Dupilumab Reduces Disease Activity in Patients with Chronic Spontaneous Urticaria: LIBERTY-CSU CUPID Study A

Chronic Spontaneous Urticaria

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Background

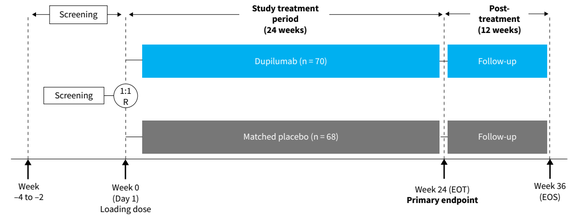
- Chronic spontaneous urticaria (CSU) is a chronic inflammatory disease characterized by wheals, angioedema, or both that recur for more than 6 weeks.[1,2]
- In most cases, CSU spontaneously resolves within 2 to 5 years, but for approximately 20% of patients, CSU can persist for >5 years.[4]
- Approximately 20% patients experience more than one lifetime episode of CSU.[5]
- Many patients continue to experience substantial disease burden despite treatment with standard-of-care H1-antihistamines (H1-AH).[6,7]
- Dupilumab is currently being investigated as a potential novel therapy for the treament patients with CSU who remain symptomatic despite H1-AH treatment.

Methods

LIBERTY-CSU CUPID Study A

- **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 antihistamine (H1-AH) use; Urticaria Activity Score over 7 days (UAS7) ≥16 and Itch Severity Score over 7 days (ISS7) ≥8; omalizumab-naive; patients with active atopic dermatitis were excluded.
- **Background therapy**: Study-defined H1-AH (up to 4-fold the licensed dose)
- **Study assessments**
  - Urticaria Activity Score over 7 days (UAS7, range 0–42): sum of the Hives Severity Score over 7 days (HSS7) and Itch Severity Score over 7 days (ISS7). UAS7 is a validated patient-reported outcome measure (PROM) that categorizes disease activity as; urticaria-free = 0; well-controlled urticaria = 1–6; mild urticaria = 7–15; moderate urticaria = 16–27; severe urticaria = 28–42[3].
- **Efficacy endpoints**
  - Proportion of patients with UAS7 ≤6 from Week 1 to Week 36
  - Proportion of patients with UAS7 =0 from Week 1 to Week 36
- **Safety outcomes**
  - Treatment-emergent adverse events (TEAE) and severe adverse events (SAE)

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 subcutaneous [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; q2w, every 2 weeks; q4w, every 4 weeks.

Objective

- **To report efficacy of dupilumab on disease activity over time in patients with antihistamine-refractory CSU from the LIBERTY-CSU CUPID Study A (NCT04180488).**

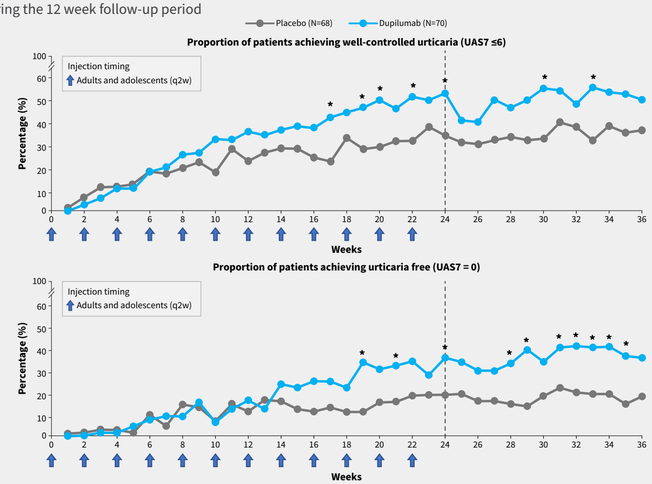
Conclusions

- **The results of this study demonstrate the beneficial effects of dupilumab in omalizumab-naïve patients with CSU who remain symptomatic despite H1-AH treatment.**
- **A numerically greater proportion of patients achieved well-controlled urticaria (UAS ≤6)[1] or urticaria-free (UAS7 =0)[1] with dupilumab versus placebo.**
- **Dupilumab was well tolerated, and the overall safety was generally consistent with the known dupilumab safety profile.**

Results

Figure 2. Proportion of patients who achieve UAS7 ≤ 6 and UAS7 = 0 over time

- Dupilumab treatment resulted in a numerically greater proportion of patients achieving well-controlled urticaria (UAS7 ≤6) from Week 8 and urticaria-free (UAS7 = 0) status from Week 14, vs placebo.
- At Week 24, significantly more dupilumab-treated patients achieved UAS7 ≤6 and UAS7 = 0 ($P = 0.0379$ and $P = 0.0411$, respectively). Following discontinuation of dupilumab at Week 24, symptom control in responder patients persisted during the 12 week follow-up period



*P <0.05; UAS7, Urticaria Activity Score over 7 days
All P values are nominal and not adjusted for multiplicity.

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)
Mean baseline UAS7 (SD)	30.8 (8.2)	31.9 (7.2)	31.3 (7.7)
Mean baseline ISS7 (SD)	15.7 (4.1)	16.1 (4.0)	15.9 (4.0)

Data are presented as mean (standard deviation) unless otherwise stated. BMI, body mass index; CSU, chronic spontaneous urticaria; ISS7, Itch Severity Score over 7 days; SD, standard deviation; 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. Patients may have reported more than one SAE. 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.

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Acknowledgments: Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifiers: NCT04180488. Medical writing/editorial assistance was provided by Hodan Ibrahim, PhD, of Excerpta Medica, 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 Bio, Tribute Pharmaceuticals, UCB, Uriach – speaker and/or consultant and/or institutional research support. **Kaplan A:** Abb-RISA, Annexon, AstraZeneca, Biomarin, Celldex, Genentech, Novartis, Phavaris, Roche, sanofi-aventis – speaker and/or consultant. **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. **Gimenez-Arnau A:** Almirall, Amgen, Avene, Novartis, Faes Farma, Genentech, GSK, Instituto Carlos III-FEDER, Menarini, LEO Pharma, MSD, Sanofi, Thermo Fisher , Uriach Pharma – medical advisor, educational activities and/or institutional research support. **Ensina LF:** Abbvie, Novartis, Sanofi – speaker and/or consultant. **Hide M:** Kaken Pharmaceutical, Kyorin Pharmaceutical, Kyowa-Kirin, Mitsubishi Tanabe Pharma, MSD, Novartis, Sanofi, Taiho Pharmaceutical, Teikoku Seiyaku, Uriach – speaker and/or consultant. **Cyr S:** Regeneron Pharmaceuticals, Inc. – employee and shareholder. **Praestgaard A, Gonzalez T, Sugerman P:** Sanofi – employees, may hold stock and/or stock options in the company.

Presented at the American Academy of Allergy, Asthma and Immunology annual meeting (AAAAI 2024); Washington, DC, USA; February 23-26, 2024.

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