Prospective, Randomized, Double-Masked, Vehicle-Controlled Study to Evaluate the Safety and Efficacy of Topical Risuteganib (ALG-1007) in the Treatment of Dry Eye Disease

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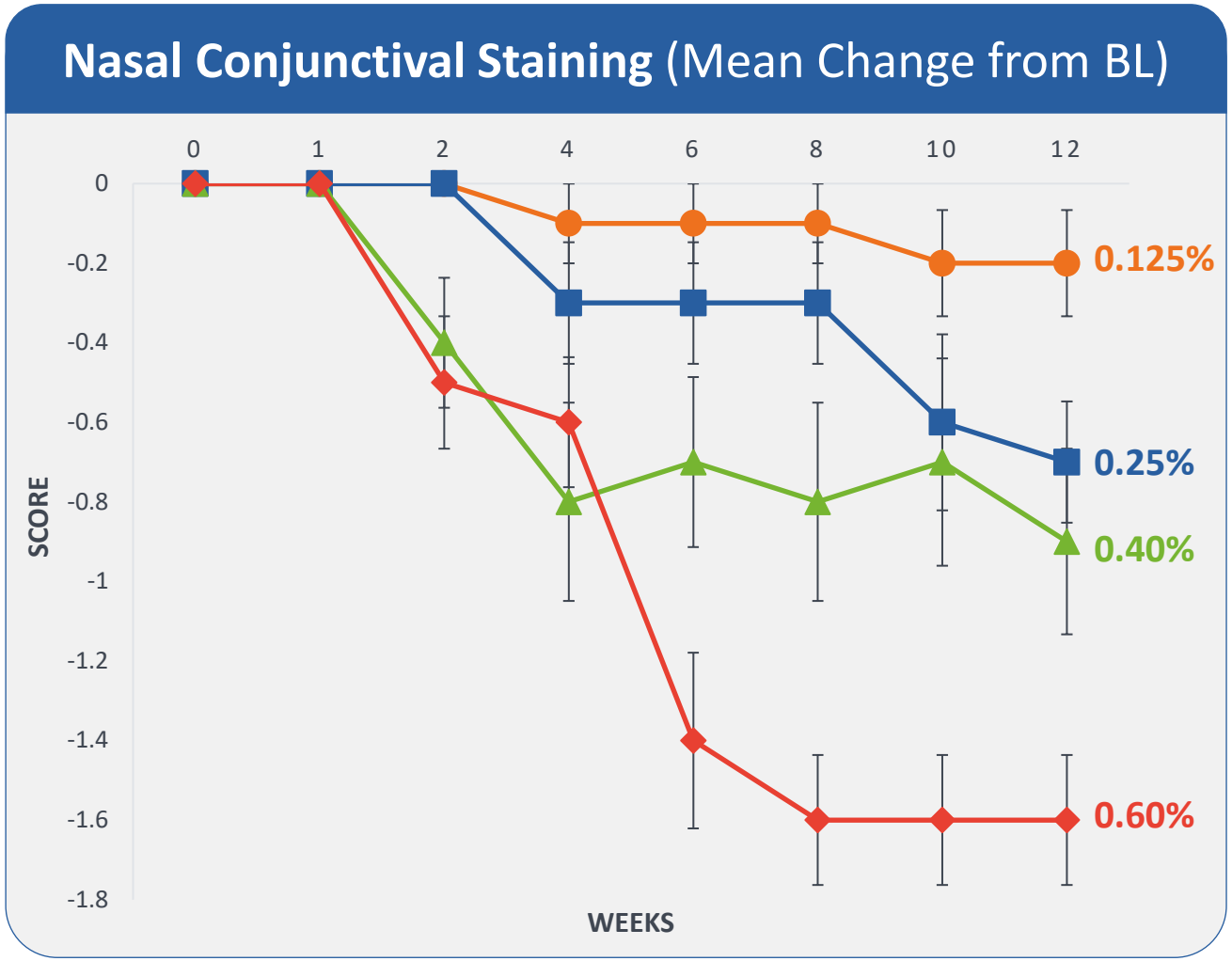
ASCRS
July 24, 2021

Financial Disclosures

Background

- Growing evidence shows that Dry Eye Disease (DED) is associated with **inflammation** and **oxidative stress due to mitochondrial dysfunction**.[1]
- Risuteganib's ability to downregulate these pathways makes it a promising candidate for DED treatment.[2]
- Initial dose-ranging DED ex-US study (2019) in 40 eyes demonstrated a dose-response.[3]
  - 4 groups: 0.125%, 0.25%, 0.4% and 0.6%
  - 10 patients per group
  - 1 drop 2x/day
- 0.6% showed the strongest efficacy

Results from Initial Dose-Ranging Study *(p<0.001)*



1. Dogru M, Kojima T, Simsek C, Tsubota K. Potential Role of Oxidative Stress in Ocular Surface Inflammation and Dry Eye Disease. Invest Ophthalmol Vis Sci. 2018 Nov 1;59(14):DES163-DES168. doi: 10.1167/iovs.17-23402. PMID: 30481822. 2. Yang P, Shao Z, Besley NA, Neal SE, Buehne KL, Park J, Karageozian H, Karageozian V, Ryde IT, Meyer JN, Jaffe GJ. Risuteganib Protects against Hydroquinone-induced Injury in Human RPE Cells. Invest Ophthalmol Vis Sci. 2020 Aug 3;61(10):35. doi: 10.1167/iovs.61.10.35. PMID: 32818234; PMCID: PMC7443126. 3. Lindstrom R, *et al*. Safety and efficacy of ALG- 1007 topical ophthalmic solution – A synthetic peptide that regulates inflammation, in patients with dry eye disease: An exploratory Phase I, open-label, single-center clinical study. Am J Ophthalmic Clin Trials 2020;3:10.

Objectives

- Determine the safety & efficacy of topical 0.6% RSG (best dose from previous study)

- Test against control

- Determine the contribution of each ingredient to the effect

Study Design

- Conducted January 2020 – May 2020
- Prospective, randomized, double masked, vehicle-controlled study
- 1 site ex-US, 12-week study
- 1 drop 2x per day
- 4 study arms (n=16 per arm)
  1. Vehicle
  2. Vehicle + 0.125% Sodium Hyaluronate (**SH**)
  3. Vehicle + 0.6% Risuteganib (**RSG**)
  4. **ALG-1007:** Vehicle + 0.125% **SH** + 0.6% **RSG**

Assessments

- Signs
  - TBUT
  - Cornea staining – 0 to 4
  - Conjunctiva staining – 0 to 4
- Symptoms
  - Dry Eye Management Scale (DEMS) – 0 to 10
  - Visual Analog Scale (VAS) – 0 to 100

Study Population

Inclusion Criteria

- Symptoms of DED for ≥ 6 months
- Must meet all criteria:
  - Inferior cornea staining score ≥ 2
  - Nasal conjunctival staining score ≥ 2
  - Dry Eye Management Scale (DEMS) score ≥ 5

Exclusion Criteria

- History of: ocular herpetic keratitis, ocular surgery in the past 6 months, LASIK surgery, use of glaucoma medicine
- Subjects with DED secondary to scarring or destruction of conjunctival goblet cells (i.e., chemical burn)
- Current use of active DED treatment (i.e., lifitegrast, cyclosporine, mast cell stabilizers, anti-histamine, corticosteroids). Washout period of 45 days is required for subjects who are on active DED treatment

Statistical Analysis

Sample Size Calculation

Based on previous study, an analysis comparing each active arm with placebo, adjusting for multiplicity by the use of Dunnett comparisons, will yield over 95% power with the planned sample size of 64 subjects.

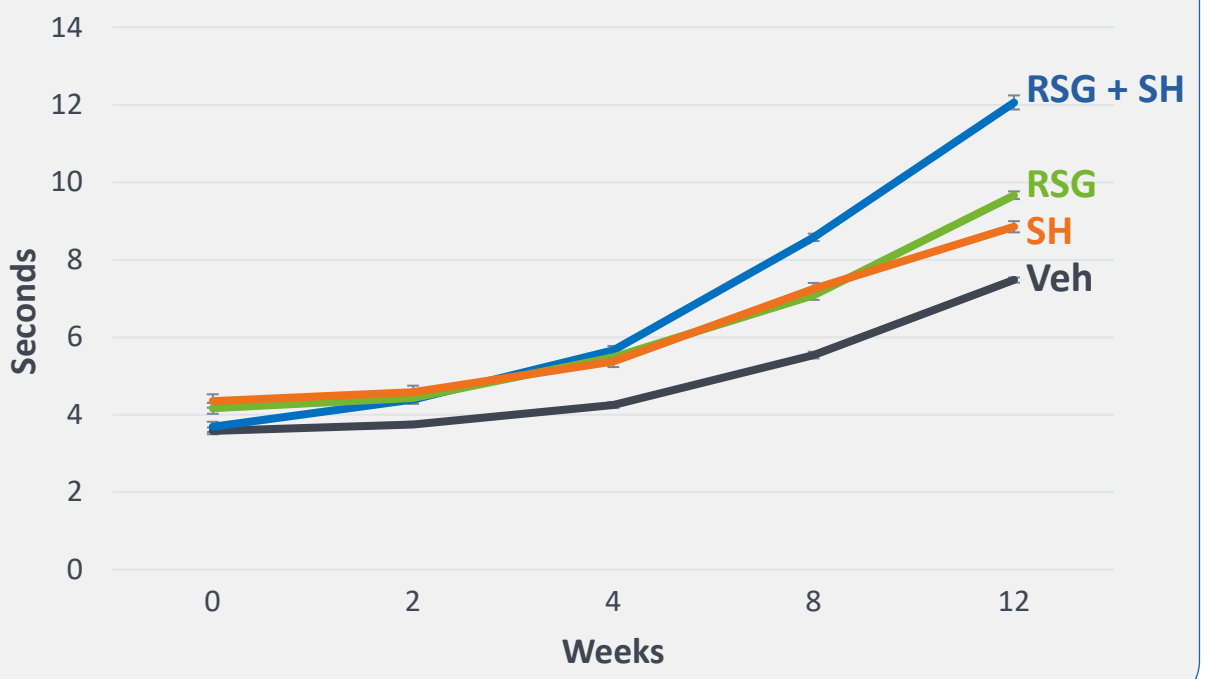
Change from baseline in signs and symptoms were summarized at each visit.

Change from baseline in signs and symptoms were analyzed at week 12. A repeated-measures ANOVA was used, due to the dependence between paired eyes.

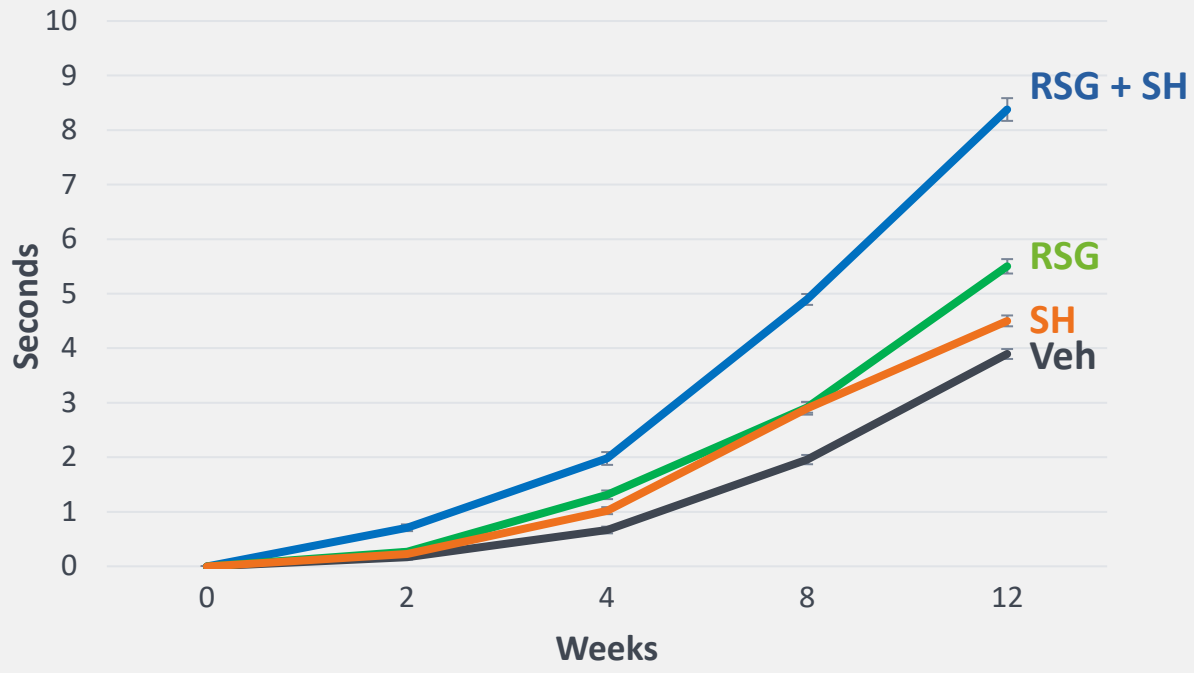
All possible group comparisons were made using post-hoc adjustment by the Tukey-Kramer method.

Results: Tear Break up Time (TBUT)

TBUT (n=16 per arm)



TBUT CFB (n=16 per arm)

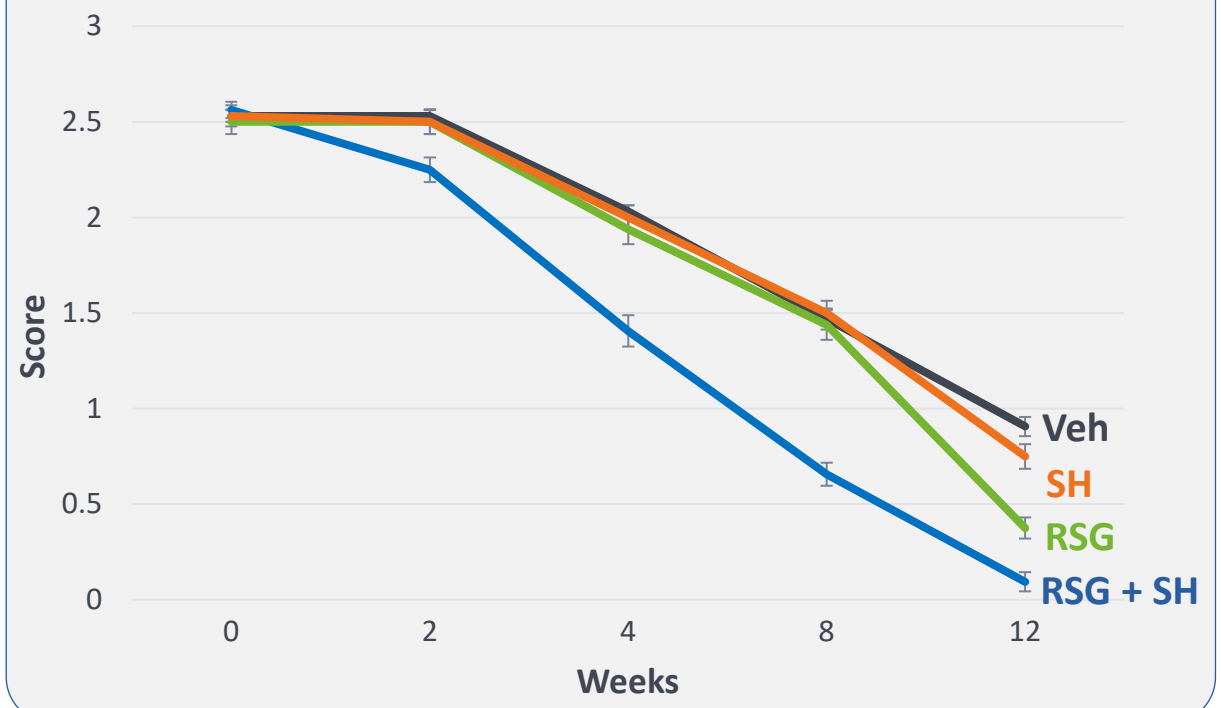


Arm	Comparator arm	P-value (Tukey-Kramer adjusted)
ALG 1007 (Veh + SH + RSG)	Veh	<.0001
ALG 1007 (Veh + SH + RSG)	Veh + SH	<.0001
Veh + RSG	Veh	<.0001
Veh + RSG	Veh + SH	0.0027

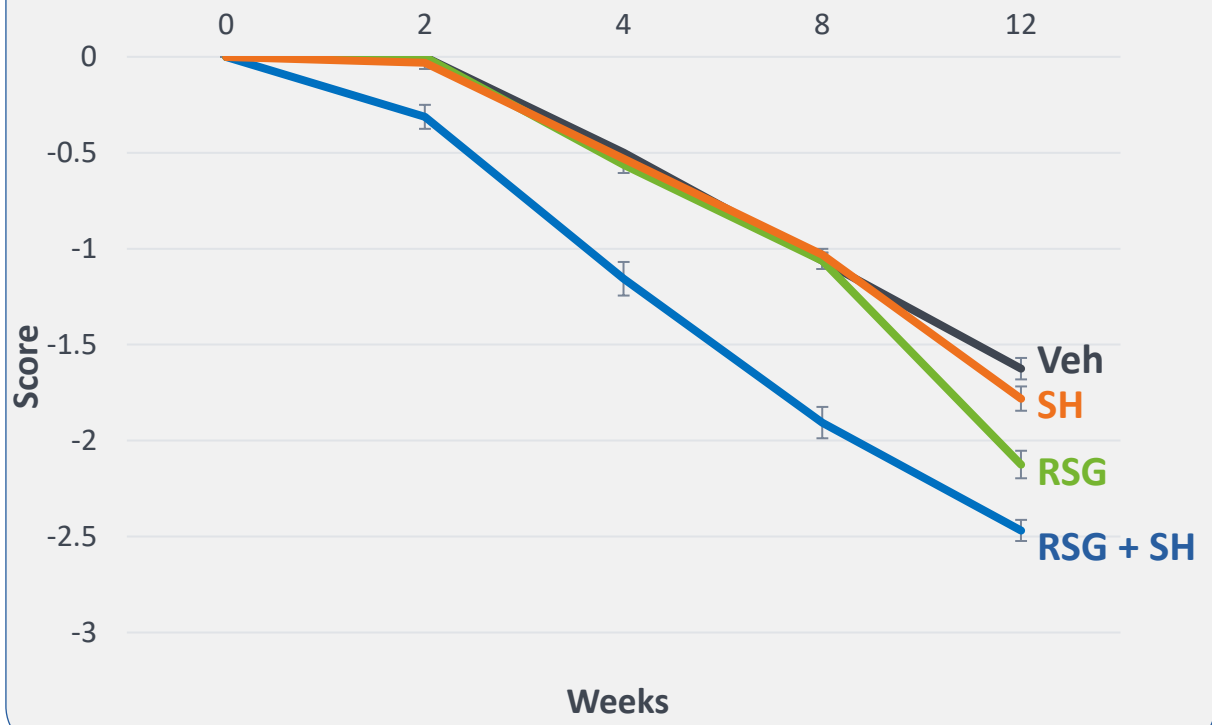
Error bar = 1 SEM

Results: Cornea Inferior Staining

Cornea Inferior (n=16 per arm)



Cornea Inferior CFB (n=16 per arm)

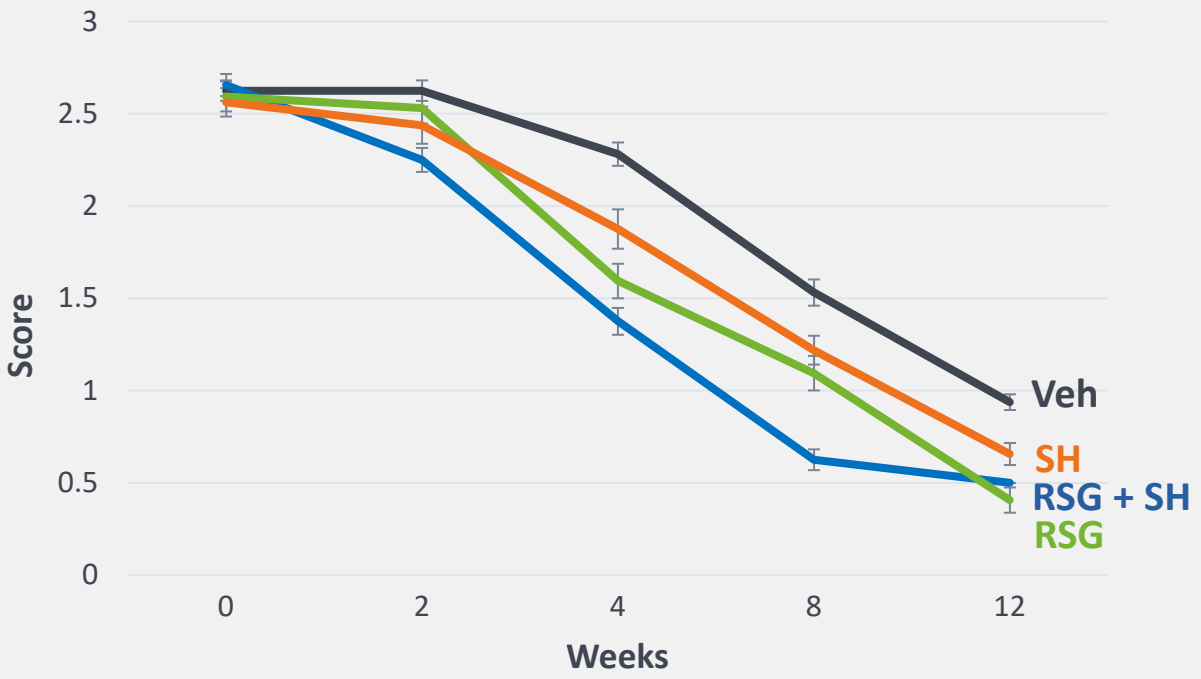


Arm	Comparator arm	P-value (Tukey-Kramer adjusted)
ALG 1007 (Veh + SH + RSG)	Veh	<.0001
ALG 1007 (Veh + SH + RSG)	Veh + SH	<.0001
Veh + RSG	Veh	<.0001
Veh + RSG	Veh + SH	<.0001

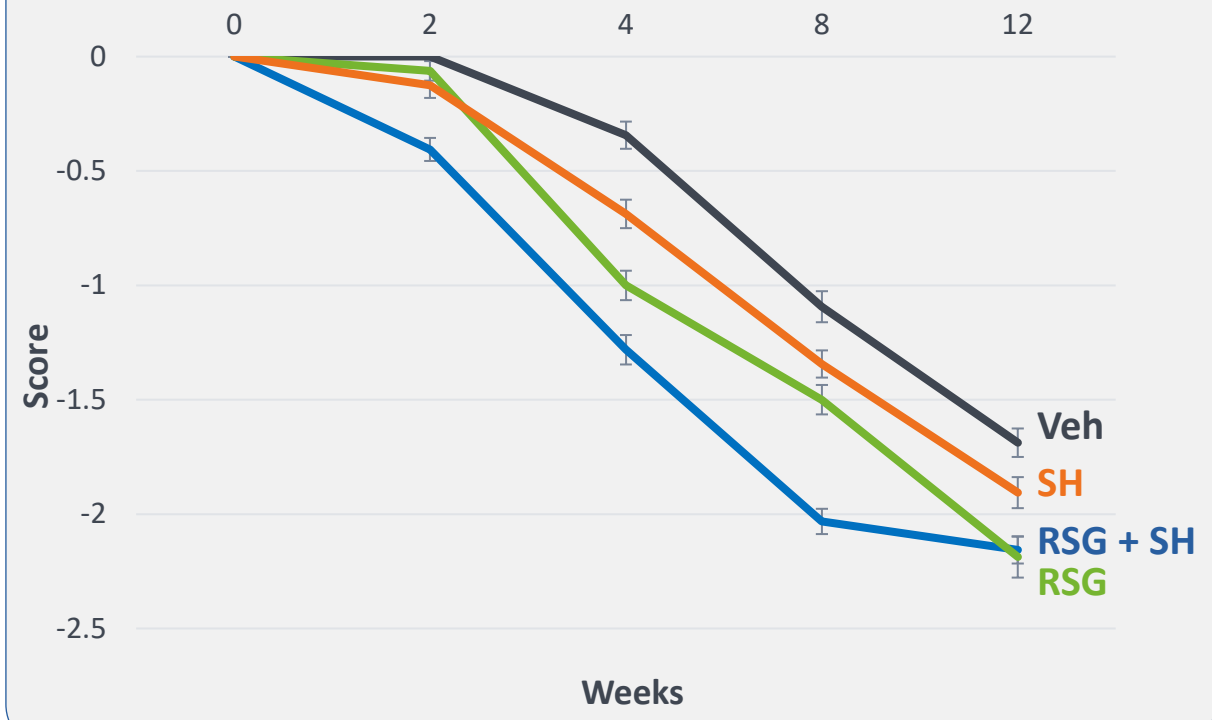
Error bar = 1 SEM

Results: Nasal Conjunctiva Staining

Nasal Conjunctiva (n=16 per arm)



Nasal Conjunctiva CFB (n=16 per arm)

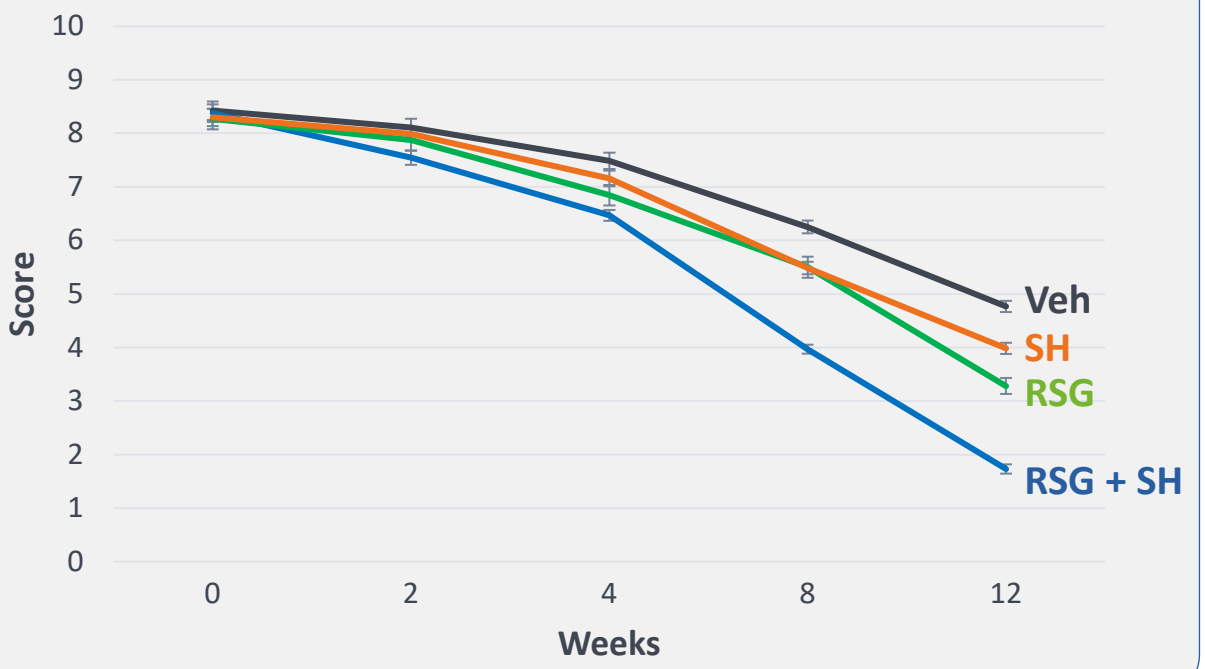


Arm	Comparator arm	P-value (Tukey-Kramer adjusted)
ALG 1007 (Veh + SH + RSG)	Veh	<.0001
ALG 1007 (Veh + SH + RSG)	Veh + SH	.0004
Veh + RSG	Veh	<.0001
Veh + RSG	Veh + SH	.0055

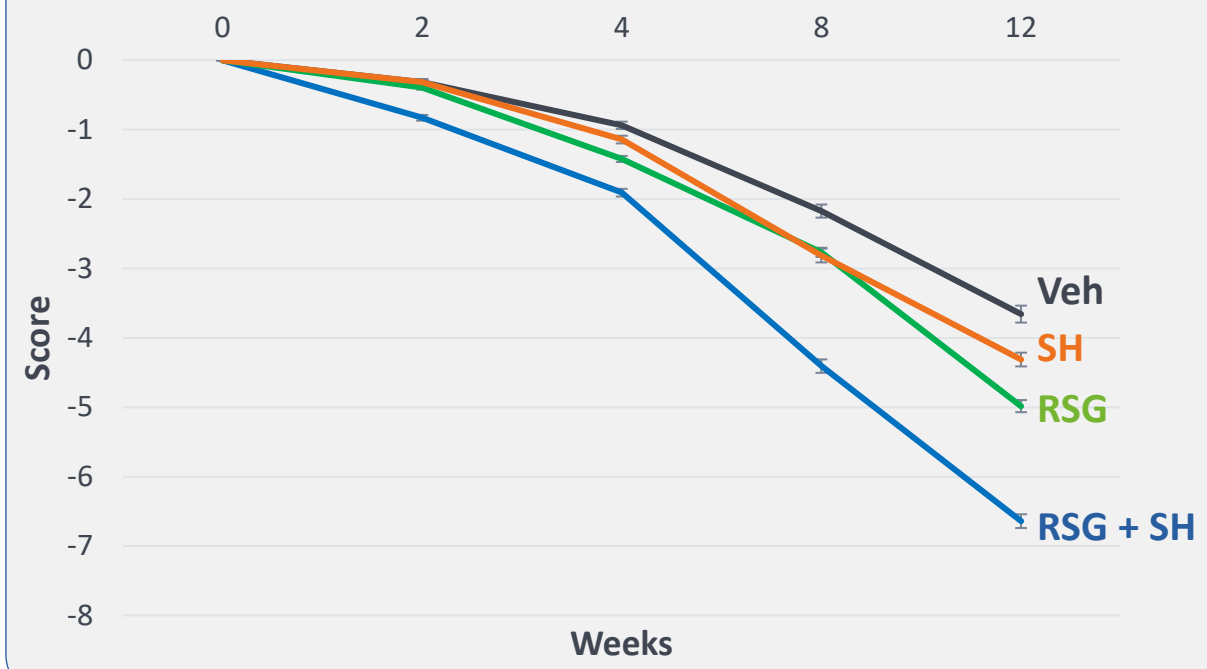
Error bar = 1 SEM

Results: Dry Eye Management Scale (DEMS)

DEMS (n=16 per arm)



DEMS CFB (n=16 per arm)

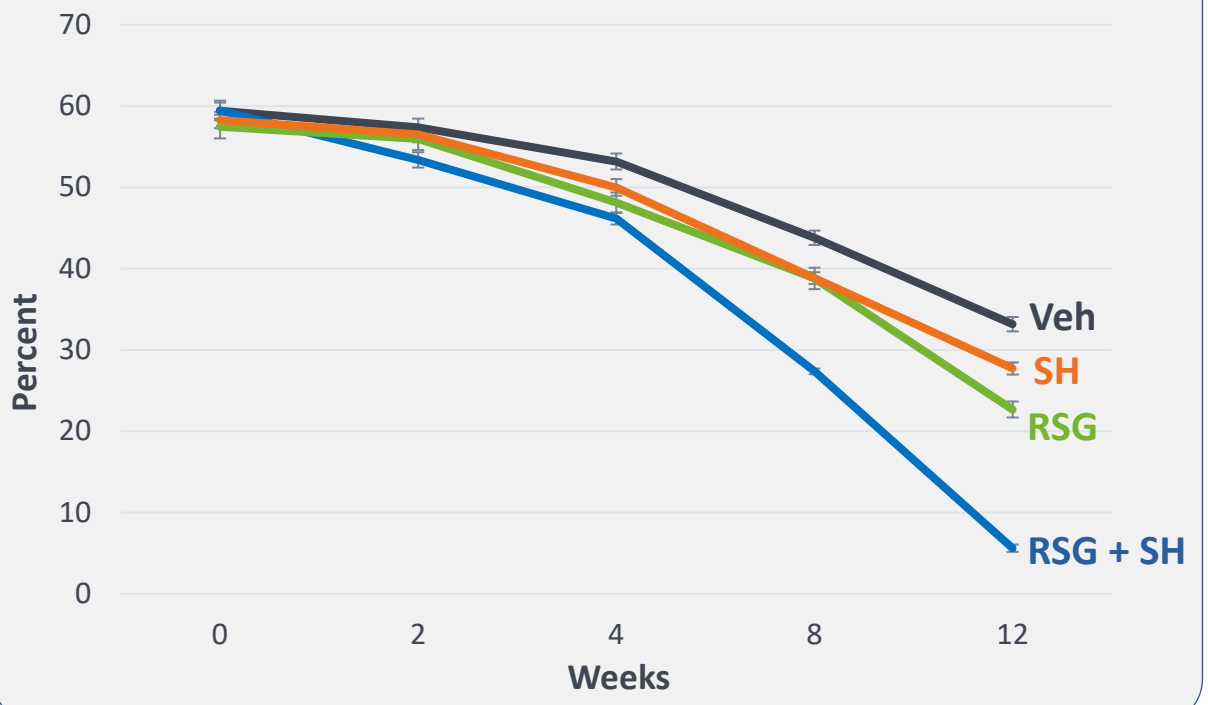


Arm	Comparator arm	P-value (Tukey-Kramer adjusted)
ALG 1007 (Veh + SH + RSG)	Veh	<.0001
ALG 1007 (Veh + SH + RSG)	Veh + SH	<.0001
Veh + RSG	Veh	<.0001
Veh + RSG	Veh + SH	.0004

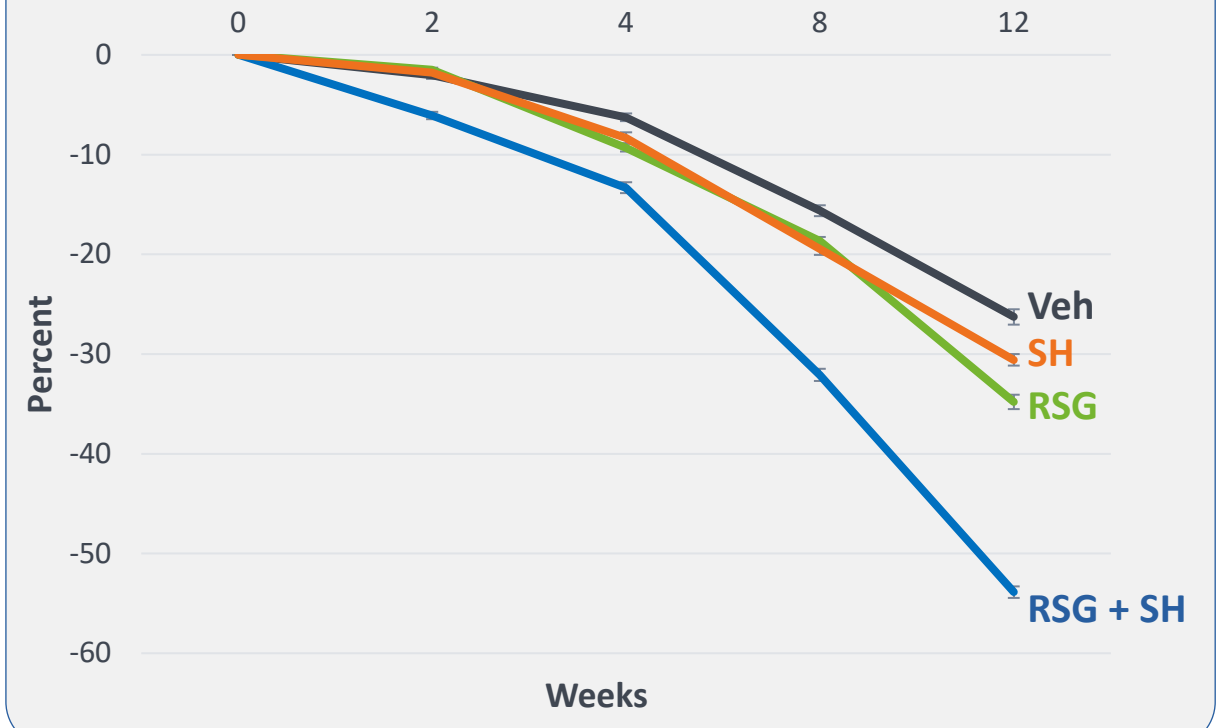
Error bar = 1 SEM

Results: Visual Analog Scale (VAS)

VAS Combined (n=16 per arm)



VAS Combined CFB (n=16 per arm)



Arm	Comparator arm	P-value (Tukey-Kramer adjusted)
ALG 1007 (Veh + SH + RSG)	Veh	<.0001
ALG 1007 (Veh + SH + RSG)	Veh + SH	<.0001
Veh + RSG	Veh	<.0001
Veh + RSG	Veh + SH	.0009

Error bar = 1 SEM

Conclusions

- Efficacy was observed in increasing order (Veh < Veh+SH < Veh+RSG < ALG1007)
- Statistically significant difference between active & control groups
- No AEs, ocular irritation or prolonged blurring of vision reported.
- Study suggests promising results for ALG1007 for the treatment of signs & symptoms of DED
- These results support the development of a larger US Phase 2b study

THANK YOU