A Randomized, Multi-Center, Double-Masked, Vehicle-Controlled, Parallel-Group Phase 2b Allergic Conjunctivitis Clinical Trial of Topical Ocular ADX-102, a Novel Aldehyde Sequestering Agent

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INTRODUCTION

Pro-inflammatory aldehyde mediators potentiate allergic (TH2) and auto-immune (TH1) inflammation. ADX-102 (reproxalap) represents a new immune-modulating drug class focused on the sequestration of pro-inflammatory aldehyde-containing mediators, which we refer to as RASP (Reactive Aldehyde Species that are Pro-inflammatory). ADX-102 is in development for the treatment of the immediate post-histaminic inflammatory phase of allergic conjunctivitis (AC) and other ocular inflammatory diseases. Post-histaminic AC, which begins 5 to 10 minutes following allergen exposure, is distinct from the acute histamine-mediated phase of AC that is partially prophylactically modulated by antihistamines.

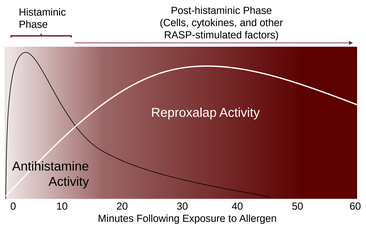

Figure 1. Schematic depicting histaminic vs post-histaminic RASP mediated post allergen challenge phases.

Histamine rises and falls more rapidly than post-histaminic factors. Thus, the activity of antihistamines is acute and transient, whereas the activity of RASP sequestration increases over time. Based on the activity seen in Phase 2a, a Phase 2b clinical trial was performed to evaluate the safety and efficacy of 0.1% and 0.5% topical ocular ADX-102 in the Conjunctival Allergen Challenge (Ora-CAC®) model in subjects with AC.

MATERIALS and METHODS

A randomized, multi-center, double-masked, vehicle-controlled, parallel-group trial of 0.1% and 0.5% ADX-102 topical ophthalmic solution was conducted in 154 subjects with seasonal and perennial AC at 5 US sites. Subjects with a history of AC were required to have a reproducible moderate to severe bilateral ocular allergic reaction following baseline CAC visits. Subjects were randomized (1:1:1) to receive 0.1% ADX-102, 0.5% ADX-102, or vehicle drops bilaterally. Subjects were challenged ~60 minutes after dosing (1-hour duration CAC). Approximately 14 days later, subjects were dosed again and challenged ~10 minutes after dosing (10-minute onset CAC). Subject-reported ocular itching (range 0 to 4) was recorded from 5 to 60 minutes post-CAC.

RESULTS

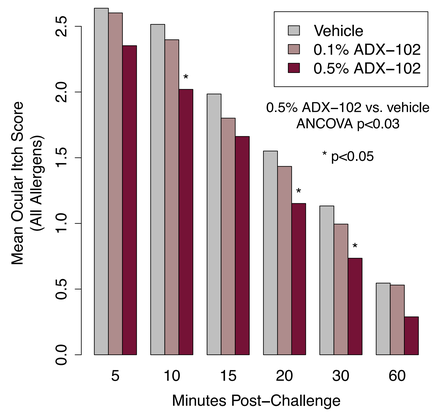

Figure 2. ADX-102 at the 10-minute onset CAC visit was statistically superior to control in reducing allergic ocular itch in seasonal and perennial AC patients 10 to 60 minutes after allergen challenge, during the post-histaminic phase.

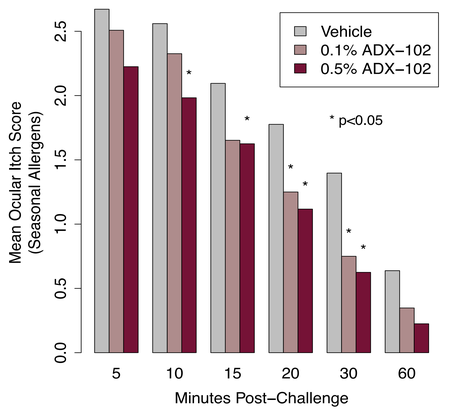

Figure 3. ADX-102 at the 10-minute onset CAC visit was statistically superior to control in reducing allergic ocular itch in seasonal AC patients 10 to 60 minutes after allergen challenge, during the post-histaminic phase.

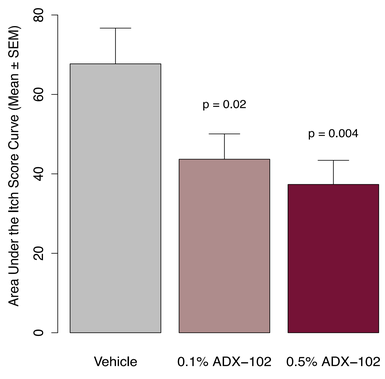

Figure 4. Area under the curve (10 to 60 minutes post-challenge) from the 10-minute onset CAC visit indicated a durable effect of ADX-102 in reducing ocular itch score in seasonal AC patients in a manner that is statistically superior to that of control.

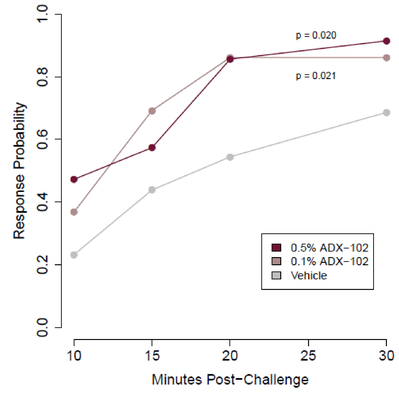

Figure 5. When a responder is defined as a patient that improves one point from peak baseline itch score, odds ratio analysis from the 10-minute onset CAC visit indicated that ADX-102-treated seasonal AC patients were more than three times as likely to achieve clinical response.

SUMMARY

The primary objective of this trial was to evaluate the efficacy of 0.1% ADX-102 and 0.5% ADX-102 ophthalmic solutions compared to vehicle in the treatment of allergen-induced conjunctivitis using the conjunctival allergen challenge (Ora-CAC®) model. Subject-reported ocular itching was statistically lower in the 0.5% ADX-102 group vs. the vehicle group 10 minutes, 20 minutes and 30 minutes post-challenge, and also across all time points in aggregate (p<0.03), at the 10-minute onset of action CAC visit. A dose-response relationship was observed. At the 1-hour duration CAC visit, a similar pattern of activity was seen, but was not statistically significant.

In seasonal AC patients, who generally responded to drug treatment more robustly than perennial patients, statistically significant results were observed at individual time points in both ADX-102 groups, and ocular itch score area under the curve 10 to 60 minutes post-challenge was statistically lower in the ADX-102 groups than the vehicle group. Responder analysis in seasonal allergic conjunctivitis patients (1-point improvement from baseline on the ocular itching scale) supported the clinical relevance of the results. The responder odds ratio vs. vehicle was greater than 3 (p=0.02) for each of the ADX-102 groups.

Both concentrations of ADX-102 were safe and well tolerated.

CONCLUSIONS

ADX-102 treatment was effective in the treatment of itching during the immediate post-histaminic inflammatory phase of AC. A consistent dose response was observed.

The durability of activity of ADX-102 over one-hour post-challenge in the CAC model exceeds that reported for antihistamines.

Disclosures: Gomes (E), Brady (E), Hollander (E), Clark (E)