Long-term dupilumab treatment is not associated with an increased overall risk of infections in adults with moderate-to-severe atopic dermatitis

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Introduction/Background: Patients with atopic dermatitis (AD) have an increased risk of cutaneous, extracutaneous, and systemic infections with a considerable associated cost burden. Certain treatments used to manage AD, such as immunosuppressants and Janus kinase inhibitors, can increase the risk of infection. Data from the LIBERTY AD open-label extension study (OLE; NCT01949311) indicate that continuous dupilumab treatment for up to 4 years in adults with moderate-to-severe AD is not associated with an increased risk of overall systemic or cutaneous infections.¹
**Objectives:** To report exposure-adjusted incidence rates (EAIR) of infections in adults with moderate-to-severe AD treated with dupilumab for up to 5 years.

**Methods:** The OLE was a phase 3, multicenter, open-label extension trial that enrolled adults with moderate-to-severe AD who had participated in any dupilumab parent study (phase 1–3). During the OLE, patients were treated with 300mg dupilumab weekly (qw). 226 patients transitioned to 300mg every 2 weeks starting from Week 108 to align with approved dosage. Concomitant topical treatments for AD were permitted. The EAIR (patients with ≥1 event/100 patient-years [nP/100PY]) was calculated for treatment-emergent infections (Medical Dictionary for Regulatory Activities [MedDRA] System Organ Class [SOC] infections and infestations) and skin infections for the overall study population (N=2,677). Skin infections were defined as adjudicated non-herpetic skin infections from the SOC infections and infestations plus, conservatively, all MedDRA Preferred Terms (PT) in MedDRA High Level Term herpes viral infections. Because the OLE lacked a control arm, infection data from adults with moderate-to-severe AD receiving placebo qw + topical corticosteroids (TCS) in the 1-year LIBERTY AD CHRONOS trial (NCT02260986; n=315) are included for comparison. Data are presented as observed.

**Results:** From the 2,677 patients enrolled, 2,207/557/334 completed treatment up to Week 52/148/260. The most common reasons for study withdrawal during the OLE were dupilumab approval and commercialization (810/1,380 patients; 58.7% of withdrawals) and patient withdrawal (248/1,380 [18.0%]). Treatment-emergent adverse events led to permanent discontinuation in 101 (3.8%) patients. The EAIR of patients with ≥1 treatment-emergent infection was lower in this OLE vs the placebo qw + TCS arm of the 1-year CHRONOS trial (70.7 vs 107.0 nP/100PY). Over this 5-year OLE, 50 patients (0.9 nP/100PY) had ≥1 serious infection, 53 (0.9 nP/100PY) had ≥1 severe infection, and 20 (0.3 nP/100PY) experienced ≥1 infection resulting in permanent treatment discontinuation. Skin infections were reported in 535 patients (11.0 nP/100PY), comprising non-herpetic skin infections (249 patients; 4.6 nP/100 PY) and herpes viral infections (343 patients; 6.6 nP/100 PY). The EAIR of skin infections...
decreased throughout the OLE (1 year: 17.2 nP/100 PY; 3 years: 11.9 nP/100 PY; 5 years: 11.0 nP/100 PY) and was lower than the CHRONOS placebo qw + TCS arm (29.5 nP/100 PY). The most common PTs (≥5.0 nP/100PY) from the SOC infections and infestations were nasopharyngitis (774 patients; 17.6 nP/100PY), upper respiratory tract infection (365 patients; 7.0 nP/100PY), and conjunctivitis (277 patients; 5.2 nP/100PY; representing conjunctivitis of unspecified or undetermined etiology, including non-infectious cases). Conjunctivitis was the most common infection PT leading to treatment discontinuation (10 patients; 0.2 nP/100PY). The EAIR of serious infections remained stable during the OLE (1 year: 0.8 nP/100PY; 3 years: 0.9 nP/100PY; 5 years: 0.9 nP/100PY).

**Conclusions:** Long-term dupilumab treatment in adults with moderate-to-severe AD does not increase risk of systemic or cutaneous infections. Rates of treatment-emergent infections, including skin infections, in the OLE for up to 5 years were low, compared with patients receiving placebo + TCS in a 1-year study. Serious infection rates remained low and stable over the 5-year OLE. This report reinforces the known long-term safety profile of dupilumab from an infection perspective.

**Keywords:** atopic dermatitis, dupilumab, long-term, safety, infections

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References:


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