Author’s response to reviews

Title: Network Meta-analysis and Cost per Responder of Targeted Immunomodulators in the Treatment of Active Psoriatic Arthritis

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Author’s response to reviews:

James Mockridge
Editor
BMC Rheumatology

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To Dr. Mockridge and the BMC Rheumatology editors,

Thank you and the peer-reviewers again for inviting us to revise and resubmit our manuscript for publication in the BMC Rheumatology Journal. Attached is a revised version of our manuscript (Manuscript ID BRHM-D-17-00035) entitled: “Network Meta-analysis and Cost per Responder of Targeted Immunomodulators in the Treatment of Active Psoriatic Arthritis”.

All of the comments we received helped us to strengthen the manuscript. Point-by-point responses are detailed within the following pages of this letter. We have provided the clean version of this revision for your review.

Thank you,

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Reviewer 1:

This is an interesting manuscript that assessed the comparative efficacy of different treatments available for Psoriatic Arthritis. To date, no head-to-head studies were performed to determine the most efficacious treatment in Psoriatic Arthritis between the different biologic and small molecules drugs, so network analysis that indirectly compare different clinical trial could be useful. The study is well written and methodologically well performed. I have only some suggestions to improve the quality of the manuscript.

1) Since the efficacy of biologic and small molecules could be improved by the association with classic synthetic DMARDs, it would be useful to verify how many patients in the different clinical trials were treated with classic DMARDs

Response: Thank you for the comment. We agree that proportion with classic DMARDs use provides valuable information on the treatment history of PsA patient among different trials. We have added the number of patients with conventional DMARDs use and with MTX use at baseline in Supplementary Table 1.
2) The recent Treat-to-target recommendations for PsA introduced the concept of remission or low disease activity as the target of therapy. If available in the different trials, it would be useful to compare even the percentage of patients achieving minimal disease activity.

Response: Thank you for the comment. We assessed whether low/minimal disease activity (MDA) was reported as an endpoint among the trials. Since MDA in PsA was defined in Coates 2010, only certolizumab pegol trial RAPID-PsA (Mease 2014) in the current evidence network reported MDA. A network meta-analysis in MDA is therefore not feasible due to limited data.

Reviewer 2:

The paper herein is interesting and explores the efficacy and the costs of biologic treatment in PsA.

How did the author calculate the cost per drug?

Response: Thank you for the question. Drug costs over the first 24 weeks of treatment were calculated based on FDA-approved dosing schedule for PsA in the package inserts, acquisition costs, and infusion costs. Wholesale acquisition costs were obtained from ReadyPrice®. Infusion costs only applies to infliximab and were based on treatment costs of an 80-kilogram adult. Infusion costs were obtained from US Department of Health and Human Services using corresponding CPT codes. The calculation of drug costs is described in detail in Cost section under Methods on page 7.

The authors should better discuss their results especially compared with other review already performed and present in the literature.

Response: Thank you for the comment. We reviewed existing literature on NMA in PsA, summarized their findings, and compared them with our study in the Discussion section (line 238, page 12; line 270, page 13). The following studies were evaluated in the discussion: 1) Cawson 2014 evaluated cost-effectiveness of anti-TNF agents from the UK NHS perspective; 2) Thorlund 2012 evaluated PsARC responses in the same set of RCTs as Cawson 2014. Both Cawson 2014 and Thorlund 2012 used inconsistent time points for outcome measures; 3) McInnes 2016 evaluated the comparative effectiveness of licensed biologics and apremilast for PsA at Weeks 12-16; 4) Dongze 2017 assessed efficacy and safety of anti-IL agents for active PsA at Week 24. For biologic-naïve patients with PsA, we evaluated three meta-analyses: McInnes 2016 and Ungprasert 2016 assessed the efficacy of biologics and apremilast in biologic-
naïve PsA population; Yang 2015 assessed PsARC and ACR 20 response rates of TIMs in a Taiwanese setting. The above-mentioned studies in biologic-naïve patients only considered joint outcomes from Weeks 12-16, whereas our study assessed both skin and joint outcomes as well as the cost-effectiveness of TIMs at Week 24.

I suggest to include the following reference:


Semin Arthritis Rheum. 2016 Apr;45(5):519-32

Pharmacoeconomic burden in the treatment of psoriatic arthritis: from systematic reviews to real clinical practice studies. Lubrano E, Spadaro A. BMC Musculoskelet Disord. 2014 Jan 20;15:25

Response: Thank you for the comment. We have added both references in the manuscript (first reference as Reference #4 in Background section, line 85, page 5; second reference as Reference #30 in Discussion section, line 243, page 12).