Dupilumab Demonstrates a Higher Likelihood of Achieving Improvements in Signs, Symptoms, and Quality of Life vs. Tralokinumab at Week 16: Results from a Bucher Indirect Treatment Comparison

Atopic Dermatitis

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Background

- Dupilumab and tralokinumab are US Food and Drug Administration (FDA)-approved biologics for treating patients with moderate-to-severe atopic dermatitis (AD) aged ≥6 months and ≥12 years, respectively, who are not adequately managed by topical treatments.[1,2]
- In the absence of direct head-to-head trials between dupilumab and tralokinumab, Bucher indirect treatment comparisons (ITCs) are employed, which anchor treatment effects to a common comparator (e.g., placebo) to evaluate the relative efficacy of drugs.
- The Bucher ITC is a robust and widely accepted method that helps clinicians in making informed decisions.

Objective

- **To report the results of a placebo-adjusted Bucher ITC comparing the efficacy of dupilumab+TCS vs. tralokinumab+TCS at Week 16.**

Conclusions

- **Dupilumab+TCS demonstrated a significantly higher likelihood of achieving improvements in signs, symptoms and quality of life compared to tralokinumab+TCS at Week 16 in patients with moderate-to-severe AD.**

Methods

- The placebo-adjusted Bucher ITC included the published data from the two similarly designed phase 3 trials:
  - LIBERTY AD CHRONOS (NCT02260986): dupilumab 300 mg q2w+topical corticosteroid (TCS) and placebo+TCS
  - ECZTRA 3 (NCT03363854, before rerandomization at Week 16): tralokinumab 300 mg q2w+TCS and placebo+TCS
- For both the studies, data from Week 16 were used, employing non-responder imputation.

Evaluated efficacy endpoints

- The proportions of patients achieving the following binary endpoints were assessed:
  - Investigator's Global Assessment score 0/1 (IGA 0/1; clear/almost clear)
  - 75% and 90% improvements in the Eczema Area and Severity Index (EASI-75 and EASI-90)
  - ≥4-point improvement in the Peak Pruritus Numerical Rating Scale score (PP-NRS)
  - ≥4-point improvement in the Dermatology Life Quality Index (DLQI≥4)

Statistical Analysis

- This Bucher ITC was performed with the frequentist approach using R software (v 4.20; netmeta package) with a fixed-effect model.
- The differences in response rates between treatment groups compared with placebo for all binary endpoints were analyzed using the Cochran–Mantel–Haenszel test.
- Relative effects were quantified using odds ratio (OR) with 95% confidence intervals (CIs).

Results

- A total of 801 patients (**LIBERTY AD CHRONOS** – placebo+TCS: 315; dupilumab+TCS: 106; **ECZTRA 3** – placebo+TCS: 127; tralokinumab+TCS: 253) were included in the Bucher ITC (**Table 1**).
- The baseline disease characteristics indicated comparable severity between the two trial populations based on IGA and PP-NRS. However, LIBERTY AD CHRONOS showed slightly higher baseline EASI scores, while ECZTRA 3 showed slightly higher DLQI scores (**Table 1**).

Table 1. Baseline characteristics of the study population included in the Bucher ITC

Study ID	LIBERTY AD CHRONOS (NCT02260986)		ECZTRA 3 (NCT03363854)	
Intervention	**Placebo+TCS (*N*=315)**	**Dupilumab q2w+TCS (*N*=106)**	**Placebo+TCS (*N*=127)**	**Tralokinumab q2w+TCS (*N*=253)**
IGA score, *n* (%)				
4 (severe AD)	147 (47.0)	53 (50.0)	60 (47.2)	116 (45.8)
3 (moderate AD)	168 (53.0)	53 (50.0)	66 (52.0)	136 (53.8)
Missing	–	–	1 (0.8)	1 (0.4)
EASI score, median (Q1–Q3)	29.6 (22.2–40.8)	30.9 (22.3–41.6)	26.5 (19.9–39.3)	24.7 (18.4–35.9)
PP-NRS score, median (Q1–Q3)	7.6[a] (6.3–8.6)	7.7[a] (6.6–8.5)	8.0[b] (7.0–9.0)	8.0[b] (6.6–8.7)
DLQI score, median (Q1–Q3)	14.0 (9.0–20.0)	13.5 (8.0–20.0)	18.0 (12.0–23.0)	18.0 (12.0–23.0)

All patients who have received rescue medications were considered "non-responders," and missing data were imputed as non-response.
[a]LIBERTY AD CHRONOS: Peak daily pruritus NRS was used; [b]ECZTRA 3: The worst daily pruritus NRS was used. For both scales, range 0 [no itch] to 10 [worst itch imaginable].
AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; ITC, indirect treatment comparison; PP-NRS, Peak Pruritus Numerical Rating Scale; q2w, every 2 weeks; Q1, first quartile Q3, third quartile; TCS, topical corticosteroid.

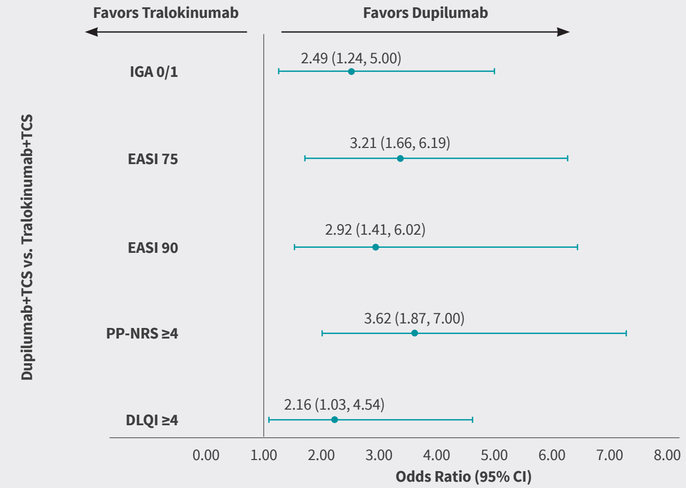
Table 2. Difference in proportions of patients achieving the efficacy endpoints with dupilumab+TCS vs. placebo+TCS and tralokinumab+TCS vs. placebo+TCS at Week 16

Study ID	LIBERTY AD CHRONOS (NCT02260986)			ECZTRA 3 (NCT03363854)		
Intervention	**Placebo+TCS (*N*=315)**	**Dupilumab q2w+TCS (*N*=106)**	**Difference vs. Placebo+TCS (95% CI)**	**Placebo+TCS (*N*=126)**	**Tralokinumab q2w+TCS (*N*=252)**	**Difference vs. Placebo+TCS (95% CI)**
IGA-0/1, *n* (%)	39 (12.4)	41 (38.7)	26 (16.3–36.3)	33 (26.2)	98 (38.9)	12.4 (2.9–21.9)
EASI-75, *n* (%)	73 (23.2)	73 (68.9)	46 (35.7–55.7)	45 (35.7)	141 (56.0)	20.2 (9.8–30.6)
EASI-90, *n* (%)	35 (11.1)	42 (39.6)	29 (18.6–38.5)	27 (21.4)	83 (32.9)	11.4 (2.1–20.7)
PP-NRS≥4, *n*/*N* (%)	59/299[a] (19.7)	60/102[a] (58.8)	39 (28.5–49.7)	43/126[b] (34.1)	113/249[b] (45.4)	11.3 (0.9–21.6)
DLQI≥4, *n*/*N* (%)	129/300[c](43.0)	81/100[c] (81.0)	38 (28.5–47.5)	81/123[c] (65.9)	207/248[c] (83.5)	17.6 (8.0–27.1)

[a]Sample size included patients with baseline PP-NRS score ≥4. [b]Sample size included patients with baseline pruritus NRS weekly average of ≤4. [c]Sample size included patients with baseline DLQI score ≥4.
AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; q2w, every 2 weeks; TCS, topical corticosteroid.

- The patients treated with dupilumab q2w+TCS had a significantly higher likelihood of achieving IGA 0/1, EASI-75, EASI-90, PP-NRS≥4, and DLQI≥4 vs. trlokinumab q2w+TCS at Week 16 (**Figure 1**).

Figure 1. Forest plot of the relative efficacy of dupilumab+TCS and tralokinumab+TCS for the endpoints at Week 16



CI, confidence interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; TCS, topical corticosteroid.

- Limitations of this study include those innate to ITC comparisons, including a lack of direct evidence (ITCs provide an approximation of relative efficacy).

REFERENCES
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CONFLICTS OF INTEREST
YC– Aixial Group – employee (contracted by Sanofi), may hold shares and/or stock options in the company;
BC, **MB**, **KN**, **CCC**, **AR** – Sanofi – employees, may hold stock and/or stock options in the company;
ZW – Regeneron Pharmaceuticals Inc. – employee and shareholder.

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