerated in patients with moderate-to-severe plaque psoriasis: a randomized controlled trial with open-label extension. Br J Dermatol. 2008;159(5):1177-85.

83. Gelfand J, Joshi A, Shin D, et al. 393 A trial to determine the effect of psoriasis treatment (adalimumab, phototherapy, and placebo) on cardiometabolic disease: The vascular inflammation in psoriasis (VIP) trial. Journal of Investigative Dermatology. 2018;138(5):S67.

84. Gelfand JM, Shin DB, Duffin KC, et al. A Randomized Placebo-Controlled Trial of Secukinumab on Aortic Vascular Inflammation in Moderate-to-Severe Plaque Psoriasis (VIP-S). J Invest Dermatol. 2020;140(9):1784-93 e2.

85. Gelfand JM, Shin DB, Alavi A, et al. A Phase IV, Randomized, Double-Blind, Placebo-Controlled Crossover Study of the Effects of Ustekinumab on Vascular Inflammation in Psoriasis (the VIP-U Trial). J Invest Dermatol. 2020;140(1):85-93 e2.

86. Blauvelt A, Papp KA, Griffiths CE, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol. 2017;76(3):405-17.

87. Reich K, Armstrong AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. J Am Acad Dermatol. 2017;76(3):418-31.

88. Gordon KB, Duffin KC, Bissonnette R, et al. A phase 2 trial of guselkumab versus adalimumab for plaque psoriasis. New England Journal of Medicine. 2015;373(2):136-44.

89. Yang HZ, Wang K, Jin HZ, et al. Infliximab monotherapy for Chinese patients with moderate to severe plaque psoriasis: a randomized, double-blind, placebo-controlled multicenter trial. Chin Med J (Engl). 2012;125(11):1845-51.