Systematic Review & Indirect Network Meta-Analysis

EFFICACY AND SAFETY OF OZORALIZUMAB *vs.* MOXIBUSTION FOR RHEUMATOID ARTHRITIS

Luthfiana Rofhani Susanti[1], Arifa Mustika[2*], Lita Diah Rahmawati[3], Citrawati Dyah Kencono Wungu[4,5]

[1]Medical Study Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[2]Department of Anatomy, Histology, and Pharmacology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[3]Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
[4]Department of Physiology and Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[5]Institute of Tropical Disease, Universitas Airlangga, Surabaya, Indonesia

ABSTRACT

Rheumatoid arthritis is a chronic inflammatory disease that symmetrically damages the synovial membrane, affecting approximately 13% of the global population. Systemic complications and substantial declines in quality of life may result from untreated rheumatoid arthritis. This study investigated the safety and efficacy of moxibustion and ozoralizumab in reducing disease activity scores in rheumatoid arthritis patients. Between July 2023 and February 2025, we conducted a thorough search on four online databases (PubMed, Cochrane, Scopus, and ProQuest) using keywords, reference searches, and other methods following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The obtained randomized controlled trials (RCTs) were assessed using the Cochrane Risk of Bias 2 (ROB2) tool. MetaInsight version 5.2.1 was utilized to perform the indirect network meta-analysis, using mean difference (MD) as the summary statistics. The measurement of the Disease Activity Score 28 (DAS28) indicated that ozoralizumab had a more significant effect on rheumatoid arthritis compared to placebo (MD=-1.88, 95% CI=-2.24-(-1.52)) and moxibustion (MD=-0.69, 95% CI=-1.07-0.31). Ozoralizumab demonstrated mild, moderate, and severe side effects, whereas moxibustion displayed modest side effects in comparison to placebo. In summary, both ozoralizumab and moxibustion reduced DAS28 in patients with rheumatoid arthritis, with ozoralizumab proving to be the more effective treatment. However, the adverse effects of ozoralizumab were more varied than those of moxibustion.

Keywords: Ozoralizumab; moxibustion; rheumatoid arthritis; Disease Activity Score 28 (DAS28); medicine

***Correspondence:** Arifa Mustika, Department of Anatomy, Histology, and Pharmacology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia Email: arifa-m@fk.unair.ac.id

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Highlights:
1. This study investigated ozoralizumab, a convincing novel tumor necrosis factor alpha (TNF-α) inhibitor for rheumatoid arthritis.
2. Moxibustion, an alternative non-pharmacological therapy for rheumatoid arthritis, was compared to ozoralizumab in this study.
3. The findings demonstrated the efficacy of both ozoralizumab and moxibustion, with a caveat that ozoralizumab may be more effective but presents a broader range of side effects.

INTRODUCTION

Rheumatoid arthritis, an inflammatory condition, causes chronic and increasing inflammation, primarily affecting the synovial membrane of the joints. In this medical condition, the immune system attacks the joint tissues, resulting in damage identifiable by an increase in immune system cells, such as macrophages and T lymphocytes. Rheumatoid arthritis has a global prevalence of 13%, which affects around 2.4 million individuals of the total population. The prevalence of rheumatoid arthritis in Indonesia is 7.30%, with a majority of patients being women (Health Research and Development Agency 2018, World Health

Organization 2022). Due to its chronic nature, rheumatoid arthritis necessitates long-term treatment to manage symptoms and halt disease progression. Patients frequently experience exacerbations that require special attention to prevent further burden (Hidayat et al. 2021).

Treatments for rheumatoid arthritis encompass non-pharmacological strategies, including therapeutic guidance and rehabilitation, alongside a range of drugs. Biologic disease-modifying anti-rheumatic drugs (bDMARDs), especially for patients unresponsive to conventional therapy, have shown promising results in reducing symptoms (Kerschbaumer et al. 2020, Hidayat et al. 2021). One of the latest innovations is ozoralizumab (OZR), which has shown effectiveness in inhibiting tumor necrosis factor alpha (TNF-α). The effects of this medication on rheumatoid arthritis have been demonstrated by the findings of phase III clinical trials (Takeuchi et al. 2022, Tanaka et al. 2023).

Multiple studies, including those conducted by Deng & Shen (2013), Shen et al. (2019), Zhong et al. (2020), have indicated that moxibustion is gaining attention as a promising alternative to medication therapy, due to its anti-inflammatory properties and minimal side effects. The measurement of the Disease Activity Score 28 (DAS28) to evaluate therapy efficacy is essential for determining treatment response and progress (Wells et al. 2009, Savitri et al. 2019, Nasir et al. 2022, Pisaniello et al. 2022). Additionally, conducting an indirect network meta-analysis (NMA) is also important when there are no direct comparisons of treatments, such as ozoralizumab and moxibustion for rheumatoid arthritis. The meta-analysis works by linking each treatment to a common comparator, such as placebo, allowing indirect comparisons even in the absence of head-to-head studies (Li et al. 2011). This approach assesses the relative effectiveness or safety of treatments by employing statistical models that integrate data from various studies. Consequently, this study was conducted to thoroughly examine the potential adverse effects and efficacy of moxibustion and ozoralizumab in decreasing disease activity in rheumatoid arthritis, utilizing the indirect network meta-analysis method.

MATERIALS AND METHODS

This systematic review and indirect network meta-analysis complied with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al. 2021). Between July 2023 and February 2025, literature searches were conducted using the Boolean operators across the PubMed, Cochrane, Scopus, and ProQuest databases. The research question for this systematic review was "What are the efficacy and side effects of ozoralizumab and moxibustion in reducing disease activity score as measured by the DAS28 assessment in patients with rheumatoid arthritis?". This study utilized the following Medical Subject Headings (MeSH) phrases and additional synonyms to organize the keywords in the literature search: (("Rheumatoid Arthritis") OR ("RA")) AND (("Ozoralizumab") OR ("OZR")) OR (("Moxibustion")) AND ("Placebo")) AND (("DAS28") OR ("Disease Activity Score-28")) AND ("Side Effect").

The literature selected for this study adhered to the subsequent inclusion criteria: (1) studies administering ozoralizumab medication to rheumatoid arthritis patients with a placebo comparison; (2) studies administering moxibustion therapy to rheumatoid arthritis patients with a placebo comparison; (3) studies evaluating ozoralizumab administration, specifically regarding its efficacy as measured by the DAS28 assessment and its safety level; and (4) literature presenting a study classified as a randomized control trial (RCT). Meanwhile, the exclusion criteria were determined as follows: (1) studies with titles and abstracts irrelevant to the research topic of this systematic review; (2) studies utilizing duplicate data; (3) publications lacking available full texts free of charge; (4) articles published in languages other than English or Indonesian; and (5) studies presented in the form of conference abstracts, review articles, case series, or case reports (Porritt et al. 2014).

The quality of the literature was evaluated using the Cochrane Risk of Bias 2 (RoB) tool. This assessment focused on several factors, including outcome measurement, the selection of reported results, missing outcome data, the randomization process, and any deviations from the intended intervention. Each of these factors indicated one of the three levels of potential bias: high risk, low risk, or some concern (Flemyng et al. 2023).

The data extraction for this investigation was carried out using Microsoft Excel. The collected data underwent an indirect network meta-analysis, which involved calculating the treatment effect using the mean, standard deviation (SD), and 95% confidence interval (CI) for each study, as well as determining the overall treatment effect through mean difference (MD) as a summary of the analysis results (Kiefer et al. 2015, Higgins et al. 2024). The indirect network meta-analysis was conducted using MetaInsight version 5.2.1 to summarize the analysis results (Owen et al. 2019). The comprehensive findings of the indirect network meta-analysis were illustrated in a frequentist network meta-analysis forest plot, then presented alongside the Litmus Rank-O-Gram derived from the cumulative ranking curve and the

surface under the cumulative ranking curve (SUCRA) values. The protocol for this indirect network meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO), under identifier No. CRD42024529373.

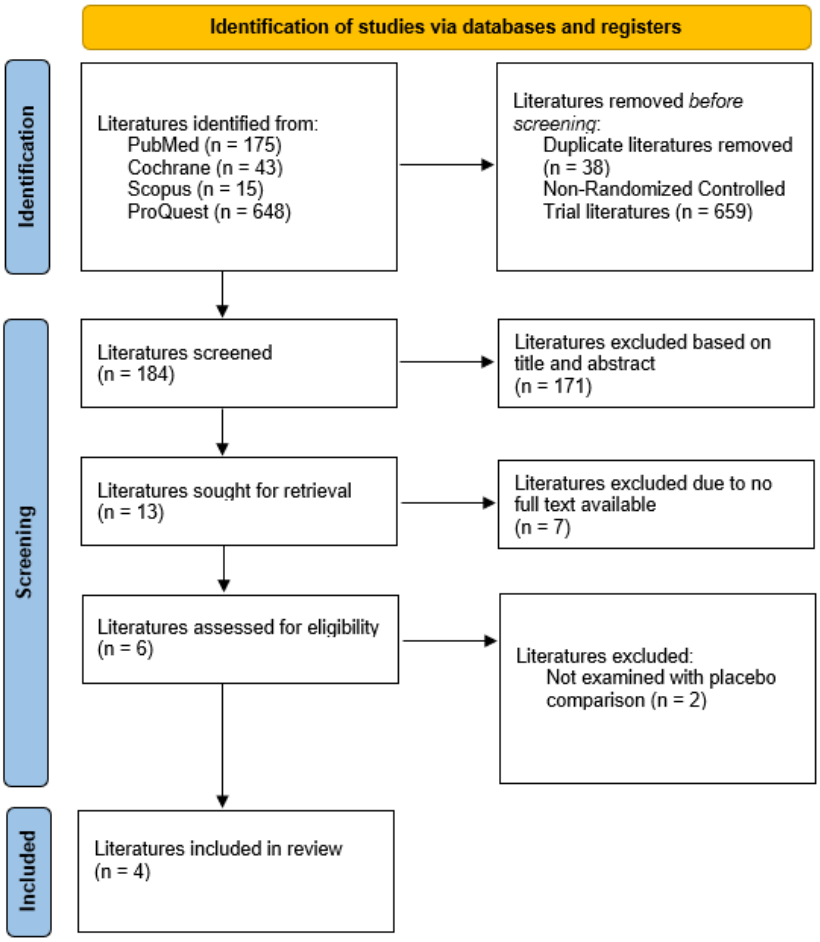

Figure 1. PRISMA flow diagram of the literature search.

RESULTS

The preliminary phase involved the identification of literature through the use of keywords. As of February 2025, the literature search yielded 881 publications from the following databases: PubMed (n=175), Cochrane (n=43), Scopus (n=15), and ProQuest (n=648). However, 38 publications were eliminated due to duplication, and 659 publications were excluded through automated methods, leaving 184 papers available for screening. A total of 171 publications were omitted following the screening of titles and abstracts. Subsequently, the remaining 13 pieces of literature were assessed for full-text availability, resulting in the inclusion of 6 full-text articles and the exclusion of 7 publications. The effectiveness of ozoralizumab and moxibustion therapy in decreasing disease activity, assessed by the DAS28 evaluation, in patients with rheumatoid arthritis was analyzed through a review of four selected trials, since two of the six studies did not use placebo as a comparative intervention. The PRISMA flow diagram in Figure 1 shows the comprehensive processes involved in obtaining the studies. The Cochrane RoB2 tool was utilized to assess the quality of the selected studies. All four studies analyzed exhibited a low risk of bias. The details of the literature assessment are encapsulated in Figure 2.

The results of the data extraction were summarized in a modified collection sheet from Cochrane for the literature presenting randomized controlled trials. The collected information included the name of the original investigator, article title, year of publication, study design, study location, sample size, population characteristics, and the details of the intervention. The summarized results of the data extraction are presented in Table 1.

Table 1. Characteristics of the included literature.

Title	First author	Year of publication	Research design	Research place
Phase II/III Results of a Trial of Anti-Tumor Necrosis Factor Multivalent NANOBODY Compound Ozoralizumab in Patients With Rheumatoid Arthritis	Tsutomu Takeuchi	2022	This multicenter, randomized, placebo-controlled study comprised a 24-week double-blind treatment phase (period A) followed by a 28-week open-label phase (period B).	Japan
Effect of Moxibustion on HIF-1α and VEGF Levels in Patients with Rheumatoid Arthritis	Yuanyuan Gong	2019	RA patients meeting the study criteria were randomly assigned to either treatment or control groups, with the randomization supervised by a separate researcher. Although moxibustion therapy could not be hidden from patients or medical personnel, the outcome data were kept blind to prevent bias.	Chengdu University of Traditional Chinese Medicine, China
The Efficacy of Moxibustion on the Serum Levels of CXCL1 and β-EP in Patients with Rheumatoid Arthritis	Siyu Tao	2021	A statistician oversaw the randomization process, ensuring that patients were assigned equally to both treatment and control groups. As maintaining complete blinding was challenging because of the moxibustion technique, delineating the responsibilities of practitioners, evaluators, and analysts contributed to maintaining accuracy.	Traditional Chinese Medicine Hospital, Sichuan Province, China
The Effects and Potential Mechanisms of Moxibustion for Rheumatoid Arthritis-Related Pain: A Randomized, Controlled Trial	Chenxi Liao	2023	RA patients were randomly assigned 1:1 to either control or moxibustion groups, with a collaborator handling the randomization. Even though the acupuncturist was aware of the administered treatment, the data remained masked during both the collection and analysis phases.	Chengdu University of Traditional Chinese Medicine, China

Legends: RA=rheumatoid arthritis; HIF-1α=hypoxia inducible factor-1alpha; VEGF=vascular endothelial growth factor; CXCL1=C-X-C motif chemokine ligand 1; β-EP=beta-endorphin.

	Randomization Process	*Deviations from intended interventions*	*Missing outcome data*	*Measurement of the outcome*	*Selection of the reported result*	*Overall Bias*		
(Takeuchi et al., 2022)	+	+	+	+	+	+	+	*Low risk*
(Gong et al., 2019)	+	+	+	+	+	+	!	*Some concerns*
(Tao et al., 2021)	+	+	+	+	+	+	-	*High risk*
(Liao et al., 2023)	+	+	+	+	+	+		

Figure 2. Assessment of the selected literature quality.

The four studies presented by Gong et al. (2019), Tao et al. (2021), Takeuchi et al. (2022), Liao et al. (2023) were all carried out in Asia. All studies were randomized controlled clinical trials utilizing a placebo as the comparative intervention. The single study conducted by Takeuchi et al. (2022) used a double-blind method, whereas the other three studies did not employ the same method. However, the studies that did not use a double-blind method ensured that the data remained masked from the data collectors, statistical analysts, and/or efficacy evaluators (Gong et al. 2019, Tao et al. 2021, Liao et al. 2023).

A total of 545 participants were involved in the studies selected for this indirect network meta-analysis and systematic review. The mean age reported in the literature ranged from 47.73 to 55.0 years. The duration of rheumatoid arthritis among the patients varied from 5.85 to 7.4 years in three out of the four studies (Gong et al. 2019, Takeuchi et al. 2022, Liao et al. 2023). Only the study conducted by Tao et al. (2021) excluded the participant demographics concerning sex, average age, and average duration of rheumatoid arthritis. The 2010 criteria established by the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) were employed to diagnose rheumatoid arthritis in all research participants (Gong et al. 2019, Tao et al. 2021, Takeuchi et al. 2022, Liao et al. 2023). In three out of the four studies Gong et al. (2019), Tao et al. (2021), Liao et al. (2023), patients using glucocorticoid or anti-rheumatic medications, except methotrexate and leflunomide, were omitted. One of the four studies Takeuchi et al. (2022) determined that methotrexate (MTX) was administered for a minimum of 12 weeks prior to baseline, with no alteration in the methotrexate dosage for at least six weeks before baseline. The details regarding research participants, diagnosis criteria, and the duration of rheumatoid arthritis are enumerated in Table 2.

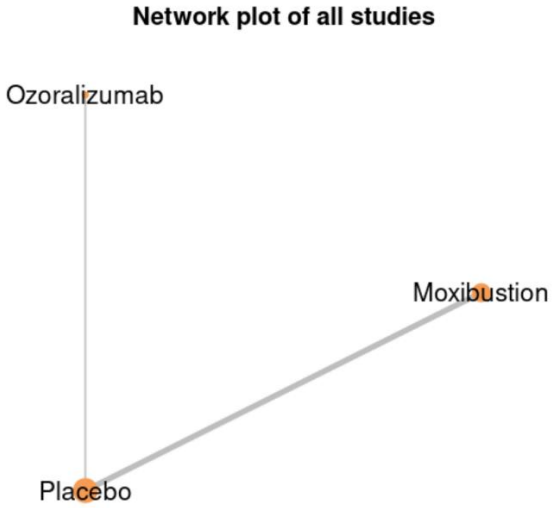

Figure 3. Network plot illustrating the relationship between ozoralizumab therapy and moxibustion in rheumatoid arthritis patients according to the DAS28 assessment.

Table 3 shows the duration of intervention, revealing discrepancies among the selected studies. The ozoralizumab intervention for the research subjects lasted 24 weeks (Takeuchi et al. 2022). Meanwhile, the moxibustion intervention was administered two times per week for a duration of eight weeks (Gong et al. 2019, Tao et al. 2021, Liao et al. 2023).

Figure 3 depicts a network plot that delineates the outcomes of ozoralizumab therapy in conjunction with moxibustion in patients with rheumatoid arthritis. The map indicated the presence of variations in the disease activity score according to the DAS28 assessment. The DAS28 assessment results were statistically analyzed to compare the effectiveness of ozoralizumab therapy versus moxibustion in individuals with rheumatoid arthritis. The results of the analysis are illustrated in the forest plot presented in Figure 4.

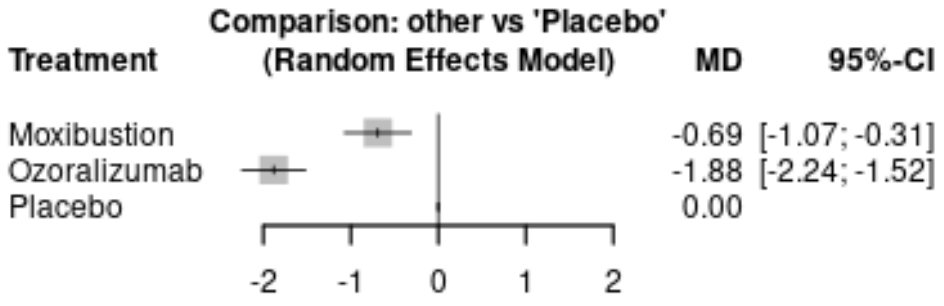

Figure 4. Forest plot comparing ozoralizumab therapy to moxibustion in rheumatoid arthritis patients, assessed by changes in DAS28.

Table 2. Characteristics of the research subjects.

First author, year	Diagnosis criteria	RA duration (year)	Total participants		Age (year)	History of therapy, examination, etc.
			Female	Male		
Takeuchi et al. (2022)	Insufficient response to MTX and fulfillment of the ACR/EULAR 2010 RA classification criteria	7.4±7.1	285	96	55.0±11.2	Patients with active RA were eligible if they exhibited hs-CRP levels of ≥0.6 mg/dl, ESR of ≥28 mm/h, TJC68 ≥6, and SJC66 of ≥6. The MTX therapy required continuity for a minimum of 12 weeks prior to the baseline, with no alterations in dosage (6–16 mg/week). Patients with active or latent tuberculosis, or those with abnormal chest X-ray results, were included unless they had received treatment using isoniazid.
Gong et al. (2019)	The ACR/EULAR 2010 RA classification criteria	5.85±4.52	34	3	48.02±10.81	Participants aged 18–65 years who were in good health, had a DAS28 of >3.2, and adhered to the study requirements were deemed eligible. The exclusions encompassed pregnant or breastfeeding women as well as individuals with psychiatric disorders, significant joint deformities, other autoimmune diseases, multiple severe health issues, cancers, or aversion to moxibustion therapy.
Tao et al. (2021)	The ACR/EULAR 2010 RA classification criteria	N/A	61		N/A	Participants aged 18–70 years exhibiting a DAS28 of >3.2 and a stable mental condition while not receiving any anti-rheumatic drugs for 24 weeks were deemed eligible. The exclusions were applied for individuals with severe joint deformities (stage IV), patients younger than 18 or older than 70, patients with infectious diseases, cancers, significant congenital conditions, and intellectual disabilities, and those unable to complete the assessments.
Liao et al. (2023)	The ACR/EULAR 2010 RA classification criteria	6.95±6.71	59	7	47.73±10.14	The eligible participants were 18–65 years old, had a DAS28 of >3.2, had not consumed glucocorticoids or anti-rheumatic medications in the last 24 weeks, and were not involved in other clinical trials. Excluded from the study were patients with stage IV exhibiting significant joint impairment, pregnant or nursing women, and individuals with psychiatric disorders, autoimmune diseases, complications from malignancies, or contraindications to moxibustion.
Total			545			

Legends: RA=rheumatoid arthritis; MTX=methotrexate; ACR/EULAR=American College of Rheumatology/European League Against Rheumatism; hs-CRP=high sensitivity C-reactive protein; ESR=erythrocyte sedimentation rate; TJC68=68 tender joint counts; SJC66=66 swollen joint counts; DAS28=Disease Activity Score 28; N/A=not available.

Table 3. Characteristics of the research interventions.

First author, year	Duration of administration	Dosage, meridian points, and administration frequency
Takeuchi et al. (2022)	24 weeks	In the double-blind study, three groups were administered subcutaneous injections of ozoralizumab (30 mg or 80 mg) or placebo four times a year, alongside MTX treatment (6–16 mg/week) over a 24-week duration.
Gong et al. (2019)	8 weeks	According to the doctor's recommendations for long-term treatment, all patients received either MTX (2.5 mg/pill) or leflunomide (10 mg/pill). The treatment group also received moxibustion at specific acupoints (Ashi, Zusanli, and BL23 on both sides) in two sessions, each lasting four weeks.
Tao et al. (2021)	8 weeks	In the treatment group, moxibustion was applied at bilateral Zusanli (ST36), Shenshu (BL23), and Ashi points, in conjunction with oral MTX (7.5 mg weekly) and folic acid (10 mg weekly). Eight moxibustion sessions were conducted over a four-week period.
Liao et al. (2023)	8 weeks	The control group was given only standard treatment comprising oral MTX (7.5 mg) and folic acid (10 mg) weekly for eight weeks. In contrast, the treatment group received moxibustion therapy incorporated into their pharmaceutical regimen, targeting the ST36, BL23, and Ashi points. The moxibustion group underwent 16 sessions, conducted biweekly over the course of eight weeks.

Legend: Note: MTX=methotrexate

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The studycomparing moxibustion to placebo demonstrated that moxibustion reduced DAS28 scores more effectively than placebo. This finding was evidenced by an effect value of -0.69 with a 95% CI of -1.07 to 0.31. In addition, studies comparing ozoralizumab to placebo revealed that the drug exhibited a more pronounced effectivity in decreasing DAS28 scores than placebo. The result was indicated by an effect value of -1.88 and a 95% CI ranging from -2.24 to -1.52.

Table 4. Side effects of ozoralizumab administration.

First author, year	Type of intervention	Intensity (%)		
		Mild	Moderate	Severe
Takeuchi et al. (2022)	Placebo	56	10.7	2
	Ozoralizumab	65.6	18.8	3

Figure 5 illustrates the results of the efficacy comparison between ozoralizumab therapy and moxibustion for rheumatoid arthritis, evaluated by changes in DAS28 and expressed using SUCRA values in a Litmus Rank-O-Gram. A decrease in disease activity, as indicated by alterations in the DAS28 measurement results, demonstrated that ozoralizumab was more effective in reducing clinical symptoms compared to placebo.

Table 5. Side effects of moxibustion administration.

First author, year	Type of intervention	Intensity (%)		
		Mild	Moderate	Severe
Gong et al. (2019)	Placebo	0	0	0
	Moxibustion	0	0	0
Tao et al. (2021)	Placebo	N/A	N/A	N/A
	Moxibustion	N/A	N/A	N/A
Liao et al. (2023)	Placebo	0	0	0
	Moxibustion	5.8	0	0

The investigation of ozoralizumab administration in rheumatoid arthritis patients, as shown in Table 4, revealed minimal occurrences of mild side effects, with a prevalence rate difference of 9.6% between placebo and ozoralizumab, as reported by Takeuchi et al. (2022). A significant difference was observed in the prevalence rate of moderate-intensity side effects between placebo and ozoralizumab, at 8.1%. Severe side effects were frequently observed with ozoralizumab therapy. However, the difference in the occurrence of severe side effects between placebo and ozoralizumab was approximately 1%, as noted by Takeuchi et al. (2022).

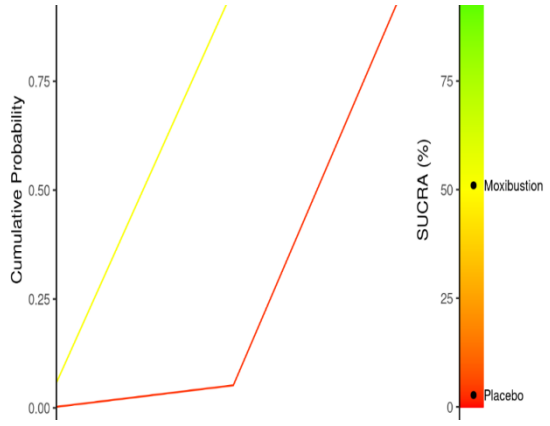

Figure 5. Order of efficacy comparison between ozoralizumab intervention and moxibustion in rheumatoid arthritis patients, according to the DAS28 assessment.

The research findings regarding the side effects of moxibustion intervention in rheumatoid arthritis patients are listed in Table 5. The intervention indicated the absence of mild, moderate, or severe side effects according to Gong et al. (2019). However, mild side effects were prevalent, occurring in 5.8% of participants in the study conducted by Liao et al. (2023). Only Tao et al. (2021) did not investigate the adverse consequences of administering moxibustion therapy to individuals with rheumatoid arthritis.

DISCUSSION

The aim of this systematic review and indirect network meta-analysis was to assess the effectiveness of moxibustion, a non-pharmacological intervention, in comparison to ozoralizumab, a novel pharmaceutical treatment, in altering DAS28 in rheumatoid arthritis patients. Four studies meeting the inclusion criteria were identified, all of which were randomized controlled trials conducted in Asia, with 545 research participants. One of the studies focused on ozoralizumab, while the other three examined moxibustion. The study carried out by Takeuchi et al. (2022) involved 381 participants and compared ozoralizumab to placebo.

Women made up the majority of participants in the four studies included in this systematic review. This is consistent with the statistic indicating that 75% of patients with rheumatoid arthritis globally are female (World Health Organization 2022). Rheumatoid arthritis in women may impact the DAS28 assessment. Female patients with rheumatoid arthritis typically demonstrate higher disease activity scores, despite exhibiting a similar progression to male patients (Tipsing & Sawanyawisuth 2021).

Only one study, conducted by Liao et al. (2023), discussed the duration of rheumatoid arthritis, revealing a common duration exceeding three months. The duration of rheumatoid arthritis is significant in the analysis of the disease since a prolonged disease duration can lead to an elevated activity score (Tipsing & Sawanyawisuth 2021). In addition, although mean age is a contributing factor, baseline data regarding participants' age was absent from the analysis in any of the studies. Three of the four studies also reported restrictions on medication use, including anti-rheumatics, glucocorticoids, and stipulated stable methotrexate administration before baseline (Gong et al. 2019, Takeuchi et al. 2022, Liao et al. 2023).

One of the four studies investigated the effects of ozoralizumab at doses of 30 mg and 80 mg over a period ranging from 24 to 52 weeks. According to Kerschbaumer et al. (2020), ozoralizumab is classified as a bDMARD that targets TNF-α. The administration of this medication has demonstrated a significant reduction in disease activity scores in comparison to placebo. Commonly used TNF-α inhibitor drugs include adalimumab, golimumab, and infliximab (Hidayat et al. 2021).

The other three studies focused on moxibustion therapy at the ST36, BL23, and AShi acupoints, administered biweekly for a duration of eight weeks (Gong et al. 2019, Tao et al. 2021, Liao et al. 2023). Additionally, the studies also included a control group that received standard treatments, such as methotrexate and leflunomide. In administering moxibustion, mugwort is used to induce mild inflammatory effects. This intervention is considered safer for patients with a fear of needles (Shen et al. 2019).

The DAS28 comparison between the ozoralizumab and moxibustion groups in rheumatoid arthritis patients exhibited significant differences. The analysis revealed that ozoralizumab was more effective in reducing DAS28, as supported by the frequency network meta-analysis forest plot, which indicated an effect value of -0.73 (CI=-1.69–0.22) for moxibustion compared to placebo. Conversely, the study comparing ozoralizumab to placebo demonstrated an effect value of -1.15 (CI=-2.25–(-0.05)). The SUCRA analysis in this study unveiled the intervention efficacy ranking of ozoralizumab in comparison to moxibustion according to the mean change in DAS28 assessment results among rheumatoid arthritis patients. According to the SUCRA ranking, ozoralizumab exhibited the

highest efficacy. Ozoralizumab is a sophisticated inhibitor that neutralizes both membrane-bound and soluble forms of TNF-α by combining two anti-TNF-α, i.e., NANOBODY® variable heavy domains of heavy chain (VHHs) with the humanized anti-human serum albumin (HSA) NANOBODY® VHH (Takeuchi 2023). On the other hand, moxibustion functions by warming the meridians and harmonizing Yin and Yang, which aids in enhancing the circulation of *Qi* and blood while also offering anti-inflammatory benefits through immunological regulation (Deng & Shen 2013, Zhong et al. 2020). The suppression of TNF-α by ozoralizumab results in a notable decrease in disease activity scores, especially DAS28. This finding is in line with the results obtained from the administration of other TNF-α inhibitors (Kerschbaumer et al. 2020).

Takeuchi et al. (2022) revealed that the administration of ozoralizumab resulted in a range of side effects, from mild to severe, due to its direct effect on the immune response. In comparison, moxibustion was linked to only mild side effects, occurring at a prevalence rate of approximately 5.8%, while some studies indicated no adverse effects at all (Gong et al. 2019, Liao et al. 2023). The side effects of ozoralizumab and moxibustion are classified as mild, moderate, or severe. The mild effects of ozoralizumab include injection site reactions, headaches, and mild gastrointestinal discomfort, whereas moderate effects involve infections or organ disorders that require medical intervention. The severe side effects of ozoralizumab are life-threatening reactions, including serious infections or organ damage. The mild effects of moxibustion are skin redness or discomfort, while moderate effects may encompass burns or dizziness. The severe reactions of moxibustion, although rare, may involve severe burns or allergic responses requiring medical intervention. Both treatments necessitate monitoring for adverse effects. Moxibustion is generally safe, with fewer risks of serious reactions compared to other therapies.

Strength and limitations

This study investigated the mechanism of action of ozoralizumab, a novel TNF-α inhibitor, and compared it with moxibustion as a traditional therapy. By using the comparative data from this study, practitioners can improve decision-making regarding the most effective therapy options and decrease the chances of negative outcomes. Furthermore, this study endorsed moxibustion as an alternative for rheumatoid arthritis patients unresponsive to conventional treatment. The findings of this study may serve as a foundation for developing more effective and safer therapies, either by merging the benefits of both treatments or by formulating new drugs with a mechanism akin to ozoralizumab but with reduced side effects.

The limitations of this study include the lack of randomized controlled trials, especially those providing placebo control data for ozoralizumab therapy. The majority of research on ozoralizumab is concentrated in Japan, whereas moxibustion has been extensively studied in China. Moreover, the incomplete incorporation of assessment components and participant data might introduce bias into the conclusions. Substantial variations in participants' sex and the absence of treatment history details might potentially introduce additional bias.

CONCLUSION

Both ozoralizumab and moxibustion therapies can lower the Disease Activity Score 28 (DAS28) in patients with rheumatoid arthritis, with ozoralizumab showing greater effectiveness in this aspect. However, ozoralizumab demonstrates a wider range of side effects compared to moxibustion, which typically leads to only moderate adverse effects. This highlights the need for further research to directly compare the efficacy and safety of both treatments.

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Conflict of interest

None.

Funding disclosure

None.

Author contribution

LRS contributed to the conception and design of this study, analyzed and interpreted the data, drafted the article, and collected and assembled the data. AM, LDR, and CDKW participated in the critical revision of the article for important intellectual content and gave final approval of the article. Additionally, CDKW provided statistical expertise.

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