

Comparison of infliximab and ustekinumab for the treatment of moderate-to-severe psoriasis: an indirect comparison meta-analysis

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Objectives: As no direct comparisons have been made between infliximab and ustekinumab, the present study's aim was to estimate these drugs' relative efficacy in the treatment of moderate-to-severe psoriasis.

Methods: Eleven randomized controlled trials of infliximab 5 mg/kg and ustekinumab 45 mg or 90 mg, reporting Psoriasis Area and Severity Index (PASI) 75 and PASI 90 end points, were identified from a systematic literature review. Of these, five were excluded because they had inappropriate intervention (n = 1), inappropriate patient population (n = 3), or a small sample size (n = 1). Ultimately, six studies were included in the networks. Log odds ratio (OR) of achieving PASI 75 or PASI 90 was used as the treatment effect in fixed- and random-effects mixed treatment comparison meta-analysis.

Results: Based on the results of the random-effects model, when compared to infliximab 5 mg/kg, the OR of ustekinumab 90 mg and ustekinumab 45 mg achieving a PASI 75 following 12 weeks of treatment was 0.57 CrI (0.19, 1.29) and 0.44 (0.15, 0.99), respectively. Similarly, the odds of achieving PASI 90 was 0.77 (0.09, 2.70) for ustekinumab 90 mg and 0.63 (0.07, 2.20) for ustekinumab 45 mg. Infliximab 5 mg/kg had the highest probability of being the most effective of all treatments considered, in attaining a PASI 75 (92%) and PASI 90 response (76%). Ustekinumab 90 mg had the highest probability of being ranked second in attaining a PASI 75 (84%) and PASI 90 response (62%). Results from the random- and fixed-effects models were consistent.

Conclusion: A greater proportion of patients with plaque psoriasis are expected to achieve a PASI 75 or PASI 90 response when treated with infliximab 5 mg/kg than with ustekinumab 90 mg or 45 mg.

Keywords: TNF inhibitor, Interleukin 12/23 inhibitor, biologic therapy, comparative effectiveness, randomized clinical trial, PASI score

Introduction

Plaque psoriasis is a chronic, inflammatory, autoimmune disorder that is thought to be due to an increased flux of leukocyte, specifically T-cells, to the dermis and epidermis. This influx induces increased cytokine production, altering the epidermal skin-cell cycle, and causing the skin to shed more frequently,¹ resulting in raised patches of dead skin – the psoriatic plaques.^{1,2}

Because of the primary role of T-cells in the pathology of psoriasis, biologic agents have been developed to target these cells and their functions.^{3,4} There are three monoclonal antibodies (adalimumab, infliximab and ustekinumab) and two circulating receptor fusion proteins (alefacept and etanercept) available for the treatment of plaque psoriasis in the United Kingdom and the United States.

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To the authors' knowledge, there have been no randomized controlled trials (RCTs) comparing all available biologic therapies, and the authors have used meta-analytic techniques to estimate the comparative efficacy and safety of these agents.^{5–11} Three meta-analyses^{10–12} did not include ustekinumab and three^{5,6,9} provided results of pairwise comparisons of active treatment with placebo, but did not present a comparative assessment of the efficacy or safety of the biologics. In a published meta-analysis that compared the efficacy of anti-TNFs in 2009, infliximab showed significantly superior efficacy than other anti-TNFs. While in a head to head randomized trial compared to etanercept, ustekinumab achieved better outcomes.¹³ However, a comparison between infliximab and ustekinumab has never been made, and hence there is a lack of knowledge and need for comparison of these two products in the literature. In 2009, the National Institute for Health and Clinical Excellence (NICE)⁷ released a guidance document on the use of ustekinumab in the treatment of moderate-to-severe psoriasis that relied, in part, upon the results of an economic model that utilized data from a mixed treatment comparison of adalimumab, efalizumab, infliximab, and etanercept. However, the meta-analysis was not included in the guidance, and, to our knowledge, is not in the public domain. Recently, Reich et al⁸ used a probit model to estimate the comparative efficacy and probability of response of all biologics approved for the treatment of plaque psoriasis in Europe. With updated clinical trial information and a different method, the objective of this study is to compare the efficacy of infliximab 5 mg/kg, ustekinumab 45 mg, and ustekinumab 90 mg for the treatment of moderate-to-severe psoriasis in adults who have plaque psoriasis and provide an estimate of the efficacy ranking for each comparator by conducting a mixed-treatment comparison (MTC) meta-analysis.

Materials and methods

Systematic literature search

A systematic search of the electronic database PubMed, from database inception to April 5, 2011, was performed to identify evidence for inclusion in the meta-analysis. RCTs that reported the results of head-to-head or placebo-controlled comparisons of infliximab and ustekinumab were eligible for inclusion. Primary end points to measure efficacy of treatments included Psoriasis Area and Severity Index (PASI) 75 and PASI 90, while PASI 50 was not included. Studies must have provided baseline and end point, or baseline and change from baseline data (number or proportion of patients achieving PASI 75 or PASI 90 scores¹⁴) and time of

measurement (ie, weeks from baseline) for each outcome of interest. The search was limited to reports published in the English language (Table 1).

Statistical analyses

To allow synthesis of both direct (head-to-head) and indirect evidence from available RCTs, Bayesian meta-analytic techniques¹⁵ were used to perform an MTC meta-analysis.¹⁶ Outcomes were analyzed as binary data using both fixed-effects and random-effects models.^{15,17} The log odds ratio (OR) was used as the measure of treatment effect. The likelihood of achieving a PASI 75 or PASI 90 response was estimated using the pooled estimate for placebo as the reference treatment.

Models were fitted with Markov chain Monte Carlo (MCMC) techniques using WinBUGS version 1.4.3; MRC Biostatistics Unit, Cambridge, UK.¹⁸ Convergence was measured using the deviance information criterion (DIC), as proposed by Spiegelhalter et al.¹⁹ For analyses that included multi-arm trials, a correlation structure was included in the models. Consistency between indirect and direct evidence was explored by comparing the results of traditional meta-analyses of head-to-head comparisons to those of the network meta-analysis.²⁰ MCMC sampling was used to estimate the probability of a treatment being superior to the others (ranking) using, as a proxy, the proportion of simulations where this situation was true.

Sensitivity analyses were conducted to explore the degree to which base case findings were affected by changes in methods, data from individual studies, or the choice of distributions for the vague priors, and stratifying patients by baseline PASI score.

Statistical heterogeneity was assessed using I^2 , the proportion of total variation in the estimates of treatment effect between studies.²¹ Higher values of I^2 are evidence that a random effects model is preferable to a fixed effects model due to the heterogeneity present.²¹

Table 1 Search strategy

#1	Search "Psoriasis" [Mesh] OR "Arthritis, Psoriatic" [Mesh]	25783
#2	Search infliximab OR mab ca2 OR ustekinumab OR cnto-1275 OR briakinumab	6602
#3	Search (psoriasis [Title]) OR psoriatic arthritis [Title]	16334
#4	Search #1 OR #3	26755
#5	Search #2 AND #4	776
#6	Search #5 limits: randomized controlled trial, English, all adult: 19+ years	34

Note: cnto-1275 is the experimental name for ustekinumab.

Abbreviation: mab ca2, chimeric A2 monoclonal antibody.

Due to the limited number of studies available for each comparison, the assessment of publication bias using funnel plots was not feasible.

Results

Systematic literature review

The literature search identified 34 studies, of which 12 were rejected: five were not RCTs, and seven did not report PASI 75 or PASI 90. Thus, 22 studies were available for potential inclusion in the review. Of those, 16 were excluded because they had an inappropriate outcome measure ($n = 8$); inappropriate study design ($n = 2$); were duplicate studies ($n = 1$); reported an inappropriate intervention ($n = 1$); included an inappropriate patient population ($n = 3$); or had a small sample

size (≤ 10) ($n = 1$) (Figure 1). Thus, six studies,^{22–27} three for infliximab,^{24,25,27} and three for ustekinumab^{22,23,26} (Table 2) were included in the networks (Figure 2).

Patients were between 35 and 46 years of age and there were slightly more males than females. All had plaque psoriasis with just less than 30% body surface area involvement. Disease duration ranged from 17 to 20 years, baseline PASI scores ranged from 19 to 22, and between 22% and 37% of patients had a diagnosis of psoriatic arthritis. All patients had previous exposure to disease-modifying antirheumatic agents, and less than 30% had received biologics at some time prior to study entry. A single study²⁷ reported that approximately 80% of patients had nail psoriasis. Individual study results are provided in Table 3.

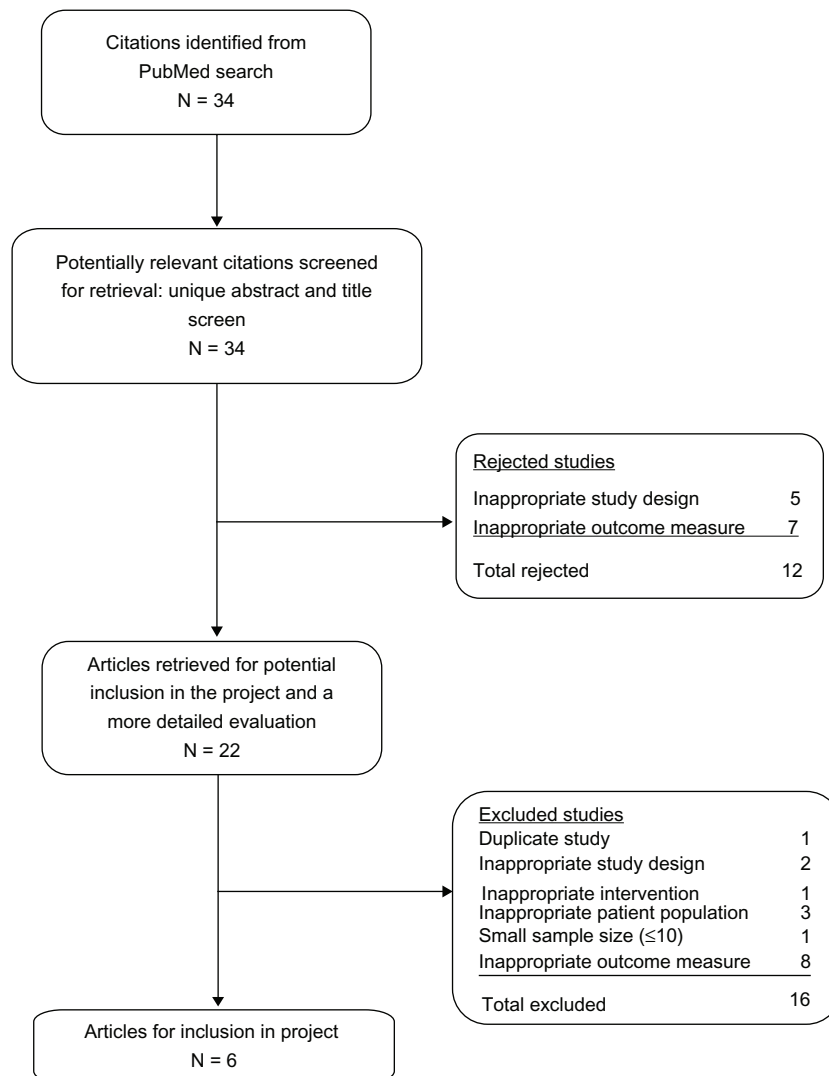


Figure 1 Flow diagram of study selection.

Table 2 Characteristics of studies included in the meta-analysis

Author; study; country	Treatment	N	Male (%)	Mean (SD)	Age (years)	Baseline PASI	Disease duration (years)	BSA (%) involved	Proportion who had taken prior to study entry (%)		Proportion diagnosed (%) ^a
									DMARDs	Biologics	PsA
Papp et al; ²²	UST 45 mg	409	69.2	45.1 (12.1)	19.4 (6.8)	19.3 (11.7)	25.9 (15.5)	54.5	38.4	26.2	NR
PHOENIX 2;	UST 90 mg	411	66.7	46.6 (12.1)	20.1 (7.5)	20.3 (12.3)	27.1 (17.4)	54.5	36.5	22.0	NR
Europe, USA, Canada	PLA	410	69.0	47.0 (12.5)	19.4 (7.5)	20.8 (12.25)	26.1 (17.4)	58.8	38.8	25.6	NR
Leonardi et al; ²³	UST 45 mg	255	68.6	44.8 (12.5)	20.5 (8.6)	19.7 (11.7)	27.2 (17.5)	55.3	52.5	29.0	NR
PHOENIX I;	UST 90 mg	256	67.6	46.2 (11.3)	19.7 (7.6)	19.6 (11.1)	25.2 (15.0)	55.1	50.8	36.7	NR
Belgium, Canada, USA	PLA	255	71.8	44.8 (11.3)	20.4 (8.6)	20.4 (11.7)	27.7 (17.4)	55.7	50.2	35.3	NR
Menter et al; ²⁴	INF 3 mg/kg	313	65.8	43.4 (12.6)	20.1 (7.9)	18.1 (11.8)	28.0 (16.3)	32.6	15.7	27.8	NR
EXPRESS II;	INF 5 mg/kg	314	65.0	44.5 (13.0)	20.4 (7.5)	19.1 (11.7)	28.7 (16.4)	34.7	14.3	28.3	NR
Europe, USA, Canada	PLA	208	69.2	44.4 (12.5)	19.8 (7.7)	17.8 (10.8)	28.4 (17.6)	33.7	13	26.0	NR
Gottlieb et al; ²⁵	INF 3 mg/kg	99	70.7	Median: 45	Median: 20	Median: 18	Median: 29	86.9	32.3	32.3	NR
USA	INF 5 mg/kg	99	73.7	Median: 44	Median: 20	Median: 16	Median: 25	88.9	33.3	29.3	NR
	PLA	51	60.8	Median: 45	Median: 18	Median: 16	Median: 26	82.4	31.4	33.3	NR
Griffiths et al; ²⁶	ETA 50 mg	347	70.9	45.7 (13.4)	18.6 (6.2)	18.8 (12.1)	23.8 (13.9)	57.3	11.8	27.4	NR
ACCEPT;	UST 45 mg	209	63.6	45.1 (12.6)	20.5 (9.2)	18.9 (11.8)	26.7 (17.8)	61.7	12.4	29.7	NR
Europe, USA, Canada	UST 90 mg	347	67.4	44.8 (12.3)	19.9 (8.4)	18.7 (11.8)	26.1 (17.6)	52.4	10.4	27.4	NR
Reich et al; ²⁷	INF 5 mg/kg	301	69.0	42.6 (11.7)	22.9 (9.3)	19.1 (11.0)	≥ 10.0	75.0 ^b	NR	31.0	81.0
Europe Canada	PLA	77	79.0	43.8 (12.6)	22.8 (8.7)	17.3 (11.1)	≥ 10.0	67.0 ^b	NR	29.0	86.0

Notes: ^a100% of the patients had plaque psoriasis; ^bcalculated by adding proportions for methotrexate and ciclosporin.

Abbreviations: BSA, body surface area; DMARDs, disease-modifying antirheumatic agents; ETA, etanercept; INF, infliximab; MTX, methotrexate; NPs, nail psoriasis; NR, not reported; NSAIDs, nonsteroidal anti-inflammatory drugs; PASI, Psoriasis Area and Severity Index; PLA, placebo; Ps, psoriasis; PsA, psoriatic arthritis; SD, standard deviation; UST, ustekinumab.

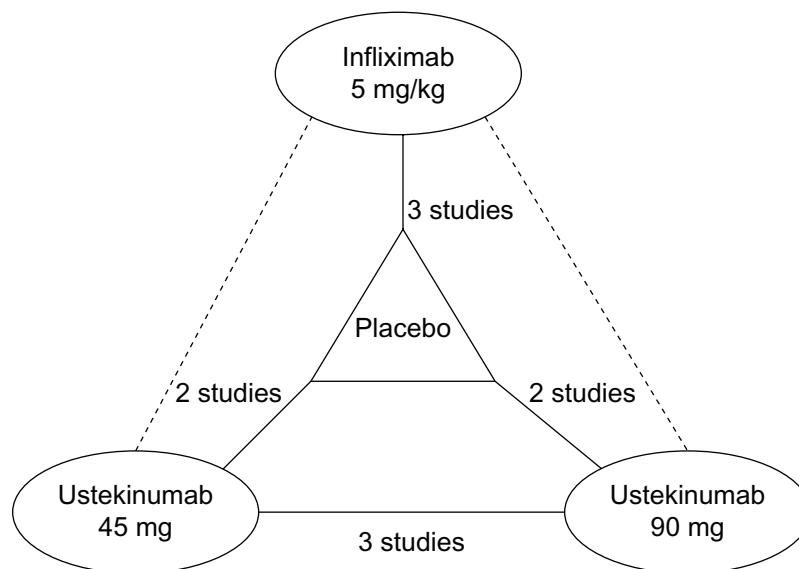


Figure 2 Network for comparison of selected biologics for the treatment of plaque psoriasis.

Note: Solid lines represent direct comparisons (ie, randomized controlled trial evidence), while dashed lines represent indirect comparisons (ie, generated by the model).

Network meta-analysis

PASI 75: pooled estimates of treatment effect

Infliximab 5 mg/kg and ustekinumab 45 mg and 90 mg were statistically significantly more effective than placebo in attaining a PASI 75 response when used for the treatment of plaque psoriasis. Results from the fixed- and random-effects models suggest that there is a statistically significant difference between infliximab 5 mg/kg and ustekinumab 45 mg (OR = 0.42; 95% credible interval [CrI]: 0.16, 0.87) and (OR = 0.44; 95% CrI: 0.15, 0.99, respectively). The comparison between infliximab 5 mg/kg and ustekinumab 90 mg did not, however, reach statistical significance in either model (OR = 0.54; 95% CrI: 0.21, 1.13 for the fixed-effects model and OR = 0.57;

95% CrI: 0.19, 1.29 for the random-effects model). Ustekinumab 90 mg was statistically significantly more effective than ustekinumab 45 mg in attaining a PASI 75 response in the fixed-effects model (OR = 1.31; 95% CrI: 1.07, 1.59), though this result was not reflected in the random-effects model (Table 4).

Of all treatments considered, infliximab 5 mg/kg had the greatest probability (95% in the fixed-effects model, and 92% in the random-effects model) of ranking as the most effective treatment for attaining a PASI 75. Ustekinumab 90 mg ranked second (95% in the fixed-effects model and 84% in the random-effects model), and ustekinumab 45 mg ranked third (99% in the fixed-effects model and 89% in the random-effects model). Placebo were the least

Table 3 Efficacy results of studies included in the meta-analysis

Study details		Proportion of patients achieving							
Author; year; trial	Time for endpoint measurement (weeks)	PASI 75				PASI 90			
		PLA	INF 5 mg/kg	UST 45 mg	UST 90 mg	PLA	INF 5 mg/kg	UST 45 mg	UST 90 mg
Papp et al; ²² 2008; PHOENIX 2	12	15/410		273/409	311/411	3/410		173/409	209/411
Leonardi et al; ²³ 2008; PHOENIX I	12	8/255		171/255	170/256	5/255		106/255	94/256
Menter et al; ²⁴ 2007; EXPRESS II	10	4/208	237/314			1/208	142/314		
Gottlieb et al; ²⁵ 2004	10	3/51	86/99			1/51	57/99		
Griffiths et al; ²⁶ 2010; ACCEPT	12			141/209	256/347			76/209	155/347
Reich et al; ²⁷ 2005	10	2/77	241/301			1/77	172/301		

Abbreviations: INF, infliximab; PASI, Psoriasis Area and Severity Index; PLA, placebo; UST, ustekinumab.

Table 4 Likelihood of achieving the desired outcome, by treatment comparison

Intervention	Odds ratio (95% CrI ^a) for achieving PASI 75 or PASI 90			
	Placebo	Infliximab 5 mg/kg	Ustekinumab 45 mg	Ustekinumab 90 mg
PASI 75 fixed-effects model				
Placebo	1			
Infliximab 5 mg	164.40 (78.35, 330.10)	1		
Ustekinumab 45 mg	59.76 (37.89, 92.25)	0.42 (0.16, 0.87)	1	
Ustekinumab 90 mg	77.89 (49.34, 121.10)	0.54 (0.21, 1.13)	1.31 (1.07, 1.59)	1
PASI 75 random-effects model				
Placebo	1			
Infliximab 5 mg	164.60 (71.35, 339.10)	1		
Ustekinumab 45 mg	61.2 (32.33, 107.00)	0.44 (0.15, 0.99)	1	
Ustekinumab 90 mg	78.96 (41.98, 136.90)	0.57 (0.19, 1.29)	1.33 (0.79, 2.10)	1
PASI 90 fixed-effects model				
Placebo	1			
Infliximab 5 mg	172.60 (46.69, 525.20)	1		
Ustekinumab 45 mg	65.45 (32.10, 127.80)	0.56 (0.10, 1.63)	1	
Ustekinumab 90 mg	79.61 (39.24, 155.20)	0.69 (0.12, 2.00)	1.22 (1.01, 1.47)	1
PASI 90 random-effects model				
Placebo	1			
Infliximab 5 mg	192.10 (41.62, 676.70)	1		
Ustekinumab 45 mg	69.93 (22.79, 167.40)	0.63 (0.07, 2.20)	1	
Ustekinumab 90 mg	85.79 (27.76, 208.30)	0.77 (0.09, 2.70)	1.35 (0.52, 2.93)	1

Notes: Comparison is for rows versus columns, eg, a greater proportion of patients will achieve PASI 75 with infliximab 5 mg/kg (row 2) than with placebo (column 1).
^aCrIs are analogous to confidence intervals in frequentist statistics.

Abbreviations: CrI, credible interval; PASI, psoriasis area and severity index.

effective, in both random- and fixed-effects models (Table 5; Figure 3).

PASI 90: pooled estimates of treatment effect

Results from both the fixed- and random-effects models showed no statistically significant difference between infliximab 5 mg/kg and either of the two ustekinumab doses for the attainment of a PASI 90 response (OR = 0.56; 95% CrI: 0.10, 1.63 and OR = 0.63; 95% CrI: 0.07, 2.20, respectively, for infliximab 5 mg/kg versus ustekinumab 45 mg, and OR = 0.69; 95% CrI: 0.12, 2.00 and OR = 0.77; 95% CrI: 0.09, 2.70, respectively, for infliximab 5 mg/kg versus ustekinumab 90 mg). Consistent with the PASI 75 results, ustekinumab 90 mg was statistically significantly more effective than ustekinumab 45 mg in attaining a PASI 90 response in the fixed-effects model (OR = 1.22; 95% CrI: 1.01, 1.47), but not the random-effects model; however, it is unlikely that this difference is clinically significant (Table 4).

Infliximab 5 mg/kg had a probability of 80% in the fixed-effect model and 76% in the random-effects model of being the most effective treatment in attaining a PASI 90 response. Ustekinumab 90 mg had a probability of 79% and 62% of being ranked second in the fixed- and random-effects models, respectively. Finally, ustekinumab 45 mg had probabilities of 86% and 67% of being ranked third in

the fixed- and random-effects models, respectively (Table 5; Figure 3).

Consistency and comparisons between models

Results of the MTC MAs were consistent with those derived from traditional meta-analyses of infliximab versus placebo, ustekinumab 45 mg versus placebo, and ustekinumab 90 mg versus placebo, for both PASI 75 and PASI 90 measurements (Tables S1–S4).

A comparison of the results of MTC meta-analyses run with and without the correlation structure showed no appreciable differences (Table S5).

DICs for the fixed- and random-effects models were comparable. For PASI 75, the DIC for the fixed-effects model was 91.089 compared to 91.744 for the random-effects models. The residual deviance values were 13.05 and 11.78, respectively. For PASI 90, the DIC was 94.692 and 92.052 for fixed- and random-effects models, respectively, and residual deviance values were 19.27 and 14.05, respectively.

Sensitivity analyses

Sensitivity analyses explored the use of uniform, logistic, and double exponential distributions as priors. Sensitivity analyses results were consistent with those of the base case estimates. Due to the limited number of studies, a sensitivity

Table 5 Ranking of interventions: probability of efficacy, by PASI

Rank	Expected efficacy rankings			
	Infliximab	Ustekinumab		Placebo
	5 mg/kg	90 mg	45 mg	
PASI 75 fixed-effects model				
1	0.95	0.05	0	0
2	0.04	0.95	0.01	0
3	0.01	0	0.99	0
4	0	0	0	1
PASI 75 random-effects model				
1	0.92	0.07	0.01	0
2	0.06	0.84	0.1	0
3	0.02	0.09	0.89	0
4	0	0	0	1
PASI 90 fixed-effects model				
1	0.8	0.2	0	0
2	0.07	0.79	0.14	0
3	0.13	0.02	0.86	0
4	0	0	0	1
PASI 90 random-effects model				
1	0.76	0.19	0.05	0
2	0.11	0.62	0.27	0
3	0.14	0.19	0.67	0
4	0	0	0	1

Abbreviation: PASI, psoriasis area and severity index.

analysis to examine the effect of stratification of studies by mean baseline PASI score was not feasible.

Heterogeneity

Notable heterogeneity was observed for comparisons of placebo and either dose of ustekinumab for the PASI 90, and for comparisons between the ustekinumab dosages for both PASI 75 and PASI 90 ($I^2 > 46\%$). Infliximab shows consistent treatment effects across studies for both the PASI 75 and PASI 90.

Discussion

The results of this MTC meta-analysis suggest that infliximab 5 mg/kg is likely to be more effective in attaining a PASI response than ustekinumab 90 mg or 45 mg in the treatment of moderate-to-severe psoriasis. Results from the fixed- and random-effects models found that infliximab had the greatest probability (92% and 95%, respectively) of ranking as the most effective treatment for attaining a PASI 75. Ustekinumab 90 mg had a probability of 95% and 84%, respectively, of ranking second, and ustekinumab 45 mg ranked third (99%

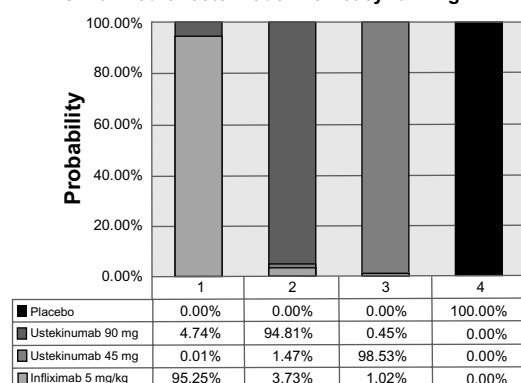
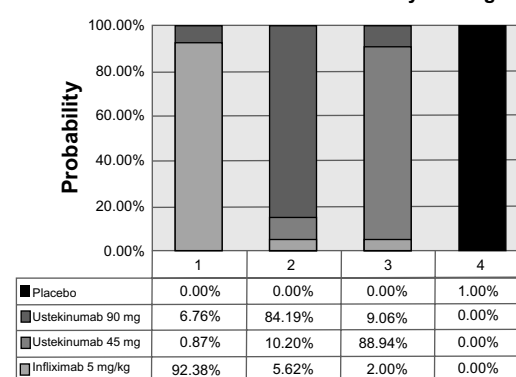
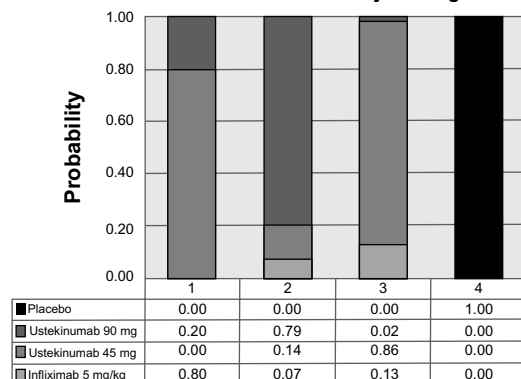
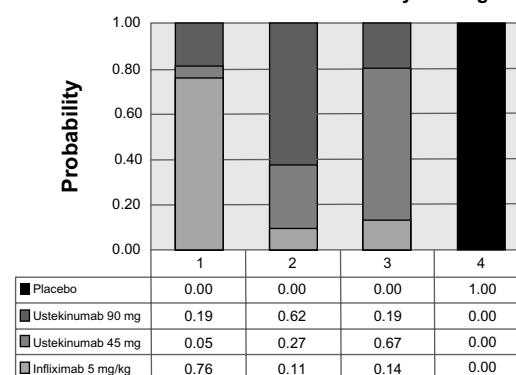
A: PASI 75 fixed-effects model – efficacy ranking**B: PASI 75 random-effects model – efficacy ranking****C: PASI 90 fixed-effects model – efficacy ranking****D: PASI 90 random-effects model – efficacy ranking**

Figure 3 Probabilities of treatment rankings: efficacy according to PASI response. Efficacy rankings of (A) PASI 75 fixed-effects model; (B) PASI 75 random-effects model; (C) PASI 90 fixed-effects model; and (D) PASI 90 random-effects model - efficacy ranking.

Abbreviation: PASI, psoriasis area and severity index.

and 89%, respectively). This result is similar to that of other published analyses that have included ustekinumab.^{7,8}

Reich et al⁸ estimated that infliximab had a probability of 93% being the most efficacious treatment in attaining a PASI 75; ustekinumab 90 mg a probability of 81% of ranking second; and ustekinumab 45 mg a probability of 79% of ranking third. In addition, they estimated that infliximab 5 mg/kg had the highest probability of achieving a PASI 50 (93%), PASI 75 (80%), and PASI 90 (55%) response, followed by ustekinumab 90 mg, ustekinumab 45 mg, adalimumab, etanercept, and efalizumab.

Overall, traditional and MTC meta-analytic estimates suggest that infliximab is likely to be the most efficacious of all the biologics for the treatment of psoriasis. These results, consistent with previous analyses, reinforced the efficacy of infliximab in psoriasis management. It is also confirmed that, although ustekinumab demonstrated statistically significant better outcomes than etanercept in one randomized clinical trial, this conclusion cannot be extended to the entire anti-TNF class. In addition, the ranking of the efficacy of all biologic therapies in psoriasis management will inform clinicians and policy makers about treatment and formulary decisions.

The main limitation of our MTC meta-analysis is the small number of RCTs available for inclusion in the networks. Thus, all estimates have wide confidence and credible intervals. However, analyses were based on the results of a systematic literature review, and it is unlikely that additional evidence on those comparators was available at the time of the search.

A search of the registry at ClinicalTrials.gov (<http://clinicaltrials.gov/>) revealed that additional data is likely to be available in the future. As more research data becomes available on the efficacy of infliximab and ustekinumab, updated MTCs will produce more precise estimates. More precise estimates may also be possible if the networks are expanded by including other biologic treatments.

A second limitation is that there was no attempt to locate data from unpublished studies. Research with statistically significant results is more likely to be published than work with null or nonsignificant results (publication bias), which may lead to overly optimistic and incorrect results.¹⁶

Third, RCTs included in the analyses reported outcomes at 10–12 weeks of therapy, and long-term outcomes were not available. This may be important, as plaque psoriasis is a chronic condition and biologics are likely to be prescribed on an ongoing basis. Notably, Reich et al¹² have reported that

significant differences between biological treatments appear to be attenuated at 24 weeks' postinitiation of therapy.

Finally, the prescribing label of ustekinumab stipulates that patients weighing over 100 kg will be treated with 90 mg therapy, while patients under 100 kg of weight will take 45 mg.²⁸ In the clinical trials of ustekinumab,^{29,30,31} however, the weight-based analyses were not reported, and it is therefore not possible to derive the results for the 45 mg and 90 mg ustekinumab for patients group with body weight under 100 kg or over 100 kg.

Conclusion

Based on this meta-analysis, patients with moderate-to-severe plaque psoriasis who are treated with infliximab 5 mg/kg are more likely than those treated with ustekinumab 90 mg and ustekinumab 45 to achieve a PASI 75 or PASI 90 response.

Disclosure

This research was supported by Merck & Co, Inc., Whitehouse Station, NJ, USA. HB, NES, MM declare no conflict of interest. TF and SSS are employees of Merck & Co, Inc.

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Supplementary tables

Table S1 Comparison of MTC MA and traditional MA results for infliximab and ustekinumab relative to placebo (PASI 75, MTC fixed-effects models)

Treatment effect versus placebo	Number of trials	Number of patients	Direct estimates (traditional meta-analyses)	MTC estimates (95% CrI)
Infliximab 5 mg	3	1050	143.86 (70.57, 293.27)	164.4 (78.35, 330.1)
Ustekinumab 45 mg	2	1916	56.32 (36.04, 87.99)	59.76 (37.89, 92.25)
Ustekinumab 90 mg	2	1679	73.04 (46.49, 114.77)	77.89 (49.34, 121.1)

Abbreviations: CrI, credible interval; MA, meta-analysis; MTC, mixed-treatment comparison; PASI, psoriasis area and severity index.

Table S2 Comparison of results from the traditional and MTC meta-analyses for infliximab and ustekinumab relative to placebo (PASI 75, MTC random-effects models)

Treatment effect versus placebo	Number of trials	Number of patients	Direct estimates (traditional meta-analyses)	MTC estimates (95% CrI)
Infliximab 5 mg	3	1050	138.68 (68.76, 279.68)	164.6 (71.35, 339.1)
Ustekinumab 45 mg	2	1916	56.20 (35.96, 87.81)	61.2 (32.33, 107)
Ustekinumab 90 mg	2	1679	73.67 (46.97, 115.56)	78.96 (41.98, 136.9)

Abbreviations: CrI, credible interval; MTC, mixed-treatment comparison; PASI, psoriasis area and severity index.

Table S3 Comparison of results from the traditional and MTC meta-analyses for infliximab and ustekinumab relative to placebo (PASI 90, MTC fixed-effects models)

Treatment effect versus placebo	Number of trials	Number of patients	Direct estimates (traditional meta-analyses)	MTC estimates (95% CrI)
Infliximab 5 mg	3	672	115.58 (36.36, 367.40)	172.6 (46.69, 525.2)
Ustekinumab 45 mg	2	1916	59.32 (29.04, 121.16)	65.45 (32.1, 127.8)
Ustekinumab 90 mg	2	1679	64.39 (31.88, 130.06)	79.61 (39.24, 155.2)

Abbreviations: CrI, credible interval; MTC, mixed-treatment comparison; PASI, psoriasis area and severity index.

Table S4 Comparison of results from the traditional and MTC meta-analyses for infliximab and ustekinumab relative to placebo (PASI 90, MTC random-effects models)

Treatment effect versus placebo	Number of trials	Number of patients	Direct estimates (traditional meta-analyses)	MTC estimates (95% CrI)
Infliximab 5 mg	3	672	106.19 (33.58, 335.76)	192.1 (41.62, 676.7)
Ustekinumab 45 mg	2	1916	56.11 (20.12, 156.48)	69.93 (22.79, 167.4)
Ustekinumab 90 mg	2	1679	61.47 (12.58, 300.28)	85.79 (27.76, 208.3)

Abbreviations: CrI, credible interval; MTC, mixed-treatment comparison; PASI, psoriasis area and severity index.

Table S5 Results of analyses with and without adjustment for correlation (PASI 75)

Comparison	OR (CrI)	
	No correlation	Correlation
Fixed-effects model		
Infliximab 5 mg vs placebo	164.4 (78.35, 330.1)	164.4 (78.35, 330.1)
Ustekinumab 45 mg vs placebo	59.76 (37.89, 92.25)	59.76 (37.89, 92.25)
Ustekinumab 90 mg vs placebo	77.89 (49.34, 121.1)	77.89 (49.34, 121.1)
Ustekinumab 45 mg vs infliximab 5 mg	0.4162 (0.1606, 0.8671)	0.4162 (0.1606, 0.8671)
Ustekinumab 90 mg vs infliximab 5 mg	0.5422 (0.2093, 1.128)	0.5422 (0.2093, 1.128)
Ustekinumab 90 mg vs ustekinumab 45 mg	1.31 (1.067, 1.591)	1.31 (1.067, 1.591)
Random-effects model		
Infliximab 5 mg vs placebo	164.6 (71.35, 339.1)	165 (70.22, 354.8)
Ustekinumab 45 mg vs placebo	61.2 (32.33, 107)	60.88 (32.76, 105.8)
Ustekinumab 90 mg vs placebo	78.96 (41.98, 136.9)	78.68 (42.38, 136.2)
Ustekinumab 45 mg vs infliximab 5 mg	0.4384 (0.1464, 0.9972)	0.4395 (0.1366, 1.019)
Ustekinumab 90 mg vs infliximab 5 mg	0.5659 (0.1874, 1.286)	0.5671 (0.1771, 1.317)
Ustekinumab 90 mg vs ustekinumab 45 mg	1.332 (0.7861, 2.1)	1.336 (0.7873, 2.118)

Abbreviations: CrI, credible interval; OR, odds ratio; PASI, psoriasis area and severity index.

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