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

WENJUN GENG, JIANHUA ZHAO, JIXING FU, HUAMIN ZHANG and SHAOHUA QIAO

Department of Dermatology, The Second Hospital of Liaocheng, Linqing, Shandong 252601, P.R. China

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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).

Correspondence to: Dr Wenjun Geng, Department of Dermatology, The Second Hospital of Liaocheng, 306 Jiankang Street, Linqing, Shandong 252601, P.R. China
E-mail: wenjungeng@126.com

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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.

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).

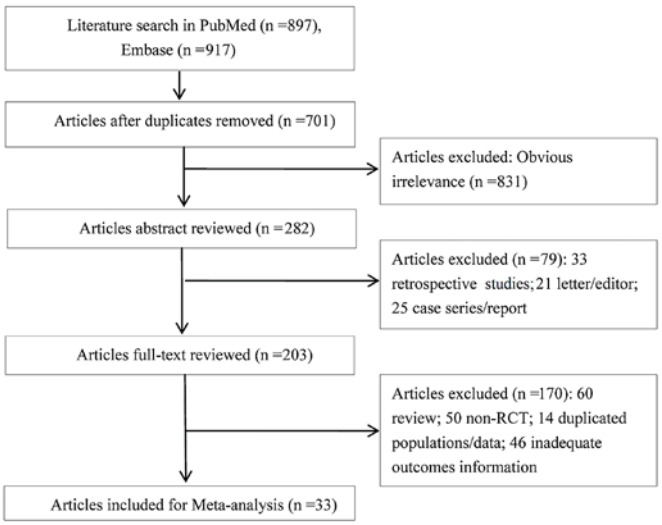

Figure 1. Process of the literature selection performed in the present meta-analysis. RCT, randomized controlled trial.

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

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

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

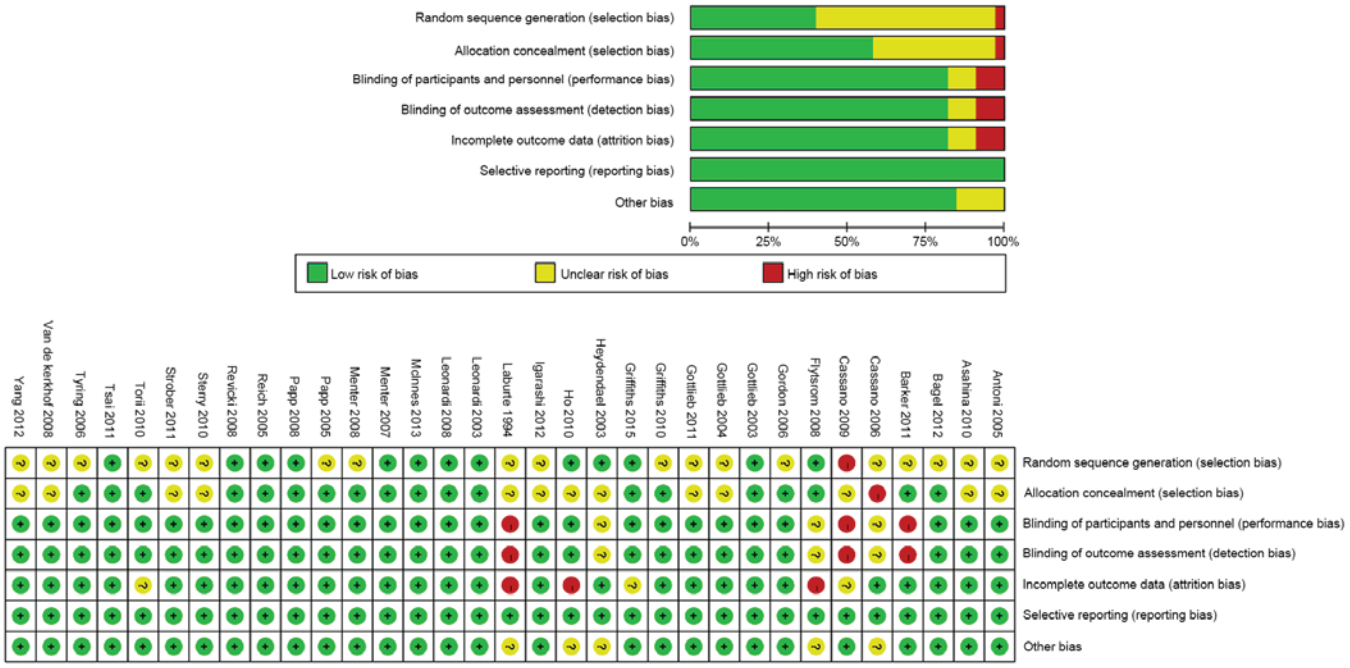

Figure 2. Risk of bias of the included studies. +, low risk of bias; ?, unclear risk of bias; -, high risk of bias. The quality evaluation map indicates that, regarding random sequence generation (selection bias) and allocation concealment (selection bias), many references have an unclear risk of bias 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.

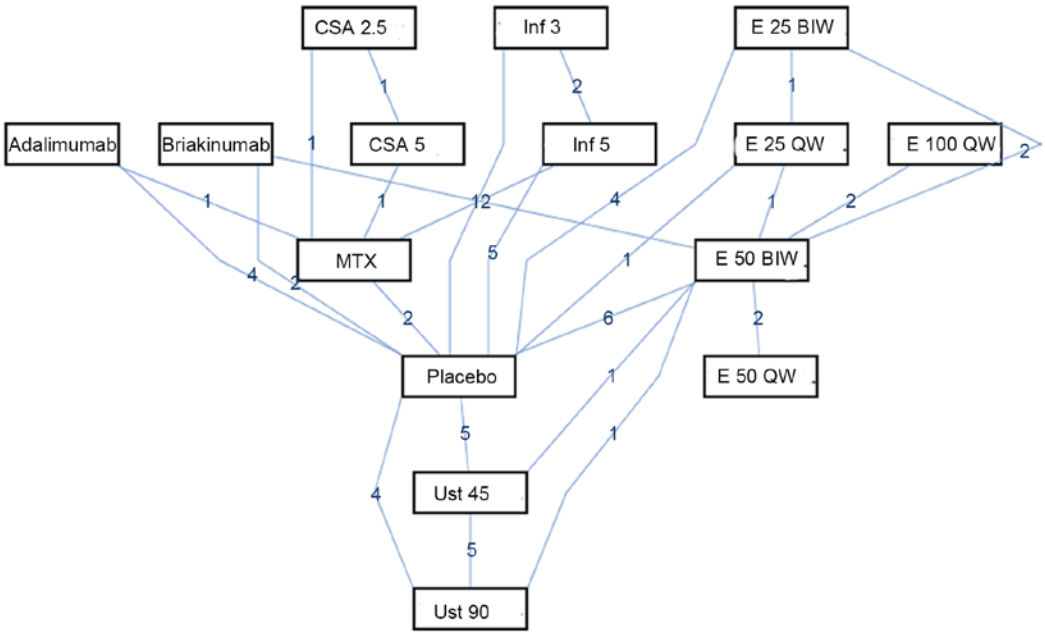

Figure 3. Network of PASI 75 response rate. The figures on the blue edges refer to the comparison times. PASI, Psoriasis Area and Severity Index. Image generated using ADDIS software 1.16.5.

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	Adalimumab	Briakinumab	CSA		Etanercept					Infliximab		MTX	Placebo	Ustekinumab	
			2.5 mg	5 mg	100 mg QW	25 mg BIW	25 mg QW	50 mg BIW	50 mg QW	3 mg	5 mg			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.

			Etanercept				Infliximab				Ustekinumab	
Drugs	Adalimumab	CSA 5 mg	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 100 mg QW	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)
Etanercept 25 mg BIW	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 25 mg QW	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)
Etanercept 50 mg BIW	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)
Infliximab 3 mg	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)
Infliximab 5 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)
MTX	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)
Placebo	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)
Ustekinumab 45 mg	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)
Ustekinumab 90 mg	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.

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

				Etanercept			Infliximab				Ustekinumab	
Drugs	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 25 mg BIW	3.03 (0.96,8.27)	11.47 (4.06,27.25)	2.00 (0.31,14.20)	-	0.23 (0.06,0.74)	2.12 (1.04,4.02)	3.13 (0.90,11.65)	4.52 (1.51,13.74)	0.56 (0.17,1.64)	0.09 (0.04,0.18)	4.79 (1.92,11.25)	5.20 (2.01,11.76)
Etanercept 25 mg QW	13.17 (3.06,58.45)	50.02 (12.01,212.82)	8.64 (1.10,79.40)	4.34 (1.36,17.31)	-	9.08 (2.86,33.94)	13.87 (2.99,74.25)	19.96 (4.65,97.31)	2.54 (0.53,10.70)	0.39 (0.11,1.48)	20.56 (5.65,85.77)	22.36 (5.77,93.02)
Etanercept 50 mg BIW	1.42 (0.54,3.57)	5.43 (2.62,10.08)	0.92 (0.15,6.31)	0.47 (0.25,0.96)	0.11 (0.03,0.35)	-	1.46 (0.51,5.15)	2.12 (0.85,6.07)	0.27 (0.10,0.70)	0.04 (0.02,0.07)	2.27 (1.21,4.37)	2.46 (1.25,4.56)
Infliximab 3 mg	0.97 (0.28,2.87)	3.71 (0.88,12.40)	0.63 (0.10,4.03)	0.32 (0.09,1.11)	0.07 (0.01,0.33)	0.68 (0.19,1.97)	-	1.45 (0.74,2.71)	0.18 (0.06,0.43)	0.03 (0.01,0.07)	1.55 (0.43,4.64)	1.68 (0.45,4.92)
Infliximab 5 mg	0.67 (0.23,1.71)	2.56 (0.70,7.58)	0.44 (0.08,2.63)	0.22 (0.07,0.66)	0.05 (0.01,0.21)	0.47 (0.16,1.18)	0.69 (0.37,1.36)	-	0.13 (0.05,0.25)	0.02 (0.01,0.04)	1.07 (0.36,2.79)	1.16 (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 (16.46,70.67)	130.12 (52.97,292.89)	22.14 (3.73,137.96)	11.08 (5.43,26.18)	2.57 (0.67,8.86)	23.55 (13.83,43.77)	35.13 (13.99,103.31)	51.03 (23.99,121.47)	6.34 (2.92,13.46)	-	53.93 (29.01,100.56)	58.50 (29.98,110.26)
Ustekinumab 45 mg	0.63 (0.23,1.58)	2.41 (0.90,5.51)	0.40 (0.06,2.91)	0.21 (0.09,0.52)	0.05 (0.01,0.18)	0.44 (0.23,0.82)	0.65 (0.22,2.31)	0.93 (0.36,2.81)	0.12 (0.04,0.31)	0.02 (0.01,0.03)	-	1.09 (0.66,1.67)
Ustekinumab 90 mg	0.58 (0.22,1.57)	2.21 (0.87,5.33)	0.38 (0.06,2.69)	0.19 (0.09,0.50)	0.04 (0.01,0.17)	0.41 (0.22,0.80)	0.60 (0.20,2.24)	0.86 (0.33,2.74)	0.11 (0.04,0.30)	0.02 (0.01,0.03)	0.92 (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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