

Z Rheumatol 2021 · 80:776–784

<https://doi.org/10.1007/s00393-020-00837-9>

Published online: 9 July 2020

© Springer Medizin Verlag GmbH, ein Teil von Springer Nature 2020

Redaktion

U. Müller-Ladner, Bad Nauheim

U. Lange, Bad Nauheim

Y. H. Lee^{1,2} · G. G. Song¹¹ Department of Rheumatology, Korea University College of Medicine, Seoul, Korea (Republic of)² Division of Rheumatology, Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seongbuk-gu, Seoul, Korea (Republic of)

Comparative efficacy and safety of secukinumab and ixekizumab in patients with active ankylosing spondylitis

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease caused by entheses and inflammation of the spinal and sacroiliac joints, which subsequently cause bone and joint erosion and gradually lead to new bone formation, syndesmophytes, and ankylosis, resulting in increased structural damage, weakness, and reduced quality of life [16, 21, 30]. Non-steroidal anti-inflammatory drugs and disease-modifying anti-rheumatic drugs are typically used in the treatment of AS. However, such medications are often ineffective for treating AS [4]. Anti-tumor necrosis factor (TNF) therapy is currently recommended for patients showing an inadequate response to conventional AS treatment [4]. However, in approximately 40% of patients with AS, anti-TNF therapy either does not achieve adequate disease control or causes unacceptable side effects [2].

Interleukin-17A (IL-17A) plays a major role in AS-related inflammatory responses [33]. In patients with AS, IL-17A and its receptor are expressed in target tissues and can mediate biological functions, leading to inflammation, injury, and tissue remodeling of the joints and entheses [29]. Secukinumab, a fully human recombinant anti-IL-17A IgG1 monoclonal antibody, is the first monoclonal IL-17 antibody to be used for AS therapy [17]. Moreover, it is the first AS-licensed non-TNF alpha inhibitor, which opened a new age of cytokine targets

outside TNF. Secukinumab is effective in treating active AS and exhibits a manageable safety profile [3, 14]; thus, treatment of AS with anti-IL-17A may be an effective alternative to TNF inhibitors (TNFIs). Another IL-17A antagonist, ixekizumab, an IgG4 humanized monoclonal antibody with high IL-17A affinity, was approved in August 2019 for treatment of AS, based on its efficacy in both TNFI-naïve and TNFI-exposed patients [23].

Studies have shown that, similar to secukinumab, ixekizumab is an effective therapeutic agent for AS [3, 8, 12, 15, 26]. However, there are no head-to-head comparative studies evaluating the efficacy and safety profiles of secukinumab and ixekizumab. A network meta-analysis can incorporate direct and indirect evidence derived from relative treatment effects across a network of randomized controlled trials (RCTs) and can thus de-

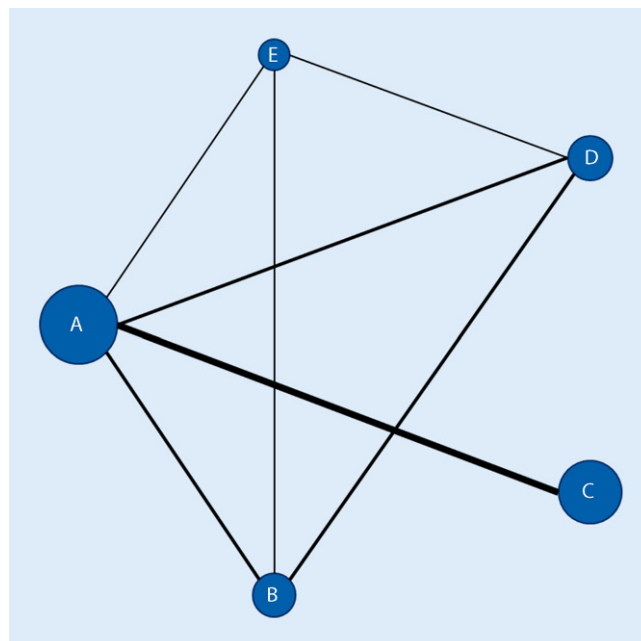


Fig. 1 ▲ Evidence network diagram of comparisons for network meta-analysis. The width of each edge is proportional to the number of randomized controlled trials comparing each pair of treatments, and the size of each treatment node is proportional to the number of randomized participants (sample size). A Placebo, B IXEQ2W, C secukinumab 150 mg, D IXEQ4W, E adalimumab 40 mg. IXEQ2W or IXEQ4W ixekizumab 80 mg every 2 weeks or 4 weeks

Table 1 Characteristics of individual studies included in the network meta-analysis

Study	Subjects	Total number	Drugs	No. of patients	ASAS20	ASAS40
Baeten-1, 2015 [3]	TNFI-naive	247	Secukinumab 150 mg	125	76	52
			Placebo	122	35	16
Baeten-2, 2015 [3]	TNFI-IR	146	Secukinumab 150 mg	72	44	26
			Placebo	74	21	8
Pavelka-1, 2017 [26]	TNFI-naive	116	Secukinumab 150 mg	57	36	25
			Placebo	59	23	14
Pavelka-1, 2017 [26]	TNFI-IR	34	Secukinumab 150 mg	17	7	5
			Placebo	17	5	2
Kivitz-1, 2018 [15]	TNFI-naive	168	Secukinumab 150 mg	85	51	34
			Placebo	83	41	25
Kivitz-2, 2018 [15]	TNFI-IR	65	Secukinumab 150 mg	31	18	11
			Placebo	34	14	15
Van der Heijde, 2018 [12]	TNFI-naive	341	IXEQ2W	83	57	43
			IXEQ4W	81	52	39
			Adalimumab 40 mg	90	53	32
			Placebo	87	35	16
Deodhav, 2019 [8]	TNFI-IR	316	IXEQ2W	98	46	30
			IXEQ4W	114	55	29
			Placebo	104	31	13

ASAS20 or 40 Assessment of Spondyloarthritis International Society 20 or 40 response criteria (improvement of $\geq 20\%$ and absolute improvement of ≥ 1 unit [on a 10-unit scale] in at least three of the four main ASAS domains, with no worsening by $\geq 20\%$ in the remaining domain) [1], **IXEQ2W or IXEQ4W** ixekizumab 80 mg every 2 weeks or 4 weeks, **TNFI-IR** tumor necrosis factor inhibitor-inadequate response

Table 2 Comparative interventions in the network meta-analysis

Comparison	Study number	Patient number
Placebo	8	580
IXEQ2W	2	181
Secukinumab 150 mg	6	387
IXEQ4W	2	195
Adalimumab 40 mg	1	90

IXEQ2W or IXEQ4W ixekizumab 80 mg every 2 weeks or 4 weeks

termine the efficacy of multiple treatments, even in the absence of direct comparative studies [7, 19, 20, 22]. Therefore, using network meta-analysis, this study compared the efficacy and safety of secukinumab and ixekizumab in patients with active AS.

Materials and methods

Identification of eligible studies and data collection

A systematic literature search was performed in MEDLINE, EMBASE, and the Cochrane Controlled Trials Database to find available research articles on the efficacy and safety of secukinumab and ix-

ekizumab in patients with active AS published until January 2020. The keywords and subject terms used in the analysis included “secukinumab,” “ixekizumab,” and “ankylosing spondylitis.” All references in the research articles were verified to find relevant studies that were not included in the online repositories. Inclusion criteria for the selection of an RCT were as follows: (1) comparison of secukinumab or ixekizumab with placebo for the treatment of patients with active AS and (2) reporting of the clinical effectiveness and safety endpoints of secukinumab or ixekizumab at week 16. The criteria for exclusion included (1) duplicate data and (2) lack of data needed for inclusion. The efficacy endpoint was

the number of patients who met either 20% (ASAS20) or 40% (ASAS40) of the response requirements in the Spondyloarthritis International Society (ASAS) evaluation. ASAS20 or ASAS40 is described as a 20 or 40% improvement, respectively, and an absolute (10-unit) improvement in at least three of the four major ASAS domains. The safety outcome was based on the number of patients with serious adverse events (SAEs) [1]. The results were collected from the original studies by two independent reviewers. Any discrepancy was resolved by consensus between the reviewers. Data from each publication included the first author’s name, publishing year, doses of secukinumab and ixekizumab, and efficacy and safety outcomes. The network meta-analysis was performed in compliance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [24].

Y. H. Lee · G. G. Song

Comparative efficacy and safety of secukinumab and ixekizumab in patients with active ankylosing spondylitis

Abstract

Objective. Evaluation of the effectiveness and safety of secukinumab and ixekizumab in active ankylosing spondylitis (AS) patients.

Methods. A Bayesian network meta-analysis was conducted using direct and indirect data from five randomized controlled trials that examined the efficacy and safety of secukinumab 150 mg every 4 weeks and ixekizumab 80 mg every 2 weeks (IXEQ2W) or every 4 weeks (IXEQ4W) in active AS patients.

Results. Data from 1433 patients were analyzed. The Assessment of Spondyloarthritis International Society evaluation 20% response rates (ASAS20) were significantly higher with secukinumab 150 mg, IXEQ2W, IXEQ2W,

and adalimumab 40 mg (odds ratio [OR] 2.75, 95% Bayesian credible interval [CrI] 2.04–3.69; OR 2.59, 95% CrI 1.69–3.98; OR 2.45, 95% CrI 1.60–3.75; and OR 1.94, 95% CrI 1.13–3.37, respectively) compared to the placebo group. Efficacies of secukinumab and ixekizumab were numerically higher compared to adalimumab 40 mg, although there was no significant difference in the ASAS20 response rates. The ASAS40 response rate showed a pattern of distribution similar to the ASAS20 response rate, with the exception of the ixekizumab group, which was associated with the most favorable surface under the cumulative ranking curve (SUCRA)

for the ASAS40 response rate. Based on the SUCRA rating, secukinumab 150 mg had the highest probability of being the best ASAS20 response rate therapy, followed by IXEQ2W, IXEQ4W, adalimumab 40 mg, and placebo. There was no significant difference between the treatments regarding the number of serious adverse events (SAEs).

Conclusion. Secukinumab and ixekizumab were effective in active AS treatment, without the risk of SAEs.

Keywords

Secukinumab · Ixekizumab · Ankylosing spondylitis · Network meta-analysis

Relative Wirksamkeit und Sicherheit von Secukinumab und Ixekizumab bei Patienten mit aktiver ankyloisierender Spondylitis

Zusammenfassung

Ziel der Arbeit. Ziel war die Beurteilung der Wirksamkeit und Sicherheit von Secukinumab und Ixekizumab bei Patienten mit aktiver ankyloisierender Spondylitis (AS).

Methoden. Eine Bayes-Netzwerk-Metaanalyse wurde anhand von direkten und indirekten Daten aus 5 randomisierten kontrollierten Studien durchgeführt, in denen die Wirksamkeit und Sicherheit von Secukinumab 150 mg alle 4 Wochen und Ixekizumab 80 mg alle 2 Wochen (IXEQ2W) oder alle 4 Wochen (IXEQ4W) bei Patienten mit aktiver AS untersucht wurde.

Ergebnisse. Es wurden Daten von 1433 Patienten ausgewertet. Die 20%-Responderaten gemäß Assessment der Spondyloarthritis International Society (ASAS20) waren unter

Secukinumab 150 mg, IXEQ2W, IXEQ2W und Adalimumab 40 mg (Odds Ratio, OR: 2,75; 95%-Bayes-Glaubwürdigkeitsintervall, 95%-CrI: 2,04–3,69; OR: 2,59; 95%-CrI: 1,69–3,98; OR: 2,45; 95%-CrI: 1,60–3,75 bzw. OR: 1,94; 95%-CrI: 1,13–3,37) signifikant höher als in der Placebogruppe. Die Wirksamkeit von Secukinumab und Ixekizumab war im Vergleich zu Adalimumab 40 mg numerisch höher, obwohl kein signifikanter Unterschied bei den ASAS20-Responderaten bestand. Die ASAS40-Responderate wies ein Verteilungsmuster auf, das dem der ASAS20-Responderate ähnlich war, mit Ausnahme der Ixekizumabgruppe, welche mit der günstigsten Oberfläche unter der kumulativen Rangkurve („surface under the cumulative ranking curve“, SUCRA) für

die ASAS40-Responderate einherging. Auf der Grundlage der Rangliste gemäß SUCRA bestand für Secukinumab 150 mg die größte Wahrscheinlichkeit, die beste Therapie in Bezug auf die ASAS20-Responderate zu sein, es folgten IXEQ2W, IXEQ4W, Adalimumab 40 mg und Placebo. Es bestand kein signifikanter Unterschied zwischen den Therapien hinsichtlich der Anzahl schwerer unerwünschter Ereignisse (SAE).

Schlussfolgerung. Secukinumab und Ixekizumab waren ohne das Risiko schwerer SAE zur Behandlung der aktiven AS wirksam.

Schlüsselwörter

Secukinumab · Ixekizumab · Spondylitis ankylosans · Netzwerk-Metaanalyse

Evaluation of statistical associations for network meta-analysis

The findings were analyzed at the same time for RCTs that compared secukinumab and ixekizumab in different arms. The efficacy and safety of secukinumab and ixekizumab in different arms were ordered based on the likelihood of being rated as the best performing regimen. Using NetMetaXL [5] and WinBUGS version 1.4.3 (MRC Bio-

statistics Unit, Institute of Public Health, Cambridge, UK), a Bayesian fixed effect model was applied for the network meta-analysis. The Monte Carlo Markov Chain approach was used to estimate the size of the pooled effect [7]. All chains were run with 10,000 iterations of burn-in, accompanied by 10,000 iterations. Relative effect information was transformed into a prediction of the best performance of a drug. The rating of each intervention, expressed as a percentage, was also calculated as

the surface under the cumulative ranking curve (SUCRA). SUCRA was 100% when the best treatment was certain and 0% when the worst treatment was certain. The league table presented the overview estimates by rating the treatments in order, starting with the highest outcome effect, as calculated by SUCRA [27]. A 95% confidence interval (CI) was recorded, along with the pairwise odds ratio (OR) and Bayesian credible interval (CrI). Trial outcomes for the different treatment arms were modified. Pooled

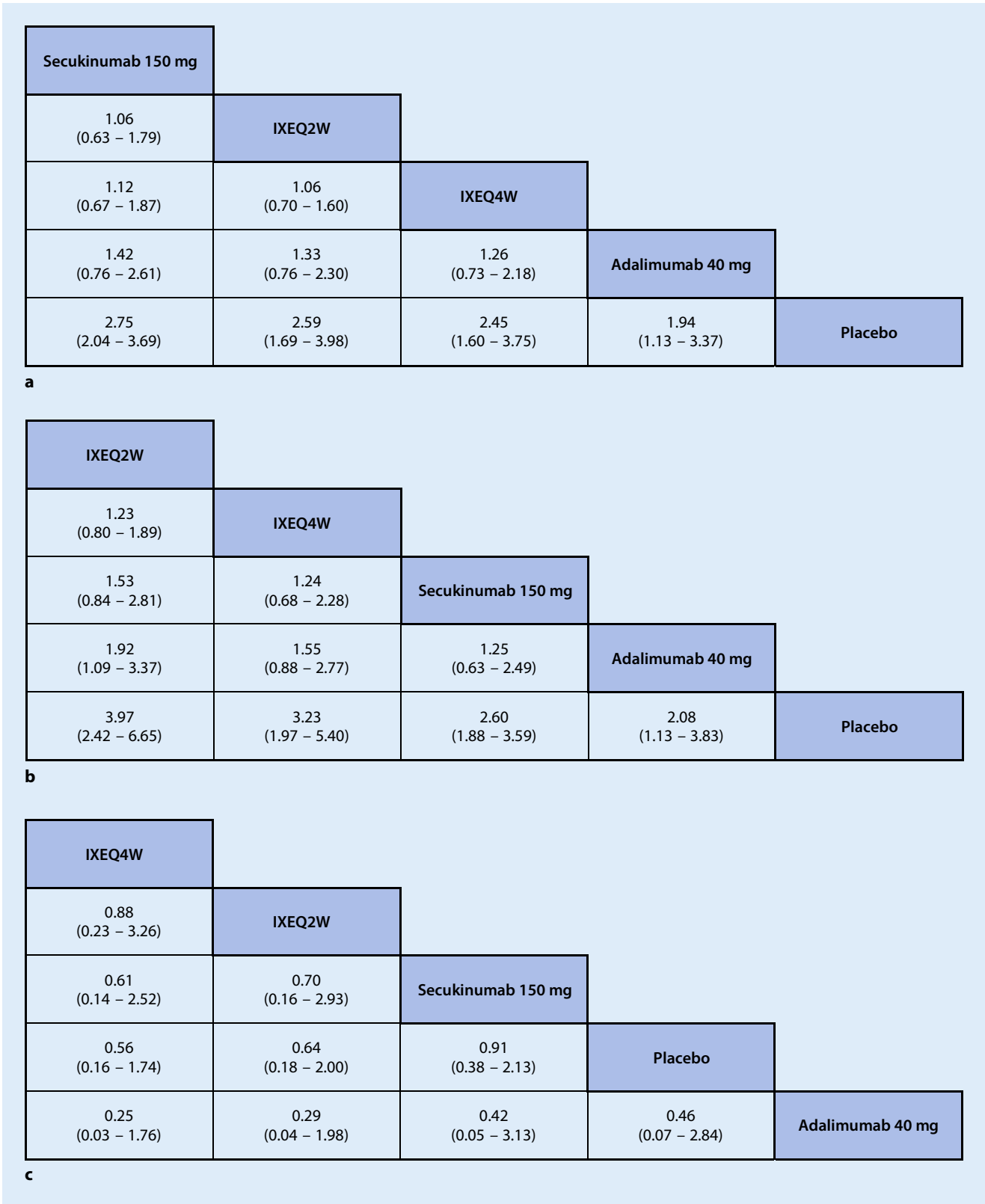


Fig. 2 ▲ Network meta-analyses comprising the effects for all contrasts along with odds ratios (ORs) and 95% credible intervals. **a** ASAS20. OR >1 means the treatment in top left is better. **b** ASAS40. **c** Safety. OR <1 means that the treatment in the top left block is better

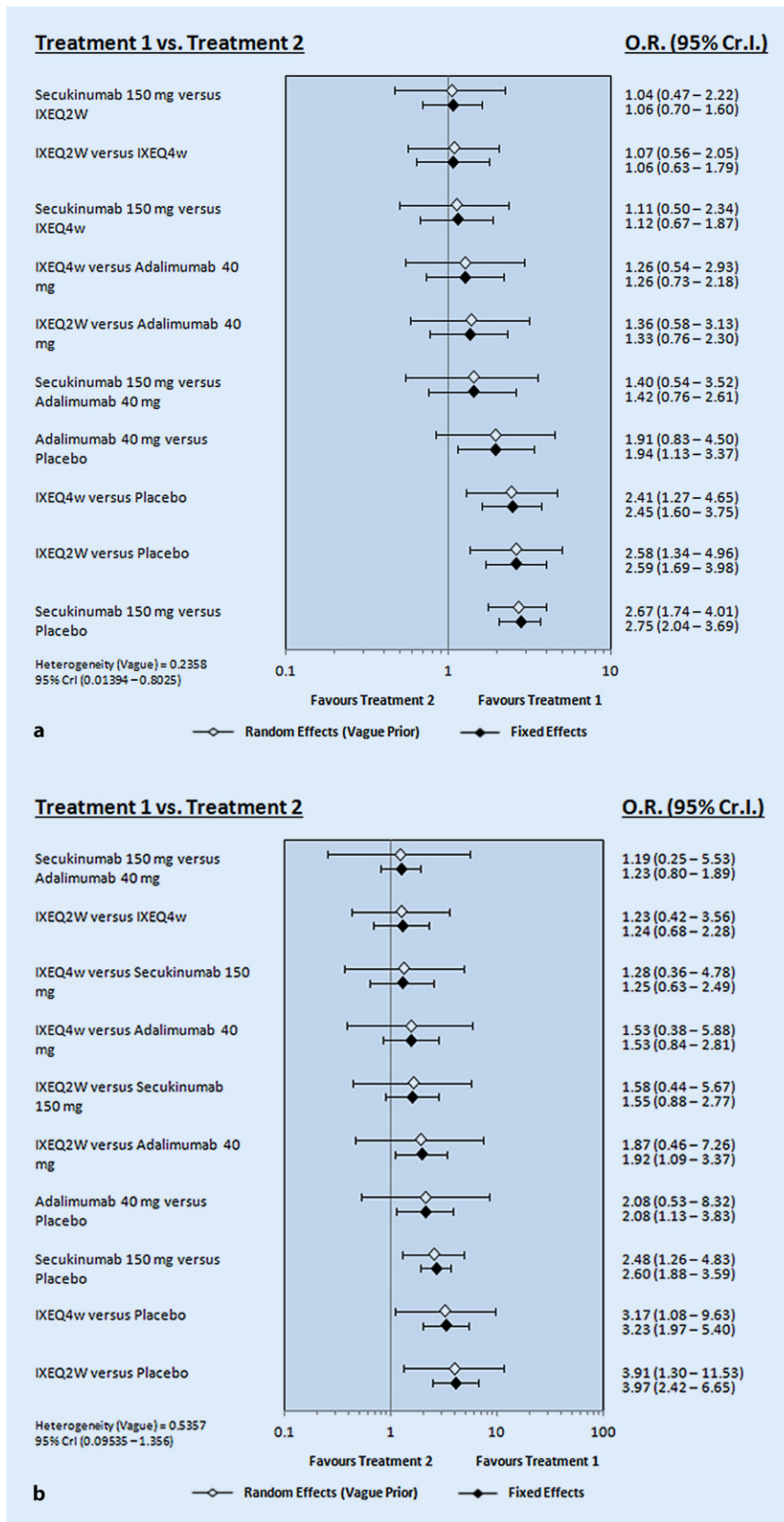


Fig. 3 ▲ Results of the Bayesian network meta-analysis of randomized controlled studies assessing the relative efficacy (a ASAS20, b ASAS40) of secukinumab and ixekizumab

tests were deemed statistically significant unless the value 1 was included in the confidence interval.

Tests for inconsistency and sensitivity

Inconsistency refers to the degree to which direct and indirect data differ [9]. Inconsistency evaluation is critical for a network meta-analysis [13]. In the inconsistencies model, to assess network inconsistencies between direct and indirect estimates in each loop, the posterior mean deviation of the individual datapoints against the posterior mean deviation in the consistency model was defined [32]. A sensitivity test was conducted with a random and fixed effect model comparison.

Results

Meta-analysis studies

Through an electronic or manual search, a total of 211 studies were identified; of these, based on the title and abstract information, 10 were selected for a full-text review. Subsequently, five studies were omitted, either due to duplicate results or a non-RCT study design. Eventually, five RCTs comprising 1433 patients (700 efficacy-related events and 44 safety-related events) that met the criteria for inclusion were analyzed ([3, 8, 12, 15, 26]; ■ Tables 1 and 2). The evidence network diagram in ■ Fig. 1 shows the data related to the number of trials that measured various treatments and the number of patients in each treatment. There were 10 pairs of comparisons, including 7 direct comparisons, and 5 treatments comprising placebo, secukinumab 150 mg, IXEQ2W, IXEQ4W, and adalimumab 40 mg (■ Fig. 1). Patients received intravenous loading infusions of secukinumab 10 mg/kg at weeks 0, 2, and 4 or subcutaneous injection of secukinumab 150 mg at weeks 0, 1, 2, and 3. This was followed by subcutaneous injection of secukinumab 150 mg every 4 weeks. Patients received 80 mg of ixekizumab every 2 weeks (IXEQ2W) or 80 mg of ixekizumab every 4 weeks (IXEQ4W), with a starting dose of either

Table 3 Rank probability in terms of efficacy based on the number of patients achieving an ASAS20 or ASAS40 response, and the safety based on the number of serious adverse events

Treatment	SUCRA
<i>Efficacy: ASAS20</i>	
Secukinumab 150 mg	0.781
IXEQ2W	0.716
IXEQ4W	0.631
Adalimumab 40 mg	0.371
Placebo	0.002
<i>Efficacy: ASAS40</i>	
IXEQ2W	0.934
IXEQ4W	0.719
Secukinumab 150 mg	0.514
Adalimumab 40 mg	0.331
Placebo	0.003
<i>Safety</i>	
IXEQ4W	0.773
IXEQ2W	0.700
Secukinumab 150 mg	0.488
Placebo	0.400
Adalimumab 40 mg	0.140

SUCRA surface under the cumulative ranking curve, IXEQ2W or IXEQ4W ixekizumab 80 mg every 2 weeks or 4 weeks

80 or 160 mg ixekizumab. Adalimumab 40 mg was administered subcutaneously every other week. **Tables 1 and 2** present the related characteristics of the studies included in the meta-analysis.

Network meta-analysis of the efficacy of secukinumab and ixekizumab

Secukinumab 150 mg was listed at the top left of the league table diagonal (**Fig. 2**) as it was associated with the most favorable ASAS20 response rate SUCRA, whereas placebo was listed at the bottom right of the league table diagonal as it was associated with the least favorable results. In the secukinumab 150 mg group, the ASAS20 response rate was significantly higher than that in the placebo group (OR 2.75, 95% CrI 2.04–3.69; **Figs. 2 and 3**). Similarly, the ASAS20 response rates were significantly higher in the IXEQ2W, IXEQ2W, and adalimumab 40 mg groups (OR 2.59, 95% CrI 1.69–3.98; OR 2.45, 95% CrI 1.60–3.75;

and OR 1.94, 95% CrI 1.13–3.37, respectively; **Figs. 2 and 3**). The efficacy of secukinumab and ixekizumab was numerically higher than that of adalimumab 40 mg (**Fig. 3**), although there was no statistically significant difference in the ASAS20 response rates. The response rate of ASAS40 showed a pattern of distribution similar to the response rate of ASAS20, except that the ixekizumab group was correlated with the most favorable response rate of SUCRA for ASAS40 (**Fig. 3**). SUCRA-based ranking probability (**Table 3**) suggested that secukinumab 150 mg had the highest likelihood of being the best treatment to achieve the ASAS20 response rate, followed by IXEQ2W, IXEQ4W, adalimumab 40 mg, and placebo (**Table 3**). The response rate of ASAS40 showed a pattern of distribution similar to the response rate of ASAS20, except that IXEQ2W and IXEQ4W had the highest probability of being the best treatment to achieve the ASAS40 response rate (**Table 3**).

Network meta-analysis of the safety of secukinumab and ixekizumab

The number of SAEs with ixekizumab was numerically smaller than those observed with secukinumab, placebo, or adalimumab 40 mg; however, the results were not statistically significant (**Table 3**; **Fig. 4**). There was no significant difference in the number of SAEs between the five treatments (**Table 3**; **Fig. 4**).

Inconsistency and sensitivity analysis

Inconsistency plots, evaluating network inconsistencies between direct and indirect estimates, showed low potential for differences that could significantly affect the results of network meta-analysis (**Fig. 5**). This was verified by the fixed and random effects model comparison, thus indicating reliable meta-analysis findings from this network (**Fig. 5**).

Discussion

In patients with active AS, a network meta-analysis was conducted to compare the efficacy and safety of secukinumab and ixekizumab with placebo. This approach was chosen because it allows an indirect comparison of multiple treatments, either incomplete or without direct comparisons. Our meta-analysis network evaluated the number of patients who received an ASAS20 or ASAS40 response and the number of SAEs in the various treatment groups. The results showed that the response rate for ASAS20 was significantly higher in the secukinumab 150 mg and ixekizumab 80 mg groups. The effectiveness of secukinumab 150 mg was numerically higher than that of ixekizumab. Nonetheless, there was no statistically significant difference between the ASAS response rates of secukinumab and ixekizumab. The response rate of ASAS40 showed a pattern of distribution similar to the response rate of ASAS20, except that ixekizumab had a numerically higher efficacy than secukinumab. With regard to safety, there was no substantial difference in the number of SAEs among the four treatment groups, indicating comparable safety among the secukinumab 150 mg, ixekizumab 80 mg, adalimumab 40 mg, and placebo groups. Our analysis confirmed the effectiveness of secukinumab and ixekizumab in AS, thus demonstrating that secukinumab and ixekizumab are good alternatives to anti-TNF.

Although the use of TNFIs has improved the treatment of AS, in a significant proportion of patients, this therapy is found to be ineffective. Thus, there is an unmet need for new AS therapies owing to drug intolerance, non-responsiveness, and therapeutic resistance seen with currently available approaches. Therefore, additional treatment strategies, with new mechanisms of action, are warranted. In the pathogenesis of AS, IL-17A plays an important role [29]. Five TNFIs and one anti-IL-17A therapy (secukinumab) have been included in the list of approved biological therapies for AS. Secukinumab is the first monoclonal antibody anti-IL-17A that provided evidence of the effectiveness of a non-TNF-targeted AS therapy as a possible treatment option for

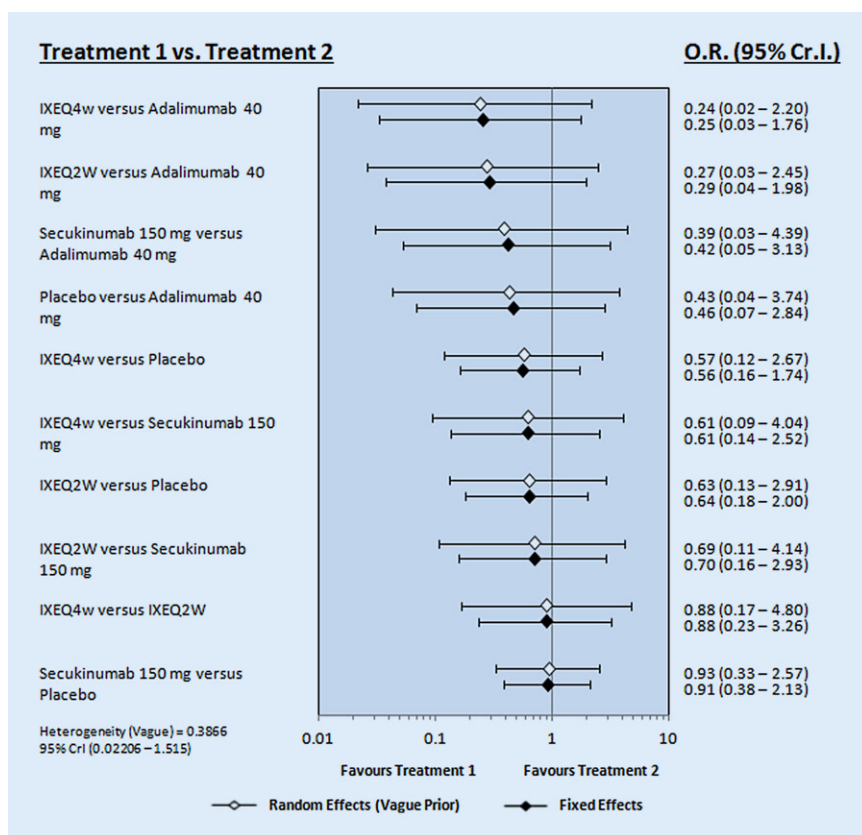


Fig. 4 ▲ Results of the Bayesian network meta-analysis of randomized controlled studies assessing the relative efficacy safety of secukinumab and ixekizumab

AS; moreover, it exhibits validated IL-17A inhibition [17]. Therefore, in either TNFI-naïve or TNFI-exposed patients or when TNFIs are contraindicated, IL-17A blockers are considered suitable treatment alternatives for AS [10]. The Food and Drug Administration (FDA) has approved doubling the previously recommended dose to 300 mg for AS based on data from the MEASURE 3 clinical trial (NCT02008916) in 2020 [26]. The European Medicines Agency (EMA) had already approved the same label update in late 2019. Recently, newer IL-17-blocking agents are being investigated as treatment options for AS. Ixekizumab, like secukinumab, is an antagonist of IL-17A [23]. Both secukinumab and ixekizumab were approved for both radiographic and non-radiographic axial spondyloarthritis (axSpA) by EMA and FDA. However, the pharmacokinetic properties of ixekizumab and secukinumab are distinct. For example, ixekizumab's *in vitro* binding affinity to IL-17A is 1.8 pmol/L com-

pared to secukinumab's 100–200 pmol/L [25].

Considering the following shortcomings, the findings of this analysis should be cautiously interpreted. First, a relatively short treatment period (16 weeks) was selected as the follow-up timepoint. The follow-up time was, therefore, too limited to determine the treatment's long-term effects. Thus, there is a need to comparatively analyze studies with longer follow-up duration. Second, as the design and patient characteristics of the selected studies were heterogeneous, the findings of this network meta-analysis may have been influenced by inter-study variations [6, 11]. The magnitude of the placebo response rates in secukinumab and ixekizumab in comparison to anti-TNF agents was comparable (28.4–41.2%, 29.8–40.2%, 20.6–32.2%, respectively), although the range of the placebo response rates in TNF inhibitors seems to be a little lower compared to those in secukinumab and ixekizumab [20]. Third, the efficacy

and safety outcomes of secukinumab and ixekizumab in AS were not fully addressed in our research. We focused solely on the effectiveness of treatments based on the number of patients who achieved ASAS20. The primary endpoint of secukinumab was the proportion of patients who met the ASAS20, whereas the primary endpoint of ixekizumab was the proportion of patients achieving an ASAS40 response. By analyzing the various results, we concentrated on the effectiveness of the treatment based on the number of patients that achieved an ASAS20 or ASAS40 response, and the safety based on the number of SAEs. In particular, due to their low frequency, the number of SAEs may not be appropriate as a safety outcome indicator. Finally, this meta-analysis included only a limited number of studies. Hence, this study was underpowered to examine the relative effectiveness and safety of the test drugs.

A Bayesian network meta-analysis allows all treatment options to be compared to conventional meta-analysis to allow simultaneous comparisons of various treatment options where direct head-to-head comparisons are not available [18, 21, 28, 31]. An estimate of the relative effectiveness is required while selecting the treatment drug [25, 28]. This is the first meta-analysis, using the Bayesian network, that performed a comprehensive and simultaneous evaluation of the efficacy and safety of secukinumab and ixekizumab in active AS. While the current data are not of the highest standard, they may be the best data available in this field, pending definitive RCTs.

In conclusion, we found that secukinumab and ixekizumab were effective in the treatment of active AS, using a Bayesian network meta-analysis of five RCTs that compared five different treatment groups. Furthermore, there was no significant safety risk associated with the treatments. Nonetheless, long-term studies are needed in a larger group of patients with active AS to further assess the relative efficacy and safety of secukinumab and ixekizumab.

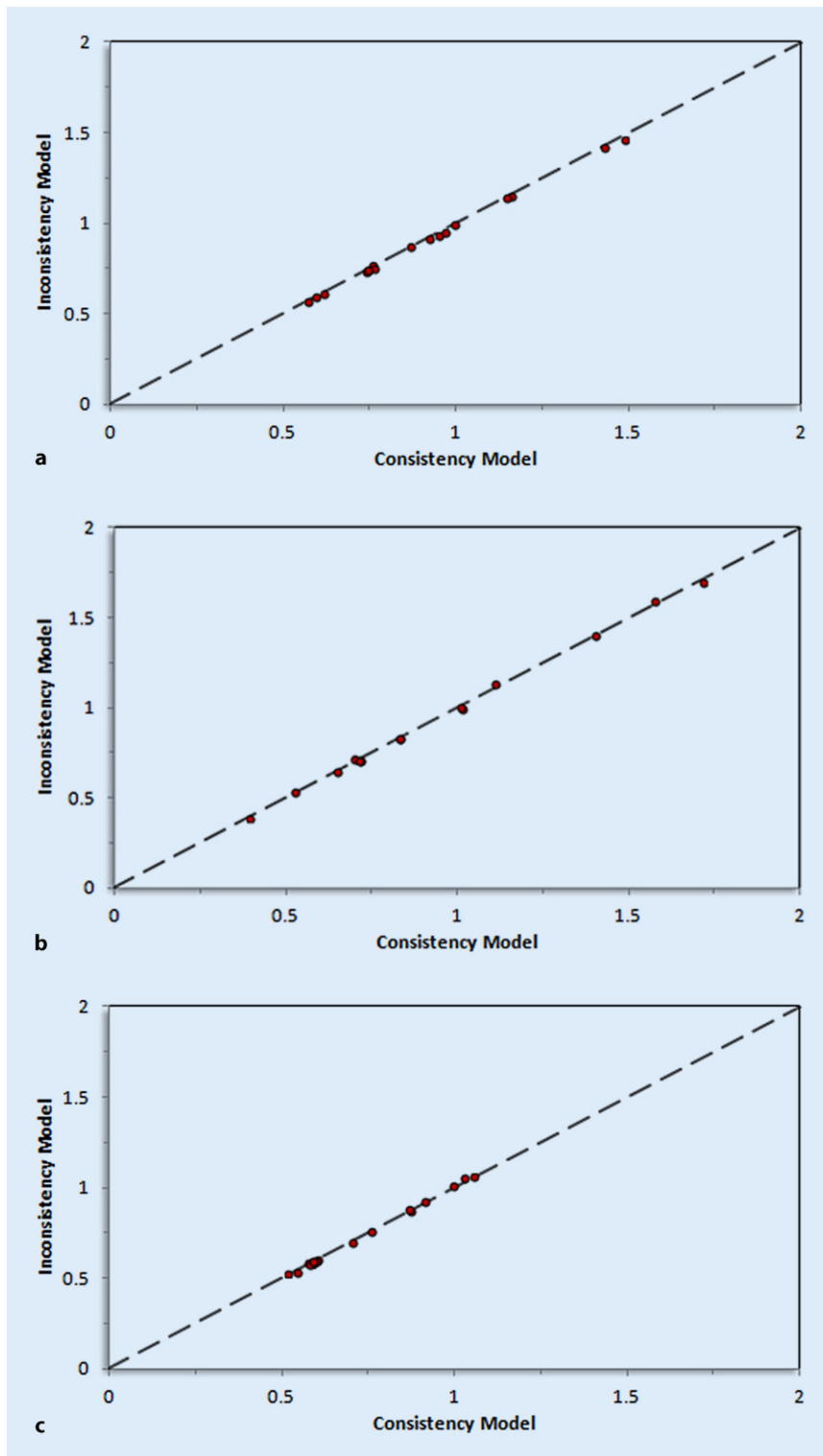


Fig. 5 ▲ Inconsistency plot for the efficacy (a ASAS20, b ASAS40) and safety (c) of secukinumab and adalimumab. Plot of the posterior mean deviance contributions of each individual datapoint for the consistency model (horizontal axis) and the unrelated mean effects model (vertical axis), along with the line of equality

Corresponding address

Y. H. Lee, MD, PhD

Division of Rheumatology, Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine 73, Goryeodae-ro, 136-705 Seongbuk-gu, Seoul, Korea (Republic of)
lyhcgh@korea.ac.kr

Funding. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Compliance with ethical guidelines

Conflict of interest. Y.H. Lee and G.G. Song have no financial or non-financial conflict of interest to declare.

For this article, no studies with human participants or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

References

1. Anderson JJ, Baron G, van der Heijde D et al (2001) Ankylosing spondylitis assessment group preliminary definition of short-term improvement in ankylosing spondylitis. *Arthritis Rheum* 44(8):1876–1886
2. Baeten D, Baraliakos X, Braun J et al (2013) Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. *Lancet* 382(9906):1705–1713
3. Baeten D, Sieper J, Braun J et al (2015) Secukinumab, an interleukin-17A inhibitor, in ankylosing spondylitis. *N Engl J Med* 373(26):2534–2548
4. Braun J, van den Berg R, Baraliakos X et al (2011) 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 70(6):896–904
5. Brown S, Hutton B, Clifford T et al (2014) A Microsoft-Excel-based tool for running and critically appraising network meta-analyses—an overview and application of NetMetaXL. *Syst Rev* 3(1):110
6. Byun S, Jung SM, Song JJ et al (2018) Hemoglobin A1c, not Glycated albumin, Can independently reflect the Ankylosing Spondylitis disease activity score. *J Rheum Dis* 25(2):131–139
7. Caldwell DM, Ades AE, Higgins JP (2005) Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 331(7521):897–900
8. Deodhar A, Poddubnyy D, Pacheco-Tena C et al (2019) Efficacy and safety of Ixekizumab in the treatment of radiographic axial spondyloarthritis: sixteen-week results from a phase III randomized, double-blind, placebo-controlled trial in patients with prior inadequate response to or intolerance of tumor necrosis factor inhibitors. *Arthritis Rheumatol* 71(4):599–611
9. Dias S, Welton NJ, Sutton AJ et al (2013) Evidence synthesis for decision making 4: inconsistency

in networks of evidence based on randomized controlled trials. *Med Decis Making* 33(5):641–656

10. Dubash S, Bridgwood C, McGonagle D et al (2019) The advent of IL-17A blockade in ankylosing spondylitis: secukinumab, ixekizumab and beyond. *Expert Rev Clin Immunol* 15(2):123–134
11. Hahn Y-S (2018) Enthesitis-related Arthritis. *J Rheum Dis* 25(4):221–230
12. Heijde D van der, Wei JC-C, Dougados M et al (2018) Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. *Lancet* 392(10163):2441–2451
13. Higgins JP, Jackson D, Barrett JK et al (2012) Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. *Res Synth Methods* 3(2):98–110
14. Kivitz A, Blanco R, Maradiaga M et al (2016) Secukinumab provides sustained improvement in physical, function, health-related quality of life, fatigue, and work productivity in patients with active psoriatic arthritis: 52-week results from an international phase 3 trial. *J Clin Rheumatol* 22(3):142–143
15. Kivitz AJ, Wagner U, Dokoupilova E et al (2018) Efficacy and safety of secukinumab 150 mg with and without loading regimen in ankylosing spondylitis: 104-week results from MEASURE 4 study. *Rheumatol Ther* 5(2):447–462
16. Koo BS, Lim JW, Shin JH et al (2018) Characteristics of uveitis in patients with ankylosing spondylitis in Korea: a single-center survey. *J Rheum Dis* 25(1):28–33
17. Langley RG, Elewski BE, Lebwohl M et al (2014) Secukinumab in plaque psoriasis—results of two phase 3 trials. *N Engl J Med* 371(4):326–338
18. Lee YH (2018) Association between the neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio and rheumatoid arthritis and their correlations with the disease activity: a meta-analysis. *J Rheum Dis* 25(3):169–178
19. Lee YH, Song GG (2020) Associations Between Circulating Interleukin-17 Levels and Systemic Lupus Erythematosus and Between Interleukin-17 Gene Polymorphisms and Disease Susceptibility: A Meta-analysis. *J Rheum Dis* 27(1):37–44
20. Lee YH, Song GG (2017) Comparative efficacy and safety of secukinumab and adalimumab in patients with active ankylosing spondylitis: a Bayesian network meta-analysis of randomized controlled trials. *J Rheum Dis* 24(4):211–219
21. Lee YH, Song GG (2018) Overall and sex-specific mortality in psoriatic arthritis and ankylosing spondylitis: A meta-analysis. *J Rheum Dis* 25(3):197–202
22. Lee YH, Song GG (2019) YKL-40 Levels in Rheumatoid Arthritis and Their Correlation with Disease Activity: A Meta-analysis. *J Rheum Dis* 26(4):257–263
23. Liu L, Lu J, Allan BW et al (2016) Generation and characterization of ixekizumab, a humanized monoclonal antibody that neutralizes interleukin-17A. *J Inflamm Res* 9:39
24. Moher D, Liberati A, Tetzlaff J et al (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 151(4):264–269
25. Paul C (2018) Ixekizumab or secukinumab in psoriasis: what difference does it make? *Br J Dermatology* 178(5):1003–1005
26. Pavelka K, Kivitz A, Dokoupilova E et al (2017) Efficacy, safety, and tolerability of secukinumab in patients with active ankylosing spondylitis: a randomized, double-blind phase 3 study, MEASURE 3. *Arthritis Res Ther* 19(1):285
27. Salanti G, Ades AE, Ioannidis JP (2011) Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol* 64(2):163–171
28. Schmitz S, Adams R, Walsh CD et al (2012) A mixed treatment comparison of the efficacy of anti-TNF agents in rheumatoid arthritis for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. *Ann Rheum Dis* 71(2):225–230
29. Shen H, Goodall JC, Hill GJS (2009) Frequency and phenotype of peripheral blood Th17 cells in ankylosing spondylitis and rheumatoid arthritis. *Arthritis Rheum* 60(6):1647–1656
30. Sieper J, Rudwaleit M, Khan MA et al (2006) Concepts and epidemiology of spondyloarthritis. *Best Pract Res Clin Rheumatol* 20(3):401–417
31. Song GG, Bae S-C, Lee YH (2012) Association between vitamin D intake and the risk of rheumatoid arthritis: a meta-analysis. *Baillieres Clin Rheumatol* 31(12):1733–1739
32. Valkenhoef G van, Lu G, de Brock B et al (2012) Automating network meta-analysis. *Res Synth Methods* 3(4):285–299
33. Wendling D, Guillot X, Prati C (2015) The IL-23/Th 17 pathway in spondyloarthritis: the royal road? *Joint Bone Spine*. <https://doi.org/10.1016/j.jbspin.2014.08.003>



© Michael Szabo, Uniklinik Jena

Hypnose bei chirurgischen Eingriffen

Hypnose lindert Schmerzen, reduziert die psychische Belastung und fördert die Genesung nach chirurgischen Eingriffen – das ist das Ergebnis einer Meta-Analyse der Unikliniken Jena und Leipzig.

Seit mehr als 50 Jahren wird die Wirksamkeit von Hypnose im Rahmen chirurgischer Eingriffe erforscht. Da psychischer Stress den Heilungsprozess negativ beeinflussen kann, soll Hypnose den Patienten die Ängste nehmen, Schmerzen verringern und die Genesung beschleunigen. Inwieweit dieses Verfahren das wirklich zu leisten vermag, untersuchten jetzt Psychologen der Unikliniken Jena und Leipzig in einer im Fachblatt *Clinical Psychology Review* veröffentlichten Meta-Analyse von über 50 Einzelstudien.

In den von der Forschungsgruppe rund um Dr. Jenny Rosendahl untersuchten Studien hatten die Patienten Hypnose jeweils zusätzlich zur Routinebehandlung vor, während oder nach Operationen erhalten. Dazu zählten beispielsweise gynäkologische oder Herzoperationen sowie diagnostische Prozeduren wie Biopsien. In der Auswertung der Studien erwies sich Hypnose als effektive Intervention: Die Wirksamkeit der Hypnose ließ sich sowohl anhand patientenrelevanter Aspekte wie psychischer Belastung oder Schmerzen belegen, als auch in Bezug auf Genesung, Medikamentenverbrauch und Dauer des Eingriffs.

Quelle: Universitätsklinikum Jena, www.uniklinikum-jena.de