# Safety of long-term dupilumab treatment in adults with moderate-to-severe atopic dermatitis: results from a 5-year open-label extension trial

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## INTRODUCTION

- Atopic dermatitis (AD) is a chronic inflammatory skin disease requiring long-term management; however, sustained AD treatment with systemic immunosuppressants is not recommended due to safety concerns
- Data from an open-label extension study (OLE; NCT01949311) previously demonstrated acceptable dupilumab safety in adult patients up to 204 weeks (approximately 4 years)

## OBJECTIVE

- **To assess the long-term safety of dupilumab administered in adult patients with AD up to 5 years (the end of this OLE study)**

## METHODS

- LIBERTY AD OLE (NCT01949311) was a phase 3, multicenter OLE trial with a duration of up to 5 years administering dupilumab 300 mg weekly (qw) to adults with moderate-to-severe AD who previously participated in dupilumab clinical trials (parent studies)
- 226 patients transitioned to 300 mg every 2 weeks (q2w) to align with approved dosage
- Concomitant treatments for AD were permitted, including topical corticosteroids (TCS) and topical calcineurin inhibitors
- Data presented include the full safety analysis set at the end of the OLE for the overall study population
- Because the OLE trial lacked a control arm, LIBERTY AD CHRONOS (NCT02260986) 52-week safety results for adults with moderate-to-severe AD receiving dupilumab 300 mg qw plus TCS were provided as a comparison

## RESULTS

- Baseline demographics and disease characteristics in the OLE study
  - 60.2% of the 2,677 patients were male and 72.3% were White
  - Mean (standard deviation, SD) age of patients was 39.2 (13.4) years and duration of AD was 29.9 (14.8) years
  - Mean (SD) Eczema Area and Severity Index, Investigator's Global Assessment, and Peak Pruritus Numerical Rating Scale scores were 16.4 (14.6), 2.7 (1.0), and 5.0 (2.5) respectively

## RESULTS (CONT.)

### Table 1. Patient disposition.

| | Total N = 2,677 n (%) |
|---|---|
| Patients who completed up to: | |
| Week 52 | 2,207 (82.4) |
| Week 100 | 1,065 (39.8) |
| Week 148 | 557 (20.8) |
| Week 172 | 362 (13.5) |
| Week 196 | 353 (13.2) |
| Week 220 | 352 (13.1) |
| Week 244 | 344 (12.9) |
| Week 260 | 334 (12.5) |
| Patients who completed study | 1,297 (48.4) |
| Patients withdrawn from study | 1,380 (51.6) |
| Study terminated by sponsor[a] | 708 (26.4) |
| Withdrawal by subject[b] | 375 (14.0) |
| Adverse event[c] | 107 (4.0) |
| Lost to follow-up | 73 (2.7) |
| Lack of efficacy | 50 (1.9) |
| Protocol deviation | 34 (1.3) |
| Pregnancy | 20 (0.7) |
| Physician decision | 9 (0.3) |
| Unknown | 4 (0.1) |

[a]Regulatory approval/commercialization. [b]Includes reasons of relocation, desire for pregnancy, did not want to discontinue treatment for safety follow-up, work/school reasons and personal/not specified reasons. [c]Includes patients receiving treatment at the time of withdrawal and those not receiving treatment during the 12-week safety follow-up period following end of treatment.

### Table 2. Safety summary.

| | OLE, Final data set Dupilumab 300 mg qw[a] N = 2,677 | | | CHRONOS Week 52, Final data set Placebo + TCS N = 315 | | | CHRONOS Week 52, Final data set Dupilumab 300 mg qw + TCS N = 315 | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. of events | Patients ≥ 1 event, n (%) | nP/100PY | No. of events | Patients ≥ 1 event, n (%) | nP/100PY | No. of events | Patients ≥ 1 event, n (%) | nP/100PY |
| TEAE | 14,717 | 2,276 (85.0) | 166.0 | 1,520 | 268 (85.1) | 325.1 | 1,500 | 263 (83.5) | 322.4 |
| Severe TEAE | 391 | 269 (10.0) | 5.0 | 46 | 28 (8.9) | 10.3 | 24 | 17 (5.4) | 5.9 |
| SAE[b] | 388 | 283 (10.6) | 5.2 | 24 | 16 (5.1) | 5.8 | 11 | 10 (3.2) | 3.4 |
| SAE related to treatment[b] | 38 | 33 (1.2) | 0.6 | 3 | 3 (1.0) | 1.1 | 2 | 2 (0.6) | 0.7 |
| TEAEs leading to discontinuation[c] | 122 | 101 (3.8) | 1.7 | 29 | 25 (7.9) | 9.1 | 10 | 9 (2.9) | 3.1 |

[a]Includes the 226 patients who switched from 300 mg qw to 300 mg q2w in Amendment 9 (Nov 2019). [b]No specific pattern was observed for incidence of SAE or SAE related to treatment. Includes 1 treatment related SAE of (PT) Serum sickness (also listed as an ADR in the USPI). This SAE was associated with an elevated ADA titer following the second dose of dupilumab 300 mg qw; study drug was permanently discontinued and the patient recovered. [c]Conjunctivitis (MedDRA PT) was the most common PT leading to treatment discontinuation in 10 (0.4%) patients.
ADR, adverse drug reaction; MedDRA, Medical Dictionary for Regulatory Activities; nP/100PY, number of patients per 100 patient-years; qw, every week; SAE, serious adverse event; TEAE, treatment-emergent adverse event; USPI, United States prescribing information.

### Table 3. Analysis of most common TEAEs.

| | OLE, Final data set Dupilumab 300 mg qw[a] N = 2,677 | | CHRONOS Week 52, Final data set Placebo + TCS N = 315 | | CHRONOS Week 52, Final data set Dupilumab 300 mg qw + TCS N = 315 | |
|---|---|---|---|---|---|---|
| | Patients ≥ 1 event, n (%) | nP/100 PY | Patients ≥ 1 event, n (%) | nP/100 PY | Patients ≥ 1 event, n (%) | nP/100PY |
| TEAEs reported in ≥ 5% of patients by PT | | | | | | |
| Nasopharyngitis | 774 (28.9) | 17.6 | 62 (19.7) | 24.9 | 62 (19.7) | 24.2 |
| Conjunctivitis[b] | 536 (20.0) | 11.1 | 25 (7.9) | 9.2 | 61 (19.4) | 23.4 |
| Atopic dermatitis | 448 (16.7) | 8.8 | 147 (46.7) | 74.3 | 55 (17.5) | 20.7 |
| Upper respiratory tract infection | 365 (13.6) | 7.0 | 32 (10.2) | 12.0 | 43 (13.7) | 15.8 |
| Headache | 218 (8.1) | 4.0 | 19 (6.0) | 7.0 | 25 (7.9) | 9.0 |
| Oral herpes | 200 (7.5) | 3.7 | 9 (2.9) | 3.2 | 15 (4.8) | 5.2 |
| Injection site reaction | 138 (5.2) | 2.5 | 25 (7.9) | 9.4 | 61 (19.4) | 24.5 |

[a]Includes the 226 patients who switched from 300 mg qw to 300 mg q2w in Amendment 9 (Nov 2019). [b]Narrow customized MedDRA query (CMQ) including the following PTs: conjunctivitis; conjunctivitis allergic, bacterial, viral; atopic keratoconjunctivitis. PT, MedDRA Preferred Term.

### Table 4. Assessment of conjunctivitis.

| | OLE, Final data set Dupilumab 300 mg qw[a] N = 2,677 | | CHRONOS Week 52, Final data set Placebo + TCS N = 315 | | CHRONOS Week 52, Final data set Dupilumab 300 mg qw + TCS N = 315 | |
|---|---|---|---|---|---|---|
| Assessment of conjunctivitis[b] | nE (%) | | nE (%) | | nE (%) | |
| Number of events, nE (%) | 894 | | 29 | | 91 | |
| Recovered/resolved | 784 (87.7)[c] | | 27 (93.0)[c] | | 81 (89.0)[c] | |
| Recovered/resolved with sequelae | 10 (1.1)[c] | | 0 | | 1 (1.1)[c] | |
| Recovering/resolving | 17 (1.9)[c] | | 1 (3.4)[c] | | 2 (2.2)[c] | |
| Not recovered/not resolved | 82 (9.2)[c] | | 1 (3.4)[c] | | 7 (7.7)[c] | |
| Unknown/missing | 1 (0.1)[c] | | 0 | | 0 | |
| | n (%) | nP/100PY | n (%) | nP/100PY | n (%) | nP/100PY |
| Number of patients with ≥ 1 event of conjunctivitis | 536 | 11.1 | 25 | 9.2 | 61 | 23.4 |
| Mild | 248 (46.3)[d] | 4.6 | 15 (60.0)[d] | 5.4 | 31 (50.8)[d] | 11.1 |
| Moderate | 261 (48.7)[d] | 4.9 | 9 (36.0)[d] | 3.2 | 28 (45.9)[d] | 10.0 |
| Severe | 27 (5.0)[d] | 0.5 | 1 (4.0)[d] | 0.4 | 2 (3.3)[d] | 0.7 |
| Related to study drug | 258 (48.1)[d] | 4.8 | 5 (20.0)[d] | 1.8 | 15 (24.6)[d] | 5.2 |
| Resulting in permanent discontinuation of study drug | 14 (2.6)[d] | 0.2 | 0 | 0 | 0 | 0 |

[a]Includes the 226 patients who switched from 300 mg qw to 300 mg q2w in Amendment 9 (Nov 2019). [b]Narrow CMQ including the following PTs: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis. [c]Percentage of outcomes calculated based on number of conjunctivitis events. [d]Percentage calculated based on number of patients with ≥ 1 conjunctivitis event. Severity classification of patients with > 1 event is based on most severe event. nE, number of events.

## CONCLUSIONS

- **The safety profile observed in this OLE trial up to 5 years is acceptable and consistent with the known safety profile of dupilumab observed in placebo-controlled studies**
- **Exposure-adjusted incidence rates (nP/100PY) of TEAEs overall did not increase over time and were lower than previously reported in the 3- and 4-year analyses of this OLE trial[1,2] and an earlier 52-week placebo-controlled trial**
- **In patients with narrow customized MedDRA query conjunctivitis TEAEs, for 95% of patients with at least one event the most severe event was assessed as mild or moderate, > 85% of events were reported as recovered/resolved, and the majority of events were not treatment limiting**

**References:** 1. Beck LA, et al. Am J Clin Dermatol. 2020;21:567-77. 2. Beck LA, et al. Am J Clin Dermatol. 2022;23 Suppl 1:393-408.

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