Inflammatory Off Treatment

**Phase 3 Multi-Center Trial Evaluating the Efficacy, Safety and Tolerability of Isunakinra (EBI-005) in Subjects with Moderate to Severe Allergic Conjunctivitis**

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**ABSTRACT**

**PURPOSE:** Although many patients with acute allergic conjunctivitis (AAC) are well controlled, large numbers of patients have late phase AAC symptoms which are inadequately treated or require high potency topical corticosteroids. The goal of this phase 2 trial was to determine the safety and efficacy of a direct topical interleukin-1 receptor inhibitor developed for the treatment of subjects with chronic allergic conjunctivitis. This double blind, randomized, vehicle-controlled, phase 2 trial in 115 subjects with AAC, Isunakinra showed a statistically significant improvement in ocular symptoms when compared to vehicle. Based on these results, we are now proceeding with a phase 3 study to evaluate topical Isunakinra compared with vehicle in subjects with both, pre-defined and post-genotyping topical interleukin-1 receptor inhibition.

**METHODS:** In this multi-center, randomized, double masked, vehicle controlled study, 115 patients with moderate to severe allergic conjunctivitis were randomized to either topical Isunakinra (25 mg/ml) or vehicle 3 times daily for 14 days. A primary endpoint of improvement from baseline in morning ocular itching in subjects treated with Isunakinra compared to vehicle for the 14 days with highest peak mean score (mean ocular itching score for Isunakinra was 152 and Vehicle was 140). There was no treatment difference between Isunakinra and vehicle in the CAC portion of the study.

**RESULTS:** Treatment was generally safe and well tolerated. In a study drop out rate was less than 10%. In addition to AC, randomized subjects also had 128 patients with systemic allergy. The discontinuations in topical treatment were generally due to treatment with oral corticosteroids (10%). In addition to AC, randomized subjects also had an additional 82 patients with systemic allergy. All discontinuations in topical treatment were generally due to treatment with oral corticosteroids (10%). In addition to AC, randomized subjects also had an additional 82 patients with systemic allergy. All discontinuations in topical treatment were generally due to treatment with oral corticosteroids (10%).

**CONCLUSIONS:** Isunakinra is a novel topical interleukin-1 receptor inhibitor developed for topical application. In this clinical study, treatment with topical Isunakinra was generally safe and well tolerated. There was no treatment difference between Isunakinra and vehicle in the CAC portion of the study.

**STUDY DESIGN**

- **Isunakinra 5 mg/ml — 3 times daily (130 subjects)**
- **Vehicle Control — 3 times daily (130 subjects)**

- **5 Eliot**

- **P3 Isunakinra (EBI-005) AC Study Results**
- **258 subjects randomized at 11 sites in U.S.**
- **Isunakinra was generally safe and well tolerated in this study.**
- **Isunakinra treated and vehicle treated subjects had an improvement in allergic conjunctivitis signs and symptoms from baseline.**
- **The study missed its primary endpoint of improvement from baseline in morning ocular itching in subjects treated with Isunakinra compared to vehicle for the 14 days with highest peak mean score (mean ocular itching score for Isunakinra was 152 and Vehicle was 140).**
- **There was no treatment difference between Isunakinra and vehicle in the CAC portion of the study.**

- **Ocular Itching Over 28 Day Study Period (ITT, SE) **
- **Ocular Redness Over 28 Day Study Period (ITT, SE)**

**STUDY RESULTS**

- **Baseline Demographics**
- **P2 trial Exploratory Analysis: Genotyping**
- **Distribution for Genotyped Subjects**
- **1.8 Million U.S.**

**REFERENCE**


**ACKNOWLEDGMENTS**

- Jay Rubin, MD San Antonio, TX Eye Clinics of South Texas
- Thomas Mundorf, MD Charlotte, NC Mundorf Eye Center

- **KEY MESSAGES**

  - The late phase allergic conjunctivitis response is an unmet medical need in AC.
  - Isunakinra (formerly EBI-005) is an interleukin-1 receptor inhibitor which demonstrated statistically significant improvement in ocular itching, total nasal symptoms and total nasal symptoms in a direct conjunctival allergen repeat challenge model in a P2 trial but did not show statistically significant separation from vehicle in this P3 environmental trial.
  - Isunakinra was generally safe and well tolerated in this study over the month study period.
  - Most subjects in this study showed an improvement from baseline for both ocular and systemic allergic conjunctivitis in both the isunakinra treated group and vehicle control group. This improvement was greater than improvement seen during treatment with topical clobetasol alone.
  - Pilot study was conducted to assess clinical relevance of high IL1 producers identified by genotyping demonstrated a group of subjects with greater responses to isunakinra therapy relative to vehicle than was seen for the overall study population (ITT).

- **PRESENTATION: #2307: Poster #C021 - SWOS Annual Meeting, Session # 3: T2, Session Title: Allergicconjunctivitis / Clinical Immunology and Allergy. This poster describes that Isunakinra in patients with moderate to severe allergic conjunctivitis was well tolerated, Sunday, May 3, 2010 from 8:00 AM to 10:15 AM PT.**

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