EFFICACY OF BRODALUMAB IN THE TREATMENT OF MODERATE-TO-SEVERE PSORIASIS: A NETWORK META-ANALYSIS

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BACKGROUND

- Plaque psoriasis is a chronic, immune-mediated inflammatory skin disorder[1,2] affecting approximately 500,000 Canadians; 25% of which are moderate-to-severe.
- Biologic therapy is considered the gold standard treatment for moderate-to-severe plaque psoriasis. Brodalumab is an interleukin (IL)-17 Receptor A inhibitor that received approval from Health Canada in 2018 for moderate-to-severe plaque psoriasis. Brodalumab effectively addresses several key concerns with existing biologic therapies, especially speed of onset and complete skin clearance in both bio-naïve and bio-experienced patients.
- Brodalumab has been compared to ustekinumab in randomized clinical trials (RCTs)[3], but there is a lack of direct evidence between brodalumab and other commonly used biologics in Canada.

OBJECTIVES

- To conduct a network meta-analysis (NMA) that compares the relative efficacy of brodalumab to other biologic agents at doses approved in Canada for the treatment of moderate-to-severe plaque psoriasis based on RCT evidence.

METHODS

- A systematic literature review of RCT was performed. The SLR used to inform the network was based on the inclusion criteria listed in Table 1.

Table 1: Inclusion criteria for studies used in the NMA

Patient Population
• Adult patients with moderate-to-severe plaque psoriasis
Interventions
• Interleukin-17 inhibitors: Brodalumab, Ixekizumab, Secukinumab • Interleukin-12/23 inhibitor: Ustekinumab • Interleukin-23 inhibitor: Guselkumab • TNF-alpha inhibitors: Infliximab, Adalimumab, Etanercept
Comparators
• Placebo • Any interventions of interest
Outcomes
• PASI 50, 75, 90, 100 responses

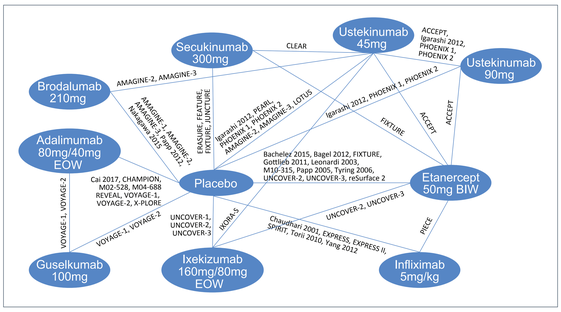
NMA: Network Meta-Analysis; PASI: Psoriasis Area Severity Index; RR: Relative Risk; TNF: Tumor Necrosis Factor.

- The quality of included studies was assessed to determine the strengths and robustness of available evidence using the Centre for Reviews and Dissemination's guidance for undertaking reviews in health care.[4]
- Psoriasis Area Severity Index (PASI) response (PASI 50, 75, 90, and 100) at the end of induction period (10-16 weeks) was analyzed using a multinomial likelihood model with probit link. Both random effects and fixed effects model analyses were conducted. Selection of model was based on the relative goodness of fit informed by total residual deviance and deviance information criterion.
- To ensure the indirect comparisons of interventions are not influenced by differences in study effects between studies, a feasibility assessment was conducted wherein the inconsistency and heterogeneity in the networks were assessed.
- Sensitivity analyses were conducted to explore potential effect modifiers such as baseline PASI score, age, weight, Dermatology Life Quality Index (DLQI) score, duration of psoriasis, and prior biologics exposure on the treatment.

RESULTS

- Embase®, MEDLINE®, and Cochrane CENTRAL were searched on 24 October 2017. A total of 43 RCTs (40 publications) were included in the NMA. The network of evidence is presented in Figure 1.

Figure 1: Network of trials for the comparison of brodalumab versus other biologics

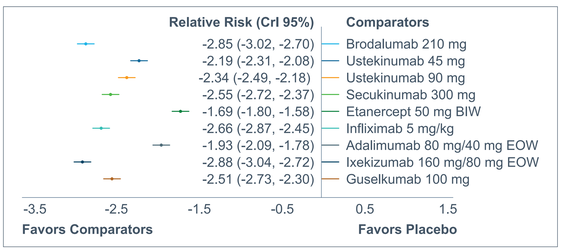


Note: Each node represents a treatment regimen included in the network. Lines represent the direct comparisons between nodes. Label along each edge represents the author of the primary reference contributing to the respective direct comparison.

RESULTS (Continued)

- The base-case results of the random effects multinomial NMA demonstrated that all biologic treatments have significantly better PASI response than placebo (Figure 2).
- Brodalumab 210 mg had significantly better results for all PASI responses than both ustekinumab 45 mg and 90 mg, secukinumab 300 mg, etanercept 50 mg twice weekly (BIW), adalimumab 80 mg/40 mg every other week (EOW) and guselkumab 100 mg, and comparable PASI responses to infliximab 5 mg/kg and ixekizumab 160 mg/80 mg EOW (Table 2).
- A larger relative risk was observed between brodalumab and all comparators except ixekizumab for PASI 100 response.

Figure 2: Treatment effects, on the probit scale, of biologics relative to placebo (random effects base case)



BIW: twice weekly; Crl: Credible Interval; EOD: every other week.

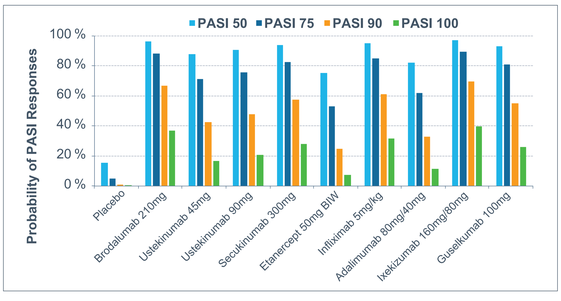
Table 2: Summary of comparisons between brodalumab 210 mg vs. other comparators for PASI 50, 75, 90, 100 (random effects model, base case)

	PASI 50		PASI 75		PASI 90		PASI 100	
Comparator	**RR**	**95% CrIs**	**RR**	**95% CrIs**	**RR**	**95% CrIs**	**RR**	**95% CrIs**
Ustekinumab 45 mg	**1.10**	**(1.07-1.14)**	**1.25**	**(1.18-1.35)**	**1.62**	**(1.02-1.21)**	**2.29**	**(1.87-2.88)**
Ustekinumab 90 mg	**1.07**	**(1.04-1.11)**	**1.18**	**(1.10-1.28)**	**1.43**	**(1.23-1.69)**	**1.86**	**(1.45-2.48)**
Ustekinumab 90 mg	**1.03**	**(1.01-1.07)**	**1.09**	**(1.02-1.17)**	**1.21**	**(1.05-1.42)**	**1.41**	**(1.10-1.87)**
Etanercept 50 mg BIW	**1.30**	**(1.23-1.40)**	**1.72**	**(1.54-1.96)**	**2.84**	**(2.35-3.52)**	**5.43**	**(4.09-7.51)**
Infliximab 5 mg/kg	1.02	(0.99-1.06)	1.05	(0.99-1.14)	1.12	(0.96-1.34)	1.24	(0.93-1.70)
Adalimumab 80 mg/40 mg EOW	**1.19**	**(1.12-1.27)**	**1.45**	**(1.30-1.66)**	**2.11**	**(1.72-2.67)**	**3.48**	**(2.52-5.00)**
Ixekizumab 160 mg/80 mg EOW	1.00	(0.98-1.02)	0.99	(1.30-1.66)	0.99	(0.88-1.11)	0.98	(0.80-1.23)
Guselkumab 100 mg	**1.04**	**(1.00-1.08)**	**1.1**	**(1.02-1.21)**	**1.24**	**(0.88-1.11)**	**1.48**	**(1.09-2.08)**

BIW: twice weekly; Crl: Credible Interval; EOD: every other week; PASI: Psoriasis Area Severity Index; RR: Relative Risk.
*Note: Statistically significant values are indicated in **bold**.*

- The estimated absolute probability of PASI responses for brodalumab and all comparators is represented in Figure 3.

Figure 3: Probability of PASI responses (i.e. PASI 50, 75, 90 and 100)



- No significant heterogeneity or inconsistencies were identified and the results were consistent across all the sensitivity analyses, indicating robustness of results.
- The base case fixed effects results were also consistent with the results from base case random effects model.

CONCLUSIONS

- These results indicated that brodalumab 210 mg can be considered a superior alternative to most biologic agents currently used for the treatment of moderate-to-severe plaque psoriasis in Canada.
- The quality of included studies was high and sensitivity analyses on baseline effect modifiers indicated no significant impact of study-level baseline characteristics on the NMA results, demonstrating that the evidence network was robust.
- These findings were consistent with the published literature, further demonstrating the robustness of results.[5]

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