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**Improvement of atopic dermatitis with dupilumab occurs equally well across different
anatomic regions: data from phase 3 clinical trials**

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DEAR EDITOR, Moderate-to-severe atopic dermatitis (AD) can affect different parts of the body, and some adults have more localized AD, such as face and neck involvement.¹ Compared with non-exposed areas, such as the trunk, exposed areas such as the face, neck, and hands could be more vulnerable to environmental allergens and irritants and can be more refractory to topical therapies. Local adverse effects of topical therapies are more likely to occur on the face and neck.¹ Additional pathologies, such as contact dermatitis, could complicate the clinical picture and response of exposed areas to treatment. Microbial factors (e.g. *Malassezia*) in specific regions may also influence AD severity on the face and neck.²

Dupilumab is a fully human VeloclImmune[®]-derived³ monoclonal antibody against interleukin (IL)-4R α that inhibits signalling of IL-4 and IL-13⁴ and is approved for treatment of inadequately controlled, moderate-to-severe AD in adults. The efficacy and safety of dupilumab has been assessed in adults with moderate-to-severe AD in several clinical trials, including two phase 3 trials of dupilumab monotherapy (LIBERTY AD SOLO 1, LIBERTY AD SOLO 2)⁵ and two phase 3 trials of dupilumab with concomitant topical corticosteroids (TCS) (LIBERTY AD CAFÉ,⁶ LIBERTY AD CHRONOS⁷). Results from these large trials showed that dupilumab significantly improved the severity and extent of AD, as measured by the Eczema Area and Severity Index (EASI), compared with placebo.

The EASI is a composite score of four anatomic regions, i.e. head/neck, upper extremities, trunk, and lower extremities.⁸ Herein, we report the disease burden by anatomic region at baseline and assess the impact of dupilumab treatment on EASI for each region in SOLO 1, SOLO 2, CAFÉ, and CHRONOS.

Methods and study designs were reported previously.^{5–7} The studies were conducted in accordance with the Declaration of Helsinki, all patients provided written informed consent, and Institutional Review Boards and Independent Ethics Committees reviewed and approved the protocols, informed consent forms, and patient information before study initiation. In this post-hoc analysis, the efficacy of subcutaneous dupilumab 300 mg every two weeks (q2w) or every week (qw) vs placebo was evaluated by assessing the least-squares (LS) mean percentage change from baseline in EASI by anatomic region at Weeks 4, 16 (all trials), and 52 (CHRONOS only). Data from SOLO1&2 were pooled by treatment group. Patients in CAFÉ and CHRONOS received a standardised concomitant TCS regimen. The full analysis set was analysed. The last-observation-carried-forward method was implemented to impute data that is missing or censored after rescue medication usage. Data were not adjusted for multiplicity, therefore *P*-values are nominal and are based on treatment difference (dupilumab vs placebo) in LS mean percentage change, using an ANCOVA model with baseline measurement as covariate and the treatment, region, and baseline IGA strata as fixed factors. Additional fixed factors included study identifier in SOLO1&2 and prior ciclosporin A use (Yes/No) in CAFÉ.

At baseline, EASI levels for each anatomic region were generally comparable throughout treatment groups in each trial (Fig. 1a–l), and relative regional contributions to the total score were lowest for the head/neck and highest for the lower extremities. This observation partly reflects relative differences in percentage body surface area (%BSA) among different regions. When absolute extent and severity of lesions were compared in different regions (i.e., without correcting for relative %BSAs), EASI levels remained lowest in the head/neck area and were highest in the upper extremities. Considering these baseline differences,

comparative assessments of EASI across anatomic regions are better achieved using percentage change rather than absolute change.

Compared with placebo, dupilumab treatment was associated with significantly greater percentage improvement in EASI from baseline to Week 16 across all anatomic regions in each trial (Fig. 1a–l). Similar results were seen at Week 4 in all trials (Fig. 1a–l) and at Week 52 in CHRONOS (Fig. 1i–l). Safety data were previously reported for the overall study populations.^{5–7} Overall rates of adverse events (AEs) were similar across treatment groups in each study; the most common AEs attributable to dupilumab were injection-site reactions and conjunctivitis.

In summary, treatment with dupilumab 300 mg q2w (approved) or qw (not approved) significantly improved disease severity in all anatomic regions in patients with moderate-to-severe AD. These data suggest that all anatomic regions are equally responsive to dupilumab treatment. Significant improvements in disease severity were observed as early as Week 4 for all anatomic regions. Week 52 data from CHRONOS indicate that improvement is maintained with continuous treatment in most patients and throughout all anatomic regions. Dupilumab had an overall acceptable safety profile in all four trials.

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Figure legend

Fig 1. LS mean percentage change in EASI from baseline, over time, by anatomic region.

EASI was obtained for the head/neck, upper extremities, trunk, and lower extremities in four phase 3 clinical trials: SOLO1&2 (pooled, a–d), CAFÉ (e–h), and CHRONOS (i–l). Patients in CAFÉ and CHRONOS received concomitant TCS. Baseline EASI data are given as mean (SD). Numbers in **bold** and non-bold font are baseline **relative scores with weighting for %BSA** (i.e. corrected by the coefficient 0.1 for head/neck, 0.2 for upper extremities, 0.3, for trunk, and 0.4 for lower extremities) and absolute scores without %BSA weighting, respectively. The analyses reported here are based on percentage reduction (i.e. improvement) from baseline, which is the same whether or not the %BSA weighting is applied. *BL*, baseline; *DPL*, dupilumab; *EASI*, Eczema Area and Severity Index; *LS*, least squares; *PBO*, placebo. *qw*, every week; *q2w*, every two weeks; *SD*, standard deviation; *SE*, standard error; *TCS*, topical corticosteroids.

