Efficacy and Safety of Nemolizumab for Treatment of Adult Atopic Dermatitis: A Meta-analysis of Randomized Clinical Trials

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To the Editor:

Nemolizumab is a recently developed human monoclonal antibody targeting the interleukin-31 receptor (IL-31R) [1-3]. In this meta-analysis, we aimed to explore the efficacy and safety of nemolizumab for the treatment of atopic dermatitis (AD).

On October 15, 2020, we conducted a systematic search of the Embase, Medline, PubMed, and Web of Science databases for randomized controlled trials (RCTs) using the search terms "nemolizumab" and "atopic dermatitis" or "eczema". A total of 4 randomized, double-blinded, and placebo-controlled clinical trials (1 phase 1 trial, 2 phase 2 trials, and 1 phase 3 trial) were included in our meta-analysis of 729 patients diagnosed with moderate-to-severe AD (Supplementary Figure 1) [4-7]. In the phase 1 trial, the doses administered were 0.3, 1.0, and 3.0 mg/kg. The 2 later phase 2 trials were independent trials with an identical clinical design that were performed to evaluate the consistency of the safety and efficacy profiles of nemolizumab, where patients received nemolizumab 0.1 mg/kg once every 4 weeks (q4w), 0.5 mg/kg q4w, 2.0 mg/kg q4w, 2.0 mg/kg q8w, 10 mg q4w, 30 mg q4w, and 90 mg q4w. In the phase 3 trial, the treatment group received a 60-mg dose of nemolizumab (Supplementary Table 1). All patients were adults, had Eczema Area and Severity Index (EASI) scores >10 or SCORAD scores >25, and a >1-year history of AD. All studies included in the systematic review exhibited a low risk of bias according to the Cochrane collaboration tool, and funnel plot and Egger test analyses revealed no significant publication bias (Supplementary Figure 2). Furthermore, the quality of each RCT was estimated using the Jadad scale, and all 4 RCTs were found to be of high quality (Supplementary Table 2).

A pooled analysis of all 4 RCTs indicated that treatment with nemolizumab resulted in significant improvements in efficacy and safety based on various clinical indices.

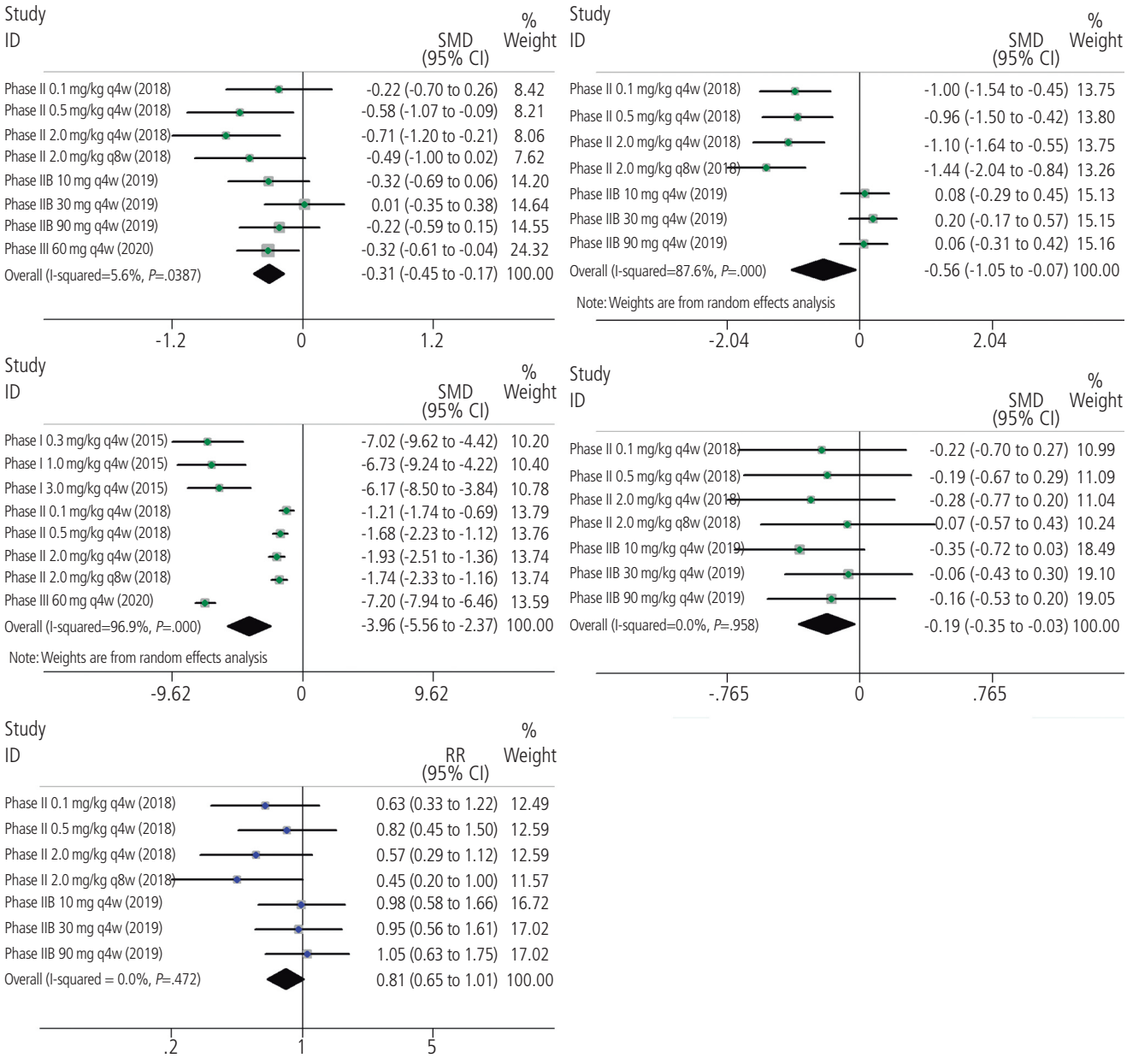

Figure. Forest plot of the efficacy of nemolizumab in the 4 randomized controlled trials based on the 5 clinical outcomes. A, Eczema Area and Severity Index score. B, Scoring Atopic Dermatitis score. C, pruritus visual analog scale. D, Body surface area score. E, Investigator global assessment score. Horizontal lines represent the 95%CIs of the standardized mean difference (SMD) or relative risk (RR) estimates. Green dots represent the SMD, blue dots represent the RR, and diamonds represent the meta-analysis summary effect estimate.

As shown in the Figure, treatment with nemolizumab led to significantly decreased EASI scores compared with the placebo group (standardized mean difference [SMD], –0.31; 95%CI, –0.45 to –0.17; *P*<.001). A meta-analysis of the 2 phase 2 RCTs suggested a significant reduction in the SCORAD score in the nemolizumab group compared with the placebo group (SMD, –0.56; 95%CI, –1.05 to –0.07; *P*=.025). A reduction in the VAS for pruritus indicates relief for patients and a significant improvement in quality of life. In the pooled nemolizumab group, the SMD of the VAS for pruritus was –3.95 (95%CI, –5.56 to –2.37; *P*<.001). The results showed a significant decrease in the SMD body surface area score in the nemolizumab group compared with the control group (SMD, –0.19; 95%CI, –0.35 to –0.03; *P*=.019). There was a significant difference in the percentage of IgA response in the nemolizumab treatment group compared with the placebo group (RR, 0.81; 95%CI, –0.65 to –1.01; *P*=.064). In addition to the overall efficacy of nemolizumab, dose-dependent efficacy was also investigated in this systematic review. Doses of 60 mg q4w,

3.0 mg/kg q4w, and 2.0 mg/kg q4w resulted in the most effective clinical improvement, while doses of 30 mg q4w and 90 mg q4w were less effective but led to significant improvements. Doses of 0.1 mg/kg q4w, 0.5 mg/kg q4w, and 10 mg q4w resulted in barely significant improvements. A Galbraith radial plot confirmed that nemolizumab regimens with doses of 0.1 mg/kg q4w, 0.5 mg/kg q4w, and 2.0 mg/kg q8w were not as safe as those with doses of 0.3 mg/kg q4w and 60 mg q4w (Supplementary Figure 3). Based on the efficacy and safety results, the optimal dose of nemolizumab for the treatment of patients with moderate-to-severe AD is likely to be 60 mg q4w.

Overall, the results of the RCTs included demonstrate that nemolizumab has an acceptable safety profile, as there was no significant difference in adverse events or severe adverse events compared with the placebo group. The adverse event rate did not differ significantly among the 4 trials (RR, 0.84; 95%CI, 0.69-1.01; *P*=.069). Furthermore, the severe adverse event rate did not differ significantly between the placebo control and nemolizumab groups (RR, 1.27; 95%CI, 0.97-1.66; *P*=.079) (Supplementary Figure 4).

Our findings clearly demonstrate that nemolizumab is a promising anti-AD medication and provide evidence that it can be used to treat AD efficiently and specifically. Further studies should be conducted to assess the long-term stability, efficacy, and safety of nemolizumab for treatment of AD.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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