ABSTRACT

Methods

In a double-masked, placebo-controlled study, 74 subjects with moderate to severe DED were randomized to receive vehicle control or EBI-005 (5 mg/ml). Subjects received the study medication three times a day for 6 weeks and were allowed to use rescue artificial tears provided by the sponsor (Refresh Plus®, Allergan Pharmaceuticals, Irvine, CA). Subjects recorded the number of vials of artificial tear used in a diary and were not allowed to use rescue tears within two hours of dosing of the study medication.

RESULTS

Subjects treated with EBI-005 used fewer rescue artificial tears than vehicle control treated subjects over the six week study period. Increased use of rescue artificial tears may play a key role in the magnitude of the vehicle response seen in many DED studies. Although not a composite driver of the clinical response in DED studies, the use of rescue artificial tears has been shown to be safe and well tolerated at both doses. These results were previously presented (Goldstein MH, 17th TFOS, 2013).

BACKGROUND

In therapeutic studies in dry eye disease (DED), the placebo response is well documented with a magnitude of effect of 20-35% on signs and symptoms of DED compared with baseline. This response is believed to be principally a result of two components: the placebo response typically seen in therapeutic drug trials and the wetting or lubricating effect of the topically applied vehicle. A third component, however, may play an important role in the vehicle response: the concomitant use of rescue artificial tears.

RESOURCES

Efficacy of the Active Ingredient

Clinical Studies in Dry Eye are impacted by multiple factors

- Key drivers include:
  - Inhibitor efficacy
  - Clinical driver (history of tear use)
  - Patient characteristics

Rescue tear use

- 11 vials (35% or 9 of 26) (p value=.005). Of the 10 heaviest artificial tear users, eight (80%) were receiving EBI-005. This effect continued for up to six weeks of treatment.

Safety and Efficacy

EBI was found to improve the signs (total corneal fluorescein staining) and symptoms of DED (patient eye questions from OSDI). These subjects who started with baseline OSDI score of under 50 showed the largest separation between the drug treated group and vehicle control group. EBI-005 was also shown to be safe and well tolerated at both doses. These results were previously presented (Goldstein MH, 17th TFOS, 2013).

MEASUREMENTS

- Natural environment study
- Double receptor controlled
- 8 centers, 36 patients
- CFS: Baseline, 14 days, and washout
- OSDI screen moderate-to-severe
- Pre-defined analysis of combined dose arms
- Rescue tear use allowed

Safety & tolerability

- 11 vials (35% or 9 of 26) (p value=.005). Of the 10 heaviest artificial tear users, eight (80%) were receiving EBI-005. This effect continued for up to six weeks of treatment.

CONCLUSIONS

- The use of rescue artificial tears has been a mainstay of treatment in dry eye disease for many years to ease the symptoms of the disease.
- Increased use of rescue artificial tears may play a key role in the magnitude of the vehicle response seen in many DED studies.
- Subjects with higher OSDI scores (greater symptoms) used more rescue artificial tears than those with lower OSDI scores.
- Subjects treated with EBI-005 used far fewer rescue artificial tears than vehicle control treated subjects over the six week study period.
- Reduction in rescue artificial tears is supportive of biological activity of topical EBI-005 in improving the symptoms of DED.
- Reduction of rescue artificial tears by patients may have important pharmacoeconomic impact and potentially decreases patient treatment burden.

KEY REFERENCES

- Foulks GN, Challenges and Pitfalls in Clinical Trials of Treatments for Dry Eye, Ophthalmology 120 (11): 2030