Dupilumab Improves Itch in Chronic Spontaneous Urticaria: **LIBERTY-CSU CUPID Study A**

DUPILUMAB

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Background

- Chronic spontaneous urticaria (CSU) is a chronic inflammatory disease characterized by wheals, angioedema, or both that recur for more than 6 weeks.[1,2]
- CSU carries a significant burden of itch that can impact patients' sleep as well as overall health and wellbeing.[3]
- In most cases, CSU spontaneously resolves within 2 to 5 years, but for approximately 20% of patients, CSU can persist for > 5 years.[4] Many patients continue to experience substantial disease burden despite treatment with H1-antihistamines (H1-AH), the standard-of-care for CSU.[3,5]

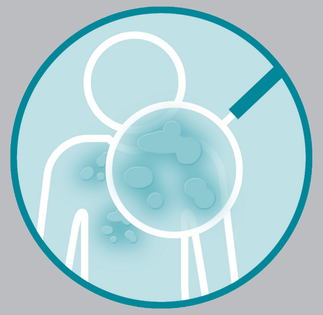
Methods

Study design

- **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.
  - **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**
  - ISS7, range 0–21: sum of daily ISS (ranging from 0 = none to 3 = intense) over 7 days. The ISS7 categorizes disease activity on a scale from 0 (none) to 3 (intense). The minimum important difference (MID) metric is used to define clinically meaningful reduction in CSU itch (≥ 5 points) reported by patients.
  - Itch-free days, range 0–7; number of days with ISS = 0 over 7 days
- **Efficacy endpoints**
  - Baseline patient characteristics
  - Number of itch-free days at Week 24
  - ISS7 at Week 24 and over time
  - Proportion of patients with an ISS7 MID response (≥5) at Week 24
- **Safety endpoints:**
  - Treatment-emergent adverse events (TEAE)
  - Serious adverse events

Objective

- **To evaluate the effect of dupilumab versus placebo on itch symptoms in patients with CSU**



Conclusions

- **Dupilumab resulted in an increased number of itch-free days and a significantly higher proportion of patients reporting an MID improvement in itch, at Week 24 compared with placebo**
- **Dupilumab was well-tolerated, and overall safety was generally consistent with the known dupilumab safety profile**

Results

Table 1. Baseline demographics and disease 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)
Disease duration, n (%)			
0–2 years	34 (50.0)	33 (47.1)	67 (48.6)
2–10 years	22 (32.4)	25 (35.7)	47 (34.1)
> 10 years	12 (17.6)	12 (17.1)	24 (17.4)
Baseline 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)

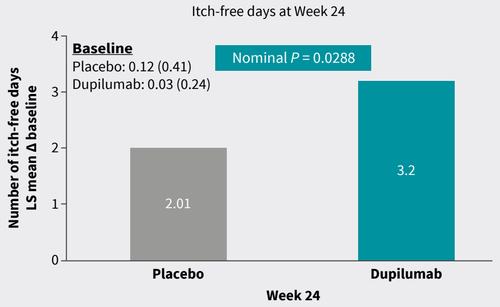
Data are presented as mean (standard deviation) unless otherwise stated.
BMI, body mass index; CSU, chronic spontaneous urticaria; H1-AH, H1-antihistamine; IU, international unit; UAS7, Urticaria Activity Score over 7 days.

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)

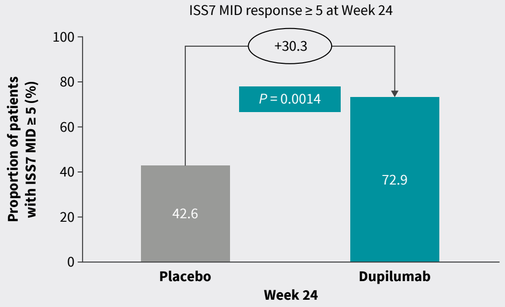
[a]Injection-site reactions by MedDRA High Level Term, n (%): placebo 9 (13.2); dupilumab 8 (11.4). Includes injection-site erythema, injection-site induration, injection-site pain, injection-site pruritus, and injection-site reactions. [b]Conjunctivitis cluster includes conjunctivitis, allergic conjunctivitis, 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; COVID-19, Coronavirus disease 2019; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; SAE, serious adverse event; SOC, system organ class; TEAE, treatment-emergent adverse event.

Figure 1. Number of itch free days in a 7-day period.



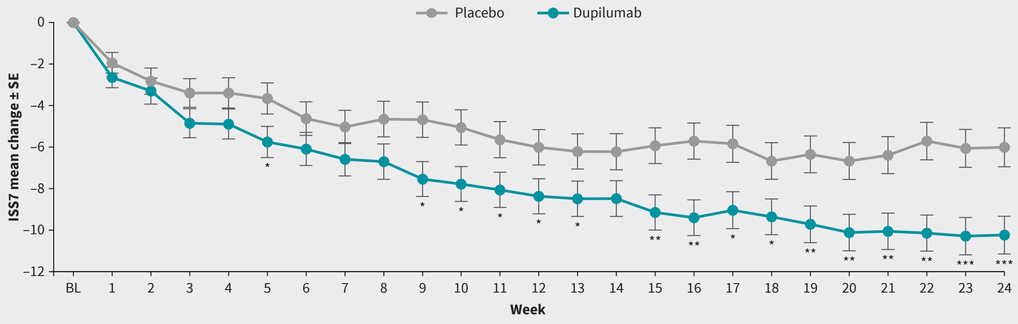
Itch-free days are quantified as the number of days with ISS = 0 over 7 days. Baseline itch-free days data are presented as mean (SD).
LS, least squares; SD, standard deviation; SE, standard error. Nominal *P*-values.

Figure 2. Proportion of participants with MID in itch response (ISS7 reduction ≥ 5) at Week 24.



ISS7, itch severity score over 7 days; MID, minimal important difference.

Figure 3. ISS7 over time and at Week 24



Nominal *P* values, except for Week 12 and 24. *$P < 0.05$, **$P < 0.005$, ***$P < 0.0005$. ISS7, itch severity score over 7 days; SE, standard error.

*This author has been included to serve as a presenter.

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Acknowledgements: Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifiers: NCT04180488. Medical writing support was provided by Hodan Ibrahim, PhD, of Excerpta Medica. Editorial assistance was provided by Tejaswi Ramisetty, Pharm D, of Sanofi, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guideline.

Disclosures: Maurer M: Allakos, Almirall, Amgen, AstraZeneca, Blueprint Medicines, Celldex Therapeutics, Faes Farma, Genentech, GI Innovation, Kyowa Kirin, LEO Pharma, Lilly, Merckle Recordati, Moxie Pharmaceutical, MSD, Novartis, Riemser, Sanofi-Aventis, Third Harmonic, Tribute Pharmaceuticals, UCB, Uriach – speaker and/or consultant and/or institutional research support. **Casale TB**: American Lung Association, Genentech, NIH, Novartis, PCORI, Sanofi – research support; AstraZeneca, Boehringer Ingelheim, Genentech, Novartis, Regeneron Pharmaceuticals Inc. – consultant; Genentech – speakers bureau. **Saini SS**: NIH, Novartis, Regeneron Pharmaceuticals, Inc. – research grants; Allakos, Aquestive, Celltrion, Escient Pharmaceuticals, GBIO, Genentech, GI Innovation, Granular Therapeutics, Innate Therapies, MedImmune, Novartis, Ono Pharmaceutical, Regeneron Pharmaceuticals, Inc., Sanofi – consultant. **Ben-Shoshan M**: Novartis, Sanofi – consultant. **Radin A, Maloney J, Mortensen E, Patel A:** Regeneron Pharmaceuticals, Inc. – employees and shareholders. **Abdulai R, Sugerman P, Bauer D, Laws E**: Sanofi – employees, may hold stock and/or stock options in the company.

Presented at the San Diego Dermatology Symposium (SDDS 2024), San Diego, CA, February 2–4, 2024. Data included in this poster were originally presented at the 12th World Congress on Itch 2023 (WCI 2023); Miami, USA; November 5–7, 2023.