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Could conjunctivitis in dupilumab treated atopic dermatitis patients be caused by colonization with *Demodex* and increased IL-17 levels? Reply from authors

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In studies in atopic dermatitis (AD), dupilumab has been associated with higher rates of conjunctivitis compared with placebo. Consistent with previous studies, in LIBERTY AD CAFÉ (NCT02755649), all cases but one were mild or moderate, most (62–89%) were recovered/resolved or recovering/resolving by end of treatment, and no patients permanently discontinued study treatment because of conjunctivitis.¹ No patients reported atopic keratoconjunctivitis in this study. Conjunctivitis rates were slightly higher in all CAFÉ treatment groups, including placebo, compared with previous studies. Baseline conjunctivitis rates were also higher and patients had more severe AD in CAFÉ than in previous studies (higher baseline EASI scores), which is consistent with the fact that they were indicated for ciclosporin. In previous studies, patients with more severe AD or comorbid allergic conjunctivitis were more likely to have conjunctivitis adverse events (AEs).² Patients with AD have greater risk of conjunctivitis than the general population, and patients with more severe AD have greater risk than those with mild disease.³ Interestingly, no imbalances in conjunctivitis AEs were observed between the dupilumab and placebo arms in studies of other allergic/atopic disorders (asthma, chronic sinusitis with nasal polyposis, eosinophilic esophagitis), suggesting that both dupilumab- and AD-related mechanisms may be involved.

In rosacea, interleukin (IL)-17-mediated pathways and *Demodex* mites may be associated with ocular inflammation and conjunctivitis. Dr. Thyssen proposed that dupilumab could exacerbate *Demodex*- and IL-17-mediated inflammatory ocular and Meibomian gland dysfunction in AD, analogous to rosacea. However, unlike in rosacea, conjunctivitis AEs in dupilumab AD studies have been relatively short in duration and generally responsive to standard treatments; patients seldom

discontinued dupilumab because of conjunctivitis. The role of *Demodex* in Meibomian gland disease is debated (Level III evidence).⁴ In contrast to Dr. Thyssen's model, dupilumab decreases IL-17 pathway gene expression in the skin of patients with AD.⁵ Nonetheless, mechanisms may be different in the eyes than the skin. Further studies are ongoing, including assessment of cytokines in tears.

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