

SUPPLEMENTARY MATERIAL

Supplementary methods

Secondary efficacy measures

The following secondary efficacy measures were evaluated at 7 (± 1), 15 (± 1), and 20 (± 1) minutes post-CAC at visits 4b and 5, using the following Ora Calibra scales.

Conjunctival redness evaluated by the investigator, 0 to 4 scale (0.5 unit increments were allowed):

- 0 = none (normal, no dilated blood vessels)
- 1 = mild, slightly dilated blood vessels
- 2 = moderate, more apparent dilation of blood vessels, with redder color, involving majority of the vessel bed
- 3 = severe, numerous and obvious dilated blood vessels, with deep red color and no chemosis, or less red with chemosis
- 4 = extremely severe, large, numerous, dilated blood vessels characterized by unusually severe deep red color regardless of chemosis and involving the entire vessel bed)

Ciliary redness evaluated by the investigator (same scale as conjunctival redness).

Episcleral redness evaluated by the investigator (same scale as conjunctival redness).

Chemosis evaluated by the investigator, 0 to 4 scale (0.5 unit increments were allowed):

- 0 = none
- 1 = mild, detectable only by slit lamp beam; definite separation of conjunctiva from sclera
- 2 = moderate, visible in normal room light; more diffuse edema
- 3 = severe, conjunctival billowing at the limbus; very diffuse and noticeable
- 4 = extremely severe, overall ballooning of conjunctiva

Eyelid swelling evaluated by the subject, 0 to 3 scale (0.5 unit increments not allowed):

- 0 = none
- 1 = mild, detectable swelling
- 2 = moderate, definite swelling
- 3 = severe, swelling with decrease in space between upper and lower lids

Tearing evaluated by the subject, 0 to 4 scale (0.5 unit increments not allowed):

- 0 = none/normal
- 1 = mild, noticeable decreased moistening
- 2 = moderate, eye feels "full" of water, lashes feel a little wet
- 3 = severe, feels like tears might drip down face, very wet lashes
- 4 = very severe, tears dripping down face

Rhinorrhea, nasal pruritus, ear or palate pruritus, and nasal congestion, each evaluated by the subject, from a 0 to 4 scale (0.5 unit increments not allowed):

- 0 = none
- 1 = mild
- 2 = moderate
- 3 = moderate/severe
- 4 = severe

Safety measures

The following safety measures were evaluated:

- Adverse events assessed at all office visits.
- Visual acuity at a distance utilizing an ETDRS chart conducted at Visit 2, 3, 4a, 4b, and 5. The cornea, conjunctiva, anterior chamber, lens, and eyelid were assessed in both eyes.
- Slit lamp biomicroscopy conducted at Visits 2, 3, 4a, 4b, and 5. Slit lamp biomicroscopic observations were graded as “Normal” or “Abnormal.” “Abnormal” findings were categorized as clinically significant (findings that could interfere with study parameters or otherwise confound the data as determined by the investigator) or not clinically significant. The cornea, conjunctiva, anterior chamber, lens, and eyelid were assessed in both eyes.
- Intraocular pressure measured at Visit 2 and Visit 5. All IOP measurements were performed in both eyes with a Goldmann applanation tonometer.
- Dilated fundoscopy measured at Visit 2 and Visit 5. Dilated fundus exams were performed using indirect ophthalmoscopy to observe the vitreous, retina, macula, choroid, and optic nerve. Observations were graded as normal or abnormal.

Supplementary Table 1. Sequence of Events and Procedures

Visit	Visit 1	Visit 2	Visit 3	Visit 4a	Visit 4b	Visit 5	Phone call
Day	-50 to -22	-21 ± 3	-14 ± 3	1	16 h (+1) from Visit 4a	8 ± 3	15 ± 3
PROCEDURE							
General Assessments							
Informed Consent and HIPAA ¹	X						
Demographic Data	X						
Medical and Medication History	x						
Update Medical and Medication History		X	X	X	X	X	X
Allergic Skin Test	X						
Urine Pregnancy Test ²		X		X		X	
Review Inclusion/Exclusion Criteria	X	X	X	X			
Randomization				X			
AE (nTEAE/TEAE) Assessment	X	X	X	X	X ³	X ⁶	X
Allergen Challenge							
Titration CAC		X					
Confirmation CAC			X				
16 h Duration of Action CAC					X		
15 m Onset of Action CAC						X	
Signs and Symptoms Assessments		X	X	X ⁴	X	X	
Relief Drop Instillation ⁵		X	X		X	X	
Visual/Systems Exams							
Visual Acuity		X	X	X	X	X ⁶	
Slit Lamp Bio microcopy		X	X	X	X	X ⁶	
Intraocular Pressure		X				X	
Dilated Fundoscopy		X				X	
Investigational product (IP)							
IP Instillation				X ⁷		X ⁸	
Drop Comfort & Descriptor Assessment				X			

¹ In the event that a subject has a medical condition, medication/contact lens washout, or needs to speak with the Investigator prior to Visit 1, the subject was given an informed consent form. Medical/medication history, demographics, skin test, and inclusion/exclusion review were performed at the time of informed consent signing prior to Visit 1 but must be confirmed at Visit 1 (with the exception of demographics and skin test).

² Urine pregnancy testing was performed, if applicable, for females of childbearing potential.

³ Performed pre-CAC and post-CAC

⁴ Only pre-CAC

⁵ Relief medication could be administered to subjects at the end of Visits 2, 3, 4b, and 5, after all evaluations were completed.

⁶ Performed pre-CAC and post-CAC as part of the safety exit exam

⁷ 16 hour (+1 hour) pre-CAC

⁸ 15 (+1) minutes pre-CAC

Supplementary Figure 1. Patient disposition (CONSORT diagram).

