Targeted Immunomodulators For The Treatment Of Moderate-to-severe Plaque Psoriasis: A Network Meta-analysis Comparing Binomial And Multinomial Approaches

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Background

- There are two common model choices to run a network meta-analysis (NMA) in psoriasis: binomial and multinomial.
- Differences in the NMA approaches may be important depending on which audience is interpreting this evidence and implementing its conclusions (e.g., researchers, economic modelers, clinicians, patients, and caregivers).

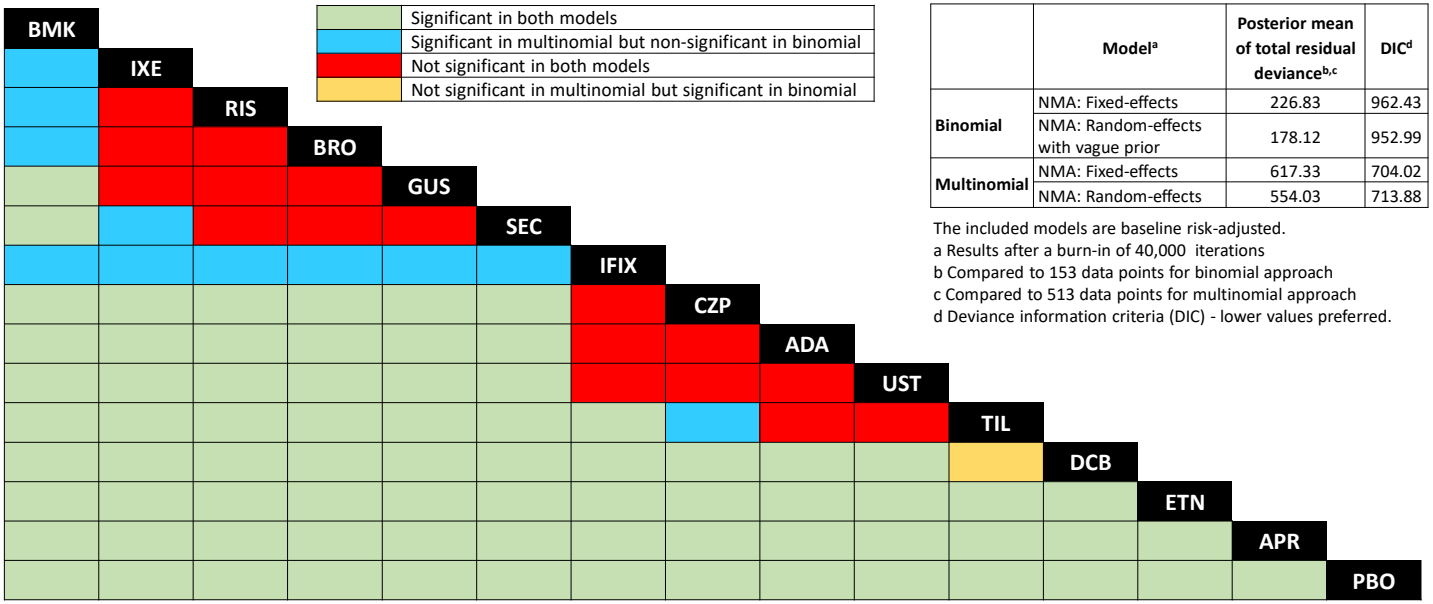
Objective

- The objective was to update ICER's 2018 systematic review and NMA on targeted immunomodulators (TIMs) for moderate-to-severe plaque psoriasis (PsO) and compare results from binomial and multinomial NMA approaches.

Methods

- We systematically identified and reviewed randomized controlled trials (RCTs) on TIMs approved for PsO that reported data on Psoriasis Area and Severity Index (PASI) outcomes at the end of an induction period (10-16 weeks).
- We searched MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials for RCTs published since the last search (January 2nd, 2018) to April 20th, 2023.
- We included two new TIMs (bimekizumab and deucravacitinib) that have been newly approved since ICER's 2018 review.
- For the binomial approach, we used a generalized linear model with a log link. The model inputs were the number of patients that achieved a PASI outcome (e.g., PASI 90) and the total number of patients.
- For the multinomial approach, we created mutually exclusive groups of the PASI data as <50, 50-74, 75-89, and 90-100 and used a multinomial likelihood model with a probit link.
- Baseline risk-adjusted random-effects Bayesian NMAs were conducted, and results were presented as relative risks (RR).
- We compared the models in terms of both significance levels and point estimates of these comparisons.

Table 1. League Table Highlighting Differences Between Binomial & Multinomial Results



Legend: The interventions are ordered from most effective (top left) to least effective (bottom right) based upon the multinomial analysis. Each box represents the comparison between binomial and multinomial results. Data represents similarities and differences in terms of significance levels ($p<0.05$).
Footnotes: ADA: adalimumab; APR: apremilast, BMK: bimekizumab, BRO: brodalumab, CZP: certolizumab pegol 200/400mg, DCB: deucravacitinib, ETN: etanercept, GUS: guselkumab, IFIX: infliximab, IXE: ixekizumab, PBO: placebo, RIS: risankizumab, SEC: secukinumab, TIL: tildrakizumab, UST: ustekinumab 45/90 mg

Table 2. Model Fit Statistics

	Model[a]	Posterior mean of total residual deviance[b,c]	DIC[d]
Binomial	NMA: Fixed-effects	226.83	962.43
	NMA: Random-effects with vague prior	178.12	952.99
Multinomial	NMA: Fixed-effects	617.33	704.02
	NMA: Random-effects	554.03	713.88

The included models are baseline risk-adjusted.
a Results after a burn-in of 40,000 iterations
b Compared to 153 data points for binomial approach
c Compared to 513 data points for multinomial approach
d Deviance information criteria (DIC) - lower values preferred.

Findings

- The updated NMA included 73 studies (25 new studies since the 2018 report) of 14 TIMs.
- All TIMs were more efficacious than placebo, with bimekizumab being the most efficacious and apremilast being the least efficacious.
- Overall, we found minimal differences between the two approaches as the relative rankings of interventions were similar.
- In the multinomial analysis, bimekizumab was more effective than all other agents in terms of PASI 90, and all met statistical significance.
- In the binomial analysis, bimekizumab was significantly more effective than all other agents except ixekizumab, risankizumab, brodalumab, and infliximab.
- Infliximab was another intervention where different findings were noted between multinomial and binomial approaches.
- The differences in point estimates between the two analyses for comparisons involving active interventions were minimal.
- The most prominent difference was that the point estimate of all agents versus placebo was much larger for the multinomial analysis, compared to the binomial analysis, with no overlapping credible intervals.

Key Takeaways

Investigators should methodologically make an a priori decision on the most appropriate model type for a given data set and should be aware of the possible differences in model types and their impact on decision-making.

Please contact Shahariar (sfahim@icer.org) for additional details.