Number Needed to Treat Among Therapies for Patients with Moderate to Severe Plaque Psoriasis: Clinical Perspective of Results from a Network Meta-Analysis

Leonardi, C, MD[1]; Fahrbach, K, PhD[2]; Neupane, B, PhD[2]; Armstrong, A, MD, MPH[3]; Gordon, K, MD[4]; Kiri, S, MSc[5]; Taieb, V, MSc[5]; McClung, L, PhD[6]

[1]Central Dermatology and Saint Louis University School of Medicine, St Louis, MO, USA; [2]Evidera, Waltham, MA, USA; [3]Keck School of Medicine USC, Los Angeles, CA, USA; [4]Medical College of Wisconsin, Milwaukee, WI, USA; [5]UCB Pharma, Slough, UK; [6]UCB Pharma, Smyrna, GA, USA

Presented at the Fall Clinical Dermatology Conference (FC21) • October 21–24, 2021 • Las Vegas, NV, USA

Introduction

- Psoriasis (PSO) is a chronic, inflammatory, multi-system disease; patients with moderate to severe plaque PSO are currently being treated with oral systemic drugs and targeted biologic therapies.[1,2]
- While the number of therapies available for the treatment of plaque PSO has increased over the last 5–10 years, data from head-to-head comparisons are scant.[3]
  - To address this limitation, we conducted a network meta-analysis (NMA), which facilitates the comparison of multiple treatments by simultaneously analyzing the direct evidence of treatments and indirect comparisons of treatments sharing a common comparator.[4]
- The number needed to treat (NNT) is a simple, clinically interpretable measure of assessing treatment benefit.[5]
  - It represents the number of patients who would need to be treated with the possible treatment options to demonstrate one additional response over established treatments or placebo.
  - An NNTof one is ideal, indicating that only one patient needs to be treated to receive an additional benefit. As the NNT increases, the less effective the intervention will be.
- A 90% and 100% improvement from baseline in Psoriasis Area and Severity Index (PASI 90 or PASI 100) are increasingly recognized as achievable clinical responses.[6]

Objective

- The objective of this analysis was to determine the NNT to achieve a PASI 90 or PASI 100 response in the short-term (10 to 16 weeks) for bimekizumab and other approved biologics for the treatment of moderate to severe PSO.

Methods

- We conducted a systematic literature review (SLR) in July 2020 to identify randomized controlled trials (RCTs) assessing the efficacy and safety of biologic and non-biologic therapies in the management of moderate to severe PSO.[7]
- Studies were included if they assessed the response to biologic therapies (at dosages approved by the Food and Drug Administration as well as some doses approved by the European Medicines Agency) and non-biologic therapies via the percentage improvement in PASI scores from baseline at 10 to 16 weeks (**Table 1**).
  - Ten to 16 weeks encompasses the range of stated primary endpoint timepoints across studies, and we have selected response data at the stated primary endpoint.
- Data from five bimekizumab trials (published phase 2b [BE ABLE 1[8]], and phase 3/3b [BE VIVID, BE READY, BE SURE, and BE RADIANT][9-12]) in PSO were included.
- A Bayesian multinomial likelihood NMA model (probit link) was conducted to compare the relative effects in achieving each of the PASI categories (i.e., 50%, 75%, 90% and 100% improvement) across treatments. Two modifications were implemented in this model:
  - The models were adjusted for the baseline risk, i.e., controlling for the relationship between placebo rate and relative effects versus placebo.
  - The multinomial assumption of the standard model was relaxed by allowing treatments to have different efficacies across the different PASI levels. This novel modification added a random-effects (RE) component to parameter z, which reflects the difficulty to achieve the next highest PASI level, and is referred to as the 'REZ' model.
- Non-biologic treatments were included in the NMA. However, only the results of biologic treatments are presented due to their increased relevance in the evolving treatment landscape in the management of moderate to severe PSO and to ensure clarity of presentation.

Methods (Cont'd)

- The NNTs of biologic treatments compared to placebo to achieve one additional PASI 90 or PASI 100 response were calculated as the reciprocal of the corresponding absolute risk differences obtained from the NMA.
  - The median and (2.5th and 97.5th) percentiles of the posterior samples, obtained from the Bayesian NMA, were used as estimates of the relative risks to achieve PASI 90 or 100 compared to placebo and their 95% credible interval (CrI).

Table 1. Inclusion/Exclusion Criteria for NMA

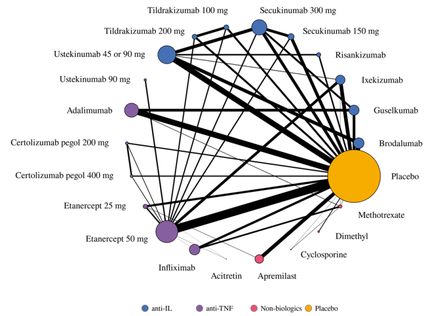
PICOS	Inclusion for Analysis	Exclusion Criteria
Population	Adult (≥18 years) patients with moderate to severe chronic plaque PSO with or without comorbid PsA Studies providing subgroup data for those with moderate to severe plaque PSO	Studies in patients primarily in PsA or with a treatment focus for PsA
Intervention/ Comparator	Protocol approved doses of systemic biologic therapies (adalimumab, bimekizumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab) Systemic non-biologics (acitretin, apremilast, cyclosporine, dimethyl fumarate, methotrexate)	Studies in biosimilar compounds
Outcomes	Any combination of PASI 50, 75, 90 and/or 100 presented as discrete/categorical outcomes	Mean change in PASI score
Study Design	Treatment induction period in randomized controlled trials	Observational/RWE studies Single-arm trials OLE follow-up periods that are not randomized
Timepoints	10 to 16 weeks	<10 weeks or >16 weeks

Abbreviations: OLE = open-label extension; PASI = Psoriasis Area and Severity Index; PICOS = population, intervention, comparison, outcomes, and study design; PsA = psoriatic arthritis; PSO = psoriasis; RWE = real-world evidence

Results

- Eighty-six RCTs (including 34,129 patients) were included in the NMA (**Figure 1**), of which 68 were placebo-controlled trials (26 trials had ≥ three arms including a placebo and an active comparator arm).

Figure 1. Network Diagram for Trials Reporting PASI Outcomes (n=86)

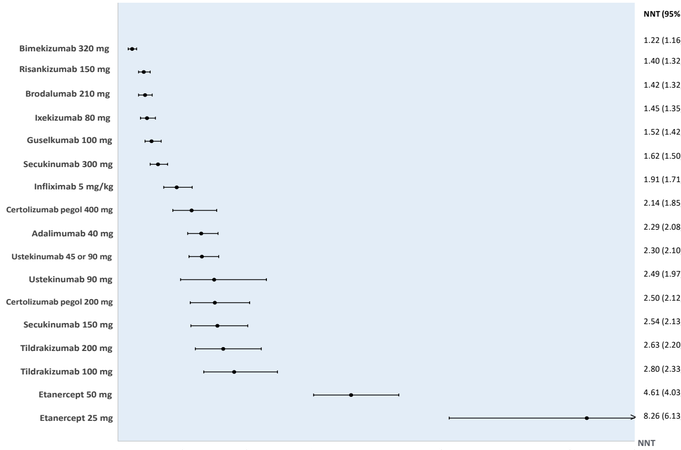


Abbreviations: IL = interleukin; PASI = Psoriasis Area and Severity Index; TNF = tumor necrosis factor

Results (Cont'd)

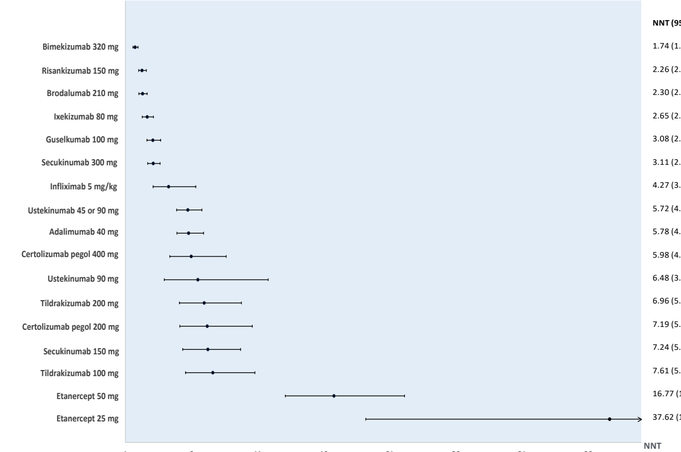
- Trial populations were generally similar with respect to age and sex. Participants in the different treatment arms were, on average, between 38.3 to 55.3 years old, and were mostly of male sex.
- Patients had moderate to severe PSO for an average duration of 11 to 24 years and the prevalence of comorbid psoriatic arthritis ranged between 2.4% and 36.8%.
- The RE, REZ model showed that interleukin inhibitors—including bimekizumab 320 mg, risankizumab 150 mg, ixekizumab 80 mg, brodalumab 210 mg, guselkumab 100 mg, and secukinumab 300 mg—were the most effective treatments in the network across all PASI response levels.
- Bimekizumab had the lowest positive NNT (closest to one) to achieve PASI 90 and PASI 100, followed by risankizumab 150 mg, ixekizumab 80 mg, and brodalumab 210 mg (**Figure 2** and **Figure 3**).
  - The NNT of bimekizumab versus placebo to achieve PASI 90 was 1.22, which means that for every 122 patients treated with bimekizumab or placebo, 100 more patients will achieve PASI 90 in the bimekizumab group compared to placebo.
  - The NNT versus placebo was 1.40 for risankizumab 150 mg, 1.45 for ixekizumab 80 mg, 1.42 for brodalumab 210 mg, 1.52 for guselkumab 100 mg, 1.62 for secukinumab 300 mg, 2.30 for ustekinumab 45 or 90 mg, 2.29 for adalimumab 40 mg, 2.80 for tildrakizumab 100 mg, and 4.61 for etanercept 50 mg.
  - The NNTs to achieve PASI 100 were: 1.74 for bimekizumab 320 mg, 2.30 for brodalumab 210 mg, 2.26 for risankizumab 150 mg, 2.65 for ixekizumab 80 mg, 3.11 for secukinumab 300 mg, 3.08 for guselkumab 100 mg, 5.72 for ustekinumab 45 or 90 mg, 5.78 for adalimumab 40 mg, 7.61 for tildrakizumab 100 mg, and 16.77 for etanercept 50 mg.

Figure 2. Number Needed to Treat (95% CrIs) for Biologic Treatments vs. Placebo for Achieving PASI 90



Abbreviations: CrI = credible interval; NNT = number needed to treat; PASI 90 =90% improvement from baseline in Psoriasis Area and Severity Index; vs = versus

Figure 3. Number Needed to Treat (95% CrIs) for Biologic Treatments vs. Placebo for Achieving PASI 100



Abbreviations: CrI = credible interval; NNT = number needed to treat; PASI 100 = 100% improvement from baseline in Psoriasis Area and Severity Index; vs = versus

Conclusions

- Fewer patients are required to be treated with bimekizumab to have one additional responder of PASI 90 and PASI 100 compared to all other agents in moderate to severe PSO.
- Interleukin inhibitors were highly effective in short-term improvement of PSO symptoms, requiring fewer patients to achieve an additional PASI response among patients with moderate to severe disease.

References

1. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072; 2. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol*. 2020;82(6):1445-1486; 3. Wright E, Yasmeen N, Malottki K, et al. Assessing the quality and coherence of network meta-analyses of biologics in plaque psoriasis: What does all this evidence synthesis tell us? *Dermatol Ther (Heidelb)*. 2021;11(1):181-220; 4. Dias S, Sutton AJ, Ades AE, Welton NJ. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making*. 2013;33(5):607-627; 5. Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med*. 1988;318(26):1728-1733; 6. Torres T, Puig L. Treatment goals for psoriasis: Should PASI 90 become the standard of care? *Actas Dermosifiliogr*. 2015;106(3):155-157; 7. Armstrong A, Reich K, Warren RB, et al. PBI3 Comparative efficacy of bimekizumab for the treatment of moderate to severe plaque psoriasis: A network meta-analysis. *Value in Health*. 2021;24:S14; 8. Papp KA, Merola JF, Gottlieb AB, et al. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: Results from BE ABLE 1, a 12-week randomized, double-blinded, placebo-controlled phase 2b trial. *J Am Acad Dermatol*. 2018;79(2):277-286.e210; 9. Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. *Lancet*. 2021;397(10273):487-498; 10. Gordon KB, Foley P, Krueger JG, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial. *Lancet*. 2021;397(10273):475-486; 11. Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus Adalimumab in Plaque Psoriasis. *N Engl J Med*. 2021;385(2):130-141; 12. Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus Secukinumab in Plaque Psoriasis. *N Engl J Med*. 2021;385(2):142-152.

Acknowledgments

We acknowledge Marissa Betts, Paulina Kazmierska, and Mahmoud Slim for their contributions to the SLR and NMA updates.

Disclosures

CL Speaker (honoraria) for AbbVie, Celgene, Eli Lilly and Novartis; served as an investigator for Actavis, AbbVie, Amgen, Boehringer Ingelheim, Celgene, Coherus, Corrona, Dermira, Eli Lilly, Galderma, Glenmark, Janssen, LEO Pharma, Merck (MSD), Novartis, Novella, Pfizer, Sandoz, Stiefel and Wyeth; consulting and advisory board honoraria for AbbVie, Amgen, Boehringer Ingelheim, Dermira, Eli Lilly, Janssen, LEO Pharma, Pfizer, Sandoz, UCB Pharma and Vitae; **KF, NB** are employees of Evidera Inc.; **AA** Data safety monitoring board member for Boehringer Ingelheim/Parexel; received research funding from BMS, Dermavent, Dermira, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, LEO Pharma, Pfizer, UCB Pharma; research investigator without compensation for Sanofi Genzyme; scientific investigator for AbbVie, BMS, Dermavent, Eli Lilly, Janssen, Leo Pharma, Modernizing Medicine, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma; speaker for AbbVie, Regeneron, Sanofi Genzyme; **KG** Consulting fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, BMS, Celgene, Dermira, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma and UCB Pharma; research support from AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis and UCB Pharma; **SK, VT, LM** are employees of UCB Pharma.

Previously presented at AMCP Nexus 2021

Funding provided by UCB Pharma