Clinical Pharmacokinetics of Oxymetazoline Cream following Topical Facial Administration for the Treatment of Erythema Associated with Rosacea

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Purpose
Oxymetazoline is FDA-approved in over-the-counter eye drops and nasal sprays and is being investigated as a topical cream to treat moderate to severe erythema associated with rosacea. The aim of this analysis was to characterize the pharmacokinetic profile of oxymetazoline following once- (QD) and twice-daily (BID) topical facial administration of oxymetazoline cream in patients with moderate to severe rosacea-associated erythema.

Methods
This was a multicenter, randomized, double-blind, parallel-group, vehicle-controlled study. Patients received 0.5%, 1.0%, or 1.5% oxymetazoline cream, QD or BID (6 hours post first dose) for 28 days. Blood samples were collected days 1 and 28 at predose, 2, 4, 6, 8, 10, 12, and 24 hours post dose with additional trough samples day 14 and a final sample day 35 after all other assessments. Oxymetazoline plasma concentrations were measured using a validated LC-MS/MS method with a lower limit of quantitation of 10 pg/mL. Pharmacokinetic analysis was conducted using non-compartmental analysis. Demographic and pharmacokinetic parameters were summarized using descriptive statistics. Patients who received ≥1 treatment were included in the pharmacokinetic and safety cohorts.

Results
356 patients were randomized; 95% (N=339) completed the study. Patients were primarily female and Caucasian. Steady state appeared to be reached by day 2 after the second and third dose for the QD and BID groups, respectively. Systemic exposure increased approximately dose proportionally. Mean maximum observed concentrations were ≤115 pg/mL across all groups. Drug accumulation on day 28 was minimal following QD dosing. Across all groups, mean effective half-life was 18-28 hours, indicating a possible depot effect. A total of 118 (33.1%) patients reported an adverse event (AE). The majority were local AEs and mild or moderate in severity; most common was headache (4.8%, N=17). Five serious AEs in 3 (0.8%) patients were reported; however, none were treatment related.

Conclusion
Steady state appeared to be reached quickly with subnanomolar systemic exposure following repeat topical administration to the maximum intended surface area (~4% BSA, entire face). Overall, topical facial application of oxymetazoline cream was well tolerated.