Long-Term Effect of Dupilumab With Concomitant Topical Corticosteroids on POEM in Adults With Moderate-to-Severe Atopic Dermatitis: LIBERTY AD CHRONOS Trial

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BACKGROUND

- The Patient-Oriented Eczema Measure (POEM) is a validated, 7-item questionnaire, which assesses patient-reported frequency of atopic dermatitis (AD) symptoms from the previous week[1–3]
  - The Harmonising Outcome Measures for Eczema initiative recommends POEM as the core outcome instrument for measuring patient-reported AD symptoms in clinical trials[4]
- Dupilumab is a fully human monoclonal antibody[5,6] that blocks the shared receptor component for interleukin (IL)-4 and IL-13, thus inhibiting signaling of both IL-4 and IL-13, which are key and central drivers of type 2 inflammation in multiple diseases[7]
- In the 52-week, phase 3, randomized, double-blinded LIBERTY AD CHRONOS trial (NCT02260986), dupilumab with concomitant topical corticosteroids (TCS) vs placebo with TCS significantly improved AD signs, symptoms, and patient quality of life with an acceptable safety profile[8]

OBJECTIVE

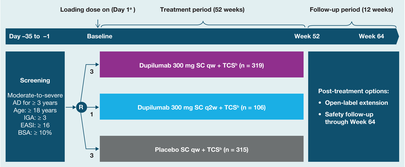
- **To analyze the effect of dupilumab with concomitant TCS on POEM in a 52-week, phase 3 trial in adults with moderate-to-severe AD using data from the LIBERTY AD CHRONOS trial**

METHODS

Study design

- The detailed study design, patient population, efficacy, and safety of the CHRONOS study have been previously reported[8]

Figure 1. CHRONOS study design.



*Dupilumab, 600 mg loading dose; placebo, matching placebo. †Patients were required to use TCS for the entire treatment period. BSA, body surface area; IGA, Investigator's Global Assessment; EASI, Eczema Area and Severity Index; R, randomization; qw, weekly; q2w, every 2 weeks; SC, subcutaneous.

METHODS (CONT.)

Endpoints

- Outcomes assessed in this analysis included
  - Least squares (LS) mean change from baseline to Week 52 in total POEM score
  - Proportion of patients in severity grades classified according to POEM scores through Week 52
  - Proportion of patients in each category of the 7 items of POEM through Week 52
    - 0 = No days
    - 1 = 1–2 days
    - 2 = 3–4 days
    - 3 = 5–6 days
    - 4 = Every day

Analysis

- The analysis presented here is focused on the placebo + TCS group (control) and the dupilumab 300 mg q2w + TCS group (approved dose in adults)
- Efficacy was analyzed in all randomized patients (full analysis set)
- Safety was analyzed in the safety analysis set, which included all patients who received ≥ 1 dose of study drug

RESULTS

Table 1. Baseline demographics and disease characteristics (full analysis set).

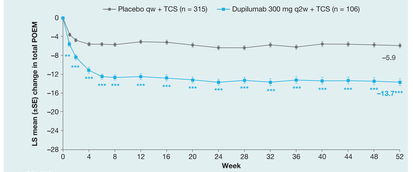
	Scoring	Placebo qw + TCS (n = 315)	Dupilumab 300 mg q2w + TCS (n = 106)
Age, mean (SD), years	–	36.6 (13.01)	39.6 (13.98)
Male, n (%)	–	193 (61.30)	62 (58.50)
Total POEM, mean (SD)	0–28	20.0 (5.99)	20.3 (5.68)
Itchy skin	0–4	3.8 (0.54)	3.9 (0.43)
Sleep disturbance	0–4	2.2 (1.48)	2.4 (1.39)
Bleeding skin	0–4	2.2 (1.44)	2.2 (1.36)
Weeping/oozing skin	0–4	1.8 (1.47)	1.9 (1.53)
Cracked skin	0–4	2.9 (1.36)	3.0 (1.28)
Flaking skin	0–4	3.2 (1.18)	3.2 (1.32)
Dry/rough skin	0–4	3.7 (0.73)	3.7 (0.75)
AD severity according to POEM, n (%)			
Mild	0–7	8 (2.5)	2 (1.9)
Moderate	8–19	128 (40.6)	39 (36.8)
Severe	20–28	178 (56.8)	65 (61.3)

SD, standard deviation.

RESULTS (CONT.)

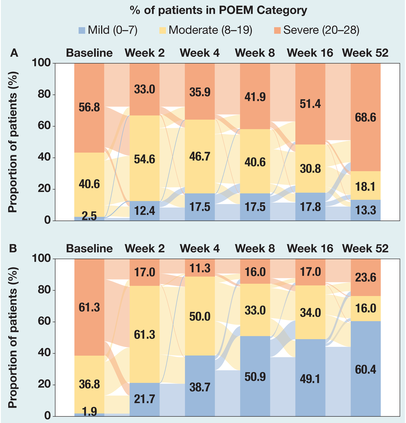
Efficacy

Figure 2. Change in total POEM score from baseline up to Week 52.



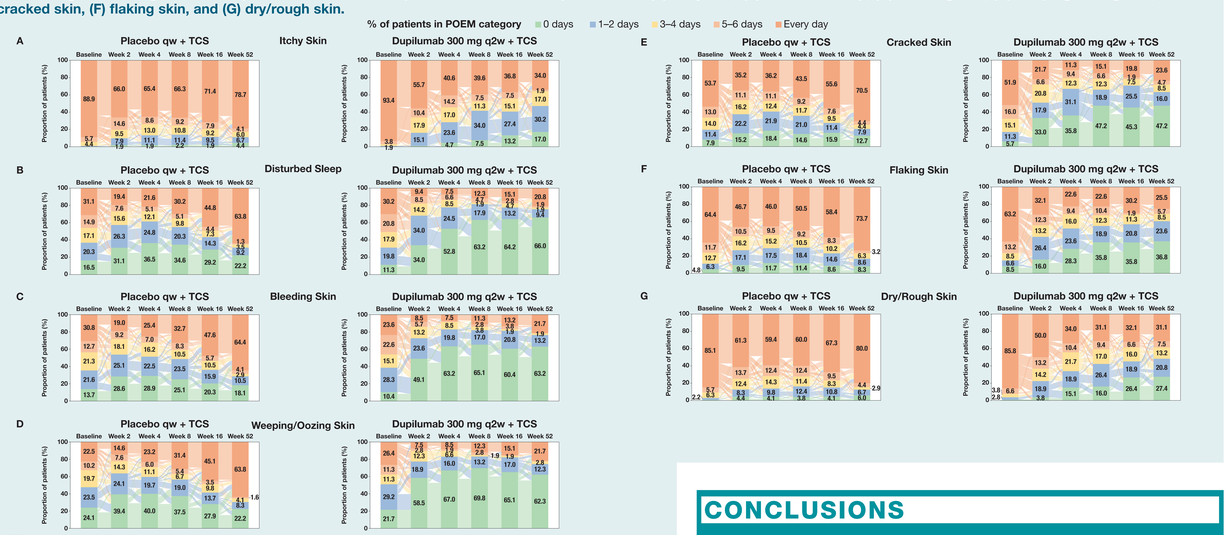
**P < 0.01, ***P < 0.0001 vs placebo. SE, standard error

Figure 3. Categorical change in AD severity according to total POEM score in (A) placebo + TCS group and (B) dupilumab 300 mg q2w group.



Missing POEM scores were imputed into "Severe" category.

Figure 4. Categorical change in each response on the individual questions of the POEM questionnaire (A) itchy skin, (B) disturbed sleep, (C) bleeding skin, (D) weeping/oozing skin, (E) cracked skin, (F) flaking skin, and (G) dry/rough skin.



Missing POEM scores were imputed into "Every day" category.

Safety

Table 2. Overall safety summary of patients during the 52-week treatment period (safety analysis set).

Patients with, n (%)	Placebo qw + TCS (n = 315)	Dupilumab 300 mg q2w + TCS (n = 110)	Dupilumab 300 mg qw + TCS (n = 315)
Any TEAE	268 (85.1)	97 (88.2)	263 (83.5)
TEAEs leading to discontinuation	25 (7.9)	2 (1.8)	9 (2.9)
Death	0	0	1 (0.3)
Any TE SAE	16 (5.1)	4 (3.6)	10 (3.2)
Nasopharyngitis[a,b]	62 (19.7)	25 (22.7)	62 (19.7)
Dermatitis atopic[a,b]	147 (46.7)	22 (20.0)	55 (17.5)
Injection-site reaction[a,b]	25 (7.9)	16 (14.5)	61 (19.4)
Conjunctivitis[b,c]	25 (7.9)	15 (13.6)	61 (19.4)

[a]Patients with ≥ 1 such event. [b]MedDRA PT. [c]Narrow conjunctivitis including MedDRA PTs of conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis. MedDRA, Medical Dictionary for Regulatory Activities; PT, Preferred Term; TEAE, Treatment-emergent adverse event; TE SAE, Treatment-emergent serious adverse event

CONCLUSIONS

- **Dupilumab + TCS significantly improved the total POEM score over the 52-week study period, and significant improvements were observed in all individual domains, with most patients reporting "mild" symptoms by the end of the study**
- **More patients receiving dupilumab + TCS vs control reported "0 days" of signs and symptoms on the 7 POEM items at Week 52**

References: 1. Charman CR, et al. Arch Dermatol. 2004;140:1513-9. 2. Schmitt J, et al. J Allergy Clin Immunol. 2007;120:1389-98. 3. Gerbens LA, et al. Allergy. 2017;72:146-63. 4. Chalmers JR, et al. Br J Dermatol. 2016;175:69-79. 5. Macdonald LE, et al. Proc Natl Acad Sci U S A. 2014;111:5147-52. 6. Murphy AJ, et al. Proc Natl Acad Sci U S A. 2014;111:5153-8. 7. Gandhi NA, et al. Expert Rev Clin Immunol. 2017;13:425-37. 8. Blauvelt A, et al. Lancet. 2017;389:2287-303.

Acknowledgments: Data first presented at the 78th Annual Meeting of the American Academy of Dermatology (AAD 2020); Denver, CO, USA; March 20–24, 2020.
Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifier: LIBERTY AD CHRONOS (NCT02260986). Medical writing/editorial assistance provided by Toby Leigh Bartholomew, PhD, of Excerpta Medica, funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosures: Silverberg JI: AbbVie, Celgene, Eli Lilly, GSK, Incyte, Kiniksa Pharmaceuticals, LEO Pharma, Realm Therapeutics, Regeneron Pharmaceuticals, Inc. – investigator; AbbVie, Eli Lilly, Galderma, GSK, Incyte, Kiniksa Pharmaceuticals, LEO Pharma, MedImmune (AstraZeneca), Menlo Therapeutics, Pfizer, Realm Therapeutics, Regeneron Pharmaceuticals, Inc. – consultant; Regeneron Pharmaceuticals, Inc. – speaker. **Lockshin B:** Eli Lilly, Regeneron Pharmaceuticals, Inc. – investigator, speaker; Anacor, Dermira, Franklin Bioscience, LEO Pharma – investigator; AbbVie – investigator, speaker, consultant. **Gooderham M:** AbbVie, Akros, Amgen, Arcutis Antiobix, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus BioSciences, Dermira, Eli Lilly, Galderma, GSK, Janssen, Kyowa Kirin, LEO Pharma, Merck, MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Sanofi Genzyme, Sun Pharma, UCB, Valeant/Bausch – investigator, advisor, and/or speaker. **Chen Z, Gadkari A:** Regeneron Pharmaceuticals, Inc. – employees and shareholders. **Rossi AB:** Sanofi Genzyme – employee, may hold stock and/or stock options in the company.

Presented at the 5th Fall Clinical Dermatology Conference for PAs & NPs (FCPANP).