Dupilumab Treatment Reduces Total IgE Levels in Patients 6 Months and Older With Moderate-to-Severe Atopic Dermatitis

Elaine C. Siegfried[1,2], Michael J. Cork[3,4], Mark Boguniewicz[5,6], Mette Deleuran[7], Eric L. Simpson[8], Zhen Chen[9], Drew Clearfield[9], Parul Shah[9], Ainara Rodríguez Marco[10]

[1]Saint Louis University, St. Louis, MO, USA; [2]Cardinal Glennon Children's Hospital, St. Louis, MO, USA; [3]University of Sheffield, Sheffield, UK; [4]Sheffield Children's Hospital, Sheffield, UK; [5]National Jewish Health, Denver, CO, USA; [6]University of Colorado School of Medicine, Denver, CO, USA; [7]Aarhus University Hospital, Aarhus, Denmark; [8]Oregon Health and Science University, Portland, OR, USA; [9]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [10]Sanofi, Madrid, Spain

BACKGROUND

- Patients with moderate-to-severe atopic dermatitis (AD) demonstrate elevated serum levels of total immunoglobulin E (IgE),[1] a type 2 inflammatory biomarker, that may correlate with AD disease severity in both children[2] and adults[3,4]
- Dupilumab studies have previously demonstrated the suppression of type 2 biomarkers across multiple atopic, allergic diseases in adults[5]

OBJECTIVE

- **To report the effect of dupilumab on total serum IgE levels after 16 weeks of treatment, in patients 6 months of age and older with moderate-to-severe AD enrolled in phase 3 clinical trials**

METHODS

- Patients with moderate-to-severe AD were enrolled for 16 weeks in any of six randomized, placebo-controlled, phase 3 studies:
  - LIBERTY AD PRESCHOOL (NCT03346434 part B)
    - Patients aged 6 months to 5 years were treated with:
      - Dupilumab 200/300 mg every 4 weeks (q4w) + topical corticosteroids (TCS; n = 83)
      - Placebo + TCS (n = 79)
  - LIBERTY AD PEDS (NCT03345914)
    - Patients aged 6–11 years were treated with:
      - Dupilumab 100/200 mg every 2 weeks (q2w) + TCS (n = 122)
      - Dupilumab 300 mg q4w + TCS (n = 122)
      - Placebo + TCS (n = 123)
  - LIBERTY AD ADOL (NCT03054428)
    - Patients aged 12–17 years were treated with:
      - Dupilumab 200/300 mg q2w (n = 82)
      - Dupilumab 300 mg q4w (n = 84)
      - Placebo (n = 85)
  - LIBERTY AD CHRONOS/SOL01/SOLO2 (NCT02260986/NCT02277743/NCT02277769)
    - Patients aged 18 years and over were treated with (TCS were allowed only in CHRONOS):
      - Dupilumab 300 mg q2w (n = 563)
      - Dupilumab 300 mg every week (qw) (n = 781)
      - Placebo (n = 775)
- Impact on serum IgE levels was assessed for dupilumab combined doses and placebo through:
  - Median absolute total serum IgE levels (kU/L) at baseline and Week 16
  - Median percentage change from baseline in total serum IgE levels at Week 16
- Impact on disease severity was assessed from baseline to Week 16 for dupilumab combined doses and placebo through:
  - SCORing Atopic Dermatitis (SCORAD; range: 0–103)
  - Eczema Area and Severity Index (EASI; range: 0–72)

RESULTS

- Baseline demographics and disease characteristics were well balanced in each age group. Baseline disease characteristics were also similar between age groups (**Table 1**)
- At Week 16, dupilumab treatment significantly ($P < 0.0001$) reduced median total serum IgE levels (kU/L [Q1–Q3]) compared with placebo in patients aged 6 months to 5 years (843 [207–3,300] vs 3,625 [540.5–8,585]), 6–11 years (1,519 [532–3,808] vs 3,862 [1,166–9,999]), 12–17 years (1,391 [436–2,842] vs 4,569 [800.5–10,000]), and 18 years and over (1,340 [229–4,360] vs 3,722 [555–10,000])
- Since the studies involved analogous designs, and similar trends were observed in both baseline disease characteristics and disease evolution at Week 16 in all 6 of them, their results were pooled for this analysis

Table 1. Baseline demographics and disease characteristics across the different age groups.

Demographics	Patients aged 6 months to 5 years		Patients aged 6–11 years		Patients aged 12–17 years		Patients aged 18 years and over[a]	
	Placebo + TCS (n = 79)	Dupilumab 200/300 mg q4w + TCS (n = 83)	Placebo + TCS (n = 123)	Dupilumab combined[b] (n = 244)	Placebo (n = 85)	Dupilumab combined[c] (n = 166)	Placebo (n = 775)	Dupilumab combined[d] (n = 1,344)
Age, years, mean (SD)	3.8 (1.3)	3.9 (1.2)	8.3 (1.8)	8.5 (1.7)	14.5 (1.8)	14.5 (1.7)	37.7 (13.6)	38.0 (14.2)
Sex, male, n (%)	55 (69.6)	44 (53.0)	61 (49.6)	122 (50.0)	53 (62.4)	95 (57.2)	443 (57.2)	801 (59.6)
Weight, kg, mean (SD)	16.7 (3.6)	17.1 (4.4)	31.5 (10.8)	31.5 (10.1)	64.4 (21.5)	65.7 (22.3)	75.7 (18.4)	76.2 (18.4)
AD characteristics								
Baseline EASI score (range: 0–72), mean (SD)	33.1 (12.2)	35.1 (13.9)	39.0 (12.0)	37.3 (11.7)	35.5 (14.0)	35.5 (14.3)	33.4 (13.8)	32.4 (13.2)
Baseline SCORAD score (range: 0–103), mean (SD)	72.2 (11.4)	72.7 (13.0)	72.9 (12.0)	74.0 (11.4)	70.4 (13.3)	70.2 (14.0)	67.6 (14.1)	66.8 (13.5)

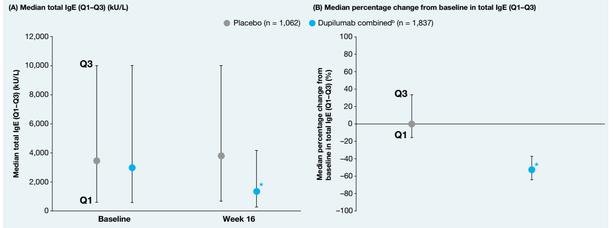
[a]Data pooled from three phase 3 adult trials (LIBERTY AD CHRONOS/SOL01/SOL02); TCS were allowed only in CHRONOS. [b]Dupilumab 300 mg q4w and dupilumab 100/200 mg q2w + TCS. [c]Dupilumab 300 mg q4w and dupilumab 200/300 mg q2w. [d]Dupilumab 300 mg q2w and dupilumab 300 mg qw. SD, standard deviation.

Table 2. Results for all age groups.[a]

IgE analysis	All age groups[a]	
	Placebo (n = 1,062)	Dupilumab combined[b] (n = 1,837)
Total IgE (kU/L), median (IQR)		
Baseline	3,435.0 (582.0 to 10,000.0)	2,952.0 (577.0 to 10,000.0)
Week 16	3,794.0 (679.0 to 10,000.0)	1,344.0 (271.0 to 4,165.0)
Percentage change from baseline at Week 16, median (IQR)	0 (–15.64 to +33.50)	–52.11 (–63.99 to –37.04)
AD characteristics		
SCORAD, mean (SD)		
Baseline	68.8 (13.8)	68.6 (13.6)
Week 16	47.5 (21.2)	28.4 (17.5)
EASI, mean (SD)		
Baseline	34.2 (13.6)	33.5 (13.2)
Week 16	19.6 (15.5)	8.5 (9.9)

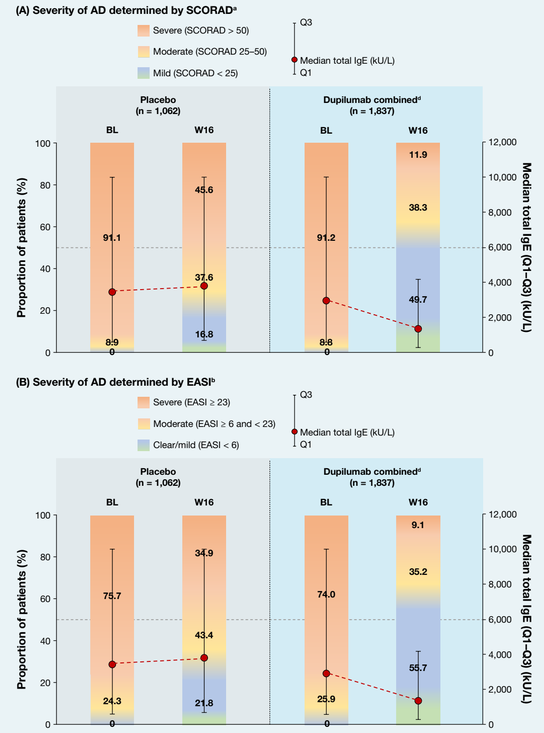
[a]Data pooled from six phase 3 trials (LIBERTY AD PRESCHOOL/PEDS/ADOL/CHRONOS/SOLO1/SOLO2); TCS were allowed only in PRESCHOOL, PEDS, and CHRONOS. [b]Dupilumab 200/300 mg q4w, dupilumab 200/300 mg q2w, dupilumab 100/200 mg q2w, and dupilumab 300 mg qw. IQR, interquartile range.

Figure 1. (A) Median total IgE (kU/L) at baseline and Week 16, and (B) median percentage change from baseline in total IgE (kU/L) at Week 16 in all age groups.[a]



[a]Data pooled from six phase 3 trials (LIBERTY AD PRESCHOOL/PEDS/ADOL/CHRONOS/SOLO1/SOLO2); TCS were allowed only in PRESCHOOL, PEDS, and CHRONOS. [b]Dupilumab 200/300 mg q4w, dupilumab 200/300 mg q2w, dupilumab 100/200 mg q2w, and dupilumab 300 mg qw. *$P < 0.0001$ vs placebo. Q1, first quartile; Q3, third quartile.

Figure 2. Proportion of patients with severity of AD determined by (A) SCORAD[a] and (B) EASI[b] at baseline and Week 16, and median total IgE levels (Q1–Q3) at baseline and Week 16 in all age groups.[c]



[a]Severity strata for SCORAD based on validated published scales.[6] [b]Severity strata for EASI based on validated published scales.[7] [c]Data pooled from six phase 3 trials (LIBERTY AD PRESCHOOL/PEDS/ADOL/CHRONOS/SOLO1/SOLO2); TCS were allowed only in PRESCHOOL, PEDS, and CHRONOS. [d]Dupilumab 200/300 mg q4w, dupilumab 200/300 mg q2w, dupilumab 100/200 mg q2w, and dupilumab 300 mg qw. BL, baseline; W16, Week 16.

CONCLUSIONS

- **Dupilumab treatment results in reduction of total serum IgE levels across all age groups in patients with moderate-to-severe AD**
- **This observation reflects the attenuation of systemic type 2 inflammation by dupilumab treatment in patients of all ages**
- **The reduction of AD signs, such as SCORAD and EASI, was observed in addition to this reduction of total serum IgE levels across all age groups in patients with moderate-to-severe AD**

SAFETY

- Overall safety was consistent with the known dupilumab safety profile

References: 1. Valenta R, et al. J Invest Dermatol. 1996;107:203-8. 2. Mothes N, et al. J Allergy Clin Immunol. 2005;116:706-9. 3. Valenta R, et al. J Allergy Clin Immunol. 2000;105:432-7. 4. Badloe FMS, et al. Clin Transl Allergy. 2020;10:34. 5. Hamilton JD, et al. Clin Exp Allergy. 2021;51:915-31. 6. Orange AP, et al. Br J Dermatol. 2007;157:645-8. 7. Chopra R, et al. Br J Dermatol. 2017;177:1316-21.

Acknowledgments and funding sources: Data first presented at the 79th Annual American Academy of Allergy, Asthma & Immunology Meeting (AAAAI 2023); Feb 25-28, 2023; San Antonio, TX, United States. Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc., ClinicalTrials.gov Identifiers: NCT03346434 part B, NCT03345914, NCT03054428, NCT02260986, NCT02277743, NCT02277769. Rainbow graphs developed by Ana B. Rossi and Marthe Vuillet of Sanofi. Medical writing/editorial assistance was provided by Benjamin Danet, PhD, of Excerpta Medica, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guideline.

Disclosures: Siegfried EC: Dermavant, Eli Lilly, Pfizer, Regeneron Pharmaceuticals Inc., Verrica Pharmaceuticals – consultant; GSK, LEO Pharma, Novan – data and safety monitoring board; Eli Lilly, Janssen, Regeneron Pharmaceuticals Inc., Stiefel, Verrica Pharmaceuticals – Principal Investigator in clinical trials. **Cork MJ:** AbbVie, Astellas Pharma, Boots, Dermavant, Galapagos, Galderma, Hyphens Pharma, Johnson & Johnson, LEO Pharma, L'Oréal, Menlo Therapeutics, Novartis, Oxagen, Pfizer, Procter & Gamble, Reckitt Benckiser, Regeneron Pharmaceuticals Inc., Sanofi – investigator and/or consultant. **Boguniewicz M:** Regeneron Pharmaceuticals Inc., Sanofi – research grants, consulting. **Deleuran M:** AbbVie, Aslan Pharmaceuticals, Arena Pharmaceuticals, Eli Lilly, Incyte, La Roche-Posay, LEO Pharma, Pfizer, Pierre Fabre, Regeneron Pharmaceuticals Inc., Sanofi – research support, consulting/advisory board agreements, and/or honoraria for lectures. **Simpson EL:** Amgen, BMS, Chugai, Galderma, Genentech, Lilly, MedImmune, Sanofi-Regeneron Pharmaceuticals Inc., Tioga Pharmaceuticals, Vanda Pharmaceuticals – grants/research support; Anacor Pharmaceuticals, BMS, Galderma, Genentech, Medicis Pharmaceutical, Merck, Sanofi-Regeneron Pharmaceuticals Inc. – consultant. **Chen Z, Clearfield D, Shah P:** Regeneron Pharmaceuticals Inc. – employees and shareholders. **Rodríguez Marco A:** Sanofi – employee, may hold stock and/or stock options in the company.

Presented at the 5th Annual Revolutionizing Atopic Dermatitis (RAD) Conference; Washington, DC, USA; April 29–May 1, 2023.