

Efficacy of several biological therapies for treating moderate to severe psoriasis: A network meta-analysis

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Abstract. The aim of the present meta-analysis was to systematically assess the efficacy of the various treatments available for moderate to severe psoriasis. PubMed and Embase databases were systematically searched to select relevant studies up to February 2015. Odds ratios (ORs) and their 95% confidence intervals (CIs) were used as effect estimates. In addition, the Psoriasis Area and Severity Index (PASI) 50, PASI 75 and PASI 90 responses for the therapies were systematically assessed. A total of 33 randomized controlled trials were included in the present study. For the PASI 75 response rate, infliximab (5 mg) may be the most effective option for the treatment of moderate to severe psoriasis. Furthermore, the pooled results of the PASI 50 response rate demonstrated that infliximab (5 mg) and ustekinumab (90 mg) may be superior to other drugs for treating moderate to severe psoriasis. For the PASI 90 response rate, infliximab (5 mg), ustekinumab (90 mg) and briakinumab (weeks 0 and 4, 200 mg; week 8, 100 mg) exhibited improved results compared with other treatments. In conclusion, infliximab (5 mg) may be a superior option to treat moderate to severe psoriasis due to the relatively high PASI scores. However, despite the high PASI 90 responses, further studies are required to identify the efficacy of ustekinumab (90 mg) and briakinumab.

Introduction

Psoriasis is a common immune-mediated skin disease. The prevalence of psoriasis in adults ranges between 0.91 and 8.5% worldwide and the incidence of psoriasis is higher in adults than in children (1). Psoriasis is characterized by symptoms of plaque, pustular and other skin lesions. Chronic plaque psoriasis accounts for 90% of all psoriasis cases (2,3).

A number of biological therapies are used to treat moderate to severe psoriasis, including etanercept, briakinumab, ustekinumab, adalimumab and infliximab (4-8). Etanercept, adalimumab and infliximab are monoclonal antibodies against tumor necrosis factor (TNF), which function by neutralizing the biological activity of TNF for treating the TNF-mediated inflammation (5,9). By contrast, ustekinumab and briakinumab are human monoclonal antibodies against interleukin (IL)-12/23p40 (8). These biological therapies are used to treat psoriasis and improved clinical outcomes have been observed. However, the efficacy of these therapies has been not systematically reviewed.

In the present study, a network meta-analysis was performed to review and compare the efficacy of these aforementioned biological therapies of psoriasis. The Psoriasis Area and Severity Index (PASI) response (10) was used as an indicator for assessing the effect of treatment on the severity of psoriasis. PASI 50, PASI 75 and PASI 90 responses for the therapies were systematically assessed. The pooled results provide further information on selecting the most suitable treatments for moderate to severe psoriasis.

Materials and methods

Data sources. The PubMed (www.ncbi.nlm.nih.gov/pubmed) and Embase (www.elsevier.com/solutions/embase-biomedical-research) databases were systematically searched in order to select relevant studies up to February 2015. The search terms included the following: Psoriasis, methotrexate (MTX), cyclosporin A (CSA), ustekinumab, etanercept, infliximab, briakinumab and adalimumab.

Inclusion and exclusion criteria. Studies with the following characteristics were included in the current meta-analysis: i) Randomized controlled trials (RCTs) reporting the treatment of moderate to severe psoriasis with the aforementioned drugs. Moderate to severe psoriasis is defined as body surface area >10 or psoriasis area and severity index >10 and dermatology life quality index >10 (11); ii) studies including the adults as participants; and iii) studies reporting the PASI response rate (50, 75 and 90%). Any reviews, case reports and letters were excluded from the meta-analysis. Any studies investigating patients with mild psoriasis and those written in a language other than English were also excluded.

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Data extraction and quality assessment. Two reviewers independently extracted the following data: The name of the first author, publication year, sample size, intervention, demographic characteristics of the included patients and PASI response rate. The controversies were discussed with a third reviewer to reach consensus. The methodological quality of the included studies was evaluated by the Cochrane Collaboration Risk of Bias Tool (12).

Statistical analysis. All analyses were performed using the ADDIS software version 1.16.5 (Drug Information and Monitoring Systems, Groningen, The Netherlands). Odds ratios (ORs) and their 95% confidence intervals (CIs) were pooled. The network analysis performed was based on the Bayesian framework. Data were evaluated by Markov chain Monte Carlo methods and all analyses were performed using the random effects model. The consistency of the RCTs was assessed by Node-splitting analysis, and the consistency model was used if $P > 0.05$. Otherwise, the inconsistency model was used to pool the odd ratios (13).

Results

Study selection. As presented in Fig. 1, a total of 897 studies were identified from PubMed and 917 studies from Embase by the initial search. Subsequent to excluding any duplicates, 1,113 studies remained. A total of 831 irrelevant studies were excluded by reviewing the titles and abstracts. In addition, 249 studies that did not meet the inclusion criteria were excluded. Finally, 33 RCTs were included in the present study (4-9,14-40).

Characteristics of the included studies. As presented in Table I, the demographic characteristics, including age, sex and weight of the patients in the included studies were similar. Included RCTs were published between 1994 and 2015. The mean duration of psoriasis of the included patients ranged between 11.1 and 21.5 years. Quality assessment demonstrated that the quality of the included RCTs was relatively high. With respect to random sequence generation (selection bias), a number of studies were assessed as having an unclear risk of bias. With regards to blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias) and incomplete outcome data (attrition bias), a small proportion of studies were assessed as having high risk of bias (Fig. 2) and were excluded from the current study. However, the studies by Laburte *et al* (25) and Cassano *et al* (15) were not excluded as they met with the inclusion criteria despite having quite a poor rating.

Network meta-analysis. Based on the results of node-splitting analysis (Table II), the effect sizes were pooled using an inconsistency model. Regarding the PASI 75 response rate, infliximab (5 mg) was the most effective option for the treatment of moderate to severe psoriasis (Table III and Fig. 3). The pooled results of the PASI 50 response rate demonstrated that infliximab (5 mg) and ustekinumab (90 mg) may be superior to other drugs for treating moderate to severe psoriasis (Table IV). In addition, regarding the PASI 90 response rate, treatment with infliximab (5 mg), ustekinumab

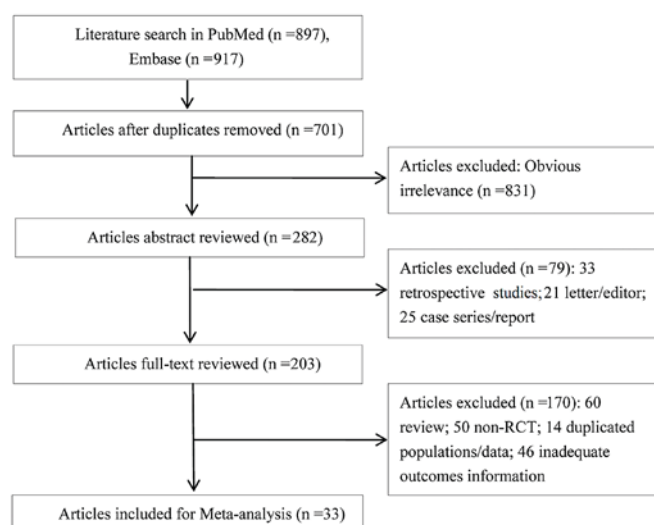


Figure 1. Process of the literature selection performed in the present meta-analysis. RCT, randomized controlled trial.

(90 mg) and briakinumab (weeks 0 and 4, 200 mg; week 8, 100 mg) indicated improved results compared with other agents (Table V). Finally, the drugs can be ranked in the following order according to their efficacy, defined as their PASI 90 response rate: Briakinumab > ustekinumab (90 mg) > infliximab (5 mg) > ustekinumab (45 mg) > adalimumab > infliximab (3 mg) > etanercept (50 mg BIW) > CSA (5 mg) > etanercept (25 mg BIW) > MTX > etanercept (25 mg QW) > placebo (Table VI). The odds ratio value of infliximab (5 mg) compared with the other drugs was >1, therefore, infliximab (5 mg) was regarded as the best treatment agent, although it ranked as third in terms of efficacy.

Discussion

In the present study, a network meta-analysis was performed to systematically review and compare the efficacy of seven drugs used at different doses for treating moderate to severe psoriasis. Based on the results of the network analysis, infliximab (5 mg) may be an appropriate option to treat moderate to severe psoriasis.

Psoriasis has been reported to be associated with a high concentration of TNF- α (41) and infliximab treatment can neutralize the biological activity of TNF- α (42). However, the role of the TNF- α in the pathogenesis of psoriasis remains unclear. Previous studies have reported that TNF- α may serve an important role in the upstream of the inflammatory responses of psoriasis (43,44). An *in vitro* study determined that infliximab was able to inhibit the activation of skin-homing T cells and impair the antigen-presenting capacity of immature dendritic cells in psoriasis patients (43). However, another TNF- α inhibitor, etanercept, has been found to be effective in the treatment of psoriasis by reducing the Th17 cell products, as well as the production of IL-17, IL-22, IL-23 and inducible NO synthase from dendritic cells (44). Thus, it has been suggested that the infliximab may serve a different role with other treatments on moderate to severe psoriasis.

Although the present meta-analysis indicated that infliximab treatment had a high PASI score, a higher percentage

Table I. Characteristics of the included studies.

First author	Year	Follow-up	Treatment	N	Age (years)	M/F	Weight (kg)	Duration of psoriasis (years)	PASI score	PASI 75	PASI 50	PASI 90	(Refs.)
Laburtie <i>et al</i>	1994	0.2-18.3 months	CSA 5 mg CSA 2.5 mg	132 119	40.7±12.3 42.0±12.6	90/42 86/33	72.9±3.4 77.4±15.5	17.7±11.1 18.4±11.1	25.1±8.0 24.9±7.0	117 57	NA NA	NA NA	(25)
Gordon <i>et al</i>	2006	60 weeks	Adalimumab Placebo	45 52	46 (20-71) 43 (20-70)	32/13 34/18	93 (63-159) 94 (50-147)	21 (1.3-57.9) 19 (1.0-39.9)	16.7 (5.4-39.0) 16.0 (5.5-40.4)	24 2	NA NA	NA NA	(17)
Menter <i>et al</i>	2008	16 weeks	Adalimumab Placebo	814 398	44.1±13.2 45.4±13.4	546/268 257/141	92.3±23.0 94.1±23.0	18.1±11.91 18.4±11.94	19.0±7.08 18.8±7.09	578 28	NA NA	366 8	(2)
Asahina <i>et al</i>	2010	24 weeks	Adalimumab Placebo	38 46	47.8±12.81 43.9±10.75	32/6 41/5	69.7±15.48 71.3±15.28	14.2±9.29 15.5±8.83	25.44±8.98 29.10±11.77	24 2	31 9	15 0	(5)
Revicki <i>et al</i>	2008	16 weeks	Adalimumab MTX Placebo	108 110 53	42.8±12.3 41.9±11.9 40.7±11.4	37/71 36/74 18/35	NA NA NA	17.6±10.0 19.0±10.3 18.9±8.7	20.1±7.4 19.5±7.4 19.2±6.9	86 66 10	95 68 16	55 15 6	(34)
Leonardi <i>et al</i>	2003	12 weeks	Etanercept 50 mg BIW Etanercept 25 mg BIW Etanercept 25 mg QW Placebo	164 162 160 166	44.8±0.8 45.4±1.0 44.4±0.9 45.6±1.0	107/57 109/53 118/42 105/61	NA NA NA NA	18.6±0.9 18.5±0.9 19.3±0.9 18.4±0.9	18.4±0.7 18.5±0.7 18.2±0.7 18.3±0.6	81 55 23 6	121 94 65 24	36 19 5 1	(27)
Papp <i>et al</i>	2005	12 weeks	Etanercept 50 mg BIW Etanercept 25 mg BIW Placebo	194 196 193	44.5 (21.0-80.0) 46.0 (20.0-87.0) 44.0 (18.0-80.0)	130/64 128/68 124/69	NA NA NA	18.1 (0.8-60.5) 21.5 (0.8-64.6) 17.5 (1.4-51.2)	16.1 (7.0-57.3) 16.9 (4.0-51.2) 16.0 (7.0-62.4)	96 67 6	150 126 18	40 21 1	(32)
Tyring <i>et al</i>	2006	12 weeks	Etanercept 50 mg BIW Placebo	311 307	45.8±12.8 45.6±12.1	203/108 216/91	NA NA	20.1±12.3 19.7±11.4	18.3±7.6 18.1±7.4	146 15	230 43	65 3	(37)
van de Kerkhof <i>et al</i>	2008	12 weeks	Etanercept 25 mg BIW Placebo	96 46	45.9±12.8 43.6±12.6	59/36 25/21	83.4±16.0 79.1±20.2	19.3±11.3 17.3±8.2	21.4±9.3 21.0±8.7	36 1	66 4	13 1	(38)
Cassano <i>et al</i>	2010	12 weeks	Etanercept 50 mg BIW Etanercept 100 mg QW	36 36	NA NA	NA NA	NA NA	NA NA	NA NA	19 13	33 27	NA NA	(40)
Strober <i>et al</i>	2011	12 weeks	Etanercept 50 mg BIW Briakinumab Placebo	139 139 72	45.2±14.8 44.9±12.9 45.0±13.9	85/54 93/46 46/26	96.9±24.9 96.1±24.5 92.9±25.2	15.2±12.1 16.3±12.0 15.5±11.7	18.5±6.0 19.4±7.9 18.3±6.4	55 112 5	NA NA NA	19 77 3	(8)
Gottlieb <i>et al</i>	2011	12 weeks	Etanercept 50 mg BIW Briakinumab Placebo	141 138 68	43.1±12.5 43.6±14.3 44.0±13.6	98/43 89/49 47/21	94.5±20.4 93.2±22.9 96.5±27.2	17.0±12.7 16.1±12.5 19.1±13.2	19.4±8.0 18.4±7.2 18.5±6.9	78 113 5	NA NA NA	32 81 1	(19)
Bagel <i>et al</i>	2012	12 weeks	Etanercept 50 mg BIW Placebo	62 62	39 (18.0-71.0) 42 (18.0-70.0)	29/33 26/36	30.2 (18.2-44.2) 30.2 (18.2-44.2)	17.5 (1-45) 11.9 (1-49)	15.5 (8-46) 15.2 (10-41)	37 3	53 4	16 1	(8)
Gottlieb <i>et al</i>	2003	10 weeks	Infliximab 5 mg Infliximab 3 mg Placebo	99 99 51	44 (34, 53) 45 (37, 55) 45 (30, 52)	73/26 70/29 31/20	NA NA NA	16 (10, 25) 18 (12, 24) 16 (6, 22)	20 (14, 28) 20 (15, 26) 18 (15, 27)	87 71 3	96 83 11	47 45 1	(20)
Reich <i>et al</i>	2005	24 weeks	Infliximab 5 mg Placebo	301 77	42.6±11.7 43.8±12.6	207/94 61/16	NA NA	19.1±11.0 17.3±11.1	22.9±9.3 22.8±8.7	227 3	248 6	161 1	(33)
Menter <i>et al</i>	2007	14 weeks	Infliximab 5 mg Infliximab 3 mg	314 313	44.5±13.0 43.4±12.6	204/110 206/107	92.2±23.2 92.0±22.5	19.1±11.7 18.1±11.8	20.4±7.5 20.1±7.9	193 149	252 213	113 75	(29)
Torii and Nakagawa	2010	14 weeks	Infliximab 5 mg Placebo	35 19	46.9±13.0 43.3±12.3	22/13 14/5	68.5±13.4 69.7±8.9	14.2±8.9 11.1±6.5	31.9±12.8 33.1±15.6	25 2	29 2	17 1	(35)

Table I. Continued.

First author	Year	Follow-up	Treatment	N	Age (years)	M/F	Weight (kg)	Duration of psoriasis (years)	PASI score	PASI 75	PASI 50	PASI 90	(Refs.)
Yang <i>et al</i>	2012	10 weeks	Infliximab 5 mg Placebo	84 45	39.4±12.3 40.1±11.1	60/24 35/10	68.2±9.2 67.4±9.9	16.0±10.8 16.0±8.9	NA NA	68 1	79 6	48 0	(39)
Barker <i>et al</i>	2011	26 weeks	Infliximab 5 mg MTX	653 215	44.1 (±18-78) 41.9 (±18-69)	438/215 148/67	84.5±18.6 83.8±18.2	18.8±11.6 17.0±10.3	21.4±8.0 21.1±7.6	502 66	529 103	333 32	(14)
Leonardi <i>et al</i>	2008	12 weeks	Ustekinumab 90 mg Ustekinumab 45 mg Placebo	256 255 255	46.2±11.3 44.8±12.5 44.8±11.3	173/83 175/80 183/72	93.8±23.9 93.7±23.8 94.2±23.5	19.6±11.1 19.7±11.7 20.4±11.7	19.7±7.6 20.5±8.6 20.4±8.6	170 171 8	220 213 26	94 106 5	(26)
Papp <i>et al</i>	2008	12 weeks	Ustekinumab 90 mg Ustekinumab 45 mg Placebo	411 409 410	46.6±12.1 45.1±12.1 47.0±12.5	274/137 283/126 283/127	91.5±21.3 90.3±21.0 91.1±21.6	20.3±12.3 19.3±11.7 20.8±12.2	20.1±7.5 19.4±6.8 19.4±7.5	311 273 15	367 342 41	209 173 3	(31)
Griffiths	2010	36 weeks	Ustekinumab 90 mg Ustekinumab 45 mg Etanercept 50 mg BIW	247 209 347	NA NA NA	NA NA NA	NA NA NA	NA NA NA	NA NA NA	183 142 198	NA NA NA	111 75 80	(21)
Tsai <i>et al</i>	2011	12 weeks	Ustekinumab 45 mg Placebo	61 60	40.9±12.7 40.4±10.1	50/11 53/7	73.1±12.7 74.6±13.0	11.9±7.5 13.9±7.3	25.2±11.9 22.9±8.6	41 3	51 8	30 1	(36)
Igarashi <i>et al</i>	2012	12 weeks	Ustekinumab 45 mg Ustekinumab 90 mg Placebo	64 62 32	M: 45.0 M: 44.0 M: 49.0	53/11 47/15 26/6	73.2±15.4 71.1±14.0 71.2±10.9	15.8±8.2 17.3±10.7 16.0±11.2	30.1±12.9 28.7±11.2 30.3±11.8	38 42 2	53 52 4	21 27 1	(24)
Heydendael <i>et al</i>	2003	17-52 weeks	CSA 2.5 mg MTX	42 43	41.6±13.0 38.3±12.4	29/13 28/15	NA NA	NA NA	14.0±6.6 13.4±3.6	30 26	NA NA	NA NA	(22)
Flytstrom <i>et al</i>	2008		CSA 5 mg MTX	31 37	45 (18-70) 48 (23-78)	27/4 28/9	87 (61-130) 85 (56-132)	NA NA	15.5±6.3 14.1±7.0	18 22	27 24	9 4	(16)
Ho <i>et al</i>	2010	6 months	MTX Placebo	20 20	38.45 (21-68) 43.45 (27-61)	18/2 18/2	NA NA	NA NA	NA NA	13 16	NA NA	0 5	(23)
Gottlieb <i>et al</i>	2003	24 weeks	Etanercept 25 mg BIW Placebo	57 55	48.2 (25-72) 46.5 (18-77)	33/24 37/18	Mean: 91.8 Mean: 90.7	23±1.6 20±1.7	17.8±1.1 19.5±1.3	17 1	40 6	6 0	(20)
Cassano <i>et al</i>	2006	12 weeks	Etanercept 50 mg BIW Etanercept 100 mg QW	53 55	42.3 (18-73)	57/52	NA NA	NA NA	8.7 (5.4-11.6)	29 28	39 43	NA NA	(15)
Sterry <i>et al</i>	2010	12 weeks	Etanercept 50 mg BIW Etanercept 50 mg QW	379 373	46±11 47±11	243/136 230/143	NA NA	19±12 19±11	20±11 19±10	208 134	NA NA	NA NA	(7)
Antoni <i>et al</i>	2005	16 weeks	Infliximab 5 mg Placebo	52 52	45.7±11.1 45.2±9.7	30/22 30/22	NA NA	19.4±11.6 16.9±10.9	5.1±5.9 4.2±5.8	35 0	NA NA	NA NA	(4)
McInnes <i>et al</i>	2013	12 weeks	Ustekinumab 45 mg Ustekinumab 90 mg Placebo	205 204 206	48.0 (39.0-55.0) 47.0 (38.5-54.0) 48.0 (39.0-57.0)	106/99 116/88 108/98	NA NA NA	12.0 (4.1-22.2) 14.1 (5.4-22.4) 13.1 (5.3-23.5)	7.1 (3.3-15.3) 8.4 (4.8-14.7) 8.8 (4.4-14.3)	83 93 16	NA NA NA	NA NA NA	(28)
Griffiths <i>et al</i>	2015	12 weeks	Etanercept 50 mg QW Etanercept 50 mg BIW	371 377	46.9±11.4 46.1±11.4	229 241	NA NA	18.6±11.4 19.2±11.9	19.0±9.8 19.8±10.7	148 226	NA NA	NA NA	(6)

Data are presented as the mean ± standard deviation, or as the median (range). PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly; M/F, male/female; NA, not available; Ref, study reference number; M, mean value.

Table II. Node-splitting analysis.

Name	Direct effect	Indirect effect	Overall	P-value
PASI 75				
Adalimumab, MTX	-1.03 (-2.13, 0.09)	-0.13 (-1.44, 1.31)	-0.81 (-1.64, 0.10)	0.28
CSA 2.5 mg, CSA 5 mg	2.15 (1.15, 3.13)	-0.55 (-2.24, 1.08)	1.47 (0.44, 2.41)	0.01
CSA 2.5 mg, MTX	-0.51 (-1.71, 0.64)	2.24 (0.71, 3.77)	0.46 (-0.62, 1.48)	0.01
CSA 5 mg, MTX	0.02 (-1.18, 1.24)	-2.70 (-4.23, -1.12)	-1.01 (-2.06, 0.07)	0.01
Etanercept 25 mg BIW, Etanercept 50 mg BIW	0.64 (-0.08, 1.35)	-0.05 (-1.03, 0.89)	0.41 (-0.27, 1.01)	0.23
Etanercept 50 mg BIW, Placebo	-3.02 (-3.57, -2.49)	-3.18 (-4.11, -2.32)	-3.03 (-3.51, -2.58)	0.74
Etanercept 50 mg BIW, Ustekinumab 45 mg	0.46 (-0.61, 1.51)	0.51 (-0.19, 1.18)	0.48 (-0.15, 1.08)	0.9
Etanercept 50 mg BIW, Ustekinumab 90 mg	0.77 (-0.29, 1.80)	0.54 (-0.20, 1.20)	0.62 (-0.00, 1.23)	0.69
Infliximab 3 mg, Placebo	-3.86 (-5.56, -2.35)	-3.95 (-5.09, -2.86)	-3.95 (-4.95, -3.01)	0.94
Infliximab 5 mg, MTX	-2.01 (-3.06, -1.04)	-2.18 (-3.45, -0.84)	-2.08 (-2.86, -1.25)	0.83
Infliximab 5 mg, Placebo	-4.83 (-5.77, -4.02)	-4.65 (-6.16, -3.25)	-4.73 (-5.50, -4.08)	0.81
MTX, Placebo	-2.53 (-3.72, -1.49)	-2.70 (-3.69, -1.78)	-2.66 (-3.50, -1.92)	0.81
Placebo, Ustekinumab 45 mg	3.54 (2.96, 4.11)	3.44 (2.39, 4.44)	3.52 (2.99, 4.02)	0.83
Placebo, Ustekinumab 90 mg	3.60 (2.97, 4.18)	3.83 (2.83, 4.83)	3.65 (3.11, 4.17)	0.65
PASI 50				
Adalimumab, MTX	-1.51 (-2.41, -0.70)	0.04 (-1.06, 1.18)	-1.10 (-2.03, -0.21)	0.02
Etanercept 25 mg BIW, Etanercept 50 mg BIW	0.64 (-0.05, 1.38)	0.73 (-0.20, 1.76)	0.61 (0.02, 1.21)	0.88
Etanercept 50 mg BIW, Placebo	-3.13 (-3.66, -2.70)	-3.82 (-4.93, -2.73)	-3.22 (-3.78, -2.75)	0.24
Infliximab 3 mg, Placebo	-3.11 (-4.31, -1.87)	-2.93 (-4.01, -1.89)	-3.04 (-3.92, -2.25)	0.82
Infliximab 5 mg, MTX	-1.54 (-2.19, -0.88)	-3.08 (-4.17, -2.09)	-2.02 (-2.88, -1.37)	0.01
Infliximab 5 mg, Placebo	-4.45 (-5.18, -3.92)	-2.93 (-3.90, -1.90)	-4.13 (-4.79, -3.55)	0.01
MTX, Placebo	-1.42 (-2.34, -0.45)	-2.57 (-3.39, -1.73)	-2.11 (-2.85, -1.31)	0.06
PASI 90				
Adalimumab, MTX	-2.04 (-3.04, -0.99)	-0.49 (-1.91, 0.86)	-1.67 (-2.58, -0.81)	0.08
Etanercept 25 mg BIW, Etanercept 50 mg BIW	0.86 (0.14, 1.62)	-0.03 (-1.47, 1.35)	0.75 (0.04, 1.39)	0.24
Etanercept 50 mg BIW, Placebo	-3.15 (-3.90, -2.45)	-3.34 (-4.48, -2.42)	-3.16 (-3.78, -2.63)	0.76
Etanercept 50 mg BIW, Ustekinumab 45 mg	0.63 (-0.36, 1.70)	0.99 (0.12, 1.83)	0.82 (0.19, 1.48)	0.53
Etanercept 50 mg BIW, Ustekinumab 90 mg	1.00 (0.01, 2.02)	0.73 (-0.10, 1.59)	0.90 (0.22, 1.52)	0.61
Infliximab 3 mg, Placebo	-4.12 (-8.54, -2.14)	-3.54 (-4.91, -2.48)	-3.56 (-4.64, -2.64)	0.69
Infliximab 5 mg, MTX	-1.80 (-2.74, -0.87)	-2.98 (-4.73, -1.47)	-2.07 (-2.97, -1.38)	0.18
Infliximab 5 mg, Placebo	-4.46 (-6.00, -3.43)	-3.33 (-4.77, -2.10)	-3.93 (-4.80, -3.18)	0.2
MTX, Placebo	-1.24 (-2.38, -0.25)	-2.30 (-3.43, -1.40)	-1.85 (-2.60, -1.07)	0.12
Placebo, Ustekinumab 45 mg	4.15 (3.45, 4.86)	3.78 (2.83, 4.68)	3.99 (3.37, 4.61)	0.37
Placebo, Ustekinumab 90 mg	3.99 (3.22, 4.77)	4.32 (3.40, 5.28)	4.07 (3.40, 4.70)	0.44

PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly.

of adverse events were observed in infliximab-treated patients compared with those in the placebo group (18), indicating that infliximab treatment induces adverse effects. In addition, infliximab treatment increases the incidence of infusion reactions (45). However, these outcomes were not considered to be important due to the small sample size of each study or the fact that the data were unavailable. Thus, the therapeutic effect of the infliximab should be systematically assessed in further studies. Besides, the dosage and treatment duration of infliximab should be optimized according to the disease severity of psoriasis.

In the present study, briakinumab and ustekinumab (90 mg) treatments were superior to other treatments for PASI 90 response. Thus, anti-IL-12/23 monoclonal antibodies appear to be more appropriate compared with anti-TNF- α treatment for treating moderate to severe

psoriasis. However, briakinumab and ustekinumab showed no significantly improved therapeutic effect in PASI 75 and PASI 50 responses when compared with the anti-TNF- α treatments. In addition, the long-term safety profile, including severe infections and cardiac disorders, should be evaluated in further studies with large sample sizes and strict study design.

To the best of our knowledge, the present study is the first network meta-analysis for evaluating the efficacy of various treatments for moderate to severe psoriasis. The current results may provide information for clinician and patients on the selection of the suitable treatment for moderate to severe psoriasis. However, there were also several limitations in the present meta-analysis. Firstly, due to unavailable data in certain included studies, confounding variables could not be adjusted and subgroup analysis was not performed to reduce the effect

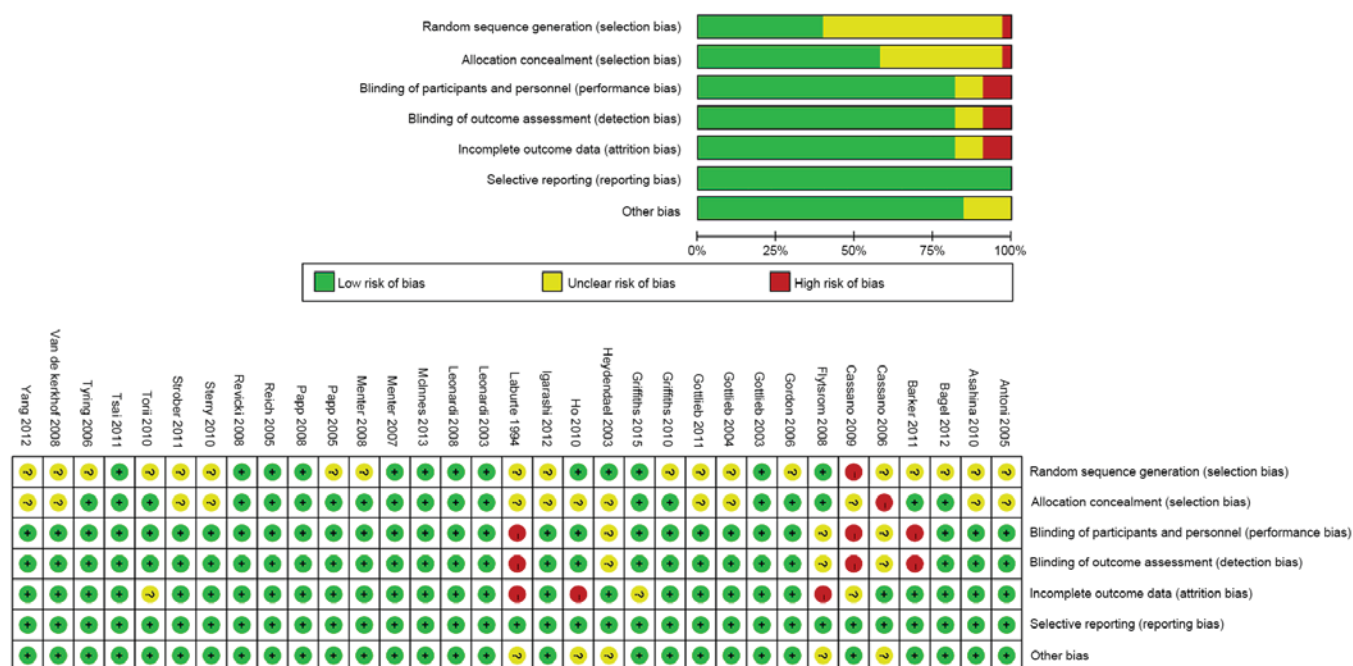


Figure 2. Risk of bias of the included studies. +, low risk of bias; ?, unclear risk of bias; -, high risk of bias. The quality evaluation map indicates that, regarding random sequence generation (selection bias) and allocation concealment (selection bias), many references have an unclear risk of bias and few references have high risk of bias. However, regarding incomplete outcome data (attrition bias), blinding of participants and personnel (performance bias) and blinding of outcome assessment (detection bias), ~10% references have high risk of bias and 10% references have an unclear risk of bias. The included references showed no evidence of selective reporting (reporting bias) in the included references-all references showed a low risk of bias.

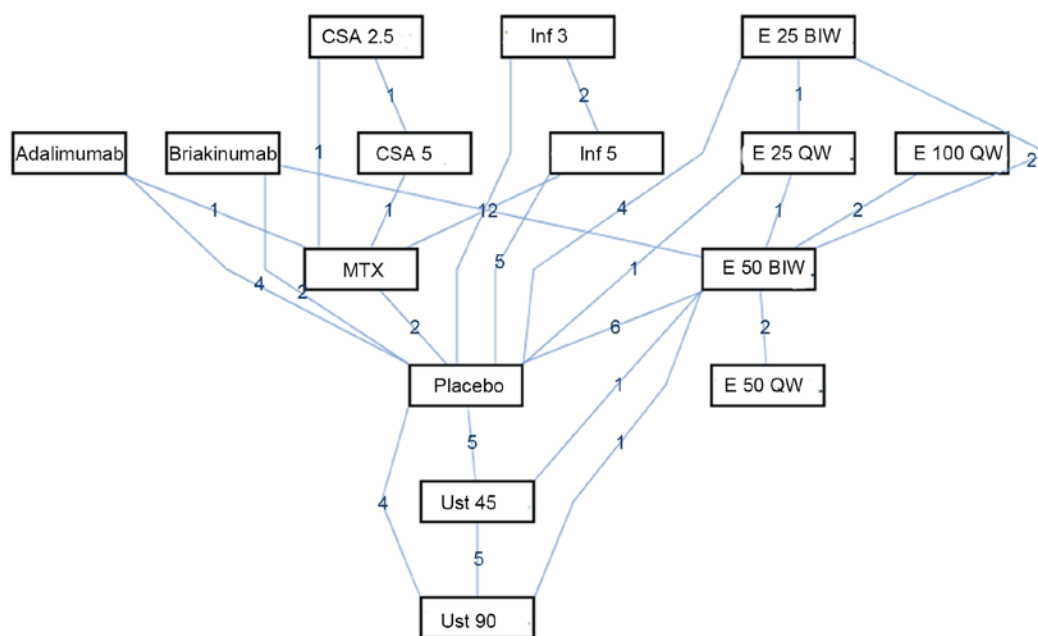


Figure 3. Network of PASI 75 response rate. The figures on the blue edges refer to the comparison times. PASI, Psoriasis Area and Severity Index. Image generated using ADDIS software 1.16.5.

of the confounding variables. Secondly, due to unknown bias, the network analyses of PASI 75 and PASI 50 responses were performed using an inconsistency model. Finally, the results of the network meta-analysis should be pooled only by a random effects model. Thus, the pooled results may be conservative and certain borderline significant effects may have been ignored (46).

In conclusion, the present meta-analysis results suggested that infliximab (5 mg) may be a superior option compared with other drugs for treating moderate to severe psoriasis due to the relatively high PASI scores of patients. However, despite the high PASI 90 responses, the efficacy of ustekinumab (90 mg) and briakinumab were also high and therefore should be investigated in further studies.

Table III. Network meta-analysis of PASI 75 response rate between drugs for treating psoriasis.

Drugs	CSA						Etanercept				Infliximab			Ustekinumab		
	Adalimumab	Briakinumab	2.5 mg	5 mg	100 mg QW	25 mg BIW	25 mg QW	50 mg BIW	50 mg QW	50 mg QW	3 mg	5 mg	MTX	Placebo	45 mg	90 mg
Adalimumab	-	2.25 (0.49,7.32)	0.31 (0.08,1.34)	1.50 (0.34,8.64)	0.37 (0.06,1.53)	0.43 (0.11,1.59)	0.10 (0.02,0.45)	0.55 (0.11,1.67)	0.25 (0.04,0.94)		1.39 (0.37,4.75)	3.04 (0.99,8.77)	0.39 (0.16,1.02)	0.03 (0.02,0.06)	0.91 (0.22,2.54)	1.04 (0.25,2.91)
Briakinumab	0.44 (0.14,2.03)	-	0.14 (0.03,1.01)	0.67 (0.12,6.22)	0.16 (0.04,0.61)	0.20 (0.07,0.69)	0.04 (0.01,0.19)	0.23 (0.05,1.03)	0.11 (0.03,0.37)		0.62 (0.18,2.46)	1.37 (0.44,4.88)	0.18 (0.05,0.70)	0.01 (0.01,0.03)	0.40 (0.15,1.02)	0.46 (0.18,1.17)
CSA 2.5 mg	3.22 (0.74,12.82)	7.11 (0.99,36.73)	-	4.98 (1.75,13.54)	1.16 (0.13,7.39)	1.43 (0.24,7.30)	0.34 (0.04,2.07)	1.74 (0.23,8.30)	0.78 (0.10,4.39)		4.42 (0.85,20.65)	9.89 (2.18,39.43)	1.29 (0.37,3.97)	0.09 (0.01,0.35)	2.88 (0.46,12.78)	3.32 (0.51,14.83)
CSA 5 mg	0.67 (0.12,2.95)	1.49 (0.16,8.29)	0.20 (0.07,0.57)	-	0.24 (0.02,1.67)	0.29 (0.04,1.67)	0.07 (0.01,0.47)	0.36 (0.03,1.95)	0.16 (0.01,1.02)		0.91 (0.12,4.84)	2.06 (0.30,9.18)	0.44 (0.14,1.57)	0.02 (0.00,0.08)	0.60 (0.07,2.96)	0.69 (0.08,3.38)
Etanercept 100 mg QW	2.73 (0.65,17.41)	6.15 (1.63,23.99)	0.86 (0.14,7.79)	4.15 (0.60,51.05)	-	1.23 (0.35,5.34)	0.28 (0.08,1.07)	1.46 (0.62,3.62)	0.66 (0.22,2.09)		3.85 (0.86,19.38)	8.51 (2.13,40.28)	1.11 (0.26,5.97)	0.07 (0.02,0.24)	2.48 (0.80,7.72)	2.85 (0.91,8.85)
Etanercept 25 mg BIW	2.32 (0.63,8.84)	5.07 (1.44,14.66)	0.70 (0.14,4.22)	3.40 (0.60,27.08)	0.82 (0.19,2.89)	-	0.28 (0.06,1.16)	1.43 (0.39,4.95)	0.55 (0.15,1.65)		3.19 (0.77,11.49)	7.09 (1.92,22.79)	0.90 (0.24,3.19)	0.06 (0.02,0.13)	2.02 (0.72,4.84)	2.32 (0.81,5.63)
Etanercept 25 mg QW	9.73 (2.22,58.96)	22.27 (5.23,85.70)	2.97 (0.48,27.13)	14.40 (2.13,179.59)	3.55 (0.94,12.49)	3.60 (0.86,16.14)	-	5.25 (1.99,13.30)	2.37 (0.73,7.27)		13.91 (2.92,65.68)	29.78 (7.31,139.88)	3.86 (0.91,20.80)	0.26 (0.05,1.37)	8.81 (2.69,28.14)	10.19 (3.01,31.84)
Etanercept 50 mg BIW	1.83 (0.60,9.27)	4.29 (0.97,18.85)	0.58 (0.12,4.32)	2.75 (0.51,30.05)	0.69 (0.28,1.62)	0.70 (0.20,2.55)	0.19 (0.08,0.50)	-	0.45 (0.23,0.89)		2.65 (0.76,10.26)	5.70 (1.94,21.09)	0.74 (0.24,3.10)	0.05 (0.01,0.21)	1.68 (0.81,3.59)	1.85 (0.48,7.46)
Etanercept 50 mg QW	4.05 (1.07,23.01)	9.31 (2.69,31.37)	1.28 (0.23,10.48)	6.17 (0.98,71.10)	1.51 (0.48,4.51)	1.81 (0.61,6.84)	0.42 (0.14,1.36)	2.21 (1.12,4.33)	-		5.75 (1.43,27.06)	12.64 (3.64,54.57)	1.65 (0.44,7.93)	0.11 (0.04,0.30)	3.75 (1.36,9.87)	4.28 (1.56,11.25)
Infliximab 3 mg	0.72 (0.21,2.67)	1.61 (0.41,5.67)	0.23 (0.05,1.17)	1.10 (0.21,8.04)	0.26 (0.05,1.16)	0.31 (0.09,1.30)	0.07 (0.02,0.34)	0.38 (0.10,1.31)	0.17 (0.04,0.70)		-	2.18 (1.10,4.75)	0.29 (0.10,0.87)	0.02 (0.01,0.05)	0.65 (0.19,1.97)	0.74 (0.21,2.29)
Infliximab 5 mg	0.33 (0.11,1.01)	0.73 (0.20,2.28)	0.10 (0.03,0.46)	0.49 (0.11,3.34)	0.12 (0.02,0.47)	0.14 (0.04,0.52)	0.03 (0.01,0.14)	0.18 (0.05,0.51)	0.08 (0.02,0.27)		0.46 (0.21,0.91)	-	0.13 (0.06,0.31)	0.01 (0.00,0.02)	0.29 (0.09,0.78)	0.34 (0.11,0.90)
MTX	2.55 (0.99,6.18)	5.57 (1.42,18.42)	0.78 (0.25,2.68)	2.25 (0.64,6.94)	0.90 (0.17,3.89)	1.11 (0.31,4.20)	0.26 (0.05,1.10)	1.35 (0.32,4.20)	0.61 (0.13,2.26)		3.49 (1.15,9.75)	7.69 (3.28,17.36)	-	0.05 (0.00,0.15)	2.26 (0.63,6.30)	2.59 (0.72,7.30)
Placebo	30.93 (16.26,58.97)	84.29 (37.74,187.34)	11.71 (2.86,69.09)	55.90 (12.23,452.23)	13.57 (4.22,41.45)	16.61 (7.77,43.27)	3.83 (0.73,18.81)	20.24 (4.73,75.32)	9.10 (3.34,24.47)		53.49 (19.24,158.08)	117.81 (54.46,286.70)	19.04 (6.83,242.20)	-	33.57 (20.28,55.73)	38.81 (22.22,64.79)
Ustekinumab 45 mg	1.09 (0.39,4.55)	2.48 (0.98,6.47)	0.35 (0.08,2.18)	1.66 (0.34,14.71)	0.40 (0.13,1.26)	0.49 (0.21,1.38)	0.11 (0.04,0.37)	0.60 (0.28,1.23)	0.27 (0.10,0.74)		1.54 (0.51,5.35)	3.43 (1.28,10.57)	0.44 (0.16,1.58)	0.03 (0.02,0.05)	-	1.19 (0.34,4.29)
Ustekinumab 90 mg	0.96 (0.34,3.97)	2.17 (0.85,5.68)	0.30 (0.07,1.95)	1.44 (0.30,13.07)	0.35 (0.11,1.10)	0.43 (0.18,1.23)	0.10 (0.03,0.33)	0.54 (0.13,2.07)	0.23 (0.09,0.64)		1.36 (0.44,4.82)	2.97 (1.11,9.46)	0.39 (0.14,1.40)	0.03 (0.02,0.05)	0.84 (0.23,2.94)	-

PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly.

Table IV. Network meta-analysis of PASI 50 response rate between drugs for treating psoriasis.

Drugs	Adalimumab	CSA 5 mg	Etanercept				Infliximab		Ustekinumab			
			100 mg QW	25 mg BIW	25 mg QW	50 mg BIW	3 mg	5 mg	MTX	Placebo	45 mg	90 mg
Adalimumab	-	1.12 (0.22,7.80)	0.59 (0.12,2.68)	0.41 (0.11,1.38)	0.17 (0.04,0.65)	0.79 (0.21,2.82)	0.61 (0.18,2.20)	1.75 (0.59,5.64)	0.29 (0.12,0.72)	0.04 (0.01,0.11)	1.40 (0.36,4.25)	1.85 (0.47,5.75)
CSA 5 mg	0.89 (0.13,4.63)	-	0.51 (0.06,3.81)	0.35 (0.05,2.02)	0.15 (0.02,0.94)	0.67 (0.10,4.15)	0.55 (0.08,3.08)	1.57 (0.27,8.03)	0.26 (0.05,1.01)	0.03 (0.00,0.13)	1.21 (0.17,6.72)	1.59 (0.22,8.98)
Etanercept	1.71 (0.37,8.01)	1.97 (0.26,16.88)	-	0.70 (0.22,2.31)	0.29 (0.08,1.10)	1.33 (0.58,3.37)	1.06 (0.27,4.26)	3.04 (0.85,11.44)	0.50 (0.12,2.03)	0.05 (0.02,0.15)	2.36 (0.70,7.67)	3.14 (0.90,10.08)
100 mg QW	2.44 (0.72,9.29)	2.83 (0.49,18.45)	1.43 (0.43,4.52)	-	0.42 (0.19,0.88)	1.88 (0.60,7.67)	1.54 (0.56,3.92)	4.35 (1.84,10.84)	0.71 (0.25,1.96)	0.08 (0.04,0.12)	3.36 (1.56,6.53)	4.51 (1.92,8.78)
Etanercept	5.82 (1.55,24.11)	6.76 (1.06,50.81)	3.47 (0.91,12.67)	2.38 (1.14,5.26)	-	4.48 (1.25,21.93)	3.67 (1.18,11.20)	10.43 (3.89,31.14)	1.70 (0.52,5.66)	0.18 (0.08,0.39)	8.06 (3.09,19.57)	10.77 (3.84,25.87)
25 mg QW	1.27 (0.36,4.71)	1.48 (0.24,9.91)	0.75 (0.30,1.74)	0.53 (0.13,1.66)	0.22 (0.05,0.80)	-	0.80 (0.26,2.15)	2.28 (0.88,5.66)	0.37 (0.12,1.08)	0.04 (0.02,0.07)	1.76 (0.72,3.61)	2.36 (0.90,4.92)
Etanercept	1.63 (0.45,5.59)	1.83 (0.33,11.99)	0.94 (0.23,3.72)	0.65 (0.26,1.79)	0.27 (0.09,0.85)	1.25 (0.47,3.79)	-	2.87 (1.49,5.97)	0.47 (0.17,1.18)	0.05 (0.02,0.11)	2.18 (0.79,5.79)	2.91 (1.00,7.85)
3 mg	0.57 (0.18,1.69)	0.64 (0.12,3.76)	0.33 (0.09,1.18)	0.23 (0.09,0.54)	0.10 (0.03,0.26)	0.44 (0.18,1.14)	0.35 (0.17,0.67)	-	0.16 (0.07,0.32)	0.01 (0.01,0.03)	0.77 (0.30,1.81)	1.01 (0.38,2.38)
Infliximab	3.47 (1.40,8.48)	3.90 (0.99,20.60)	2.01 (0.49,8.47)	1.41 (0.51,4.03)	0.59 (0.18,1.93)	2.68 (0.92,8.59)	2.13 (0.85,5.91)	6.07 (3.09,14.56)	-	0.16 (0.07,0.42)	4.73 (1.65,12.90)	6.32 (2.13,17.45)
5 mg	25.54 (8.86,70.76)	37.03 (7.41,242.17)	19.15 (6.52,56.34)	13.18 (8.43,23.22)	5.56 (2.58,12.19)	25.18 (14.53,50.34)	20.48 (8.87,47.46)	75.64 (37.84,166.80)	6.11 (2.36,14.83)	-	44.24 (26.51,73.29)	59.44 (32.83,99.32)
MTX	0.72 (0.24,2.79)	0.83 (0.15,5.84)	0.42 (0.13,1.43)	0.30 (0.15,0.64)	0.12 (0.05,0.32)	0.57 (0.28,1.38)	0.46 (0.17,1.26)	1.30 (0.55,3.33)	0.21 (0.08,0.61)	0.02 (0.01,0.04)	-	1.34 (0.77,2.22)
Placebo	0.54 (0.17,2.12)	0.63 (0.11,4.46)	0.32 (0.10,1.12)	0.22 (0.11,0.52)	0.09 (0.04,0.26)	0.42 (0.20,1.11)	0.34 (0.13,1.00)	0.99 (0.42,2.64)	0.16 (0.06,0.47)	0.02 (0.01,0.03)	0.75 (0.45,1.30)	-

PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly.

PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly.

Table V. Network meta-analysis of PASI 90 response rate between different drugs used to treat psoriasis.

Drugs	Etanercept					Infliximab					Ustekinumab		
	Adalimumab	Briakinumab	CSA 5 mg	25 mg BIW	25 mg QW	50 mg BIW	3 mg	5 mg	MTX	Placebo	45 mg	90 mg	
Adalimumab	-	3.84 (1.16,11.56)	0.66 (0.11,4.09)	0.33 (0.12,1.04)	0.08 (0.02,0.33)	0.70 (0.28,1.85)	1.03 (0.35,3.58)	1.50 (0.58,4.27)	0.19 (0.08,0.44)	0.03 (0.01,0.06)	1.60 (0.63,4.31)	1.71 (0.64,4.60)	
Briakinumab	0.26 (0.09,0.86)	-	0.17 (0.03,1.36)	0.09 (0.04,0.25)	0.02 (0.00,0.08)	0.18 (0.10,0.38)	0.27 (0.08,1.14)	0.39 (0.13,1.44)	0.05 (0.02,0.16)	0.01 (0.00,0.02)	0.42 (0.18,1.11)	0.45 (0.19,1.15)	
CSA 5 mg	1.51 (0.24,9.19)	5.76 (0.73,39.77)	-	0.50 (0.07,3.26)	0.12 (0.01,0.91)	1.09 (0.16,6.79)	1.58 (0.25,9.60)	2.27 (0.38,12.56)	0.28 (0.06,1.23)	0.05 (0.01,0.27)	2.48 (0.34,15.66)	2.65 (0.37,17.51)	
Etanercept	3.03	11.47	2.00	-	0.23	2.12	3.13	4.52	0.56	0.09	4.79	5.20	
25 mg BIW	(0.96,8.27)	(4.06,27.25)	(0.31,14.20)		(0.06,0.74)	(1.04,4.02)	(0.90,11.65)	(1.51,13.74)	(0.17,1.64)	(0.04,0.18)	(1.92,11.25)	(2.01,11.76)	
Etanercept	13.17	50.02	8.64	4.34	-	9.08	13.87	19.96	2.54	0.39	20.56	22.36	
25 mg QW	(3.06,58.45)	(12.01,212.82)	(1.10,79.40)	(1.36,17.31)		(2.86,33.94)	(2.99,74.25)	(4.65,97.31)	(0.53,10.70)	(0.11,1.48)	(5.65,85.77)	(5.77,93.02)	
Etanercept	1.42	5.43	0.92	0.47	0.11	-	1.46	2.12	0.27	0.04	2.27	2.46	
50 mg BIW	(0.54,3.57)	(2.62,10.08)	(0.15,6.31)	(0.25,0.96)	(0.03,0.35)		(0.51,5.15)	(0.85,6.07)	(0.10,0.70)	(0.02,0.07)	(1.21,4.37)	(1.25,4.56)	
Infliximab	0.97	3.71	0.63	0.32	0.07	0.68	-	1.45	0.18	0.03	1.55	1.68 (0.45,4.92)	
3 mg	(0.28,2.87)	(0.88,12.40)	(0.10,4.03)	(0.09,1.11)	(0.01,0.33)	(0.19,1.97)		(0.74,2.71)	(0.06,0.43)	(0.01,0.07)	(0.43,4.64)		
Infliximab	0.67	2.56	0.44	0.22	0.05	0.47	0.69	-	0.13	0.02	1.07	1.16	
5 mg	(0.23,1.71)	(0.70,7.58)	(0.08,2.63)	(0.07,0.66)	(0.01,0.21)	(0.16,1.18)	(0.37,1.36)		(0.05,0.25)	(0.01,0.04)	(0.36,2.79)	(0.37,3.04)	
MTX	5.31 (2.25,13.20)	20.30 (6.20,62.98)	3.55 (0.81,17.74)	1.79 (0.61,5.77)	0.39 (0.09,1.89)	3.77 (1.43,10.05)	5.50 (2.32,16.93)	7.96 (3.98,19.45)	-	0.16 (0.07,0.34)	8.58 (3.19,23.75)	9.20 (3.33,25.36)	
Placebo	33.59	130.12	22.14	11.08	2.57	23.55	35.13	51.03	6.34	-	53.93	58.50	
	(16.46,70.67)	(52.97,292.89)	(3.73,137.96)	(5.43,26.18)	(0.67,8.86)	(13.83,43.77)	(13.99,103.31)	(23.99,121.47)	(2.92,13.46)		(29.01,100.56)	(29.98,110.26)	
Ustekinumab	0.63	2.41	0.40	0.21	0.05	0.44	0.65	0.93	0.12	0.02	-	1.09	
45 mg	(0.23,1.58)	(0.90,5.51)	(0.06,2.91)	(0.09,0.52)	(0.01,0.18)	(0.23,0.82)	(0.22,2.31)	(0.36,2.81)	(0.04,0.31)	(0.01,0.03)		(0.66,1.67)	
Ustekinumab	0.58	2.21	0.38	0.19	0.04	0.41	0.60	0.86	0.11	0.02	0.92	-	
90 mg	(0.22,1.57)	(0.87,5.33)	(0.06,2.69)	(0.09,0.50)	(0.01,0.17)	(0.22,0.80)	(0.20,2.24)	(0.33,2.74)	(0.04,0.30)	(0.01,0.03)	(0.60,1.52)		

PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly.

Table VI. Rank analysis of PASI 90 response rate of the drugs for treating psoriasis.

Treatment	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6	Rank 7	Rank 8	Rank 9	Rank 10	Rank 11	Rank 12
Adalimumab	0.01	0.03	0.05	0.13	0.21	0.28	0.22	0.07	0.01	0.00	0.00	0.00
Briakinumab	0.86	0.08	0.03	0.02	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CSA 5 mg	0.03	0.07	0.04	0.06	0.07	0.09	0.14	0.25	0.17	0.05	0.01	0.00
Etanercept 25 mg BIW	0.00	0.00	0.00	0.00	0.00	0.01	0.03	0.23	0.59	0.14	0.00	0.00
Etanercept 25 mg QW	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.09	0.81	0.07
Etanercept 50 mg BIW	0.00	0.00	0.00	0.03	0.07	0.18	0.35	0.35	0.01	0.00	0.00	0.00
Infliximab 3 mg	0.02	0.04	0.09	0.09	0.22	0.24	0.20	0.09	0.02	0.00	0.00	0.00
Infliximab 5 mg	0.05	0.23	0.16	0.30	0.18	0.08	0.02	0.00	0.00	0.00	0.00	0.00
MTX	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.18	0.70	0.10	0.00
Placebo	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.93
Ustekinumab 45 mg	0.01	0.18	0.35	0.21	0.14	0.08	0.02	0.00	0.00	0.00	0.00	0.00
Ustekinumab 90 mg	0.02	0.37	0.28	0.16	0.10	0.05	0.02	0.00	0.00	0.00	0.00	0.00

Rank 1 indicates the best rating, while Rank 12 indicates the worst rating. PASI, Psoriasis Area and Severity Index; MTX, methotrexate; CSA, cyclosporin A; BIW, twice weekly; QW, once weekly.

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