ORIGINAL RESEARCH

Number Needed to Treat Network Meta-Analysis to Compare Biologic Drugs for Moderate-to-Severe Psoriasis

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ABSTRACT

Introduction: Number needed to treat (NNT) estimates are a practical metric to help identify the most effective therapies. Our objective is to compare 11 biologic drugs for moderate-to-severe psoriasis in terms of NNT.

Methods: The NNT data were obtained from a Bayesian network meta-analysis of 42 double-blind, randomized, phase 3 clinical trials for 11 biologics (adalimumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab). We determined NNT to achieve Psoriasis Area and Severity Index (PASI) 75/90/100 responses at weeks 4, 8, 12, 16, and 48/52 and Dermatology Life Quality Index (DLQI) response 0, 1 at week 12.

Results: Highest efficacy (lowest NNT) was with brodalumab and ixekizumab for PASI 90 at weeks 4, 8, and 12; ixekizumab for PASI 90/100 at week 16; and brodalumab for PASI 100 at week 12. After 48/52 weeks, risankizumab had the highest efficacy for PASI 90/100 overlapping with guselkumab, brodalumab, and ixekizumab for PASI 90 and with brodalumab and ixekizumab for PASI 100. Ixekizumab had the highest efficacy for DLQI (0,1) at week 12.

Conclusions: Brodalumab and ixekizumab had the lowest NNTs for achieving PASI responses at early time points and were not significantly different than risankizumab and guselkumab after 48/52 weeks.

Keywords: Biologics; Meta-analysis; NNT; Psoriasis

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Key Summary Points

Why carry out this study?

Number needed to treat (NNT) estimations provide a simple and practical metric for payors and providers to compare available biologic treatments for moderate-to-severe psoriasis

A network meta-analysis of 42 clinical trials for 11 biologic drugs was used to calculate NNT

A lower NNT indicates that a treatment is more effective than the comparator

What was learned from the study?

Brodalumab and ixekizumab had the highest efficacy (lowest NNT) for achieving PASI 75/90/100 responses at early time points (week 4 to week 16). After 48/52 weeks, risankizumab, guselkumab, brodalumab, and ixekizumab had the lowest NNT and were not significantly different. Ixekizumab had the highest efficacy in quality-of-life improvement (achievement of Dermatology Life Quality Index response 0,1 at week 12)

DIGITAL FEATURES

This article is published with digital features, including animated graphs, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.19323539.

INTRODUCTION

Psoriasis is a chronic disease characterized by painful, itchy skin lesions, which can greatly impact a patient's quality of life [1–3]. Currently, 11 biologics have been approved by the United States Food and Drug Administration

(FDA) for the treatment of moderate-to-severe psoriasis, which are anti-interleukin (IL)-17 agents (brodalumab, ixekizumab, and secukinumab), an anti-IL-12/-23 agent (ustekinumab), anti-IL-23 agents (guselkumab, risankizumab, and tildrakizumab), and anti-tumor necrosis factor (TNF) agents (adalimumab, certolizumab pegol, etanercept, and infliximab). Health care providers and patients benefit from an assessment of comparative efficacy to help identify the most effective and appropriate therapy. Network meta-analyses (NMA) are indirect comparisons of individual treatments versus placebo, and while NMAs have been conducted in the short- and long-term [4–8], few comprehensive long-term NMAs have focused on the number needed to treat (NNT) [9–11]. Number needed to treat is the average number of patients required to be treated with a given treatment to achieve an outcome in question. Number needed to treat estimates provide a simple and practical metric for payors and providers to compare available treatments, as a lower NNT indicates the treatment is more effective than the comparator. Comparative NNTs provide more comprehensive evidence for dermatologists in their treatment decisions.

The objective of this study is to provide a comprehensive long-term NMA focused on NNT to compare efficacy among 11 FDA-approved biologics for the treatment of moderate-to-severe psoriasis. Bayesian NMA (BNMA) was used to calculate NNT for achieving skin improvement (measured as Psoriasis Area and Severity Index [PASI] 75, PASI 90, and PASI 100 responses at weeks 4, 8, 12, 16, and 48/52) and quality-of-life improvement (measured as achievement of Dermatology Life Quality Index [DLQI] response of 0, 1 at week 12). This study uniquely includes rapid PASI response rates at weeks 4 and 8 and quality of life in terms of NNT.

METHODS

Efficacy data for this NMA analysis were collected from 42 phase 3 double-blind randomized clinical trials for 11 approved biologic treatments for moderate-to-severe psoriasis:

anti-IL-17 agents brodalumab, ixekizumab, and secukinumab; anti-IL-12/-23 agent ustekinumab; anti-IL-23 agents guselkumab, risankizumab, and tildrakizumab; and anti-TNF agents adalimumab, certolizumab pegol, etanercept, and infliximab [12–46]. These studies included patients who were ≥ 18 years of age with moderate-to-severe psoriasis, and inclusion and exclusion criteria for the studies have been previously reported. Studies used in each analysis of the NMA are in Supplementary Material Table S1.

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Outcome measures extracted for short- and long-term skin improvement were achievement of PASI 75, PASI 90, and PASI 100 at weeks 4, 8, 12, 16, and 48/52 in terms of the NNT. The outcome measure for quality-of-life improvement was achievement of DLQI (0,1) at week 12 in terms of NNT, defined as no impact or minimal impact on quality of life. Dermatology Life Quality Index (0,1) data were not available after week 12 from enough randomized controlled trials (RCTs) for NMA inclusion; thus, additional time points were not evaluated.

Systematic Literature Review

Efficacy data on outcome measures were obtained from a systematic literature review previously reported by Warren et al. [4], which is updated in this report. Briefly, a search was performed using the OvidSP platform for literature published between January 1, 1990, and August 21, 2020. The search parameters were designed to identify publications that reported data from phase 3 RCTs of biologics approved for the treatment of moderate-to-severe psoriasis. Studies included in the NMA are listed above and in Supplementary Material Table S1. The Cochrane Handbook for Systematic Reviews of Interventions guidance was followed [47].

In this update of the previous report [4], long-term analyses were included to week 48/52. All doses were included in the analyses (shown in the evidence network for NMA in Fig. 1). Our data present only FDA-approved label doses, as was done in the previous report [4]. Treatments/studies were excluded from any specific analysis where data were not available. For long-term efficacy analysis (week 48/52), studies with re-randomization at the end of the induction period (week 12/16) were excluded. The ustekinumab arm in AMAGINE-2,3 was excluded for week 48/52 analysis; data were not available for patients who were taking ustekinumab and did not receive a brodalumab rescue dose at week 16.

Statistical Analyses

Bayesian NMAs were performed on PASI 75, PASI 90, and PASI 100 response rates at different time points, separately, using normal approximation. A mixed effect model was assumed with fixed treatment effect and random baseline effect to allow various placebo response rates across different studies. Non-informative priors were used for the model parameters. The BNMA describes the joint probability distribution of these response variables, and NNTs were calculated using the response difference of each respective treatment versus placebo. Posterior distributions of the treatment effect were presented by posterior samples and summarized by posterior means and 95% credible intervals. Bayesian NMAs were conducted through an internal tool based on JAGS and R with three chains; a thinning factor of 50; burn-in iterations of 300,000; and 1,000,000 total samples. Posterior samples of NNTs to achieve PASI 75, 90, and 100 responses were obtained as reciprocals of the posterior samples of the corresponding treatment effects. Posterior means and 95% credible intervals were also summarized for NNTs.

RESULTS

The evidence network for the NMA of PASI 90 response at week 12 is presented in Fig. 1. This is representative of evidence network findings for NMA for PASI response at other time points and DLQI (0,1) at week 12. All studies included in
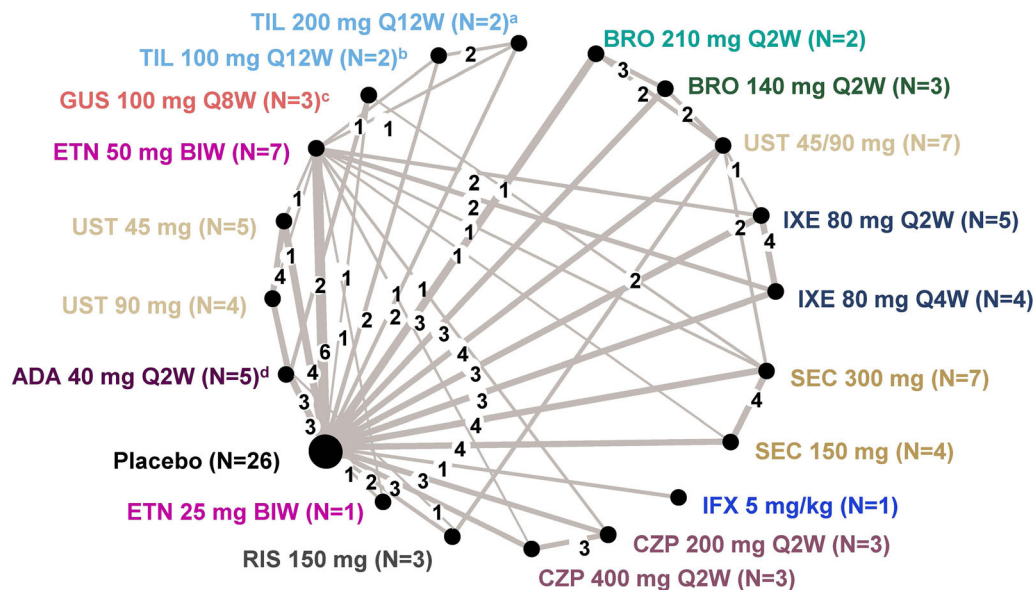
Fig. 1 Evidence network for NMA of PASI 90 at week 12. A total of 35 RCTs and 20 treatments are included. Lines represent direct comparisons using RCTs (*n*). Numbers and thicknesses of lines represent the number of RCTs included in each comparison (*N*). [a]200 mg at Weeks 0 and 4, then every 12 weeks; [b]100 mg at Weeks 0 and 4, then every 12 weeks; [c]100 mg at Weeks 0 and 4, then every 8 weeks; [d]80 mg at Week 0, 40 mg at week 1, then 40 mg Q2W. *ADA* adalimumab (anti-TNF agent), *BIW* twice weekly, *BRO* brodalumab (anti-IL-17 agent), *CZP* certolizumab pegol (anti-TNF agent), *ETN*

etanercept (anti-TNF agent), *GUS* guselkumab (anti-IL-23 agent), *IFX* infliximab (anti-TNF agent), *IXE* ixekizumab (anti-IL-17 agent), *NMA* network meta-analysis, *PASI* Psoriasis Area and Severity Index, *Q2W* every 2 weeks, *Q4W* every 4 weeks, *Q8W* every 8 weeks, *Q12W* every 12 weeks, *RCT* randomized controlled trial, *RIS* risankizumab (anti-IL-23 agent), *SEC* secukinumab (anti-IL-17 agent), *TIL* tildrakizumab (anti-IL-23 agent), *UST* ustekinumab (anti-IL-12/-23 agent)

each analysis of the NMA are in the Supplementary Material (Table S1).

Short-term Efficacy and Quality of Life in Terms of NNT

Brodalumab and ixekizumab had the highest efficacy (lowest NNT) to achieve PASI 90 and PASI 100 at weeks 4 and 8 (Table 1), the earliest time points examined in this analysis. At week 12, the lowest NNT to achieve PASI 90 was with ixekizumab (1.44, 95% credible interval [Crl] 1.39, 1.49) with density distribution overlapping with brodalumab (1.49, 95% Crl 1.43, 1.55), and the lowest NNT to achieve PASI 100 was with brodalumab (2.50, 95% Crl 2.35, 2.67) with density distribution overlapping with ixekizumab (2.61, 95% Crl 2.45, 2.79) (Fig. 2 and Table 1). At week 16, the lowest NNT to

achieve PASI 90 was with ixekizumab (1.38, 95% Crl 1.30, 1.47) with density distribution overlapping with risankizumab (1.40, 95% Crl 1.34, 1.46), and the lowest NNT to achieve PASI 100 was with ixekizumab (2.25, 95% Crl 2.04, 2.50) with density distribution overlapping with brodalumab (2.29, 95% Crl 2.04, 2.60) (Fig. 2; Table 1). Estimated mean treatment effects (relative to placebo) on PASI 90 and PASI 100 response rates are presented at weeks 12 and 16 in Fig. 3. Number needed to treat to achieve PASI 75 and estimated mean treatment effects (relative to placebo) on PASI 75 response rates are presented at weeks 4, 8, 12, and 16 in the Supplementary Material (Figure S1, Figure S2, and Table S2).

At week 12, the lowest NNT to achieve DLQI (0,1) was with ixekizumab (1.75, Crl 1.63, 1.87) followed by and overlapping in distribution

Table 1 Treatment effect (based on absolute difference with placebo) and NNT to achieve PASI 90 and PASI 100 responses at weeks 4, 8, 12, 16, and 48/52. Data are mean relative to placebo

		PASI 90			PASI 100	
Week	Biologic	Effect (95% CrI)	NNT (95% CrI)	Biologic	Effect (95% CrI)	NNT (95% CrI)
4	BRO	0.28 (0.26, 0.31)	3.53 (3.25, 3.84)	BRO	0.09 (0.07, 0.10)	11.75 (9.89, 14.15)
	IXE	0.23 (0.21, 0.26)	4.29 (3.92, 4.71)	IXE	0.07 (0.06, 0.09)	13.96 (11.63, 17.02)
	IFX	0.15 (0.10, 0.20)	6.72 (4.95, 9.60)	SEC	0.04 (0.03, 0.05)	28.01 (21.72, 37.27)
	SEC	0.13 (0.11, 0.15)	7.76 (6.84, 8.86)	GUS	0.01 (0.00, 0.01)	NE (68.45, NE)
	RIS	0.05 (0.03, 0.07)	19.03 (13.48, 28.63)	ADA	0.00 (0.00, 0.01)	NE (87.49, NE)
	ADA	0.04 (0.03, 0.05)	24.92 (18.85, 34.48)	RIS	0.00 (-0.01, 0.02)	NE (65.36, NE)
	CZP	0.03 (0.01, 0.05)	43.96 (18.30, 109.65)	TIL	0.00 (-0.01, 0.01)	NE (68.73, NE)
	GUS	0.03 (0.01, 0.04)	42.61 (23.14, 89.85)	UST	0.00 (0.00, 0.01)	NE (124.22, NE)
	UST	0.03 (0.01, 0.04)	40.41 (25.95, 69.98)	ETN	0.00 (0.00, 0.01)	NE (154.56, NE)
	TIL	0.02 (0.01, 0.04)	56.76 (24.37, 135.32)	CZP	NA	NA
	ETN	0.01 (0.01, 0.02)	82.61 (46.55, 163.40)	IFX	NA	NA
8	BRO	0.59 (0.56, 0.61)	1.71 (1.63, 1.79)	BRO	0.30 (0.27, 0.32)	3.36 (3.11, 3.65)
	IXE	0.57 (0.54, 0.59)	1.76 (1.69, 1.85)	IXE	0.25 (0.23, 0.27)	4.05 (3.71, 4.44)
	IFX	0.44 (0.37, 0.50)	2.31 (2.01, 2.67)	SEC	0.16 (0.14, 0.18)	6.28 (5.48, 7.26)
	SEC	0.43 (0.40, 0.46)	2.33 (2.18, 2.49)	RIS	0.14 (0.12, 0.17)	7.01 (5.84, 8.57)
	RIS	0.41 (0.37, 0.45)	2.42 (2.20, 2.67)	GUS	0.09 (0.06, 0.12)	11.21 (8.46, 15.55)
	GUS	0.34 (0.30, 0.37)	2.97 (2.67, 3.33)	UST	0.08 (0.06, 0.10)	12.52 (10.04, 16.01)
	ADA	0.24 (0.21, 0.28)	4.11 (3.58, 4.77)	ADA	0.07 (0.05, 0.08)	15.40 (12.33, 19.74)
	UST	0.24 (0.21, 0.27)	4.13 (3.68, 4.68)	TIL	0.06 (0.04, 0.08)	16.84 (12.09, 24.88)
	TIL	0.20 (0.16, 0.23)	5.13 (4.34, 6.15)	ETN	0.02 (0.01, 0.03)	58.06 (35.05, 108.46)
	CZP	0.17 (0.12, 0.21)	6.05 (4.72, 8.02)	CZP	NA	NA
	ETN	0.09 (0.08, 0.11)	10.66 (9.07, 12.68)	IFX	NA	NA
12	IXE	0.70 (0.67, 0.72)	1.44 (1.39, 1.49)	BRO	0.40 (0.37, 0.43)	2.50 (2.35, 2.67)
	BRO	0.67 (0.65, 0.70)	1.49 (1.43, 1.55)	IXE	0.38 (0.36, 0.41)	2.61 (2.45, 2.79)
	RIS	0.62 (0.58, 0.66)	1.62 (1.52, 1.72)	RIS	0.31 (0.27, 0.34)	3.28 (2.93, 3.70)
	SEC	0.58 (0.55, 0.61)	1.72 (1.64, 1.80)	SEC	0.28 (0.25, 0.30)	3.60 (3.30, 3.95)
	IFX	0.57 (0.51, 0.63)	1.75 (1.58, 1.96)	GUS	0.21 (0.18, 0.25)	4.76 (4.02, 5.71)
	GUS	0.54 (0.50, 0.57)	1.86 (1.74, 2.00)	UST	0.16 (0.14, 0.17)	6.35 (5.78, 7.01)
	UST	0.42 (0.39, 0.45)	2.37 (2.22, 2.54)	ADA	0.13 (0.12, 0.15)	7.47 (6.51, 8.64)
	ADA	0.37 (0.35, 0.40)	2.69 (2.51, 2.89)	TIL	0.13 (0.10, 0.15)	8.11 (6.50, 10.35)
	TIL	0.35 (0.31, 0.39)	2.87 (2.57, 3.24)	ETN	0.05 (0.04, 0.06)	19.65 (15.50, 25.58)

Table 1 continued

| Week | PASI 90 | | | PASI 100 | | |
	Biologic	Effect (95% Crl)	NNT (95% Crl)	Biologic	Effect (95% Crl)	NNT (95% Crl)
	CZP	0.34 (0.29, 0.40)	2.94 (2.51, 3.48)	CZP	NA	NA
	ETN	0.21 (0.19, 0.23)	4.83 (4.40, 5.32)	IFX	NA	NA
16	IXE	0.73 (0.68, 0.77)	1.38 (1.30, 1.47)	IXE	0.45 (0.40, 0.49)	2.25 (2.04, 2.50)
	RIS	0.71 (0.68, 0.74)	1.40 (1.34, 1.46)	BRO	0.44 (0.39, 0.49)	2.29 (2.04, 2.60)
	SEC	0.70 (0.67, 0.72)	1.43 (1.38, 1.49)	RIS	0.42 (0.39, 0.45)	2.40 (2.24, 2.58)
	BRO	0.69 (0.64, 0.74)	1.45 (1.35, 1.56)	SEC	0.38 (0.35, 0.41)	2.65 (2.46, 2.86)
	GUS	0.69 (0.66, 0.72)	1.46 (1.40, 1.52)	GUS	0.36 (0.33, 0.39)	2.8 (2.58, 3.05)
	CZP	0.48 (0.42, 0.53)	2.10 (1.87, 2.38)	ADA	0.19 (0.17, 0.21)	5.36 (4.82, 5.98)
	UST	0.45 (0.41, 0.49)	2.21 (2.03, 2.42)	UST	0.18 (0.15, 0.22)	5.50 (4.56, 6.75)
	ADA	0.44 (0.42, 0.47)	2.26 (2.14, 2.41)	TIL	0.15 (0.12, 0.18)	6.85 (5.65, 8.44)
	TIL	0.44 (0.39, 0.48)	2.30 (2.09, 2.54)	CZP	0.14 (0.09, 0.20)	7.34 (5.05, 11.48)
	ETN	0.27 (0.23, 0.30)	3.75 (3.28, 4.32)	ETN	0.07 (0.05, 0.09)	15.37 (11.61, 21.22)
	IFX	NA	NA	IFX	NA	NA
48/52	RIS	0.79 (0.75, 0.82)	1.27 (1.21, 1.34)	RIS	0.57 (0.53, 0.61)	1.77 (1.64, 1.90)
	GUS	0.76 (0.72, 0.79)	1.32 (1.26, 1.39)	BRO	0.54 (0.49, 0.59)	1.85 (1.68, 2.05)
	BRO	0.72 (0.67, 0.76)	1.40 (1.31, 1.50)	IXE	0.53 (0.48, 0.57)	1.90 (1.74, 2.07)
	IXE	0.70 (0.66, 0.75)	1.42 (1.33, 1.52)	GUS	0.47 (0.43, 0.51)	2.13 (1.95, 2.34)
	SEC	0.62 (0.59, 0.65)	1.61 (1.53, 1.69)	SEC	0.38 (0.34, 0.41)	2.66 (2.45, 2.90)
	CZP	0.58 (0.51, 0.66)	1.72 (1.51, 1.97)	CZP	0.28 (0.21, 0.35)	3.58 (2.83, 4.67)
	UST	0.47 (0.43, 0.52)	2.12 (1.91, 2.35)	UST	0.27 (0.22, 0.31)	3.74 (3.18, 4.46)
	ADA	0.46 (0.41, 0.52)	2.17 (1.92, 2.46)	ADA	0.23 (0.18, 0.27)	4.44 (3.64, 5.51)
	ETN	0.32 (0.26, 0.37)	3.20 (2.72, 3.81)	ETN	0.10 (0.07, 0.13)	10.52 (7.64, 15.22)
	IFX	NA	NA	IFX	NA	NA
	TIL	NA	NA	TIL	NA	NA

ADA adalimumab, *BRO* brodalumab, *Crl* credible interval, *CZP* certolizumab pegol, *ETN* etanercept, *GUS* guselkumab, *IFX* infliximab, *IXE* ixekizumab, *NA* not available, *NE* not evaluable as denominator is ≤ 0.01, *NNT* number needed to treat, *PASI* Psoriasis Area and Severity Index, *RIS* risankizumab, *SEC* secukinumab, *TIL* tildrakizumab, *UST* ustekinumab

with brodalumab (1.83, Crl 1.74, 1.93) and secukinumab (1.88, Crl 1.76, 2.01) (Supplementary Material Table S3).

Long-term Efficacy in Terms of NNT

After 48/52 weeks, the lowest NNT to achieve PASI 90 was with risankizumab (1.27, 95% Crl 1.21, 1.34) with density distribution overlapping with guselkumab (1.32, 95% Crl 1.26,
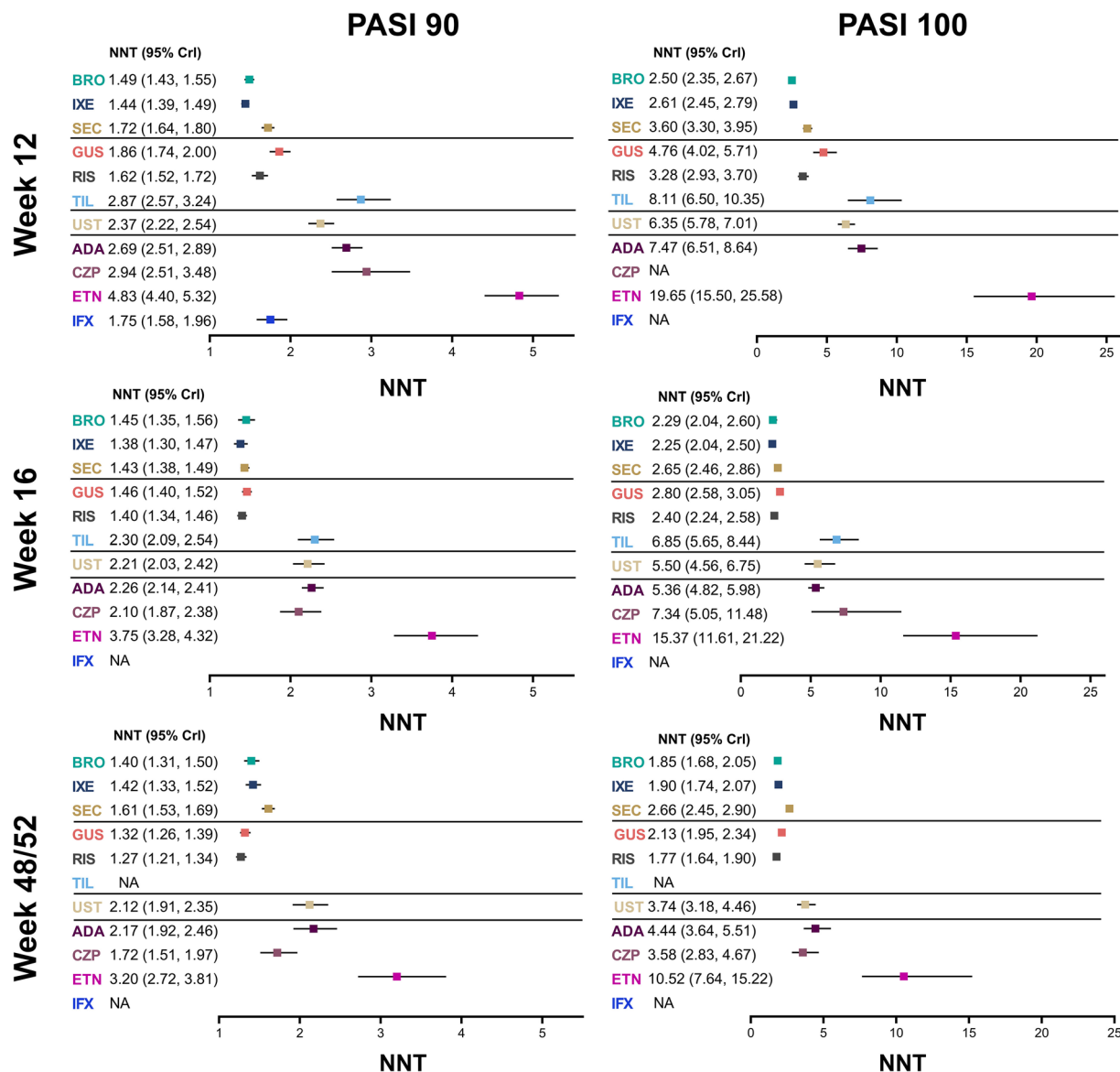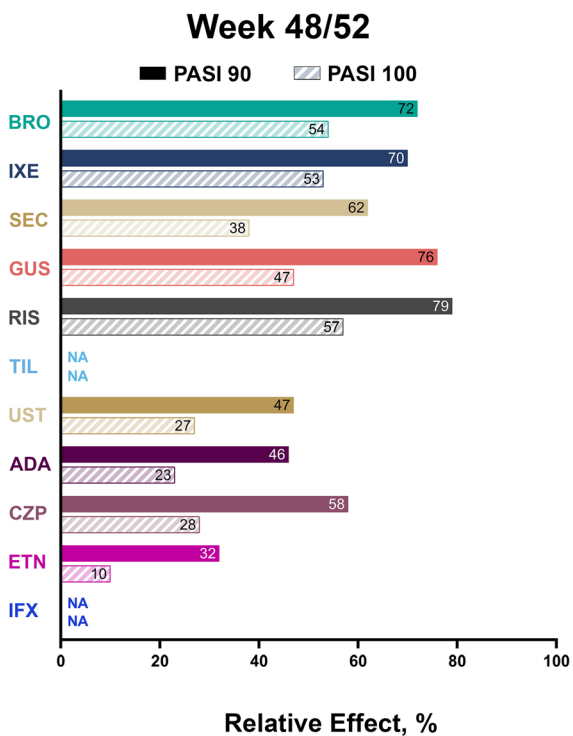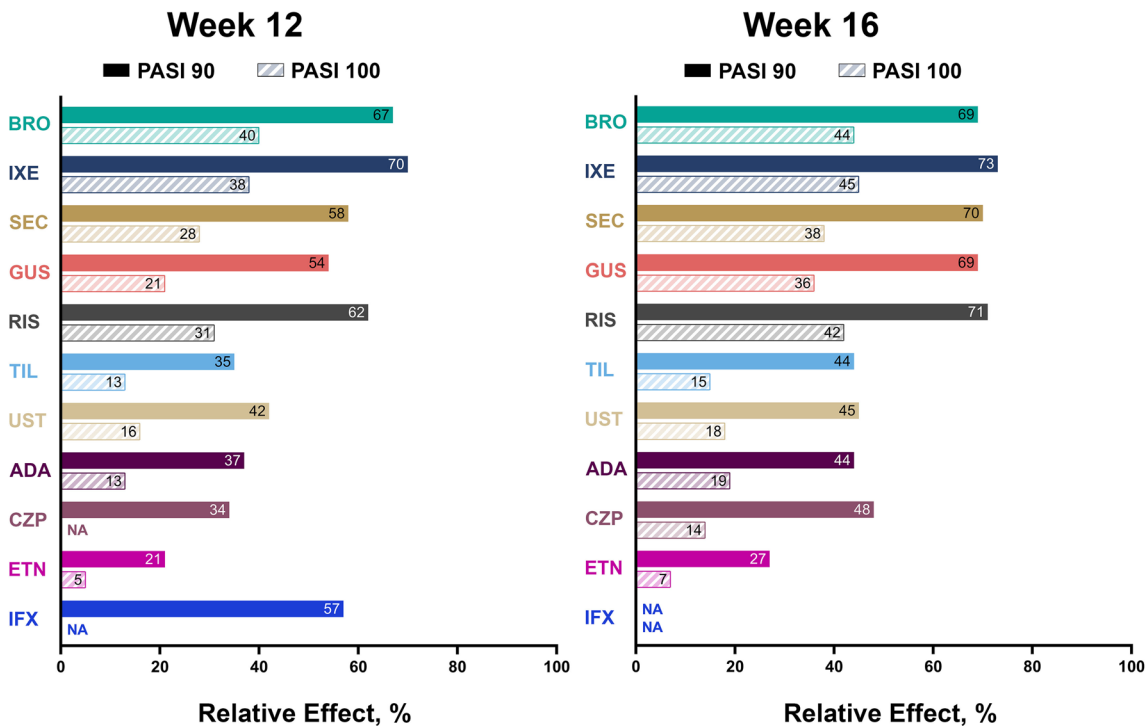
Fig. 2 NNT to achieve PASI 90 and PASI 100 responses at weeks 12, 16, and 48/52. Data are mean relative to placebo. Missing data are marked NA. Studies included in the analysis are listed in the Supplementary Material. *ADA* adalimumab, *BRO* brodalumab, *Crl* credible interval, *CZP* certolizumab pegol, *ETN* etanercept, *GUS* guselkumab, *IFX* infliximab, *IXE* ixekizumab, *NA* not applicable, *NNT* number needed to treat, *PASI* Psoriasis Area and Severity Index, *RIS* risankizumab, *SEC* secukinumab, *TIL* tildrakizumab, *UST* ustekinumab

1.39), brodalumab (1.40, 95% Crl 1.31, 1.50), and ixekizumab (1.42, 95% Crl 1.33, 1.52) (Figs. 2, 4, and Table 1). The lowest NNT to achieve PASI 100 was with risankizumab (1.77, 95% Crl 1.64, 1.90) with density distribution overlapping with brodalumab (1.85, 95% Crl 1.68, 2.05) and ixekizumab (1.90, 95% Crl 1.74, 2.07) (Fig. 2; Table 1). Estimated mean treatment effects (relative to placebo) on PASI 90 and PASI 100 response rates are presented at week 48/52 in Fig. 3. Number needed to treat to achieve PASI 75 and estimated mean treatment effects (relative to placebo) on PASI 75 response rates are presented at week 48/52 (in the the

Week 12

Week 16

Week 48/52

◄ **Fig. 3** Treatment effects on PASI 90 and 100 response rates at week 12, week 16, and week 48/52. Data are mean relative to placebo. Missing data are marked NA. Studies included in the analysis are listed in the Supplementary Material. *ADA* adalimumab, *BRO* brodalumab, *CZP* certolizumab pegol, *ETN* etanercept, *GUS* guselkumab, *IFX* infliximab, *IXE* ixekizumab, *NA* not applicable, *PASI* Psoriasis Area and Severity Index, *RIS* risankizumab, *SEC* secukinumab, *TIL* tildrakizumab, *UST* ustekinumab

Supplementary Material: Figure S1, Figure S2, and Table S2).

Network meta-analysis is comprehensive in nature and examines multiple time points over induction periods plus longer term follow-up to 1 year (48/52 weeks). Animations are provided to help the reader more fully understand these complex data. Animated videos are in the online/HTML version of the manuscript or follow the digital features link under the abstract (Video 1, relative response [proportion] based on NMA for PASI 90; Video 2, NNT to achieve PASI 90; Video 3, relative response [proportion] based on NMA for PASI 100; Video 4, NNT to achieve PASI 100).

DISCUSSION

Out of all treatments examined and consistent with previous analysis [9, 10, 48, 49], ixekizumab and brodalumab had the lowest NNTs for achievement of completely clear or nearly completely clear skin (PASI 100 and 90 responses) at early time points (as early as weeks 4 and 8) and at weeks 12 and 16 indicating rapid clearance of plaque psoriasis versus other biologic treatments for patients with moderate-to-severe psoriasis. Consistent with previous NMAs [4], there were significant differences in the performance of members within the same class. For example, brodalumab and ixekizumab had consistently lower NNTs (higher efficacy) versus secukinumab with the exception of achievement of DLQI (0,1) at week 12 where distributions overlapped. After 48/52 weeks, ixekizumab and brodalumab were comparable to anti-IL-23 agents with density distributions overlapping with risankizumab (the treatment with the lowest NNT) for PASI 90 and PASI 100 and guselkumab for PASI 90. This was consistent with a head-to-head study of ixekizumab and guselkumab that showed similar levels of complete skin clearance (PASI 100) at week 24 [50]. Anti-TNF agents had the highest NNTs (lowest efficacy) across all analyses.

Our report aligns with previous NMA findings focused on NNT [6, 9–11] but uniquely includes earlier time points (weeks 4 and 8) and quality of life (DLQI 0,1 at week 12). Compared to recent NMA with NNT estimates [9], the BNMA statistical methodology used here required fewer assumptions than other analytical methodologies, such as ordinal BNMA. We included only phase 3 RCTs, which allowed for more homogeneous comparisons between treatments and have distinct time points at weeks 4, 8, 12, and 16 (which is unique from other publications that employed a range of time points).

Several limitations, common to all meta-analyses, should be considered. An overview of NMA is available in the following online supplement [4]. As previously described, the strength of NMA is that it is a statistical methodology that allows for both direct and indirect evidence for comparison of many treatments at once, but it relies on published studies with differing specific imputation methods, study designs, and patient characteristics. The number of clinical trials is also different for each biologic drug, which might affect the results of the study. Treatment expectations and treatment goals have also evolved over time since the first psoriasis treatments were approved, and this contributes additional heterogeneity when including present day RCTs and older clinical trials within the NMA.

Patients prefer complete clearance of psoriasis, and PASI 100 is now an attainable treatment goal [51]. In this NMA focused on NNT, brodalumab and ixekizumab had the highest efficacy (lowest NNTs) in complete clearance of psoriasis as early as weeks 4 and 8 of treatment and at weeks 12 and 16. After 1 year, there was overlap in distribution in NNT to achieve PASI 100 between risankizumab (with the lowest NNT), broadlumab, and ixekizumab indicating
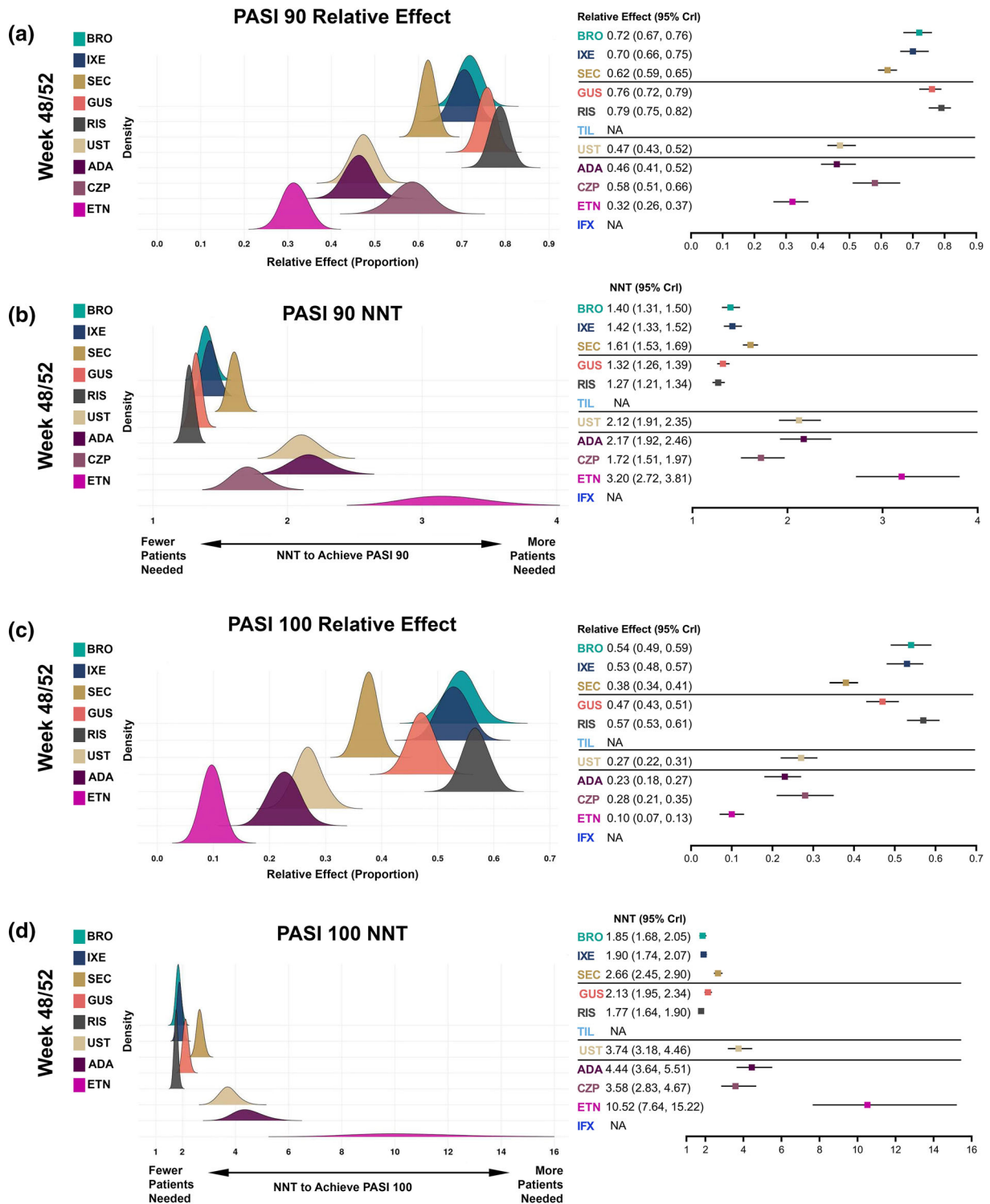
◀ **Fig. 4 a** Relative response of biologic treatments of moderate-to-severe plaque psoriasis based on BNMA for PASI 90 at week 48/52. **b** NNT to achieve PASI 90 at week 48/52. PASI 100 data are in panels (**c**) and (**d**). Missing data are marked NA. Studies included in the analysis from the studies are listed in the Supplementary Material. *ADA* adalimumab, *BNMA* Bayesian network meta-analysis, *BRO* brodalumab, *CrI* credible interval, *CZP* certolizumab pegol, *ETN* etanercept, *GUS* guselkumab, *IFX* infliximab, *IXE* ixekizumab, *NA* not applicable, *NNT* number needed to treat, *PASI* Psoriasis Area and Severity Index, *RIS* risankizumab, *SEC* secukinumab, *TIL* tildrakizumab, *UST* ustekinumab

that these biologics were not significantly different after 1 year (weeks 48/52).

ACKNOWLEDGEMENTS

preparation, data collection and analysis were performed by Kyoungah See, Zhuoer Sun, and Ying Zhang.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. The ongoing search is registered at PROSPERO (CRD42021244387).

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