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CASE STUDY

# Ophthalmic Clinical Case Study, Palovarotene (POS)

## STUDY OVERVIEW

An ophthalmic solution formulation of palovarotene (POS), a selective retinoic acid receptor γ agonist, is in Phase I trials to assess the safety, tolerability, and pharmacokinetics of ascending doses in the treatment of dry eye disease (DED).

## STUDY DETAILS

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| **Class of Drug or Device:** | Ophthalmic solution |
| **Indication:** | Dry eye disease (DED) |
| **Population Type:** | Healthy adults |
| **# of Participants:** | 48 |

## STUDY PURPOSE

The objective of this study was to determine the ocular and systemic safety, tolerability, and pharmacokinetics of ascending doses of POS in healthy adults.

## METHODS

This was a single-center, randomized, double-masked, vehicle-controlled Phase I study in healthy adults. Participants were randomized 3:1 to receive either POS (at 0.025, 0.05, or 0.10 mg/mL) or vehicle (placebo-to-match POS). Six cohorts of eight participants were planned for evaluation (six participants in the POS group and two in the vehicle group); three cohorts were each administered treatment once daily (QD) or twice daily (BID) for seven consecutive days. Escalation to the next dose required Review Committee approval. Healthy adults, 18 to 55 years of age, were eligible for this study. Safety was assessed by physical examinations, vital signs, ECGs, clinical laboratory parameters, ocular assessments, adverse events (AEs), and treatment emergent ocular adverse events (TEOAEs). Blood samples for PK assessments of POS were collected from study participants prior to and following dose administration.

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## RESULTS

36 participants were randomized to POS and 12 to vehicle. Overall, 89 TEOAEs were reported by 22 participants (61%) receiving POS and 10 TEOAEs were reported by five participants (42%) receiving vehicle. Erythema, irritation, and skin dryness of the eyelid were the most common TEOAEs in participants receiving POS. Overall, the incidence of TEOAEs and eyelid-related findings in participants treated with POS increased with ascending dose and frequency compared with participants treated with vehicle. All TEOAEs were mild (96.6%) or moderate (3.4%), and resolved without sequelae. There were no serious AEs. Similar PK profiles were observed for the QD and BID regimens following multiple ascending doses of POS. No meaningful difference was observed between the PK profile of POS following the a.m. and p.m. doses during BID treatment.

## CONCLUSION

The administration of POS was generally well tolerated at doses up to and including 0.10 mg/mL BID. These data support further investigation of the safety and efficacy of POS in patients with DED.

## ABOUT ALTASCIENCES

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