Performance of automated hyperemia assessment in allergic conjunctivitis interventional study

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Introduction
• Ocular hyperemia is an important efficacy1, safety2, and tolerability3 endpoint in ophthalmic clinical trials.
• Validated subjective standardized scales, e.g. the validated bulbar redness scale4 and McMonnies/Chapman-Davies scale5, suffer from intra- and inter-grader variability necessitating large study populations.
• Objective methods of assessing ocular hyperemia offer the potential to reduce the length and/or size of clinical trials.
• A novel automated approach called Imaging System for Ocular Surface (ISOS)6 may offer a robust method to measure hyperemia grade with the added detail of vessel morphology.

Objective
Explore the reproducibility and sensitivity of automated ocular hyperemia efficacy readout in a double-blind interventional study in allergic conjunctivitis

Methods
• Twenty three subjects were randomly assigned to receive two slit lamp photographs of their right temporal conjunctiva after seven days of either 0.1% Dexamethasone (Maxidex®) ophthalmic solution or vehicle control BID in a double blinded fashion as part of NCT02079649.
• Between slit lamp photographs, subjects were dosed with study medication just before spending 3 hours in an environmental exposure chamber (EEC) in which ragweed pollen was circulated at 3500 ± 500 particles per m³.

Methods (cont.):
• Photographs were immediately scored using the validated bulbar redness scale from 0 to 4 in 0.5 increments by one of two ophthalmologists (live scoring) and later by three fully-blinded expert graders.
• A consensus expert score was calculated for each 25x photo to minimize grader variability which was estimated by repeated scorings and modeling.
• 35 morphological parameters (e.g. vessel density, length and width, # triple points, etc.) of the conjunctival vasculature were calculated using an automatic vessel segmentation algorithm from each 25x photograph.
• Multivariate linear regression models were used to predict live and expert consensus scores from the morphological parameters.
• The Maxidex® effect was explored via a linear mixed model of change from Pre-EEC relative to vehicle group for hyperemia scores and image descriptors.
• Estimated N-sizes were made based on observed mean change and standard deviation within the Maxidex® treatment group using a paired t-test model.

Results
• Pre-EEC vs Post-EEC and vehicle treated groups
• A significant Maxidex® response (p<0.05) relative to vehicle was observed in consensus expert and automated scores with further characterization of the response offered by vessel density, vessel length, and # triple points (Figure 5).
• Improved reliability of automated hyperemia readouts offer the potential for reduced study sizes (Table 1).

Conclusions
• ISOS-based hyperemia assessment offers a deeper understanding of the hyperemia response with a high degree of reliability.
• Its application in additional indications and further implementation enhancements could dramatically improve the efficiency for future clinical trials.

References
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Disclosures
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• MIW, CLG, and SC are employees (E) of Novartis Institutes of Biomedical Research.
• BL and RD are employees (E) of ADCIS and consult (C) for Novartis.