International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 3, No. 1, 2023

Comparative Efficacy of bDMARDs and tsDMARDs for the Treatment of Rheumatoid arthritis: A Systematic Review and Network Meta-Analysis

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Abstract: To compare the relative clinical efficacy of biologic disease-modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs) (adalimumab, infliximab, certolizumab pegol, golimumab, tocilizumab, sarilumab, tofacitinib, baricitinib, upadacitinib, peficitinib, filgotinib, abatacept, anakinra, rituximab) in patients with rheumatoid arthritis (RA) who had been treated with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) without adequate response by network meta-analysis. The computer comprehensively searched PubMed, Embase, Cochrane Library, Web of Science, China Knowledge Network (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang, and VIP databases for randomized controlled trials (RCTs) of bDMARDs and tsDMARDs in the treatment of RA. The search time limit was set from the establishment of the databases to February 18, 2023. The quality assessment of the included studies was performed using the Cochrane Collaboration's tool, and the R software (version 4.1.3) calling the gemtc package (version 1.0-1) in conjunction with JAGS software was for data analysis. Efficacy outcomes included American College of Rheumatology 20%, 50%, 70% response (ACR20, ACR50, ACR70). The included 68 RCTs, totaling 32356 patients with RA were analyzed. There were 68, 64 and 63 studies reported the outcomes of ACR20, ACR50, and ACR70 respectively. The result showed that fifteen drugs all had significant difference compared with placebo. According to the SUCRA values, certolizumab pegol had the highest probability of becoming the best intervention in ACR20 and ACR50, and etanercept was ranked first in ACR70, followed by certolizumab pegol. In conclusion, bDMARDs and tsDMARDs were all effective in improving signs and symptoms in RA patients who had been treated with csDMARDs without adequate response. Certolizumab combined with csDMARDs had better performance on efficacy compared with other interventions.

Keywords: Biologic Disease-modifying Anti-rheumatic Drugs; Network Meta-analysis; Rheumatoid Arthritis; Targeted Synthetic Disease-modifying Anti-rheumatic Drugs.

1. Introduction

Rheumatoid arthritis (RA) is one of the most common chronic systemic and inflammatory diseases, and its pathological characteristics are chronic inflammation in joint synovial tissue, cell proliferation, formation of vascular opacities and infiltration of a variety of inflammatory cells, which subsequently cause destruction of articular cartilage and bone tissue [1]. Epidemiological surveys have shown that the global incidence of the disease is 0.5% ~ 1.0%, and RA tends to be more prevalent in female, with a lifetime risk of 3.6% for female and 1.7% for male [2]. RA can lead to joint dysfunction or loss, progressive disability, and even death [3].

Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) were recommended as the first treatment strategy for RA, and its representative drugs include methotrexate and leflunomide [4]. The second-line treatments of RA were biologic disease-modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs). The typical drugs of bDMARDs include tumor necrosis factor-α (TNF-α) inhibitors, interleukin-6 (IL-6) inhibitors, T-cell co-stimulation modulator, CD20 monoclonal antibodies, and interleukin-1 (IL-1) inhibitors. Janus kinase (JAK) inhibitors are representative drugs of tsDMARDs [5, 6].

Current guidelines recommend that csDMARDs in combination with one of the bDMARDs and tsDMARDs for the treatment of RA patients who had been treated with csDMARDs without adequate response, but there is no recommendation on the order of drug selection [7-9]. Therefore, we conducted this network meta-analysis to investigate the comparative efficacy of bDMARDs and tsDMARDs in RA patients who had been treated with csDMARDs without adequate response, and provide medical evidence in clinical practice.

2. Materials and Methods

2.1. Retrieval Strategy

Pubmed, Embase, Cochrane Library, Web of Science, China Knowledge Network (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang, VIP databases were comprehensively searched by computer, and clinical randomized controlled trials (RCTs) related to the treatment of RA with bDMARDs and tsDMARDs were searched, and the references of relevant articles were hand-searched to obtain relevant RCTs. The search terms included "rheumatoid arthritis", "adalimumab", "infliximab", "certolizumab pegol", "golimumab", "etanercept", "tocilizumab", "sarilumab", "tofacitinib", "baricitinib", "upadacitinib", "peficitinib", "filgotinib", "abatacept", "anakinra", "rituximab", "randomized controlled trial". The search time limit was set from the establishment of the databases to February 18, 2023.

2.2. Literature Inclusion and Exclusion Criteria

The literature inclusion criteria included: (1) Patients: adults met the 1987 ACR revised criteria or the 2010 ACR and EULAR classification criteria [10, 11]; they had been treated with csDMARDs without adequate response; they had not used bDMARDs or tsDMARDs, or had been treated with them but discontinuations of drugs for reasons other than inadequate response. No restrictions on gender, disease duration, nationality, or race. (2) Interventions: the experimental group was any one of bDMARDs or tsDMARDs, and the control group was the other one of bDMARDs or tsDMARDs, or placebo. (3) Outcomes: American College of Rheumatology 20%, 50%, and 70% response (ACR20, ACR50, and ACR70). (4) Study: RCT, language was limited to English or Chinese.

The literature exclusion criteria were as follows: (1) duplicate reports from the same research population; (2) animal or cell experimental researches; (3) review, conference abstracts, etc.; (4) retrospective researches, real world researches, etc.; (5) literature with full-text that was unobtainable.

2.3. Data Extraction and Quality Evaluation

Two researchers independently searched the literature, and conducted literature screening and data extraction. In case of disagreements, a third researcher was involved in order to solve the differences. The extracted data included name of the first author, year of publication, diagnose criteria, sample size, gender, age, interventions, outcomes. Seven aspects, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias, were evaluated and ranked as low, unclear, or high risk of bias.

2.4. Statistical Analysis

The network meta-analysis was performed using R software (version 4.1.3) calling gemtc package (version 1.0-1) in conjunction with JAGS software, based on the Bayesian framework using Markov Chain Monte Carlo (MCMC) method. Four Markov chains were used for simulation analysis, with initial value was 2.5. The iteration step was refined to 1. The number of pre-simulation iterations was 10000 for annealing, and the number of iterations was 40000 to achieve model convergence. When the potential scale reduction factors (PSRF) tend to 1, it indicates that the model convergence is satisfactory, otherwise, the number of iterations would have to continue to increase. In this study, risk ratio (RR) was used as the effect quantity, and 95% credible interval (95% CrI) that does not include 1 was used as the standard for statistical difference.

3. Results

3.1. Literature Retrieval Results

10654 related records were obtained through databases and 5 additional records were obtained from other sources. 7727 records remained after duplicates were removed. Screening was performed according to the inclusion and exclusion criteria, and 68 articles [12-79] were finally included, with a total of 68 studies for the final quantitative analysis (Fig. 1).

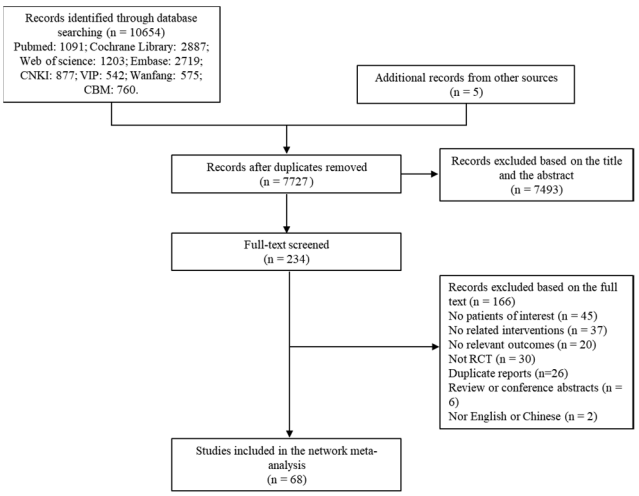

Figure 1. Flowchart of study selection process

3.2. Basic Characteristics and Quality Assessment

The network meta-analysis included 68 RCTs, totaling 32356 patients with RA. 68 RCTs, published from 1999 to 2021 were all randomized controlled trials. Among the 68 RCTs, 6 RCTs considered adalimumab as the study drug, accompanied with 7 RCTs for infliximab, 8 RCTs for certolizumab pegol, 6 RCTs for golimumab, 4 RCTs for etanercept, 6 RCTs for tocilizumab, 3 RCTs for sarilumab, 4 RCTs for tofacitinib, 4 RCTs for baricitinib, 5 RCTs for upadacitinib, 3 RCTs for peficitinib, 2 RCTs for filgotinib, 5 RCTs for abatacept, 3 RCTs for rituximab and 2 RCTs for anakinra. All patients with RA were diagnosed according to the 1987 ACR revised criteria or the 2010 ACR and EULAR classification criteria. Among the 68 RCTs, 40 and 21 RCTs had a low risk in random sequence generation and concealment of allocation, respectively. 67 RCTs performed blinding on the patients and research investigators; 25 RCTs performed blinding to the outcome indicators. There was a low risk of bias on incomplete outcome data and selective reporting in 67 and 62 RCTs respectively, and the risk of other bias was unclear.

3.3. Network Meta-analysis Results

3.3.1. ACR20

The network meta-analysis was conducted on 68 RCTs, including 16 interventions and 31461 patients (Fig. 2A). The consistency of interventions explored by the node split model was good, so the consistency model was applied. The PSRF value of the network meta-analysis was 1, indicating a good convergence. There were significant differences in the comparison between the fifteen drugs and the placebo, with RR ranging from 1.53 (95% CrI: 1.09, 2.15) for filigotinib to 2.74 (95% CrI: 2.20, 3.44) for certolizumab pegol. There were significant differences between adalimumab and certolizumab pegol (RR: 0.69, 95% CrI: 0.53, 0.88), infliximab and certolizumab pegol (RR: 0.72, 95% CrI: 0.53, 0.98), certolizumab pegol and baricitinib (RR: 1.44, 95% CrI: 1.03, 2.04), certolizumab pegol and upadacitinib (RR: 1.42, 95% CrI: 1.03, 1.97), certolizumab pegol and peficitinib (RR: 1.57, 95% CrI: 1.05, 2.39), certolizumab pegol and peficitinib (RR: 1.79, 95% CrI: 1.20, 2.68), certolizumab pegol and abatacept (RR: 1.40, 95% CrI: 1.02, 1.95), certolizumab pegol and anakinra (RR: 1.68, 95% CrI: 1.02, 2.77) (Fig. 3). According to the SUCRA values, certolizumab pegol (94.90%) had the highest probability of becoming the best

treatment measure in ACR20, followed by tocilizumab (73.05%) (Fig. 6).

3.3.2. ACR50

The network meta-analysis was conducted on 64 RCTs, including 16 interventions and 29026 patients (Fig. 2B). The consistency of interventions explored by the node split model was good, so the consistency model was applied. The PSRF value of the network meta-analysis was 1, indicating a good convergence. There were significant differences in the comparison between the fifteen drugs and the placebo, with RR ranging from 2.26 (95% CrI: 1.36, 3.84) for filigotinib to 4.10 (95% CrI: 2.82, 6.00) for certolizumab pegol. There was no significant difference between the drugs when they were indirectly compared between them (Fig. 4). According to the SUCRA values, certolizumab pegol (86.82%) had the highest probability to become the best treatment measure in ACR50, followed by etanercept (77.39%) (Fig. 6).

3.3.3. ACR70

The network meta-analysis was conducted on 63 RCTs, including 16 interventions and 28434 patients (Fig. 2C). The consistency of interventions explored by the node split model was good, so the consistency model was applied. The PSRF value of the network meta-analysis was 1, indicating a good convergence. There were significant differences in the comparison between the fifteen drugs and the placebo, with RR ranging from 2.58 (95% CrI: 1.19, 5.93) for rituximab to 8.68 (95% CrI: 3.10, 31.98) for etanercept. There was no significant difference in the indirect comparison between the fifiteen drugs (Fig. 5). According to the SUCRA values, etanercept (86.36%) had the highest probability of becoming the best treatment measure in ACR70, followed by certolizumab pegol (79.54%) (Fig. 6).

Figure 2. Network diagram of interventions.

Each circle represents a drug. The connected circles represent the two drugs that have been compared in studies. The width of the lines is proportional to the number of trails.

Abbreviation: ACR20, American College of Rheumatology 20% response; ACR50, American College of Rheumatology 50% response; ACR70, American College of Rheumatology 70% response; ADA, adalimumab; INF, infliximab; CER, certolizumab pegol; GOL, golimumab; ETA, etanercept; TOC, tocilizumab; SAR, sarilumab; TOF, tofacitinib; BAR, baricitinib; UPA, upadacitinib; PEF, peficitinib; FIL, filgotinib; ABA, abatacept; RIT, rituximab; ANA, anakinra.

ADA	1.05 (0.81, 1.37)	**1.46 (1.13, 1.88)**	1.13 (0.84, 1.51)	1.20 (0.84, 1.70)	1.20 (0.90, 1.59)	1.10 (0.77, 1.60)	1.19 (0.90, 1.59)	1.01 (0.76, 1.34)	1.03 (0.78, 1.34)	0.93 (0.63, 1.35)	0.81 (0.57, 1.16)	1.04 (0.79, 1.35)	1.10 (0.74, 1.64)	0.87 (0.54, 1.40)	**0.53 (0.45, 0.62)**
0.95 (0.73, 1.23)	INF	**1.38 (1.02, 1.89)**	1.07 (0.77, 1.49)	1.14 (0.77, 1.67)	1.14 (0.82, 1.57)	1.05 (0.71, 1.57)	1.13 (0.79, 1.62)	0.96 (0.68, 1.34)	0.98 (0.71, 1.34)	0.88 (0.58, 1.32)	0.77 (0.52, 1.15)	0.98 (0.73, 1.33)	1.04 (0.68, 1.60)	0.82 (0.50, 1.36)	**0.51 (0.41, 0.62)**
0.69 (0.53, 0.88)	**0.72 (0.53, 0.98)**	CER	0.78 (0.56, 1.08)	0.82 (0.55, 1.21)	0.82 (0.59, 1.14)	0.76 (0.51, 1.14)	0.82 (0.58, 1.17)	**0.69 (0.49, 0.97)**	**0.71 (0.51, 0.97)**	**0.64 (0.42, 0.95)**	**0.56 (0.37, 0.83)**	**0.71 (0.51, 0.98)**	0.75 (0.49, 1.16)	0.60 (0.36, 0.98)	**0.37 (0.29, 0.45)**
0.88 (0.66, 1.18)	0.93 (0.67, 1.29)	1.29 (0.93, 1.80)	GOL	1.06 (0.71, 1.58)	1.06 (0.75, 1.49)	0.98 (0.65, 1.49)	1.05 (0.73, 1.54)	0.89 (0.62, 1.27)	0.91 (0.65, 1.28)	0.82 (0.54, 1.25)	0.72 (0.47, 1.09)	0.92 (0.65, 1.29)	0.97 (0.62, 1.52)	0.77 (0.46, 1.29)	**0.47 (0.37, 0.60)**
0.84 (0.59, 1.19)	0.88 (0.60, 1.30)	1.22 (0.83, 1.80)	0.94 (0.63, 1.41)	ETA	1.00 (0.68, 1.49)	0.92 (0.58, 1.47)	0.99 (0.65, 1.53)	0.84 (0.56, 1.27)	0.86 (0.58, 1.28)	0.77 (0.48, 1.24)	0.68 (0.43, 1.08)	0.87 (0.58, 1.30)	0.92 (0.56, 1.50)	0.73 (0.42, 1.27)	**0.44 (0.32, 0.61)**
0.84 (0.63, 1.11)	0.88 (0.64, 1.21)	1.22 (0.88, 1.69)	0.94 (0.67, 1.33)	1.00 (0.67, 1.48)	TOC	0.92 (0.61, 1.40)	0.99 (0.69, 1.45)	0.84 (0.59, 1.20)	0.86 (0.61, 1.20)	0.77 (0.50, 1.17)	0.68 (0.45, 1.03)	0.87 (0.62, 1.21)	0.92 (0.59, 1.42)	0.72 (0.44, 1.21)	**0.44 (0.35, 0.56)**
0.91 (0.62, 1.30)	0.95 (0.64, 1.42)	1.32 (0.88, 1.97)	1.03 (0.67, 1.55)	1.08 (0.68, 1.71)	1.09 (0.72, 1.63)	SAR	1.08 (0.70, 1.67)	0.91 (0.59, 1.39)	0.93 (0.61, 1.40)	0.84 (0.52, 1.35)	0.74 (0.46, 1.18)	0.94 (0.62, 1.42)	1.00 (0.60, 1.64)	0.79 (0.45, 1.38)	**0.48 (0.34, 0.67)**
0.84 (0.63, 1.11)	0.89 (0.62, 1.26)	1.23 (0.86, 1.74)	0.95 (0.65, 1.38)	1.01 (0.65, 1.53)	1.01 (0.69, 1.45)	0.93 (0.60, 1.44)	TOF	0.85 (0.58, 1.23)	0.87 (0.60, 1.24)	0.78 (0.49, 1.21)	0.69 (0.44, 1.05)	0.87 (0.60, 1.25)	0.92 (0.58, 1.47)	0.73 (0.43, 1.24)	**0.45 (0.33, 0.59)**
0.99 (0.74, 1.32)	1.04 (0.74, 1.46)	**1.44 (1.03, 2.04)**	1.12 (0.79, 1.60)	1.19 (0.79, 1.79)	1.19 (0.83, 1.69)	1.09 (0.72, 1.68)	1.18 (0.81, 1.73)	BAR	1.02 (0.72, 1.45)	0.92 (0.59, 1.41)	0.81 (0.53, 1.24)	1.03 (0.72, 1.46)	1.09 (0.69, 1.71)	0.86 (0.51, 1.45)	**0.53 (0.41, 0.68)**
0.97 (0.74, 1.28)	1.02 (0.75, 1.42)	**1.42 (1.03, 1.97)**	1.10 (0.78, 1.55)	1.16 (0.78, 1.73)	1.16 (0.84, 1.63)	1.07 (0.71, 1.63)	1.16 (0.81, 1.68)	0.98 (0.69, 1.39)	UPA	0.90 (0.59, 1.37)	0.79 (0.53, 1.19)	1.01 (0.72, 1.41)	1.07 (0.69, 1.66)	0.84 (0.51, 1.41)	**0.52 (0.41, 0.66)**
1.08 (0.74, 1.59)	1.14 (0.76, 1.72)	**1.57 (1.05, 2.39)**	1.22 (0.80, 1.87)	1.29 (0.81, 2.08)	1.29 (0.85, 1.98)	1.19 (0.74, 1.94)	1.28 (0.83, 2.03)	1.09 (0.71, 1.68)	1.11 (0.73, 1.69)	PEF	0.88 (0.54, 1.43)	1.12 (0.74, 1.71)	1.19 (0.72, 1.97)	0.94 (0.53, 1.66)	**0.57 (0.41, 0.81)**
1.23 (0.87, 1.75)	1.29 (0.87, 1.94)	**1.79 (1.20, 2.68)**	1.39 (0.91, 2.11)	1.47 (0.92, 2.34)	1.47 (0.97, 2.23)	1.35 (0.84, 2.19)	1.46 (0.95, 2.27)	1.24 (0.81, 1.90)	1.26 (0.84, 1.90)	1.14 (0.70, 1.84)	FIL	1.27 (0.84, 1.92)	1.35 (0.82, 2.22)	1.07 (0.61, 1.88)	**0.65 (0.47, 0.92)**
0.96 (0.74, 1.26)	1.02 (0.75, 1.37)	**1.40 (1.02, 1.95)**	1.09 (0.78, 1.53)	1.15 (0.77, 1.71)	1.15 (0.82, 1.61)	1.06 (0.71, 1.61)	1.15 (0.80, 1.66)	0.97 (0.68, 1.38)	0.99 (0.71, 1.38)	0.89 (0.58, 1.35)	0.79 (0.52, 1.18)	ABA	1.06 (0.68, 1.65)	0.84 (0.50, 1.40)	**0.51 (0.40, 0.65)**
0.91 (0.61, 1.36)	0.96 (0.62, 1.47)	1.32 (0.86, 2.04)	1.03 (0.66, 1.60)	1.09 (0.67, 1.77)	1.09 (0.70, 1.69)	1.00 (0.61, 1.66)	1.08 (0.68, 1.73)	0.92 (0.58, 1.44)	0.94 (0.60, 1.45)	0.84 (0.51, 1.39)	0.74 (0.45, 1.22)	0.94 (0.61, 1.46)	RIT	0.79 (0.44, 1.42)	**0.48 (0.33, 0.70)**
1.15 (0.71, 1.85)	1.21 (0.74, 2.00)	**1.68 (1.02, 2.77)**	1.30 (0.78, 2.17)	1.38 (0.79, 2.40)	1.38 (0.83, 2.29)	1.27 (0.72, 2.24)	1.37 (0.81, 2.35)	1.16 (0.69, 1.95)	1.18 (0.71, 1.96)	1.07 (0.60, 1.87)	0.94 (0.53, 1.64)	1.20 (0.71, 1.99)	1.27 (0.71, 2.26)	ANA	**0.61 (0.39, 0.96)**
1.88 (1.61, 2.20)	**1.98 (1.60, 2.47)**	**2.74 (2.20, 3.44)**	**2.12 (1.67, 2.72)**	**2.25 (1.64, 3.09)**	**2.25 (1.78, 2.86)**	**2.07 (1.49, 2.92)**	**2.23 (1.70, 2.99)**	**1.89 (1.46, 2.46)**	**1.93 (1.53, 2.45)**	**1.74 (1.23, 2.46)**	**1.53 (1.09, 2.15)**	**1.95 (1.54, 2.48)**	**2.06 (1.43, 2.99)**	**1.63 (1.04, 2.57)**	PLB

Figure 3. Comparisons for ACR20 of the network meta-analysis.

Abbreviation: ADA, adalimumab; INF, infliximab; CER, certolizumab pegol; GOL, golimumab; ETA, etanercept; TOC, tocilizumab; SAR, sarilumab; TOF, tofacitinib; BAR, baricitinib; UPA, upadacitinib; PEF, peficitinib; FIL, filgotinib; ABA, abatacept; RIT, rituximab; ANA, anakinra.

4. Discussion

The study included 32356 patients of 68 RCTs used a network meta-analysis to investigate the comparative efficacy of bDMARDs and tsDMARDs for the treatment of RA patients who had been treated with csDMARDs without adequate response. The quality of included studies was generally high. Sixteen interventions, including placebo, were included in ACR20, ACR50, and ACR70. In terms of efficacy, tumor necrosis factor-α inhibitors, interleukin-6 inhibitors, interleukin-1 inhibitors, JAK inhibitors, T-cell co-stimulation modulator, and CD20 monoclonal antibody all had significant differences compared with placebo, which indicated that the typical drugs of bDMARDs and tsDMARDs were effective in relieving symptoms and signs. It could be seen that the ranking of certolizumab pegol was higher than other

interventions. This may be due to the fact that polyethylene glycolization technology was used for certolizumab pegol, which was attached to polyethylene glycol at a special site, and while maintaining the binding activity, its circulating half-life was longer compared to other drugs, which could exert drug effects in patients for a longer period of time, resulting in better efficacy [80].

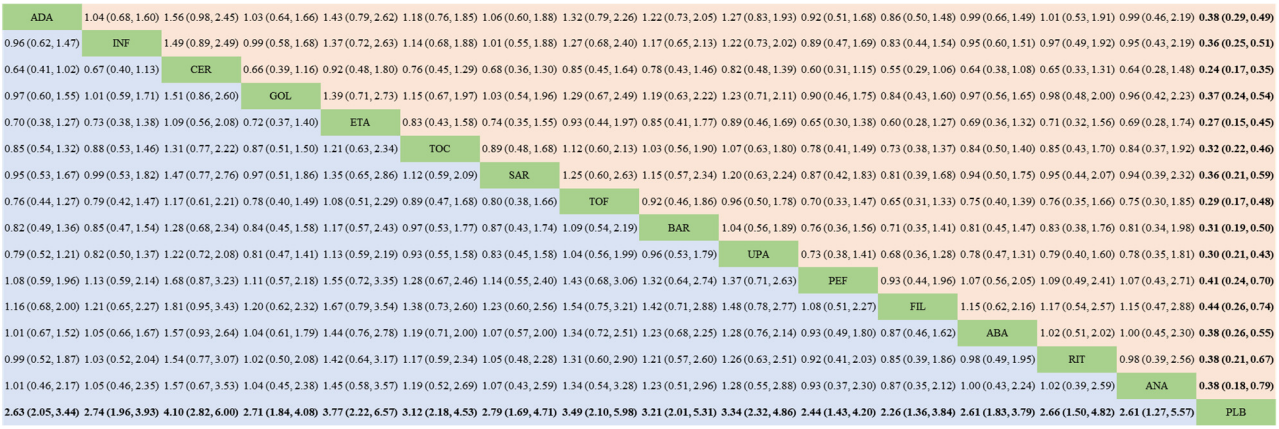

Figure 4. Comparisons for ACR50 of the network meta-analysis.

Abbreviation: ADA, adalimumab; INF, infliximab; CER, certolizumab pegol; GOL, golimumab; ETA, etanercept; TOC, tocilizumab; SAR, sarilumab; TOF, tofacitinib; BAR, baricitinib; UPA, upadacitinib; PEF, peficitinib; FIL, filgotinib; ABA, abatacept; RIT, rituximab; ANA, anakinra.

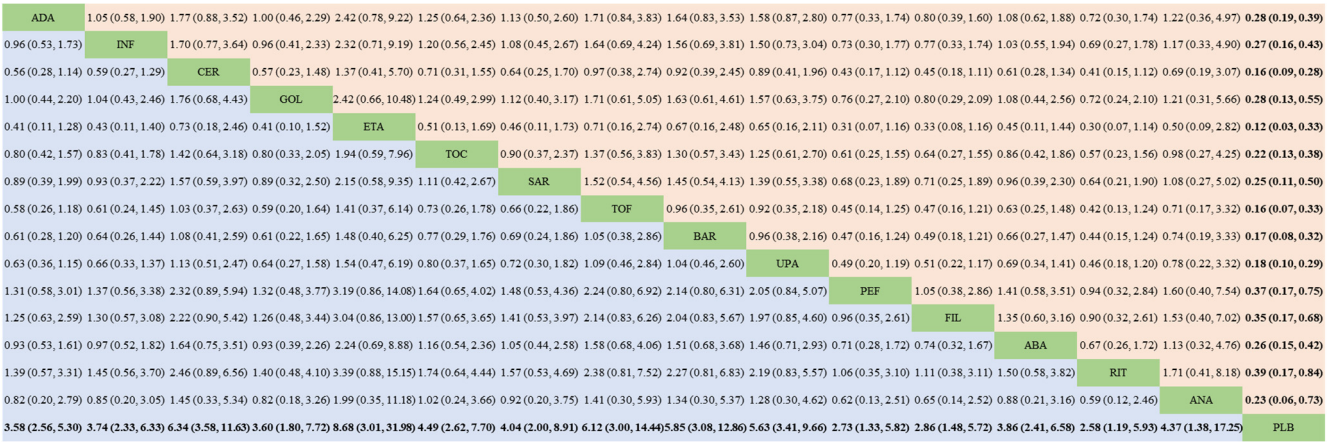

Figure 5. Comparisons for ACR70 of the network meta-analysis.

Abbreviation: ADA, adalimumab; INF, infliximab; CER, certolizumab pegol; GOL, golimumab; ETA, etanercept; TOC, tocilizumab; SAR, sarilumab; TOF, tofacitinib; BAR, baricitinib; UPA, upadacitinib; PEF, peficitinib; FIL, filgotinib; ABA, abatacept; RIT, rituximab; ANA, anakinra.

Interventions	ACR20		ACR50		ACR70	
	SUCRA (%)	RANK	SUCRA (%)	RANK	SUCRA (%)	RANK
adalimumab	40.57	12	39.92	13	39.33	12
infliximab	51.06	8	46.00	8	43.63	10
certolizumab pegol	94.90	1	86.82	1	79.54	2
golimumab	63.66	5	44.70	9	41.97	11
etanercept	71.08	4	77.39	2	86.36	1
tocilizumab	73.05	2	61.11	6	57.45	6
sarilumab	58.68	6	48.39	7	49.76	8
tofacitinib	71.28	3	71.38	3	76.27	3
baricitinib	43.56	11	63.63	5	74.46	4
upadacitinib	46.81	10	69.02	4	73.45	5
peficitinib	32.66	13	35.40	14	26.00	14
filgotinib	18.25	15	28.30	15	26.98	13
abatacept	48.40	9	40.14	12	46.33	9
rituximab	57.82	7	44.08	10	24.16	15
anakinra	28.05	14	43.66	11	54.17	7
placebo	0.17	16	0.05	16	0.14	16

Figure 6. The relative ranking of interventions based on SUCRA.

Abbreviation: ACR20, American College of Rheumatology 20% response; ACR50, American College of Rheumatology 50% response; ACR70, American College of Rheumatology 70% response; SUCRA, surface under the cumulative ranking curve

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The efficacy of the combination csDMARDs with bDMARDs or tsDMARDs was comprehensively evaluated in this study. It was the first network meta-analysis involved a total of fifteen drugs and three outcomes. However, there were some limitations which should be mentioned in this study. On the one hand, the language of included studies was English or Chinese, which may have potential selective bias. On the other hand, there was some heterogeneity in the duration of drug maintenance and time point of outcome assessment.

5. Conclusion

In conclusion, bDMARDs and tsDMARDs were all effective in improving signs and symptoms in RA patients who had been treated with csDMARDs without adequate response. Certolizumab combined with csDMARDs had better performance on efficacy compared with other interventions.

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