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Comparison of the efficacy and safety of tofacitinib and baricitinib in patients with active rheumatoid arthritis: a Bayesian network meta-analysis of randomized controlled trials

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic synovial joint inflammation, which leads to disability and a decreased quality of life [38]. The intracellular pathways, which include the Janus kinases (JAKs—JAK1, JAK2, JAK3, and tyrosine kinase 2 [Tyk2]), are critical to immune cell activation, proinflammatory cytokine production, and cytokine signaling [14]. Proinflammatory cytokines—including the interleukins 2, 6, 12, 15, and 23, interferons, and granulocyte-macrophage colony-stimulating factor (GM-CSF), which act through the JAK family—are implicated in RA [36]. Small-molecule JAK inhibitors are being clinically developed for the treatment of RA [34].

Tofacitinib (CP-690,550) is an orally administered JAK inhibitor [6]. It selectively inhibits JAK-1, JAK-2, and JAK-3, with functional cellular specificity for JAK-1 and JAK-3 over JAK-2 [7, 30]. Tofacitinib effectively modulates adaptive and innate immunity [30]. Baricitinib is a potent, selective JAK1 and JAK2 inhibitor [37]. Baricitinib shows similar inhibitory activity against both JAK1 and JAK2, but decreased activity against JAK3 and tyrosine kinase 2 [15].

Several clinical trials have attempted to evaluate the efficacy and safety of tofacitinib and baricitinib in patients with active RA with an incomplete response to methotrexate (MTX) or biologics [3, 9, 13, 16, 20, 21, 23, 39–41, 44, 45]. All of these drugs have shown considerable efficacy in placebo-controlled trials, but the relative efficacy and safety of tofacitinib and baricitinib remain unclear due to a lack of head-to-head comparisons. In the absence of head-to-head trials of relevant comparators, it is necessary to combine evidence from randomized controlled trials (RCTs) of different treatments to derive an estimate of the effect of one treatment versus another. A network meta-analysis can assess the

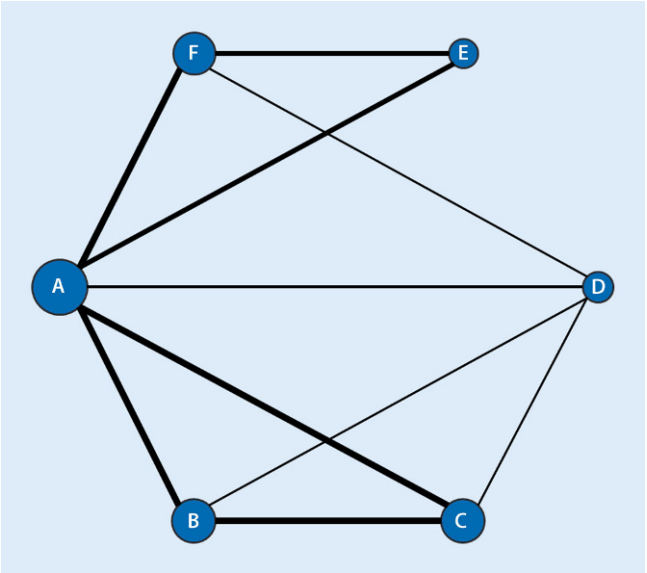

Fig. 1 ▲ Evidence network diagram of network meta-analysis comparisons. The width of each edge is proportional to the number of randomized controlled trials comparing each pair of treatments, and the size of each treatment node is proportional to the number of randomized participants (*sample size*). *A*: Placebo + MTX, *B*: Tofacitinib 5 mg + MTX, *C*: Tofacitinib 10 mg + MTX, *D*: Adalimumab + MTX, *E*: Baricitinib 2 mg + MTX, *F* Baricitinib 4 mg + MTX

Table 1 Characteristics of individual studies included in the meta-analysis and systematic review

Study [Ref]	Patient number	Subjects	Doses, twice daily (numbers)	Follow-up time point for evaluation	Jadad score
Kremer 2013 [21]	795	DMARD-IR	Placebo + MTX (159), Tb 5 mg + MTX (318), Tb 10 mg + MTX (318)	6 months	5
Van der Heijde 2013 [44]	797	MTX-IR	Placebo + MTX (160), Tb 5 mg + MTX (321), Tb 10 mg + MTX (316)	6 months	4
Burmester 2013 [3]	399	TNF-IR	Placebo + MTX (132), Tb 5 mg + MTX (133), Tb 10 mg + MTX (134)	3 months	4
Van Vollenhoven 2012 [45]	717	MTX-IR	Placebo + MTX (108), Tb 5 mg + MTX (204), Tb 10 mg + MTX (201), adalimumab 40 mg once a week + MTX (204)	3 months	4
Kremer 2012 [23]	214	MTX-IR	Placebo + MTX (69), Tb 5 mg + MTX (71), Tb 10 mg + MTX (74)	3 months	3
Tanaka 2011 [40]	84	MTX-IR	Placebo + MTX (28), Tb 5 mg + MTX (28), Tb 10 mg + MTX (28)	3 months	3
Study [ref]	**Patient number**	**Subjects**	**Doses, once daily (numbers)**	**Follow-up time point for evaluation**	**Jadad score**
Genovese 2016 [13]	527	Biologic-IR	Placebo + MTX (176), baricitinib 2 mg + MTX (174), baricitinib 4 mg + MTX (177)	3 months	3
Keystone 2015 [20]	202	MTX-IR	Placebo + MTX (98), baricitinib 2 mg + MTX (52), baricitinib 4 mg + MTX (52)	3 months	4
Tanaka 2016 [39]	97	MTX-IR	Placebo + MTX (49), baricitinib 2 mg + MTX (24), baricitinib 4 mg + MTX (24)	3 months	4
Taylor 2015 [41]	1305	MTX-IR	Placebo + MTX (488), baricitinib 4 mg + MTX (487), adalimumab 40 mg once a week + MTX (330)	3 months	3
Dougados 2015 [9]	684	DMARD-IR	Placebo + MTX (228), baricitinib 2 mg + MTX (229), baricitinib 4 mg + MTX (227)	3 months	3
Greenwald 2010 [16]	62	DMARD-IR	Placebo + MTX (31), baricitinib 4 mg + MTX (31)	3 months	3

DMARD disease-modifying anti-rheumatic drug, *MTX* methotrexate, *IR* incomplete response, *Tb* tofacitinib

comparative efficacy of multiple interventions by combining evidence across a network of RCTs, even in the absence of head-to-head comparisons [4, 5], in contrast to a traditional meta-analysis [26, 28]. The present study aimed to use a network meta-analysis to investigate the relative efficacy and safety of tofacitinib and baricitinib in patients with active RA and an inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) or biologics.

Materials and methods

Identification of eligible studies and data extraction

We conducted an exhaustive search for studies that examined the efficacy and safety of tofacitinib and baricitinib in patients with active RA who showed an inadequate response to DMARDs including MTX or biologics. A literature search was performed using MEDLINE, EMBASE, the Cochrane Controlled Trials Register, and the American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) conference proceedings to identify available articles (up to April 2018). The following key words and subject terms were used in the search: "tofacitinib", "baricitinib", and "rheumatoid arthritis". All references in the studies were reviewed to identify additional works not included in the electronic databases. RCTs were included if they met the following criteria: (1) the study compared

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Abstract

Objectives. The relative efficacy and safety of tofacitinib and baricitinib were assessed in patients with rheumatoid arthritis (RA) with an inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) or biologics.
Methods. We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tofacitinib and baricitinib in combination with DMARDs in RA patients with an inadequate DMARD or biologic response.
Results. Twelve RCTs including 5883 patients met the inclusion criteria. There were 15 pairwise comparisons including 10 direct comparisons of 6 interventions. Tofacitinib 10 mg + methotrexate (MTX) and baricitinib 4 mg + MTX were among the most effective treatments for active RA with an inadequate DMARD or biologic response, followed by baricitinib 2 mg + MTX, tofacitinib 5 mg + MTX, and adalimumab + MTX. The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that tofacitinib 10 mg + MTX had the highest probability of being the best treatment to achieve the ACR20 response rate (SUCRA = 0.865), followed by baricitinib 4 mg + MTX (SUCRA = 0.774), baricitinib 2 mg + MTX (SUCRA = 0.552), tofacitinib 5 mg + MTX (SUCRA = 0.512), adalimumab + MTX (SUCRA = 0.297), and placebo + MTX (SUCRA <0.001). No significant differences were observed in the incidence of serious adverse events after treatment with tofacitinib + MTX, baricitinib + MTX, adalimumab + MTX, or placebo + MTX.
Conclusions. In RA patients with an inadequate response to DMARDs or biologics, tofacitinib 10 mg + MTX and baricitinib 4 mg + MTX were the most efficacious interventions and were not associated with a significant risk of serious adverse events.

Keywords

Tofacitinib · Baricitinib · Rheumatoid arthritis · Network meta-analysis · Janus kinase inhibitors

Vergleich der Wirksamkeit und Sicherheit von Tofacitinib und Baricitinib bei Patienten mit aktiver rheumatoider Arthritis: Bayes-Netz-Metaanalyse randomisierter kontrollierter Studien

Zusammenfassung

Ziel. Bei Patienten mit rheumatoider Arthritis (RA) und unzureichendem Ansprechen auf krankheitsmodifizierende Medikamente („disease-modifying anti-rheumatic drugs", DMARD) oder Biologika wurden die relative Wirksamkeit und Sicherheit von Tofacitinib und Baricitinib ermittelt.
Methoden. Die Autoren führten eine Bayes-Netz-Metaanalyse zur Kombination direkter und indirekter Evidenz aus randomisierten kontrollierten Studien („randomized controlled trials", RCT) durch, die der Untersuchung der Wirksamkeit und Sicherheit von Tofacitinib und Baricitinib zusätzlich zu DMARD bei RA-Patienten mit unzureichendem Ansprechen auf DMARD oder Biologika diente.
Ergebnisse. Die Einschlusskriterien erfüllten 12 RCT mit 5883 Patienten. Es wurden 15 paarweise erfolgende Vergleiche einschließlich 10 direkter Vergleiche von 6 Interventionen durchgeführt. Tofacitinib 10 mg + Methotrexat (MTX) und Baricitinib 4 mg + MTX gehörten zu den wirksamsten Therapien bei aktiver RA mit unzureichendem Ansprechen auf DMARD oder Biologika, nächstwirksam waren Baricitinib 2 mg + MTX, Tofacitinib 5 mg + MTX und Adalimumab + MTX. Die auf dem SUCRA-Wert („surface under the cumulative ranking curve") basierende Rangfolgewahrscheinlichkeit ergab für Tofacitinib 10 mg + MTX die größte Wahrscheinlichkeit, die beste Behandlung zur Erzielung einer Ansprechrate mit 20%iger Linderung der Symptome (ACR20) zu sein (SUCRA = 0,865); es folgten Baricitinib 4 mg + MTX (SUCRA = 0,774), Baricitinib 2 mg + MTX (SUCRA = 0,552), Tofacitinib 5 mg + MTX (SUCRA = 0,512), Adalimumab + MTX (SUCRA = 0,297) und Placebo + MTX (SUCRA <0,001). Bei der Inzidenz schwerer unerwünschter Ereignisse nach Behandlung mit Tofacitinib + MTX, Baricitinib + MTX, Adalimumab + MTX oder Placebo + MTX wurden keine signifikanten Unterschiede festgestellt.
Schlussfolgerung. Bei RA-Patienten mit unzureichendem Ansprechen auf DMARD oder Biologika stellten Tofacitinib 10 mg + MTX und Baricitinib 4 mg + MTX die wirksamsten Interventionen dar, sie waren dabei nicht mit einem signifikanten Risiko für schwere unerwünschte Ereignisse verbunden.

Schlüsselwörter

Tofacitinib · Baricitinib · Rheumatoide Arthritis · Netzwerk-Metaanalyse · Januskinase-Inhibitoren

tofacitinib or baricitinib with DMARDs including MTX to placebo + DMARDs including MTX for the treatment of active RA that responded inadequately to DMARDs or biologics; (2) the study provided endpoints for the clinical efficacy and safety of tofacitinib or baricitinib at 3 or 6 months; and (3) the study included patients diagnosed with RA based on the ACR criteria for RA [18] or the 2010 ACR/EULAR classification criteria [1]. The exclusion criteria were as follows: (1) the study included duplicate data; and (2) the study did not contain adequate data for inclusion. The efficacy outcome was the number of patients who fulfilled the ACR 20% improvement criteria (achieved an ACR20 response), and the safety outcome was the number of patients who experienced serious adverse events (SAEs). The following information was extracted from each study: first author, year of publication, country in which the study was conducted, dosages of tofacitinib and baricitinib, follow-up time when outcomes were evaluated, and efficacy and safety outcomes. Data were extracted from original studies by 2 independent reviewers. Any discrepancy between the reviewers was resolved by consensus or a third reviewer. We quantified the methodological quality of studies using

Table 2 Ten direct comparisons of interventions

Comparison	Study number	Patient number
Placebo + MTX vs. tofacitinib 5 mg + MTX	6	1731
Placebo + MTX vs. tofacitinib 10 mg + MTX	6	1727
Tofacitinib 5 mg + MTX vs. tofacitinib 10 mg + MTX	6	2146
Placebo + MTX vs. adalimumab + MTX	2	1130
Tofacitinib 5 mg + MTX vs. adalimumab + MTX	1	408
Tofacitinib 10 mg + MTX vs. adalimumab + MTX	1	405
Placebo + MTX vs. baricitinib 2 mg + MTX	4	1030
Placebo + MTX vs. baricitinib 4 mg + MTX	6	2068
Baricitinib 2 mg + MTX vs. baricitinib 4 mg + MTX	4	959
Adalimumab + MTX vs. baricitinib 4 mg + MTX	1	817

MTX methotrexate

Table 3 T Rank probability of the efficacy of tofacitinib and baricitinib based on the number of patients who achieved an ACR20 (A) response and the safety based on the number of serious adverse events (B)

A) Efficacy	
Treatment	*SUCRA*
Tofacitinib 10 mg + MTX	0.865
Baricitinib 4 mg + MTX	0.774
Baricitinib 2 mg + MTX	0.552
Tofacitinib 5 mg + MTX	0.512
Adalimumab + MTX	0.297
Placebo + MTX	<0.001
B) Safety	
Treatment	*SUCRA*
Adalimumab + MTX	0.877
Baricitinib 2 mg + MTX	0.782
Placebo + MTX	0.475
Baricitinib 4 mg + MTX	0.474
Tofacitinib 10 mg + MTX	0.208
Tofacitinib 5 mg + MTX	0.184

SUCRA surface under the cumulative ranking curve, *MTX* methotrexate

Jadad scores [19] ranging from 0 to 5. Quality was classified as high (a score of 3–5) or low (a score of 0–2). We conducted this network meta-analysis in accordance with the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [31].

Evaluation of statistical associations for network meta-analysis

In RCTs that compared multiple doses of tofacitinib and baricitinib in different arms, the results from the different arms were analyzed simultaneously. The efficacy and safety of tofacitinib and baricitinib in different arms were ordered according to the probability of being ranked as the best performing regimen. We performed a Bayesian random-effects network meta-analysis using NetMetaXL [2] and WinBUGS statistical analysis program version 1.4.3 (MRC Biostatistics Unit, Institute of Public Health, Cambridge, UK). The Bayesian approach offers greater flexibility in the use of more complex models and different outcome types, thereby enabling the simultaneous comparison of all treatment options. We chose a random-effects model for the network meta-analysis, as it incorporates between-study variations and utilizes a conservative method. The random network model was selected prior to the statistical analysis. We used the Markov chain Monte Carlo method to obtain pooled effect sizes [4]. All chains were run with 10,000 burn-in iterations followed by 10,000 monitoring iterations. Information on relative effects was converted to a probability that a treatment is the best, second best, etc., or to the ranking of each treatment, called the surface under the cumulative ranking curve (SUCRA; [35]), which is expressed as a percentage. The SUCRA value is 1 when a treatment is certain to be the best and 0 when a treatment is certain to be the worst. SUCRA values enable the overall ranking of treatments for a particular outcome. SUCRA simplifies the information on the effect of each treatment into a single number, thereby facilitating decision-making. The league table arranges the presentation of summary estimates by ranking the treatments in the order of the most pronounced impact on the outcome under consideration, based on the SUCRA value [35]. We reported the pairwise odds ratio (OR) and 95% credible interval (CrI; or Bayesian confidence interval) and adjusted for multiple-arm trials. Pooled results were considered statistically significant if the 95% CrI did not contain the value 1.

Inconsistency assessment

Inconsistency refers to the extent of disagreement between direct and indirect evidence [8], and assessments of inconsistency are important when conducting a network meta-analysis because an inconsistency plot yields information that can help identify the loops in which the inconsistency is present [17]. We plotted the posterior mean deviance of the individual data points in the inconsistency model against the posterior mean deviance in the consistency model to assess the network inconsistency between the direct and indirect estimates in each loop [43]. A sensitivity test was performed by comparing the random and fixed effects models.

Results

Studies included in the meta-analysis

A total of 588 studies were identified through electronic or manual searches, and 17 studies were selected for a full-text review based on the title and abstract details. However, 5 of the 17 studies were excluded due to inclusion of DMARD-naïve RA patients [12, 25], monotherapy [10, 11], or a short-term follow-up period [22]. Thus, 12 RCTs that included 5883 patients (2964 events for efficacy and 206 events for safety) met the inclusion criteria [3, 9, 13, 16, 20, 21, 23, 39–41, 44, 45]. All of the RCTs provided data related to both efficacy and safety, except for 2 that showed only efficacy data for the tofacitinib and baricitinib groups [16, 23]. The evidence

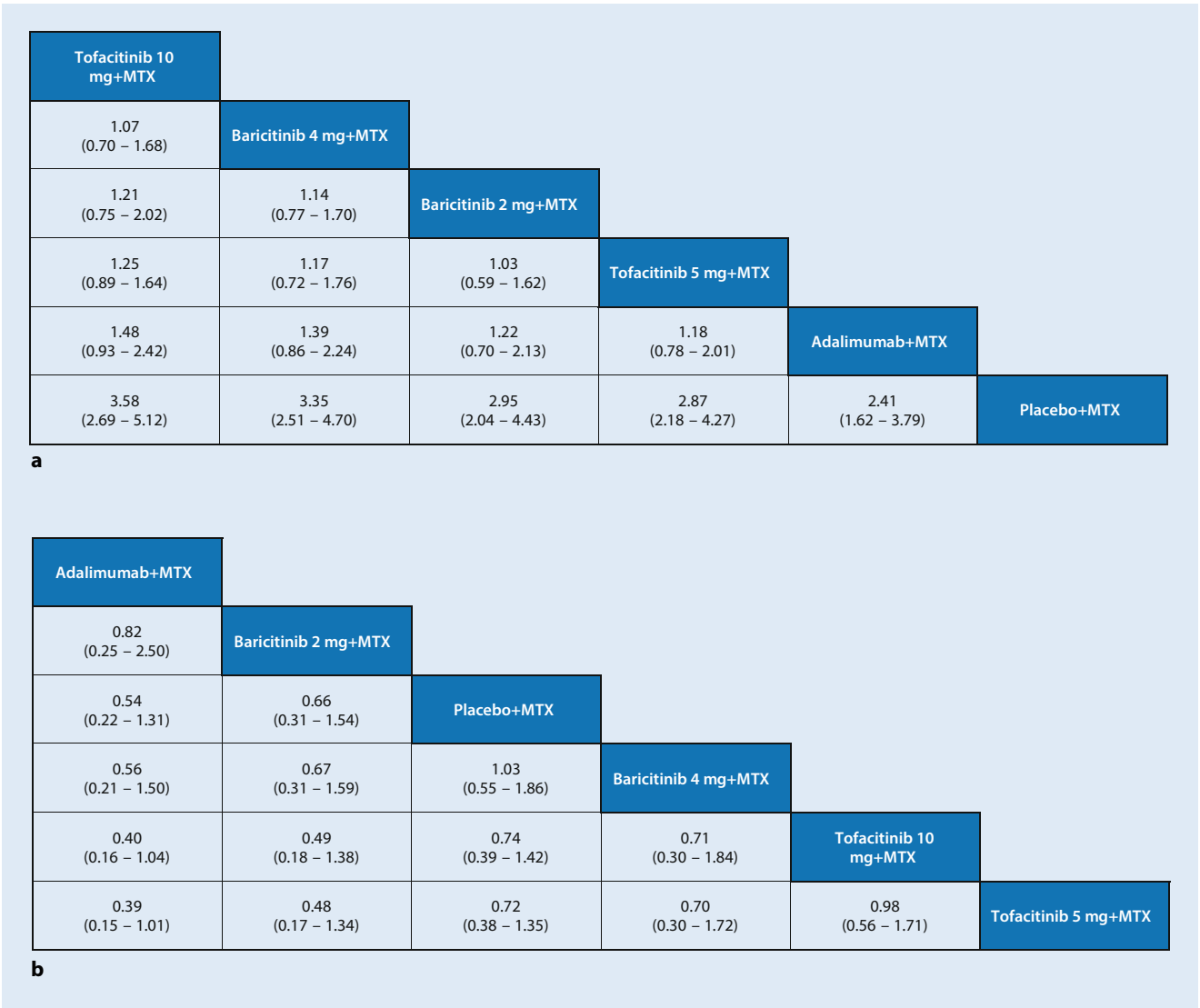

Fig. 2 ▲ League tables showing the results of the network meta-analysis comparing the effects of all drugs including odds ratios and 95% credible intervals. **a** Efficacy: Odds ratio >1 indicates that the top-left treatment is better. **b** Tolerability: Odds ratio <1 indicates that the top-left treatment is better

network diagram shows data pertaining to the number of studies that compared different treatments and the number of patients included in each treatment (**Fig. 1**, **Table 1 and 2**). While the recommended dosage of tofacitinib is 5 mg twice daily [42], some patients may benefit from an increased dose of 10 mg twice daily. Thus, we chose the dosages of 5 and 10 mg of tofacitinib twice daily. For phase II and III RCTs, the recommended dosage of baricitinib is 2 mg or 4 mg once daily. Therefore, we chose the dosages of 2 and 4 mg of baricitinib once daily. There were 15 pairwise comparisons including 10 direct comparisons and 6 interventions, including tofacitinib 5 mg + MTX, tofacitinib 10 mg + MTX, baricitinib 2 mg + MTX, baricitinib 4 mg + MTX, adalimumab 40 mg once every 2 weeks + MTX, and placebo + MTX for the network meta-analysis. The Jadad scores of the studies ranged from 3–5, indicating high study quality overall (**Table 1 and 2**). Relevant features of the studies included in the meta-analysis are provided in **Table 1 and 2**.

Network meta-analysis of the efficacy of tofacitinib and baricitinib in RCTs

Tofacitinib 10 mg + MTX is listed in the top left of the diagonal of the league table (OR, 3.58; 95% CrI, 2.69–5.12), because it was associated with the most favorable SUCRA for the ACR20 response rate, whereas placebo + MTX is listed in the bottom right of the diagonal of the league table because it was associated with the least favorable results (**Fig. 2**). All of the interventions achieved a significant ACR20 response compared with placebo + MTX (**Fig. 2**). A trend of greater efficacy with

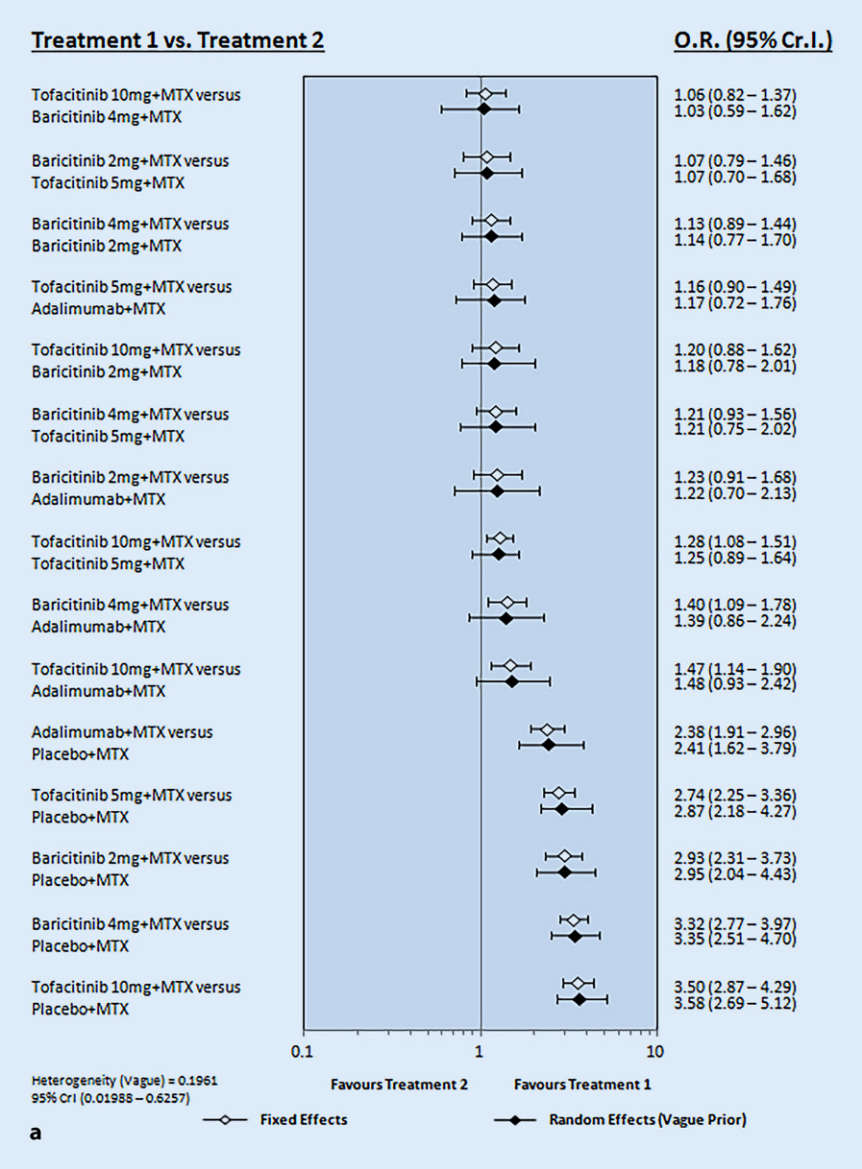

Fig. 3 ▲ Bayesian network meta-analysis results of randomized controlled studies on the relative efficacy (**a**) and safety (**b**) of tofacitinib and baricitinib. *O.R.* odds ratio, *95% Cr.I.* 95% credible interval, *MTX* methotrexate

tofacitinib 10 mg + MTX, baricitinib 4 mg + MTX, baricitinib 2 mg + MTX, and tofacitinib 5 mg + MTX than with adalimumab + MTX was noted (**Figs. 2 and 3**). The ranking probability based on SUCRA indicated that tofacitinib 10 mg + MTX had the highest probability of being the best treatment in terms of the ACR20 response rate (SUCRA = 0.865), followed by baricitinib 4 mg + MTX (SUCRA = 0.774), baricitinib 2 mg + MTX (SUCRA = 0.552), tofacitinib 5 mg + MTX (SUCRA = 0.512), adalimumab + MTX (SUCRA = 0.297), and placebo + MTX (SUCRA <0.001; **Table 3**).

Network meta-analysis of the safety of tofacitinib and baricitinib in RCTs

The number of SAEs in the adalimumab + MTX, baricitinib 2 mg + MTX, placebo + MTX, and baricitinib 4 mg + MTX groups tended to be lower than that in the tofacitinib 10 mg + MTX and tofacitinib 5 mg + MTX groups (**Figs. 2 and 3**). However, the number of SAEs did not differ significantly between the tofacitinib and baricitinib groups (**Figs. 2 and 3**). Ranking probability based on SUCRA values indicated that adalimumab + MTX, baricitinib 2 mg + MTX, and placebo + MTX had a higher probability of being the safest treatment (SUCRA = 0.877, 0.782, 0.475, respectively), followed by baricitinib 4 mg + MTX (SUCRA = 0.474), tofacitinib 10 mg + MTX (SUCRA = 0.208), and tofacitinib 5 mg + MTX (SUCRA = 0.184; **Table 3**).

Inconsistency and sensitivity analysis

The contributions to the deviance were likely to be similar and close to 1 for both models. Inconsistency plots assessing network inconsistencies between direct and indirect estimates showed a low possibility of inconsistencies that might significantly affect the results of the network meta-analysis (**Fig. 4**). In addition, the results of the random- and fixed-effects models yielded the same interpretation, indicating that the results of this network meta-analysis were robust (**Fig. 3**).

Discussion

Drugs that inhibit pathways may directly block cytokine signaling or indirectly modulate T-cell functions through the suppression of the CD80/86 expression in the dendritic cells [24, 32]. Recent studies on the treatment of RA have focused on the small molecules that can inhibit intracellular kinases (such as those from the JAK family; [34]). Treatment trends have evolved to include the increasing use of new small molecules to target the JAK pathways.

Since patients with RA may receive tofacitinib or baricitinib when they are either refractory or intolerant to MTX or biologics or when they are contraindicated, it is important to determine the optimal treatment options for these patients. In addition to efficacy, the safety of tofacitinib and baricitinib is an important factor in selecting the therapeutic approach in patients with RA. We conducted a network meta-analysis to compare the efficacy and safety of

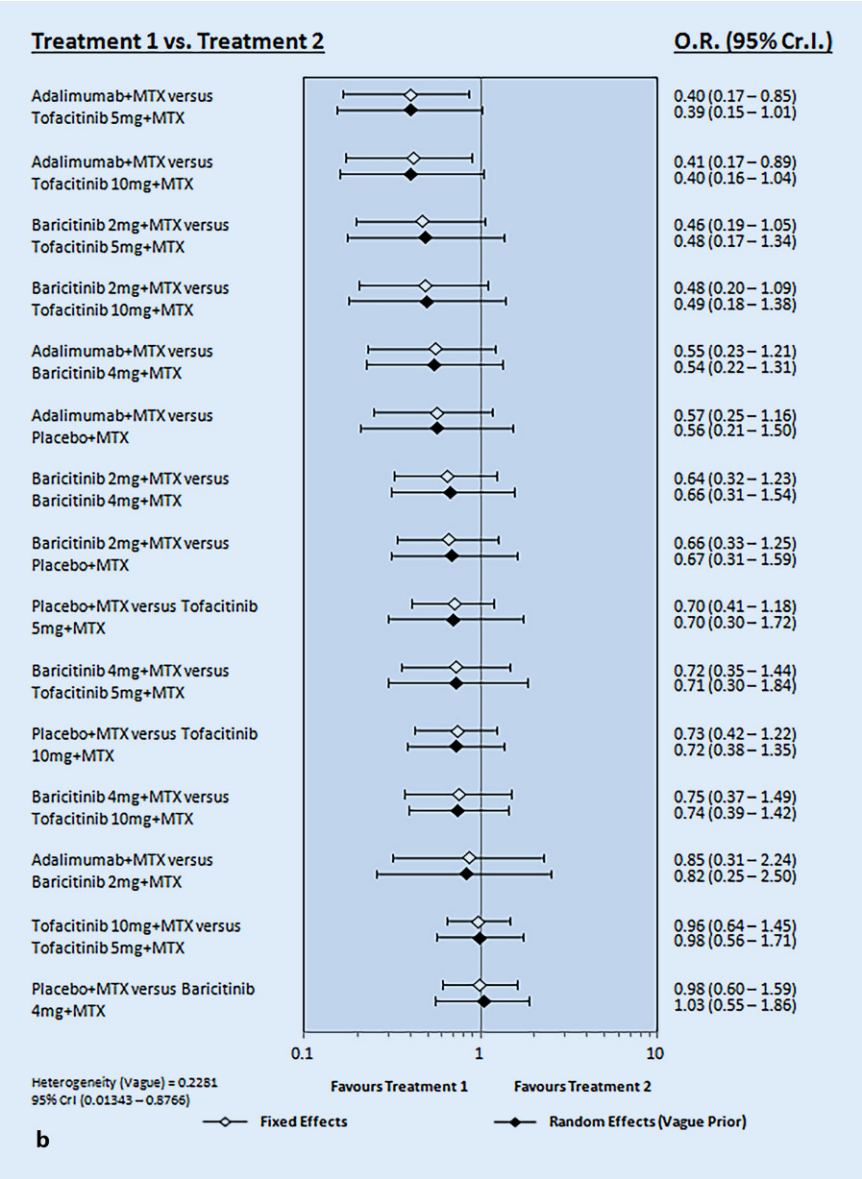

Fig. 3 ▲ (continued)

tofacitinib and baricitinib in patients with active RA who show an inadequate response to DMARDs including MTX or biologics. With regard to efficacy, our network meta-analysis suggested that tofacitinib 10 mg + MTX and baricitinib 4 mg + MTX were the most effective treatments for active RA that responded inadequately to DMARDs or biologics, followed by baricitinib 2 mg + MTX, tofacitinib 5 mg + MTX, and adalimumab + MTX. Tofacitinib + MTX and baricitinib + MTX were more likely to be the best for achieving an ACR20 response, as compared to adalimumab + MTX. Although the reason for this finding was not identified, it was suggested to be differences in efficacies between JAK inhibitors and adalimumab. In terms of safety based on the number of SAEs, tofacitinib 10 mg + MTX and tofacitinib 5 mg + MTX were associated with more SAEs and had a lower probability of being optimal in terms of SAEs than adalimumab + MTX, baricitinib 2 mg + MTX, placebo + MTX, and baricitinib 4 mg + MTX. However, no significant difference was observed in the number of SAEs among the 6 interventions, suggesting comparable safety among the different tofacitinib and baricitinib regimens and the placebo.

The results of this network meta-analysis, which combined evidence from both direct and indirect comparisons for evaluation of the relative efficacy and safety of baricitinib, were in accordance with those of previous meta-analyses of direct comparisons showing that treatment with tofacitinib and baricitinib led to a statistically significant improvement according to the response criteria (ACR20) compared to placebo and that there were no statistically significant differences between tofacitinib and placebo in terms of SAEs [27, 29]. However, our network meta-analysis differs from previous meta-analyses in that we were able to generate a rank order for the relative efficacy and safety of tofacitinib and baricitinib in patients with active RA.

However, our results should be interpreted with caution, as this study had some limitations. First, the follow-up time points were limited to 3 or 6 months. Therefore, the follow-up duration was too short to evaluate the long-term effects, and longer comparative studies are needed. Second, the design and patient characteristics of the included trials were heterogeneous; therefore, there is a risk that the differences across the studies affected the results of the analysis. Third, this study did not comprehensively address the efficacy and safety outcomes of tofacitinib and baricitinib in RA patients. It focused solely on the effectiveness based on the number of patients that achieved an ACR20 response and on the safety according to the number of SAEs, without an assessment of various other outcomes [33].

In conclusion, we conducted a Bayesian network meta-analysis involving 12 RCTs and found that tofacitinib 10 mg + MTX and baricitinib 4 mg + MTX were the most efficacious interventions for RA patients with an inadequate response to DMARD or biologics therapy and that neither was associated with a significant risk of SAEs. Long-term studies are warranted to determine the relative efficacy and safety of tofacitinib and baricitinib in a large number of patients with active RA that is inadequately responsive to MTX or biologics.

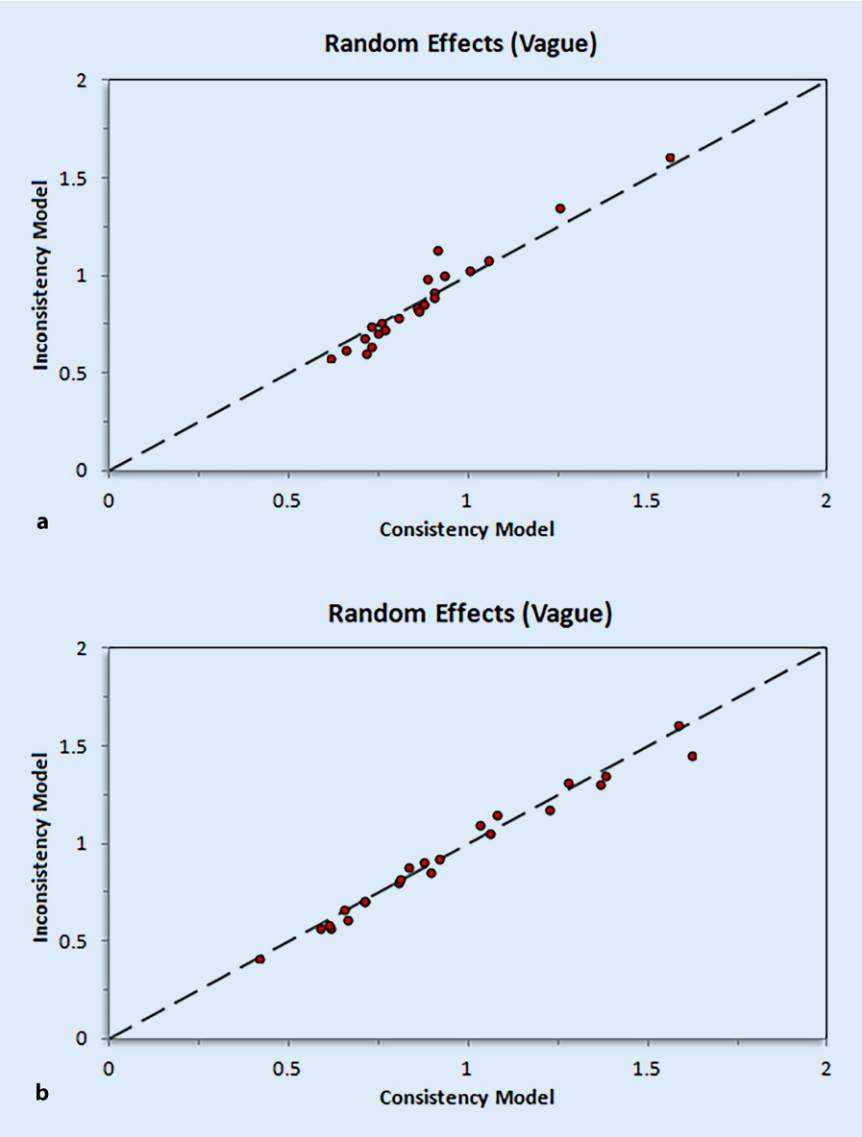

Fig. 4 ▲ Inconsistency plot for the efficacy (**a**) and safety (**b**) of tofacitinib and baricitinib. Plot of the individual data points' posterior mean deviance contributions for the consistency model (*horizontal axis*) and the unrelated mean effects model (*vertical axis*) along with the line of equality

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Compliance with ethical guidelines

Conflict of interest. S.-C. Bae and Y. H. Lee have no financial or non-financial conflict of interest to declare.

This article does not contain any studies with human participants or animals performed by any of the authors.

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Verbesserung der Lehre im PJ

Viele Mediziner haben wenig positive Erinnerungen an ihr Praktisches Jahr (PJ) des Medizinstudiums. Auch für die Kliniken ist hinsichtlich der Ressource „Zeit" die Einbindung der medizinischen Lehre oft schwierig, es entstehen für beide Seiten unerfreuliche und konfliktträchtige Situationen. Zusätzlich ist an vielen Einrichtungen zum Teil eine deutliche Diskrepanz zwischen der Fremdeinschätzung durch die Studierenden und der Selbsteinschätzung der Lehrstuhlinhaber und ihrer Lehrbeauftragten zur Qualität ihrer Lehre festzustellen.

Um den PJ-Studierenden dauerhaft Lehre auf hohem Niveau zu bieten und die Lehrenden zu unterstützen, hat die Medizinische Fakultät der Universität des Saarlandes UdS 2016 ein Zehn-Punkte-Programm an Sofortmaßnahmen zu Verbesserung der PJ-Lehre aufgestellt und erfolgreich eine PJ-Faculty etabliert. Dies hat an der gesamten Fakultät zu einem deutlichen Motivationsschub geführt und garantiert deren Nachhaltigkeit.

In Ausgabe 1/19 von *Der Ophthalmologe* wird das Zehn-Punkte-Programm ausführlich vorgestellt, das sich auch auf andere Standorte und Einrichtungen übertragen lässt. Der Beitrag ist frei zugänglich.

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