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[8], Marta Casillas[8], Gaia Gallo[8], 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; [6]Maths In Health B.V., Klimmen, The Netherlands

Sponsored by Eli Lilly and Company

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

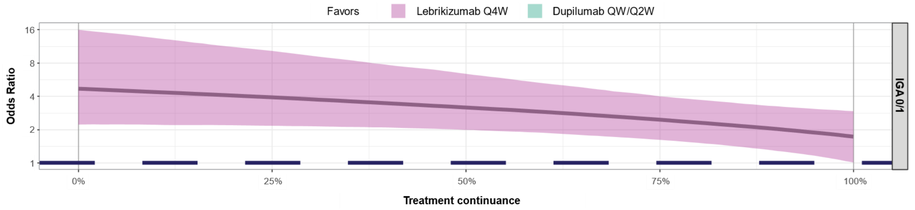
CONCLUSIONS

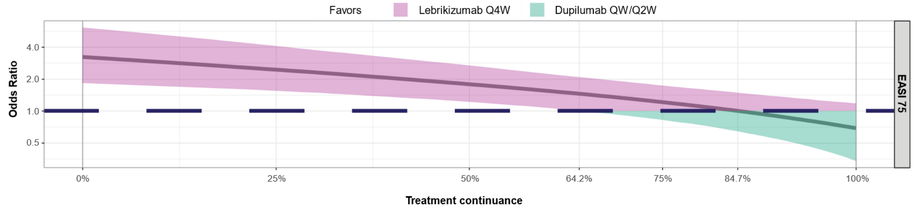
- This indirect comparative analysis demonstrates that biologics differ in their maintenance of population-level efficacy at varying treatment continuance rates
- Treatment responses were significantly higher for lebrikizumab than dupilumab or tralokinumab at most continuance rates, especially lower 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%

Fall Clinical 2024; Las Vegas, USA; 24-27 October 2024

KEY RESULTS

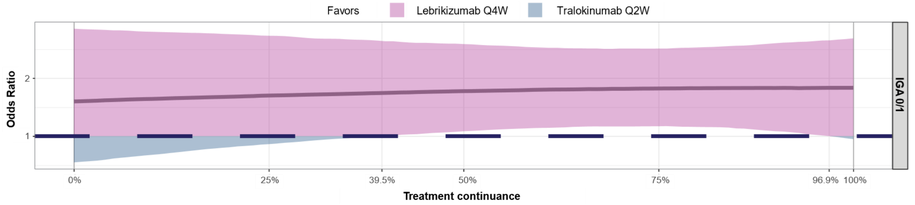
Durability index odds ratios for lebrikizumab and dupilumab for IGA 0/1 and EASI 75 from 0% to 100% treatment continuance

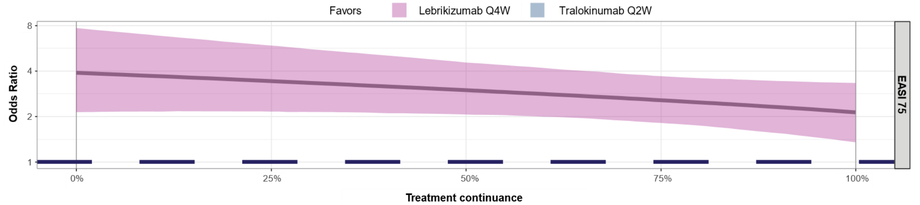




- IGA 0/1: Lebrikizumab had statistically significantly better odds of durability at week 52 than dupilumab for continuance rates from 0% (OR 4.69, 95% CrI: 2.23–15.96) to 100% (1.73, 1.01–2.94)
- EASI 75: Lebrikizumab had significantly better odds of durability than dupilumab at continuance rates from 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

1. Hosoya K, et a. Patient Prefer Adherence. 2023;17:861-872.
2. Blauvelt A, et al. *Br J Dermatol*. 2023;188(6):740-748.
3. Wollenberg A, et al. *Br J Dermatol*. 2021;184(3):437-449.
4. Worm M, et al. *JAMA Dermatol*. 2020;156(2):131-143.

Acknowledgments: This analysis was funded by Eli Lilly and Company. Medical writing support was provided by Michael Franklin (PPD, a Thermo Fisher company) in accordance with Good Publication Practice (GPP3) guidelines and funded by Eli Lilly and Company.

Disclosures: JIS has served as advisor, speaker, or consultant for AbbVie, Asana Biosciences, Dermavant Sciences, Galderma, GlaxoSmithKline, Glenmark, Kiniksa, LEO Pharma, Lilly, Menlo Therapeutics, Novartis, Pfizer, Realm Pharma, and Regeneron-Sanofi; and is a researcher for GlaxoSmithKline. **AID** has received research funding or served as an advisor, speaker, or consultant for AbbVie, Arena Pharmaceuticals, BenevolentAI, Eli Lilly and Company, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi, Pfizer, and the International Eczema Council. **PF** has received research funding or served as an advisor, speaker, or consultant received grants from AbbVie, Amgen, Argenx, Arcutis, Aslan, AstraZeneca, Boehringer Ingelheim, Botanix, Bristol-Myers Squibb, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Celgene, Eli Lilly and Company, Evelo, Galderma, Genentech, Geneseq, GenesisCare, GlaxoSmithKline, Hexima, Incyte, Janssen, Kymab, LEO Pharma, Mayne Pharma, Merck, MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Roche, Sanofi, Sun Pharma, Teva, UCB Pharma, and Valeant. **JDL** has received grants as an investigator, honoraria for lecturing, and/or consulting fees from AbbVie, Amgen (Celgene), AOBiome, Aslan, Arbonne, Arcutis, Bausch Health (Ortho Derm), Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Exeltis, Ferndale, Galderma, Incyte, IntraDerm, Johnson & Johnson, La Roche-Posay/L’Oréal, LEO Pharma, Menlo Therapeutics, Nektar, Pfizer, Pierre Fabre, Regeneron/Sanofi Genzyme, Sun Pharma, Theraplex, UCB Pharma, Unilever, and Verrica Pharmaceuticals. **LP** has received consultancy/speaker’s honoraria from and/or participated in clinical trials sponsored by Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius-Kabi, J&J Innovative Medicine, Leo-Pharma, Lilly, Novartis, Pfizer, STADA, Sun-Pharma, and UCB. **KR** is an employee of Maths In Health B.V., which was funded by Eli Lilly and Company to provide analytical services for this publication. **MD**, **GG**, and **MC** are employees and minor shareholders of Eli Lilly and Company. **BA** is an employee of Almirall. **LSG** is an investigator and/or consultant and/or speaker for: AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB Pharma.

Scan the QR code for a list of all Lilly content presented at the congress.

Other company and product names are trademarks of their respective owners.

Scan the QR code for supplemental results showing comparisons between dupilumab and tralokinumab.

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, The Netherlands; [7]Eli Lilly and Company, Indianapolis, IN, USA;
[8]Almirall S.A., Barcelona, Spain; [6]Maths In Health B.V., Klimmen

Sponsored by Eli Lilly and Company

OBJECTIVE

- This study aims to understand whether 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

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]

METHODS

Durability index development

- 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 phase 3 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

METHODS

Durability Index Development

- 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 IGA of 0 (clear) or 1 (almost clear), with a ≥2 point reduction from baseline

* Analysis included the ADvocate 1 and 2 adult populations.

METHODS

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%

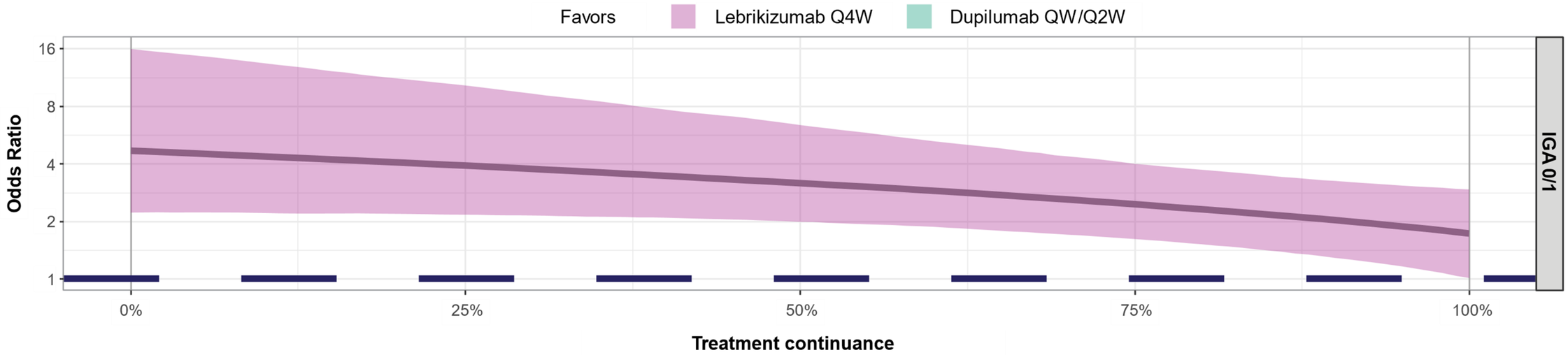
METHODS

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

KEY RESULTS

Durability index for lebrikizumab vs dupilumab for IGA 0/1 from 0% to 100% treatment continuance



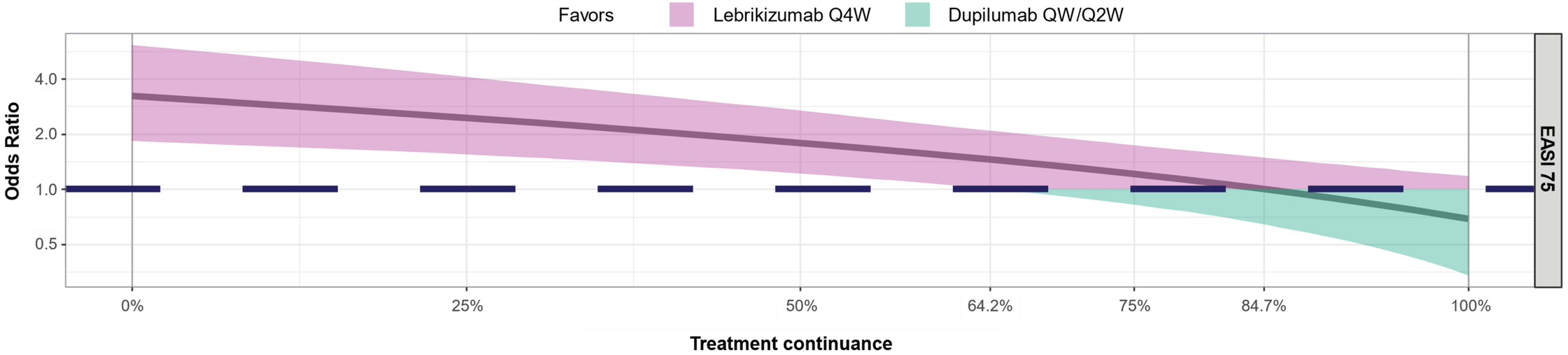
- IGA 0/1: Lebrikizumab had statistically significantly better odds of durability at week 52 than dupilumab for continuance rates from 0% (OR 4.69, 95% CrI: 2.23–15.96) to 100% (1.73, 1.01–2.94)

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

Abbreviations: CrI, credible interval; 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

KEY RESULTS

Durability index for lebrikizumab vs dupilumab for EASI 75 from 0% to 100% treatment continuance



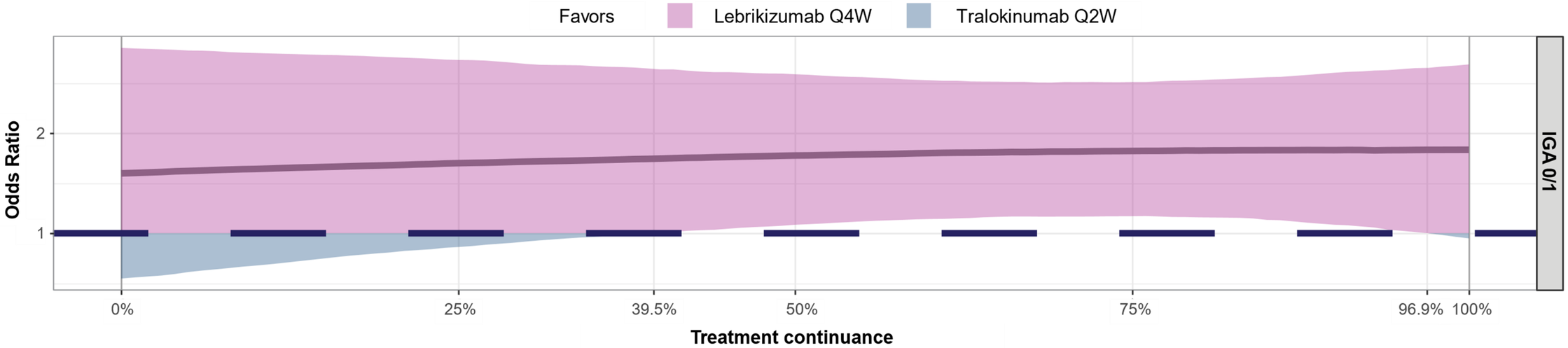
- EASI 75: Lebrikizumab had significantly better odds of durability than dupilumab at continuance rates from 0% (3.24, 1.83–6.12) to 64.2% (1.45, 1.00–2.08). Lebrikizumab also had numerically better odds from 64.2% to 84.7%, while dupilumab had numerically better odds from 84.7% to 100%.

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

Abbreviations: CrI, credible interval; EASI 75, ≥75% improvement in Eczema Area Severity Index; OR, odds ratio; Q2W, every 2 weeks; Q4W, every 4 weeks

KEY RESULTS

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



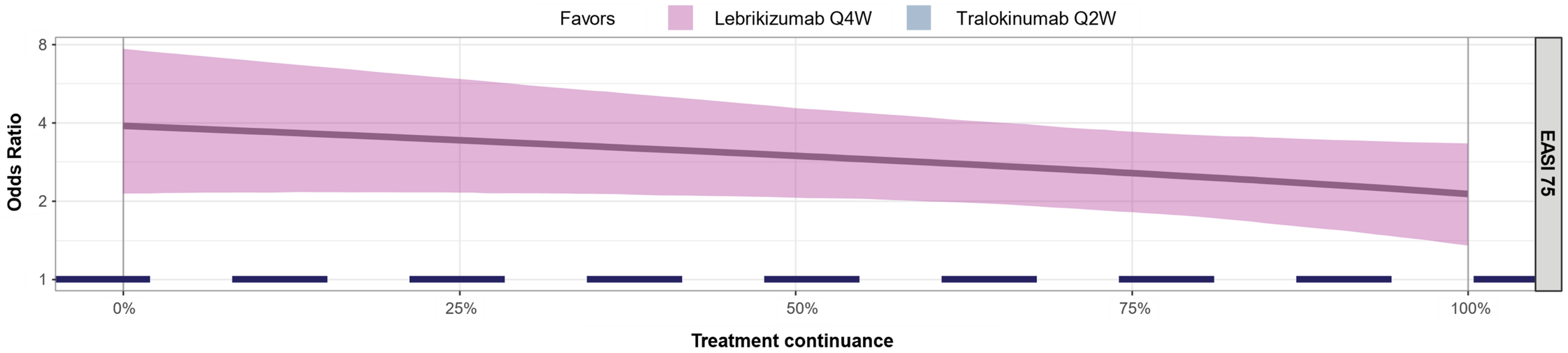
- IGA 0/1: Lebrikizumab had significantly better odds of durability than tralokinumab at continuance rates between 39.5% (OR 1.68, 95% CrI: 1.00–3.12) and 96.9% (1.79, 1.00–3.14). Lebrikizumab also had numerically better odds at continuance rates <39.5% and >96.9%.

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

Abbreviations: CrI, credible interval; 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

KEY RESULTS

Durability index for lebrikizumab and tralokinumab for EASI 75 from 0% to 100% treatment continuance



- 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 OR. **Upper and lower bands** represent 95% CrIs. **Dashed line** represents point of equivalence (i.e., no difference between drugs).

Abbreviations: CrI, credible interval; EASI 75, ≥75% improvement in Eczema Area Severity Index; OR, odds ratio; Q2W, every 2 weeks; Q4W, every 4 weeks

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%

REFERENCES

1. Hosoya K, et a. Patient Prefer Adherence. 2023;17:861-872.
2. Blauvelt A, et al. Br J Dermatol. 2023;188(6):740-748.
3. Wollenberg A, et al. Br J Dermatol. 2021;184(3):437-449.
4. Worm M, et al. JAMA Dermatol. 2020;156(2):131-143.

ACKNOWLEDGMENTS

- This analysis was funded by Eli Lilly and Company.
- Medical writing support was provided by Michael Franklin (PPD, a Thermo Fisher company) in accordance with Good Publication Practice (GPP3) guidelines and funded by Eli Lilly and Company.

DISCLOSURES

- **JIS** has served as advisor, speaker, or consultant for AbbVie, Asana Biosciences, Dermavant Sciences, Galderma, GlaxoSmithKline, Glenmark, Kiniksa, LEO Pharma, Lilly, Menlo Therapeutics, Novartis, Pfizer, Realm Pharma, and Regeneron-Sanofi; and is a researcher for GlaxoSmithKline. **AID** has received research funding or served as an advisor, speaker, or consultant for AbbVie, Arena Pharmaceuticals, BenevolentAI, Eli Lilly and Company, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi, Pfizer, and the International Eczema Council. **PF** has received research funding or served as an advisor, speaker, or consultant received grants from AbbVie, Amgen, Argenx, Arcutis, Aslan, AstraZeneca, Boehringer Ingelheim, Botanix, Bristol-Myers Squibb, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Celgene, Eli Lilly and Company, Evelo, Galderma, Genentech, Geneseq, GenesisCare, GlaxoSmithKline, Hexima, Incyte, Janssen, Kymab, LEO Pharma, Mayne Pharma, Merck, MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Roche, Sanofi, Sun Pharma, Teva, UCB Pharma, and Valeant. **JDL** has received grants as an investigator, honoraria for lecturing, and/or consulting fees from AbbVie, Amgen (Celgene), AOBiome, Aslan, Arbonne, Arcutis, Bausch Health (Ortho Derm), Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Exeltis, Ferndale, Galderma, Incyte, IntraDerm, Johnson & Johnson, La Roche-Posay/L'Oréal, LEO Pharma, Menlo Therapeutics, Nektar, Pfizer, Pierre Fabre, Regeneron/Sanofi Genzyme, Sun Pharma, Theraplex, UCB Pharma, Unilever, and Verrica Pharmaceuticals. **LP** has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius-Kabi, J&J Innovative Medicine, Leo-Pharma, Lilly, Novartis, Pfizer, STADA, Sun-Pharma, and UCB. **KR** is an employee of Maths In Health B.V., which was funded by Eli Lilly and Company to provide analytical services for this publication. **MD**, **GG**, and **MC** are employees and minor shareholders of Eli Lilly and Company. **BA** is an employee of Almirall. **LSG** is an investigator and/or consultant and/or speaker for: AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB Pharma.

SUPPLEMENTAL MATERIAL

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

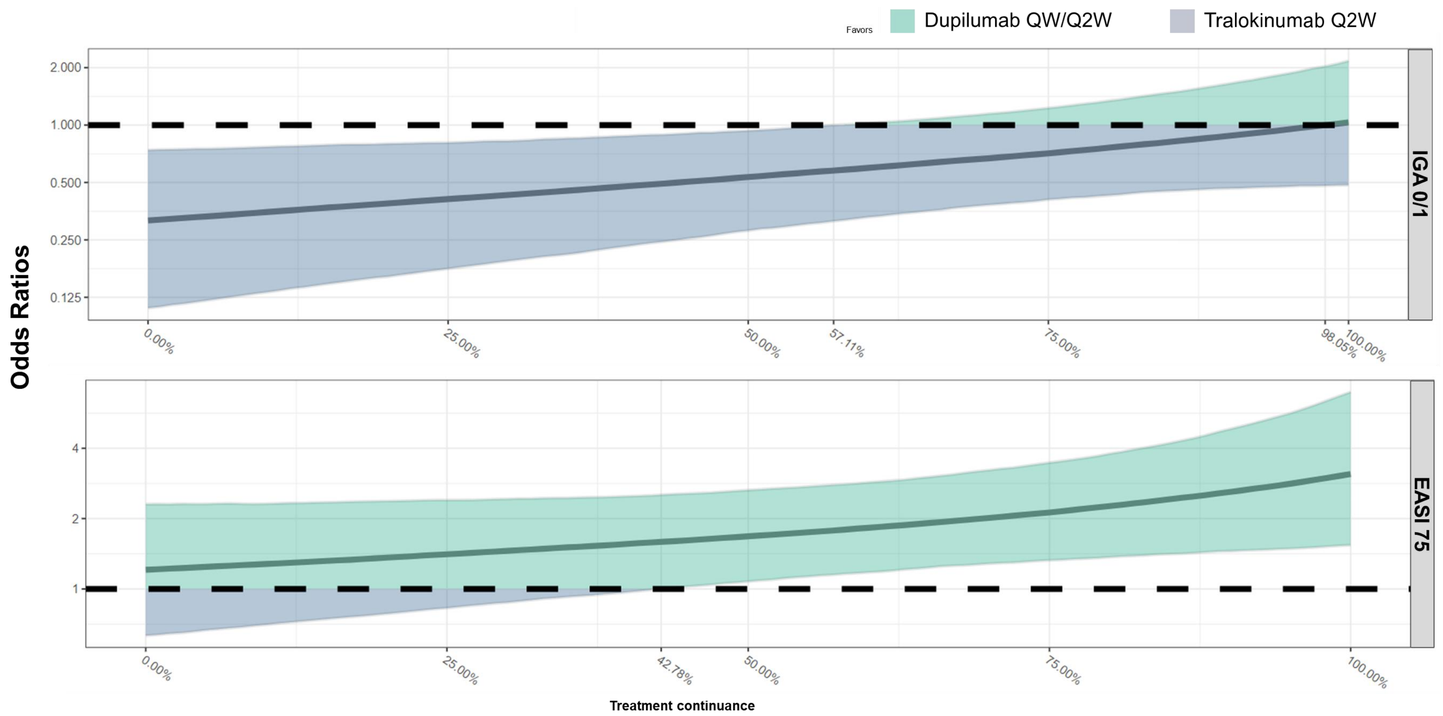
Jonathan I. Silverberg[1], Alan Irvine[2], Peter Foley[3], James Del Rosso[4], Luis Puig[5], Linda Stein Gold[6], Martin Dossenbach[7], Marta Casillas[7], Gaia Gallo[7], Buelent Akmaz[8], Kim Rand[9]

[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, The Netherlands; [7]Eli Lilly and Company, Indianapolis, IN, USA;
[8]Almirall S.A., Barcelona, Spain; [6]Maths In Health B.V., Klimmen

KEY RESULTS

Durability index for dupilumab and tralokinumab for IGA 0/1 and EASI 75 from 0% to 100% treatment continuance rates

- IGA 0/1: Tralokinumab had better odds of achieving IGA 0/1 at week 52 than dupilumab at 0% (OR 0.32, CrI: 0.11–0.74) to 57.1% (0.58, 0.31–1.00)
- EASI 75: In contrast, dupilumab had better odds of achieving EASI 75 than tralokinumab at 42.8% (OR 1.59, CrI: 1.00–2.53) to 100% (3.10, 1.54–6.96)



Solid line represents the point estimate for OR. **Upper and lower bands** represent 95% CrIs. **Dashed line** represents 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