Phase 2 Trial in Progress: Lirentelimab in Adults with Moderate-to-Severe Atopic Dermatitis Inadequately Controlled by Topical Treatments

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NCT05155085
"ATLAS"

BACKGROUND

- Atopic dermatitis (AD) is a chronic pruritic inflammatory dermatitis that affects approximately 16.5 million (7.3%) adults in the US, of which around 6.6 million (40%) have moderate-to-severe disease[1,2]
- The current standard of care includes topical treatments supplemented with corticosteroids with and without immunosuppressants[3,4]
- Patients with AD inadequately controlled by topical treatments and immunosuppressants are often treated with biologics and/or JAK inhibitors (JAKi)[5,6]
  - Some patients do not have an adequate clinical response or are unable to tolerate JAKi or available biologics[7]
- New and targeted AD treatment options are needed

SCIENTIFIC RATIONALE

- Mast cells (MCs) and eosinophils are implicated in the pathogenesis of AD[8-10]
- Sialic acid-binding Ig-like lectin (Siglec)-8 is expressed selectively on MCs and eosinophils; engagement with an antibody results in broad inhibition of MC activation and eosinophil depletion[11,12]
- Lirentelimab (AK002)* is a humanized IgG1 mAb directed against Siglec-8, which is expressed selectively on MCs and eosinophils
- Preclinical data demonstrates that lirentelimab can broadly inhibit multiple modes of MC activation that drives AD pathogenesis[13-15]

Figure 1. Lirentelimab Mechanism of Action

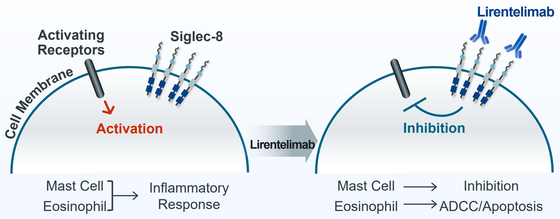
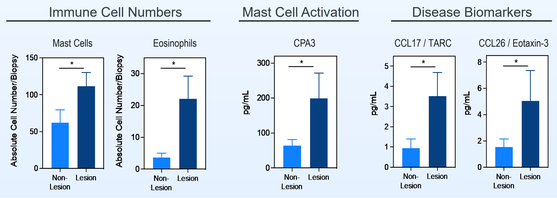


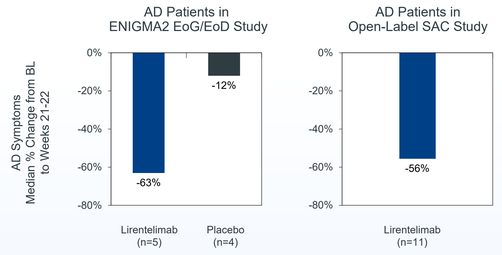
Figure 2. AD Lesional Biopsies Show Evidence of MC and Eosinophil Activity[13-15]



STUDY RATIONALE

- Lirentelimab, administered every 4 weeks as an infusion (IV), has been tested in over 700 healthy volunteers and patients with inflammatory and allergic diseases; in those with concomitant AD, improvements in AD were observed

Figure 3. Lirentelimab Improved AD Symptoms in Patients with Concomitant EoG/EoD and SAC[16,17]



- 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
- This phase 2 proof-of-concept, randomized, double-blind, placebo-controlled study, represents the evaluation of lirentelimab SC in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments (NCT05155085, "ATLAS")

STUDY POPULATION

- Adult (18-80 years) with moderate-to-severe AD inadequately controlled by topical treatments are eligible for screening

Key Inclusion Criteria:

- Male or female aged 18 - 80 years
- Chronic AD present for at least 3 years with moderate-to-severe symptoms:
  - Eczema Area and Severity Index (EASI) score ≥16
  - Involvement of ≥10% of the body surface area (BSA)
  - Investigator Global Assessment (IGA) score ≥3
- Documented recent history of inadequate response to treatment with medications such as topical corticosteroids, calcineurin inhibitors, JAKi, or PDE4 inhibitors (crisaborole)
- Patients who are biologic-naïve or biologic-exposed
- The patient will apply a stable dose of non-medicated, non-prescription, topical emollient at least twice daily for 7 consecutive days before the baseline visit

Key Exclusion Criteria:

- Current use of biologics for any indication
- Demonstrated lack of primary response to treatment with a biologic for the treatment of AD
- Treatments need to be stopped prior to study: phototherapy for AD, immunosuppressive or immunomodulatory drugs (systemic calcineurin inhibitors, mTOR inhibitors, anti-metabolites, alkylating agents, TNF inhibitors, eosinophil-depleting drugs, etc.), systemic corticosteroids, and oral JAK inhibitors
- Any ongoing use of topical corticosteroids, topical calcineurin inhibitors, topical JAK inhibitors, or topical PDE4 inhibitors
- Presence of skin comorbidities/concomitant conditions that may interfere with study assessments or interpretation of study results

STUDY DESIGN

- 130 patients will be randomized 1:1 to receive either:
  - 7 SC injections of 300mg lirentelimab every two weeks, *OR*
  - 7 doses of placebo SC every two weeks
- Patients 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 7 doses of 300mg lirentelimab SC
- All patients will be followed for approximately 12 weeks after the last dose
- All patients who receive study medication will be included in the safety analysis

Primary Efficacy Objective:

- Proportion of patients who achieve EASI-75 (≥75% improvement in EASI) at Week 14 compared with baseline

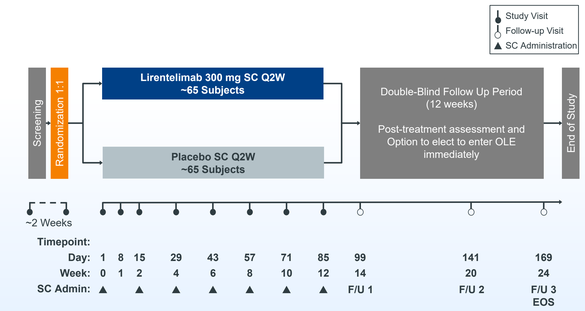
Key Secondary and Exploratory Objectives:

- Proportion of patients who achieve an IGA score of 0 or 1 AND a ≥2-point improvement at week 14
- Percent change in EASI from baseline to week 14
- Change from baseline to Week 14 in SCORAD, Pruritus NRS, VAS sleep score
- Time to EASI response
- Proportion of patients who achieve EASI-50 and EASI-90

Table 1. Key Efficacy Measures in ATLAS

Full Name of Measure	Approach
EASI: Eczema Area and Severity Index	Physician evaluation
IGA: Investigator Global Assessment	Physician evaluation
BSA: Body Surface Area	Physician evaluation
SCORAD: Scoring Atopic Dermatitis Index	Physician and Patient evaluation
ppNRS: Peak Pruritus Numeric Rating Scale	Patient Questionnaire
DLQI: Dermatology Life Quality Index	Patient Questionnaire

Figure 4. ATLAS Study Schema (Randomized Period)



STUDY SITES

Figure 5. Current ATLAS Study Sites in the USA

- This study is currently enrolling from ~70 sites in the USA and Europe

CONCLUSIONS/ DISCUSSION

- Mast cells and eosinophils are key effector cells in the pathogenesis of atopic dermatitis
- Lirentelimab (AK002) is an anti-Siglec-8 antibody has demonstrated inhibition of mast cells and rapid depletion of eosinophils in preclinical and clinical studies, and was generally well tolerated
- Given the significant unmet need despite available therapies, lirentelimab represents a potential novel targeted treatment for AD
- **This phase 2 randomized, double-blind, placebo-controlled study of lirentelimab SC in adults with moderate-to-severe AD is currently enrolling**
- Please visit clinicaltrials.gov (NCT05155085) or email atlas.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) Silverberg JI, Dermatol Clin 2017; (2) Chiesa Fuxench ZC, et al., J Invest Dermatol 2019; (3) Eichenfield LF, et al. J Am Acad Dermatol 2014; (4) Hong JJ, et al. Dermatol Ther (Heidelb) 2021; (5) Deleanu D, Nedelea I. Exp Ther Med 2019; (6) Newson M, et al., Drugs 2020; (7) Silverberg JI, et al. J Eur Acad Dermatol Venereol 2021; (8) Voss M, et al. Int J Mol Sci 2021; (9) Lee HJ, et al. Int J Mol Sci 2021; (10) Stander S.NEJM 2021 (11) Youngblood BA, et al. Cells 2020; (12) Schanin J, et al. Mucosal Immunol 2021; (13) Youngblood BA, et al., JCI Insights 2019; (14) Schanin J, et al., Mucosal Immunology 2020; (15) Benet Z, et al. Allergy Journal 2022 (EAACI); (16) ENIGMA 2 data on file; (17) Anesi S, et al. J Allergy Clin Immunol 2022

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