Lirentelimab for Antihistamine-Refractory Chronic Spontaneous Urticaria – Phase 2 Trial in Progress

NCT05528861
"MAVERICK"

Marcus Maurer MD[1,2], Martin Metz MD[1], Hanna Bonnekoh MD[1], Frank Siebenhaar MD[1], Alan T. Chang[3], Rita DeVico[3], Enoch Bortey PhD[3], Cristian Rodriguez MD[3], Craig Paterson MD[3]

[1]Institute of Allergology, Charité – Universitätsmedizin Berlin, Berlin, Germany; [2]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Berlin, Germany; [3]Allakos Inc., San Carlos, CA , USA

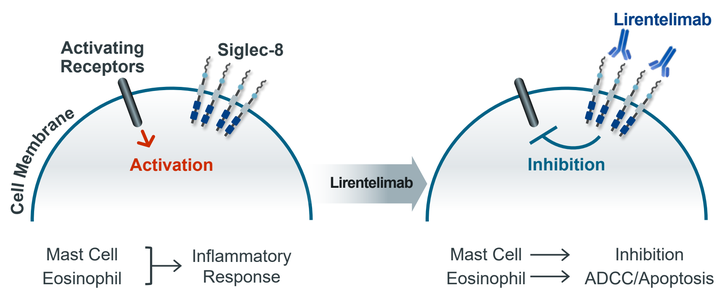
BACKGROUND

- Current treatment guidelines for the management of all forms of chronic urticaria (CU) recommend the use of a non-sedating second generation oral H1-antihistamine (sgAH) as first-line therapy[1]
  - In more than 50% of sgAH-treated patients, symptoms persist despite the use of up to 4 times the licensed dose[1,2]
- In sgAH-refractory patients with chronic spontaneous urticaria (CSU), the only licensed treatment available is omalizumab, a monoclonal anti-IgE antibody[3]
  - Despite omalizumab treatment, a substantial number of patients do not respond[3,4]
- New and targeted treatments are needed

STUDY RATIONALE

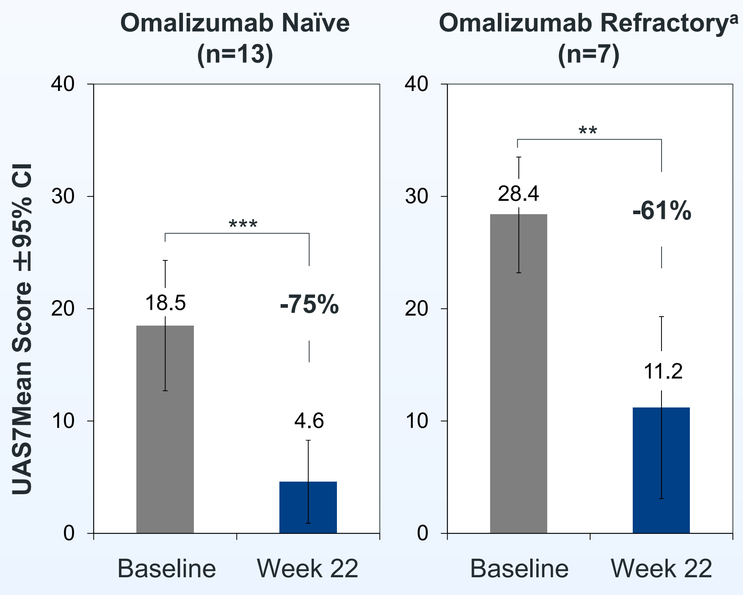
- CSU is a mast cell (MC) driven disease[1]
- Lirentelimab (AK002)* is a humanized IgG1 mAb directed against Siglec-8, which is expressed selectively on MCs and eosinophils, inhibits MCs and depletes eosinophils[5,6]

Figure 1. Lirentelimab (AK002) Mechanism of Action



- Lirentelimab, administered every 4 weeks as an infusion (IV), has been tested in over 700 healthy volunteers and patients with inflammatory and allergic diseases[7-10]
- Overall, lirentelimab IV has been well-tolerated; the most common AE being infusion related reactions (IRRs) typically associated with the initial infusion
- In a phase 1 study, a subcutaneous (SC) formulation of lirentelimab was well-tolerated with no IRRs[10]
- In an open-label phase 2a proof-of-concept study, IV lirentelimab demonstrated a clinical response in patients with sgAH-refractory CSU, naïve or refractory to omalizumab[9]

Figure 2. Change in UAS7 with Lirentelimab in the Phase 2a Proof-of-Concept Study[9]



[a] Patients who received 6 doses
**P<0.01, ***P<0.001

- The results of these studies provide a strong rationale for conducting this phase 2 randomized, double-blind trial of lirentelimab SC in omalizumab-naïve and omalizumab-exposed adults with moderate–severe sgAH-refractory CSU (NCT05528861, "MAVERICK")

STUDY POPULATION

- Adult (18-80 years) subjects with moderate-to-severe CSU inadequately controlled by sgAH are eligible for screening for the study

Key Inclusion Criteria:

- CSU diagnosis for ≥ 6 months
- Diagnosis of moderate-severe CSU refractory to sgAH:
  - Presence of hives and itch for ≥6 consecutive weeks prior to Screening;
  - UAS7 score (range 0–42) ≥16 and HSS7 score (range 0–21) ≥8
- Subjects that are omalizumab-naïve or omalizumab-exposed
- Subjects must be on a stable dose of sgAH, between 1 × and 4 × the licensed dose and frequency, for treatment of CSU for at least 1 week prior to screening

Key Exclusion Criteria:

- Current use of biologics for any indication
- Demonstrated lack of primary response to treatment with a biologic therapy (e.g., omalizumab) for the treatment of CSU
- Use of any of the following treatments need to be stopped prior to the study: immunosuppressive or immunomodulatory drugs; systemic hydroxychloroquine; intravenous immunoglobulin (IVIG); plasmapheresis; oral Janus kinase (JAK) inhibitors; H2-AH; and LTRA
- sgAH use at greater than approved doses or greater than local CSU guideline recommended doses
- Subjects having causes other than CSU for their urticaria including symptomatic dermographism, cholinergic urticaria, or any inducible urticaria
- Diseases other than CU with urticarial or angioedema symptoms, including chronic itching, that in the Investigator's opinion might influence study evaluations and results

STUDY DESIGN

- Approximately 110 subjects with sgAH-refractory CSU will be randomized 1:1 to receive either
  - 6 SC injections of 300mg lirentelimab every 2 weeks or
  - 6 doses of placebo SC every 2 weeks
- Subjects will be stratified at randomization based on omalizumab experience for the treatment of CSU (exposed/naïve) and weekly Urticaria Activity Score (UAS7) values (16-27 or 28-42)
- Subjects who complete the double-blind period of the study, contingent on meeting defined study selection criteria, will be given the option to enroll in an open-label extension (OLE) for 6 doses of 300mg lirentelimab SC
- All subjects will be followed for approximately 12 weeks after the last dose in the double-blind period
- All patients who receive study medication will be included in the safety analysis

Primary Efficacy Objective:

- Absolute change in UAS7 from baseline to Week 12

Key Secondary and Exploratory Objectives:

- Absolute change in weekly Hives Severity Score (HSS7) from baseline to Week 12
- Absolute change in weekly Itch Severity Score (ISS7) from baseline to Week 12
- Proportion of subjects achieving UAS7 = 0 at Week 12
- Proportion of subjects achieving UAS≤6 at weeks 12 and 22
- Change in UCT score at Week 12
- Proportion of subjects achieving Dermatology Life Quality Index (DLQI) = 0 or 1

Figure 3. MAVERICK Study Schema (Randomized Period)

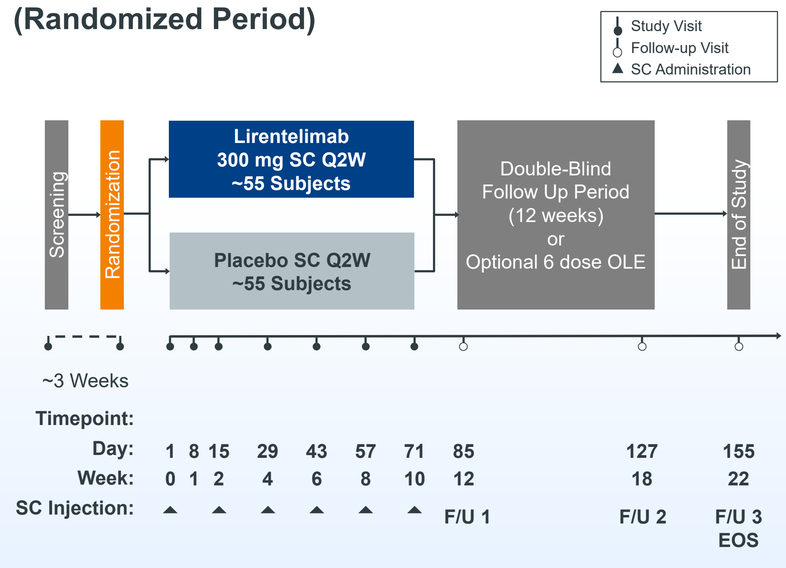


Table 1. Key Efficacy Measures in MAVERICK

Full Name of Measure	Approach
UAS: Urticaria Assessment Score	Patient questionnaire
HSS: Hives Severity Score	Patient questionnaire
ISS: Itch Severity Score	Patient questionnaire
UCT: Urticaria Control Test	Physician interview
DLQI: Dermatology Life Quality Index	Patient questionnaire

STUDY SITES

Figure 4. Current MAVERICK Study Sites in the US and Germany

- This study is planning to enroll from ~70 sites in the USA and Europe

CONCLUSION/DISCUSSION

- In a proof-of-concept trial, lirentelimab was well tolerated and demonstrated clinical activity in omalizumab-naïve and omalizumab–refractory patients with CSU
- Lirentelimab represents a potential novel approach to treat patients with CSU who are refractory to the standard care of non-sedating second generation oral H1-antihistamines
- **This phase 2 randomized, double-blind trial of lirentelimab SC in omalizumab-naïve and omalizumab-exposed adults with moderate–severe sgAH-refractory CSU is currently enrolling!**
- Please visit clinicaltrials.gov (NCT05528861) or email maverick.info@allakos.com to learn more

*Lirentelimab is an investigational medicine, its efficacy and safety profile have not been established, and it has not been approved by the FDA.

References: (1) Zuberbier T, et al. Allergy 2022.; (2) Maurer M, et al. Allergy 2011.; (3) Metz M, et al. Clin Rev Allergy Immunol 2020.; (4) Maurer M, et al. Clin Exp Allergy 2020.; (5) Youngblood BA, et al. Int Arch Allergy 2019.; (6) Youngblood BA, et al. Cells 2020.; (7) Dellon E, et al. NEJM 2020.; (8) Anesi S, et al. J Allergy Clin Immunol 2022.; (9) Altrichter S, et al. J Allergy Clin Immunol 2022.; (10) Allakos data on file.

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