Comparative Efficacy of Lebrikizumab, Dupilumab, and Tralokinumab in Maintaining Treatment Response in Atopic Dermatitis at Varying Treatment Continuance Rates

Jonathan I. Silverberg[1], Alan Irvine[2], Peter Foley[3], James Del Rosso[4], Luis Puig[5], Linda Stein Gold[6], Martin Dossenbach[7], Marta Casillas[7], Gaia Gallo[7], Buelent Akmaz[8], Kim Rand[9]

[1]George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [2]Department of Clinical Medicine, Trinity College, Dublin, Ireland; [3]The University Melbourne, Melbourne, Victoria, Australia; [4]JDR Dermatology Research Las Vegas, NV, USA; [5]Department of Dermatology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Henry Ford Hospital, Detroit, MI, USA; [7]Eli Lilly and Company, Indianapolis, IN, USA; [8]Almirall S.A., Barcelona, Spain; [9]Maths In Health B.V., Klimmen, The Netherlands

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OBJECTIVE

- This study aims to understand whether the durability of treatment effect is a critical factor to consider when managing a chronic disease such as atopic dermatitis (AD) whose symptoms can fluctuate over time.
  - In real-world settings, patients with AD may need to pause treatment or may not be completely compliant with treatment[1]
  - Recent phase 3 monotherapy trials indicate that the impact of treatment pauses may vary for dupilumab, tralokinumab, and lebrikizumab[2-4]
  - We developed the “durability index” (DI), a novel estimate of drug performance that captures a drug’s ability to maintain efficacy whether on-therapy or off-therapy at the population level

CONCLUSIONS

- This indirect comparative analysis demonstrates that biologics differ in their maintenance of population-level efficacy at varying treatment continuance rates
- Treatment responses were significantly higher for lebrikizumab than dupilumab or tralokinumab at most continuance rates, especially lower rates
- This finding suggests that lebrikizumab may have better maintenance of response in real-life settings where treatment pauses may occur and continuance rates may be below 100%

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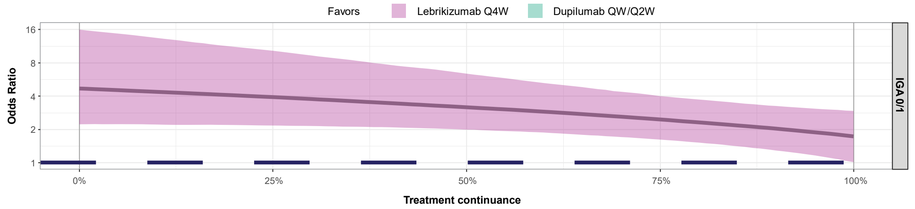
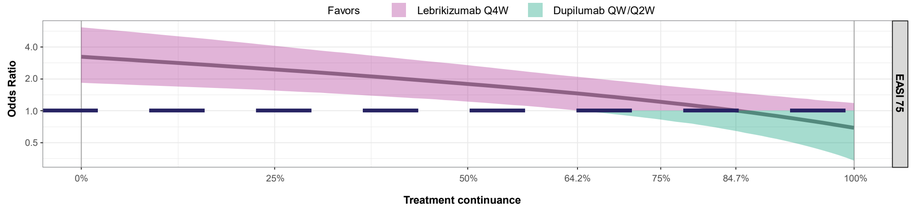
KEY RESULTS

Durability index odds ratios for lebrikizumab and dupilumab for IGA 0/1 and EASI 75 from 0% to 100% treatment continuance

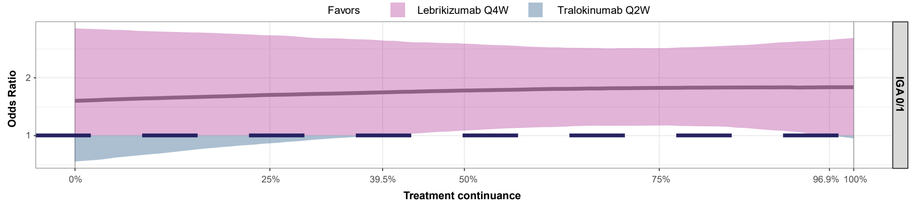


- IGA 0/1: Lebrikizumab had statistically significantly better odds of durability at week 52 than dupilumab for continuance rates from 0% (OR 4.69, 95% CrI: 2.23–15.96) to 100% (1.73, 1.01–2.94)

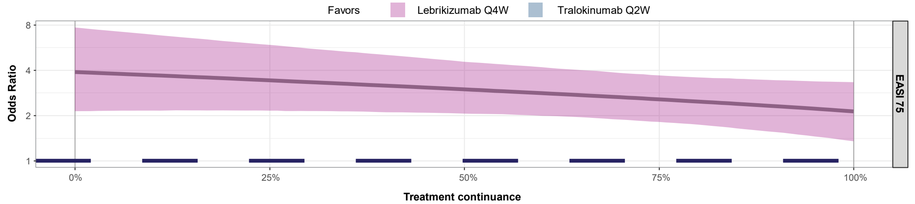


- EASI 75: Lebrikizumab had significantly better odds of durability than dupilumab at continuance rates from 0% (OR 3.24, 1.83–6.12) to 64.2% (1.45, 1.00–2.08). Lebrikizumab also had numerically better odds from 64.2% to 84.7%, while dupilumab had numerically better odds from 84.7% to 100%.

Durability index odds ratios for lebrikizumab and tralokinumab for IGA 0/1 and EASI 75 from 0% to 100% treatment continuance



- IGA 0/1: Lebrikizumab had significantly better odds of durability than tralokinumab at continuance rates between 39.5% (OR 1.68, 95% CrI: 1.00–3.12) and 96.9% (1.79, 1.00–3.14). Lebrikizumab also had numerically better odds at continuance rates <39.5% and >96.9%.



- EASI 75: Lebrikizumab had statistically significantly better odds of durability at week 52 than tralokinumab at continuance rates from 0% (OR 3.89, 2.13–7.66) to 100% (2.13, 1.35–3.32)

Solid line represents the point estimate for ORs. **Upper and lower bands** represent 95% CrIs. **Dashed line** represents the point of equivalence (i.e., no difference between drugs).

Abbreviations: CrI, credible interval; EASI 75, ≥75% improvement in Eczema Area Severity Index; IGA 0/1, Investigator’s Global Assessment of 0 (clear) or 1 (almost clear), with a ≥2 point reduction from baseline; OR, odds ratio; Q2W, every 2 weeks; Q4W, every 4 weeks

METHODS

Durability index development

- A population-adjusted indirect comparison was conducted of placebo-controlled phase 3 monotherapy trials with similar designs in post-induction periods
  - Lebrikizumab 250 mg Q4W (ADvocate1 and ADvocate2)[2]
  - Tralokinumab 300 mg Q2W (ECZTRA1 and ECZTRA 2)[3]
  - Dupilumab 300 mg QW/Q2W (SOLO 1, SOLO 2, and SOLO CONTINUE)[4]
- Patients were eligible for these trials if they had responded to biologics at week 16
  - Responders were re-randomized at week 16 to continue treatment or switch to treatment withdrawal until week 52
  - Data from these trials cannot be connected in a network meta-analysis using the withdrawal arm as a common comparator because patients in this arm received treatment during the 16-week induction period
  - The withdrawal arm, however, can be used to evaluate a drug’s effect after treatment discontinuation as a population-level measure of long-term durability of response (**Table 1**)
  - For the DI analysis, patients who used rescue medication after week 16 were considered non-responders

Table 1: Proportion of week-16 responders maintaining response at week 52 in phase 3 trials

	Treatment withdrawal	Treatment continuation
IGA 0/1		
Lebrikizumab 250 mg Q4W[2*]	40.1%	69.4%
Tralokinumab 300 mg Q2W[3]	34.0%	55.9%
Dupilumab 300 mg QW/Q2W[4]	14.3%	54.0%
EASI 75		
Lebrikizumab 250 mg Q4W[2*]	59.2%	68.7%
Tralokinumab 300 mg Q2W[3]	26.4%	57.3%
Dupilumab 300 mg QW/Q2W[4]	30.4%	71.6%

Abbreviations: EASI 75, ≥75% improvement in Eczema Area Severity Index; IGA 0/1, Investigator’s Global Assessment of 0 (clear) or 1 (almost clear), with a ≥2 point reduction from baseline; Q2W, every 2 weeks; Q4W, every 4 weeks.
* Analysis included the ADvocate 1 and 2 adult population.

Durability index definition

- The DI was developed as a novel estimate of the population-level efficacy of biologics when different proportions of patients who respond to treatment either continue or suspend treatment
- The DI can be based on varying rates of treatment continuance, from 0% to 100% continuing therapy
- The durability index was calculated as the proportion of predicted week-52 responders out of week-16 responders at varying continuance rates from 0% to 100%

Statistical analysis

- Unanchored simulated treatment comparison (STC) was used to estimate odds ratios (OR) adjusting for baseline covariates
  - STC regresses outcomes on baseline covariates, treating them as prognostic factors and including interaction terms for effect modifiers
  - Two STC logistic regression models were generated: one for week-16 outcomes and one for week 52 outcomes
- Uncertainty was handled using non-parametric bootstrapping, with 5000 resamples drawn from the active induction treatment population
- All comparisons remained consistent even when the target population and the covariates used for adjustment were varied

References

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