Dupilumab Demonstrates a **Significantly Higher Likelihood** of Achieving Improvements in **Atopic Dermatitis Signs and Itch** vs **Nemolizumab** at Week 16 in Combination With Topical Corticosteroids: Results From a **Bucher Placebo-Adjusted Indirect Comparison**

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Key Takeaway

This placebo-anchored Bucher ITC analysis demonstrates that dupilumab + TCS vs nemolizumab + TCS is significantly more likely to achieve improvements in patients' AD signs and itch at Week 16

AD

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Objective

To report the results of a placebo-anchored Bucher ITC of 16 weeks of therapy for moderate-to-severe AD, comparing the efficacy of dupilumab + TCS vs nemolizumab + TCS

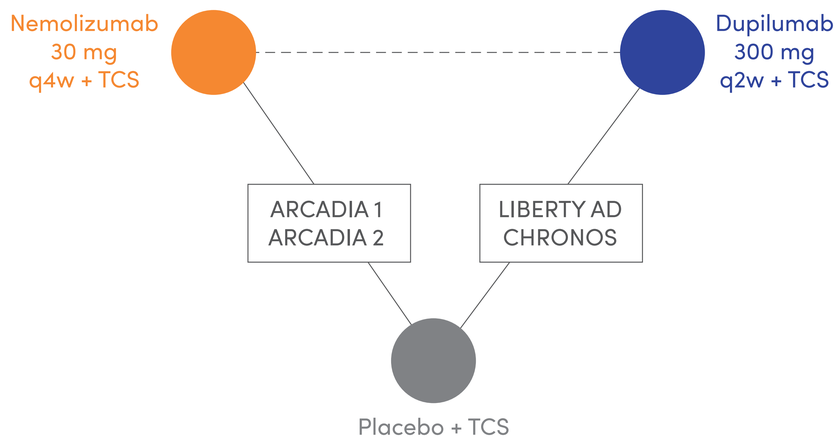
Background

- AD is a chronic type 2 inflammatory disease, which often needs long-term treatment
- Monoclonal antibodies dupilumab and nemolizumab have both demonstrated efficacy and safety in clinical trials of AD[1,2]
- No direct head-to-head comparisons between dupilumab and nemolizumab have been performed
- In the absence of direct comparisons, Bucher ITCs, in which treatment effects of drugs are anchored to a common comparator (e.g. placebo), can provide a robust and widely accepted method to evaluate relative efficacy[3,4,5]

Methods

- A placebo-anchored Bucher ITC was conducted using published phase 3 trial data from LIBERTY AD CHRONOS (NCT02260986)[1] and replicate trials ARCADIA 1 (NCT03985943)[2] and ARCADIA 2 (NCT03989349)[2]
- 16-week data were used for the following doses: dupilumab 300 mg q2w + TCS, or placebo q2w + TCS (LIBERTY AD CHRONOS), and nemolizumab 30 mg q4w + TCS, or placebo q4w + TCS (ARCADIA 1 & 2)
  - Medium-potency TCS was used for non-sensitive skin areas, while a low-potency TCS or a TCI was used in sensitive areas
  - ARCADIA trials had a mandatory run-in with TCS/TCI ≥14 days before treatment day 1, while CHRONOS did not
- Week 16 outcomes in this analysis included proportion of patients achieving IGA 0/1 (clear/almost clear skin), EASI-75, and PP-NRS Δ ≥4; non-responder imputation was used in the original trials for these binary outcomes
- ORs with 95% CIs were computed without adjustment based on published proportions[1,2]; meta-analysis ORs were generated for ARCADA 1 & 2 combined; the meta-analsyis used R and meta R package
- The NNT for achieving those 3 outcomes were computed to compare treatment benefits

Network diagram for Bucher ITC of dupilumab vs nemolizumab



Inclusion criteria and study design details for the source studies

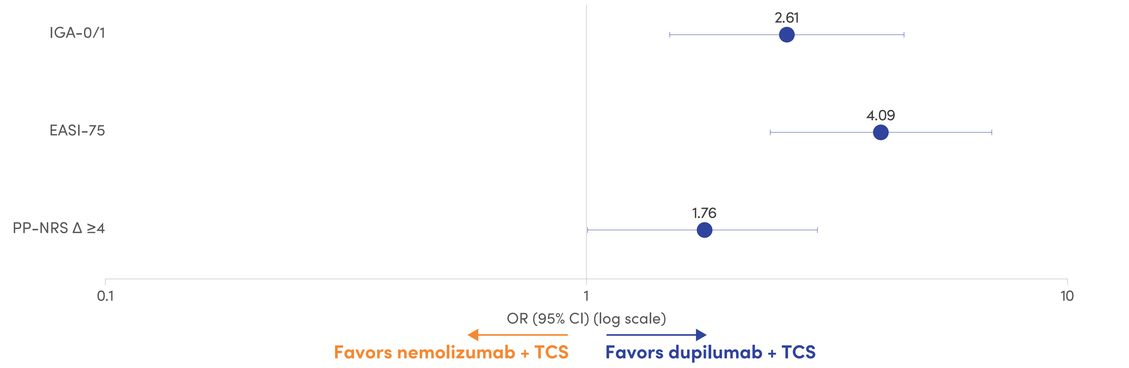
	Dupilumab	Nemolizumab
Study	**LIBERTY AD CHRONOS** (NCT02260986)[1]	**ARCADIA 1** (NCT03985943) and **ARCADIA 2** (NCT03989349)[2]
Inclusion criteria	• Adults (aged ≥18 years) • Moderate-to-severe AD (IGA=3 or 4, EASI ≥16, and BSA ≥10%) • Inadequate response to topical AD medications within 6 months prior to screening	• Adults and adolescents (aged ≥12 years) • Moderate-to-severe AD (IGA=3 or 4, EASI ≥16, and BSA ≥10%) • Inadequate response to topical AD medications within 6 months prior to screening

Results

Baseline disease characteristics were generally similar between CHRONOS and ARCADIA 1 & 2, except for % of patients with IGA=4, supporting the use of Bucher ITC

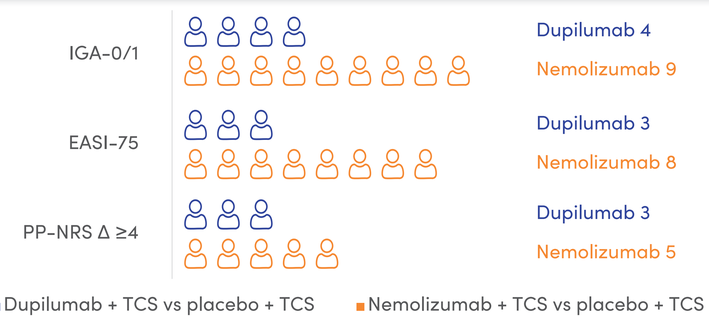
Study name (NCT number)	Treatment arms	n	Male (%)	Age (mean)	IGA-4 (%)	EASI (mean)	PP-NRS (mean)
LIBERTY AD CHRONOS (NCT02260986)	Dupilumab + TCS	106	58	40.5	47%	30.9	7.7
	Placebo + TCS	315	61	34	50%	29.6	7.6
ARCADIA 1 (NCT03989206)	Nemolizumab + TCS	620	52	33.5	29%	27.8	7.2
	Placebo + TCS	312	55	33.3	26%	27.1	7.2
ARCADIA 2 (NCT03989206)	Nemolizumab + TCS	522	48	34.9	33%	27.4	7.0
	Placebo + TCS	265	49	35.2	30%	27.6	7.1

Likelihood of achieving improvements in AD signs and itch is significantly higher for patients treated with dupilumab + TCS vs nemolizumab + TCS at Week 16



Patients treated with dupilumab + TCS vs nemolizumab + TCS had a significantly higher likelihood of achieving IGA-0/1 (OR=2.61; 95% CI 1.49–4.57), EASI-75 (OR=4.09, 95% CI 2.41–6.96), and PP-NRS Δ≥4 (OR=1.76, 95% CI 1.02–3.02) at Week 16

For each outcome – IGA 0/1, EASI-75, and PP-NRS Δ≥4 – the NNT to observe 1 additional patient achieving the outcome was lower (demonstrating greater treatment efficacy) for dupilumab + TCS compared with nemolizumab + TCS



At Week 16, response rates for the three outcomes were as follows: for IGA-0/1, 38.7% with dupilumab + TCS vs 12.4% with placebo + TCS, 36.6% with nemolizumab + TCS vs 25.3% with placebo + TCS; for EASI-75, 68.9% with dupilumab + TCS vs 23.2% with placebo + TCS, 42.9% with nemolizumab + TCS vs 29.5% with placebo + TCS; and for PP-NRS Δ ≥4, 58.8% with dupilumab + TCS vs 19.7% with placebo + TCS, 41.9% with nemolizumab + TCS vs 17.9% with placebo + TCS

Conclusions

- This placebo-anchored Bucher ITC analysis demonstrated that the likelihood of achieving improvements in AD signs and itch is significantly higher for patients treated with dupilumab + TCS vs nemolizumab + TCS at Week 16
- Based on the NNT analysis, dupilumab + TCS demonstrated greater treatment efficacy across all assessed outcomes compared with nemolizumab + TCS, requiring substantially fewer patients to be treated to achieve the same clinical benefits

AD, atopic dermatitis; BSA, Body Surface Area; CI, confidence internal; EASI-75, 75% improvement in Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NNT, number needed to treat; ITC, indirect treatment comparison; OR, odds ratio; PP-NRS, Peak Pruritus Numeric Rating Scale; q2w, every 2 weeks; q4w, every 4 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid(s).

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