Dupilumab Improves Itch and Urticaria Activity Across Several CSU Subpopulations: LIBERTY-CSU CUPID Study A

Thomas B. Casale[1], Sarbjit S. Saini[2], Allen Radin[3], Eric Mortensen[3], Elizabeth Laws[4]

[1]University of South Florida, Tampa, FL, USA; [2]Johns Hopkins Asthma and Allergy Center, Baltimore, MD, USA; [3]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [4]Sanofi, Bridgewater, NJ, USA

DUPILUMAB

Introduction

- Chronic spontaneous urticaria (CSU) is a chronic inflammatory disease characterized by wheals, angioedema, or both that recur for more than 6 weeks[1,2]
- In adults, CSU is more prevalent in females, with a female to male ratio of approximately 2 to 1[3,4]
- The adjusted prevalence of CSU is higher for non-White patients than White patients[5]
- Many patients continue to experience substantial disease burden despite treatment with H1-antihistamines (H1-AH), the standard-of-care for CSU[6,7]

Methods

- **Study design:** LIBERTY-CSU CUPID Study A was a randomized, double-blind, placebo-controlled, 24-week, phase 3 trial that evaluated the efficacy and safety of dupilumab in patients with CSU (**Figure 1**)
  - **Patient population:** Aged ≥ 6 years; diagnosis of CSU > 6 months prior to screening visit; presence of itch and hives for > 6 consecutive weeks despite H1-AH use; Urticaria Activity Score over 7 days (UAS7) ≥ 16 and Itch Severity Score over 7 days (ISS7) ≥ 8; omalizumab-naive
  - **Background therapy:** Study-defined H1-AH (up to 4-fold the licensed dose)
- **Study assessments**
  - Itch Severity Score over 7 days (range 0–21): sum of daily ISS (ranging from 0 = none to 3 = intense) over 7 days
  - Hive Severity Score over 7 days (range 0–21): sum of daily HSS (ranging from 0 = 0 hives to 3 = > 50 hives) over 7 days
  - Urticaria Activity Score over 7 days (range 0–42): sum of the daily HSS7 and ISS7 scores over 7 days
- **Outcomes**
  - Change in ISS7 from baseline (BL) at Week 24
  - Change in HSS7 from BL at Week 24
  - Change in UAS7 from BL at Week 24
- **Safety endpoints:** TEAEs, serious adverse events

Objective

- **To report the safety and efficacy of dupilumab in patients with CSU from LIBERTY-CSU CUPID Study A (NCT04180488) who remained symptomatic despite treatment with H1-AH in patients with:**
  - **High or low baseline urticaria activity**
  - **Standard or increased doses of background H1-AH**
  - **Varying disease duration**
  - **Different demographic profiles (sex and race)**

Conclusion

- **CSU patients treated with dupilumab experienced significantly reduced itch and urticaria activity. Although not powered for subgroup efficacy analyses, itch and urticaria activity reductions were observed across subpopulations, regardless of sex or race. Overall safety was generally consistent with the known dupilumab safety profile**

Study design and Results

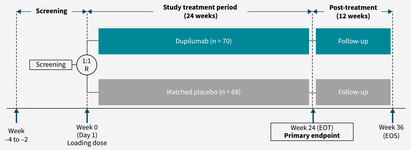
- Baseline characteristics were generally balanced across treatment groups

Table 1. Baseline demographics and clinical characteristics.

	Placebo (n = 68)	Dupilumab (n = 70)	All (N = 138)
Age, years	41.9 (14.8)	40.7 (16.2)	41.3 (15.5)
Female, n (%)	50 (73.5)	41 (58.6)	91 (65.9)
Race, n (%)			
White	48 (70.6)	47 (67.1)	95 (68.8)
Black or African American	2 (2.9)	1 (1.4)	3 (2.2)
Asian	16 (23.5)	19 (27.1)	35 (25.4)
Other	2 (2.9)	3 (4.3)	5 (3.6)
BMI, kg/m^2	27.9 (6.2)	27.4 (6.8)	27.7 (6.5)
Age at onset of CSU, years	36.7 (16.0)	35.5 (16.6)	36.1 (16.2)
Time since first diagnosis of CSU, years	5.7 (7.7)	5.8 (9.3)	5.7 (8.5)
BL total IgE, median, IU/mL	96.5	109.4	101.0
BL total IgE, Min; Max, IU/mL	1; 14827	5; 23388	1; 23388
BL H1-AH, n (%)			
Standard dose	41 (60.3)	31 (44.3)	72 (52.2)
2–4-fold standard dose	27 (39.7)	39 (55.7)	66 (47.8)

Data are presented as mean (standard deviation) unless otherwise stated. BMI, body mass index.

Figure 1. Study design.



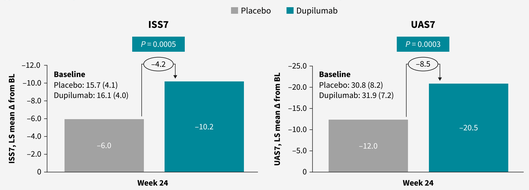
*Background study-defined H1-AH (up to 4-fold the licensed dose).
Dupilumab dosing: adults (> 18 years) and adolescents (12–17 years) ≥ 60 kg: loading dose (LD) 600 mg (two 300 mg SC injections), followed by 300 mg q2w; adolescents (12–17 years) and children (≥ 6 to < 12 years) ≥ 30 kg to < 60 kg: LD 400 mg (two 200 mg SC injections), followed by 200 mg q2w; children (≥ 6 to < 12 years) ≥ 15 kg to < 30 kg: LD 600 mg (two 300 mg SC injections), followed by 300 mg q4w. BL, baseline; EOS/T, end of study/treatment; R, randomization; SC, subcutaneous; q2w, every 2 weeks; q4w, every 4 weeks.

Table 2. Safety summary.

n %	Placebo (n = 68)	Dupilumab (n = 70)
Any TEAE	40 (58.8)	38 (54.3)
TEAEs reported in ≥ 5% of patients in any treatment group (by primary SOC and PT)		
Skin and subcutaneous tissue disorders	18 (26.5)	10 (14.3)
CSU	6 (8.8)	3 (4.3)
Angioedema	5 (7.4)	1 (1.4)
General disorders and administration-site conditions	10 (14.7)	9 (12.9)
Injection-site reactions[a]	2 (2.9)	4 (5.7)
Injection-site erythema	4 (5.9)	3 (4.3)
Selected AE		
Conjunctivitis[b]	1 (1.5)	0
Treatment-emergent SAE[c]	5 (7.4)	2 (2.9)

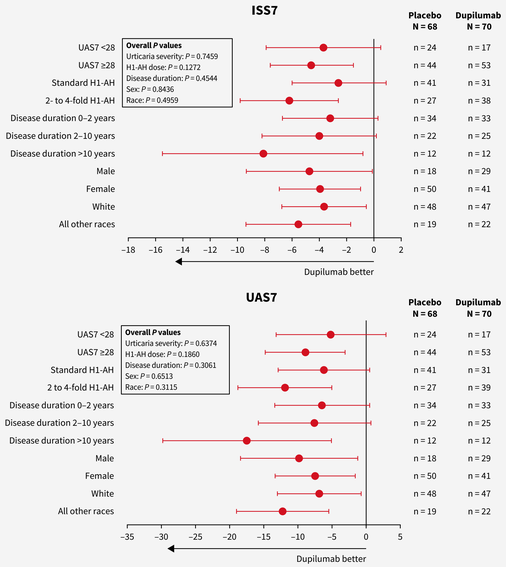
[a]Injection-site reactions by MedDRA High Level Term, n (%): placebo 9 (13.2); dupilumab 8 (11.4). Includes injection-site erythema, injection-site induration, injection-site pain, injection-site pruritus, and injection-site reactions. [b]Conjunctivitis cluster includes conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, giant papillary conjunctivitis, eye irritation, and eye inflammation. [c]SAE terms (PT) include: COVID-19 pneumonia, depression, suicide, dyspnea, hemorrhoids, upper abdominal pain, nausea, angioedema, and atopic dermatitis.
AE, adverse event; CSU, chronic spontaneous urticaria; MedDRA, Medical Dictionary for Regulatory Activities; PT, Preferred Term; SAE, serious adverse event; SOC, system organ class; TEAE, treatment-emergent adverse event.

Figure 2. Dupilumab treatment led to significant improvements in ISS7 and UAS7.



Data are presented as mean (standard deviation) unless otherwise stated.
[a]ISS7, range 0–21; primary endpoint. [b]UAS7 is a composite of ISS7 and HSS7, range 0–42; secondary endpoint. BL, baseline; ISS7, Itch Severity Score over 7 days LS, least squares, UAS7, Urticaria Activity Score over 7 days.

Figure 3. Dupilumab treatment improved ISS7 and UAS7, regardless of baseline characteristics.



Data presented as LS mean difference vs placebo (95% CI).

References: 1. Zuberbier T, et al. Allergy. 2022;77:734-66. 2. Maurer M, et al. Handb Exp Pharmacol. 2022;268:117-33. 3. Maurer M, et al. Allergy. 2011;66:317–330. 4. Fricke J, et al. Allergy. 2020;75:423–432. 5. Wertenteil S, et al. J Am Acad Dematol. 2019;81:152-6. 6. Goncalo M, et al. Br J Dermatol. 2021;184:226-36. 7. Kaplan AP. Allergy Asthma Immunol Res. 2017;9:477-82.

Acknowledgments: Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifier: NCT04180488. Medical writing/editorial assistance was provided by Corinne S. Wilson, PhD, and Hodan Ibrahim, PhD, of Excerpta Medica, and was funded by Sanofi and Regeneron Pharmaceuticals, Inc. according to the Good Publication Practice guideline.

Disclosures: Casale TB: American Lung Association, Genentech, National Institutes of Health, Novartis, PCORI, Sanofi – research support; AstraZeneca, Boehringer Ingelheim, Genentech, Novartis, Regeneron Pharmaceuticals Inc. – consultant; Genentech – speakers bureau. **Saini SS:** National Institutes of Health, Novartis, Regeneron Pharmaceuticals, Inc. – research grants; Allakos, Aquestive, Celltrion, Escient Pharmaceuticals, Genentech, GI Innovation, Granular Therapeutics, Innate Therapies, MedImmune, Novartis, Ono Pharmaceutical, Regeneron Pharmaceuticals, Inc., Sanofi – consultant. **Radin A, Mortensen E:** Regeneron Pharmaceuticals, Inc. – employees and shareholders. **Laws E:** Sanofi – employees, may hold stock and/or stock options in the company.

Presented at the American College of Allergy, Asthma, and Immunology (ACAAI) Annual Meeting, Anaheim, CA, USA, 9–13 November 2023.