Novel Small Molecule Aldehyde Sequestering Agents Demonstrate Broad Therapeutic Potential for Ocular Inflammation

Susan G. Macdonald, Ph.D.; Adna Halilovic, Ph.D.; Todd Brady, M.D., Ph.D.
Aldeyra Therapeutics, Inc.

RESULTS (continued)

In the MD model, daily reproxalap or ADX-103 treatment decreased formation of A2E by 71% or 69%, respectively, compared with vehicle controls (Figure 1). In a separate study, systemic (IP) doses of reproxalap, 5-fold greater than the effective dose in the A2E study, administered for 56 days, had no effect on dark adaptation (data not shown). Daily treatment with reproxalap or ADX-103 for 56 days had no effect on body weight, nor were any drug-related adverse effects observed.

In the LPS-induced uveitis model, ocular exam scores were significantly improved, compared to vehicle, at 6 hours and 24 hours after TO administration of reproxalap or ADX-103. After IVT administration of reproxalap or ADX-103, ocular exam scores were also significantly improved vs. vehicle. Small, although not significant, reductions in MDA adducts were observed in the reproxalap and ADX-103 groups after TO and IVT administration (data not shown). To control for variations between individual animals, a within-subject statistical analysis, examining the co-variates of treatment and time, was conducted on the retina-choroid scores from the IVT groups. Retina-choroid scores in rats were significantly improved following IVT treatment with either reproxalap or ADX-103, compared to vehicle control (Figure 7).

CONCLUSIONS

Two structurally distinct aldehyde traps have shown activity in two models of ocular inflammation following ocular (TO, IVT) and systemic (IP) administration. No evidence of ocular or systemic toxicity was noted with any route of administration. Overall, the data suggest that aldehyde sequestration has broad potential for the treatment of a range of ocular diseases in which inflammation plays a role, including diseases involving the posterior pole and the anterior chamber.

Disclosures: Macdonald (E), Halilovic (E), Brady (E)