

Efficacy and Safety of Nemolizumab for Treatment of Adult Atopic Dermatitis

Freemantle N¹, Piketty C²

¹Institute of Clinical Trials and Methodology, University College London, London, UK

²Galderma, Lausanne, Switzerland

Corresponding author

Nick Freemantle PhD

Professor of Clinical Epidemiology & Biostatistics

Institute of Clinical Trials and Methodology, University College London, 90 High Holborn 2nd Floor.

London WC1V 6LJ, UK

Email: nicholas.freemantle@ucl.ac.uk

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.18176/jiaci.0727

Key words: Nemolizumab. Adult Atopic Dermatitis.

Palabras clave: Nemolizumab. Dermatitis atópica del adulto.

To the Editor:

We were interested to read the meta-analysis by Xuemin and colleagues on the efficacy and safety of nemolizumab for treatment of adult atopic dermatitis [1]. This is an important topic and overview of the available data is timely. We concur with the conclusions of the authors that nemolizumab is a promising treatment, and Galderma is currently undertaking further phase 3 clinical trials to address this data need.

On one important point, however, we struggle to reconcile the results and conclusions of the review with our knowledge of the published data. Xuemin et al. comment that the 60mg Q4w is likely to be optimal. The one phase 3 trial that has currently completed used that dose [2], comparison on a proper like-for-like basis with a lower dose currently in late development (30mg Q4w) is actually in favor of the lower dose. The percent change in EASI Score (from baseline to week 16) for the 30 mg Q4w dose versus placebo (difference -23.7; 95% CI -8.9 to -38.5; $p=0.002$) was reported in the Silverberg phase 2b trial [3]. The treatment effect observed with EASI was greater than those observed with the 60 mg Q4w dose in the Kabashima Phase 3 trial (difference -12.6; 95% CI -1.3 to -24.0). Using the Bucher method [4] to undertake a formal indirect comparison, we observe a numerically greater benefit for 30 mg Q4w (difference -11.1; 95% CI 7.6 to -29.8) (Figure). The 30 mg dose is under evaluation in two pivotal phase 3 trials (NCT03989349, NCT03985943) and the outcomes of the two studies will substantially inform the resolution of the important question.

We do not recognize some of the data included by the reviewers in their work (for example the results above for Silverman derived from the CSR are not reflected in the report by Xuemin et al.). This is troubling. While the overall conclusions are supported by individual trials, the dosage conclusions do not reflect the available data.

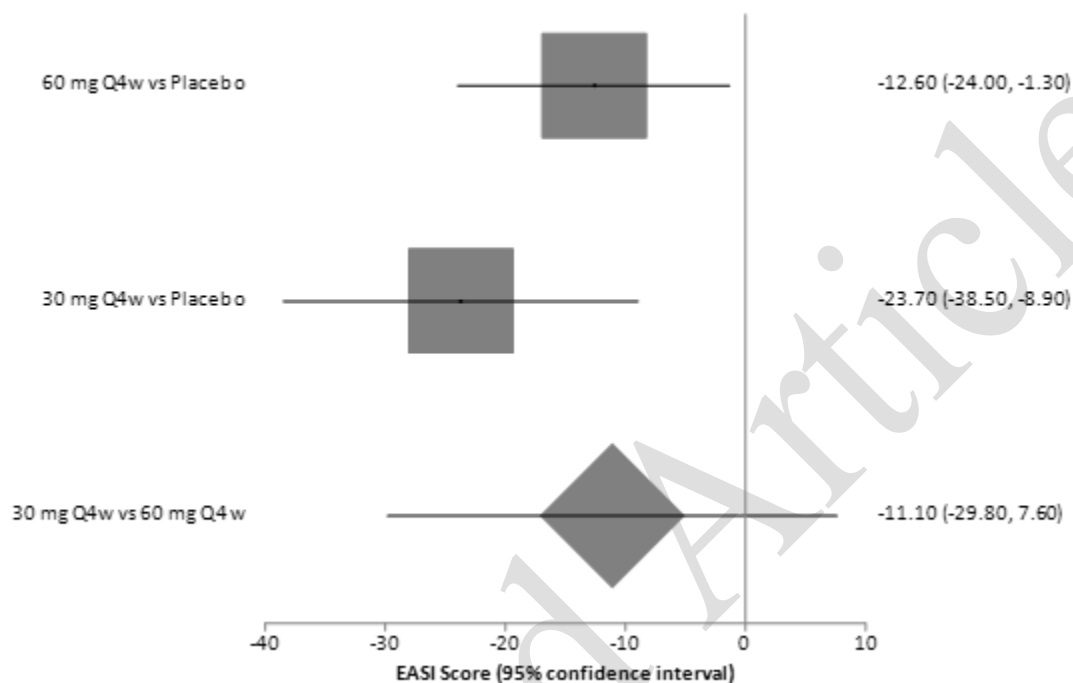
Yours Sincerely,

Funding

This work was funded by GALDERMA. NF has received consulting fees from ALK Allergan, Aimmune, AstraZeneca, MSD, Ipsen, Sanofi Aventis, Novo Nordisk, Novartis, Grifols, and speaking fees from Abbott Singapore, Sanofi Aventis. His institution receives a grant from European Association for Cardiothoracic Surgery for methodological advice and teaching. CP is an employee of Galderma.

References

- [1] Xuemin X, Lihang L, Changhua Z, Xiaofang Y, Yongshan N, Zhipeng L, et al. Efficacy and safety of nemolizumab for adult atopic dermatitis treatment: A meta-analysis of randomized clinical trials. *J Invest Allergol Clin Immunol*. 2021;31:190-2.
- [2] Kabashima K, Matsumura T, Komazaki H, Kawashima M and the Nemolizumab-JP01 Study Group. Trial of Nemolizumab and Topical Agents for Atopic Dermatitis with Pruritus. *N Engl J Med*. 2020;383:141-50.
- [3] Silverberg JI, Pinter A, Pulka G, Poulin Y, Bouaziz JD, Wollenberg A, et al. Phase 2B randomized study of nemolizumab in adults with moderate-to-severe atopic dermatitis and severe pruritus. *J Allergy Clin Immunol*. 2020;145:173-82.
- [4] Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol*. 1997;50:683-91.

Figure Legend**Figure 1.** The percent change in EASI Score (from baseline to week 16) by dose.

Note: the 60 mg Q4w versus placebo comparison is derived from Kabashima Phase 3a trial; the 30 mg Q4w versus placebo is derived from the Silverman Phase 2 trial. The difference between doses is calculated using the Butcher method.