

OCT Anatomic & Temporal Biomarkers in Uveitic Macular Edema

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1. Clearside Biomedical, Inc.

Financial Disclosures

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Background

- There is limited information on longitudinal structure-functional correlations in Uveitic Macular Edema (UME).
- In clinical practice, physicians often base treatment decisions on BCVA and/or OCT assessment.
- This study assessed these relationships, focusing on baseline anatomic features with potential prognostic value for visual response.

Phase 3 – Suprachoroidal CLS-TA

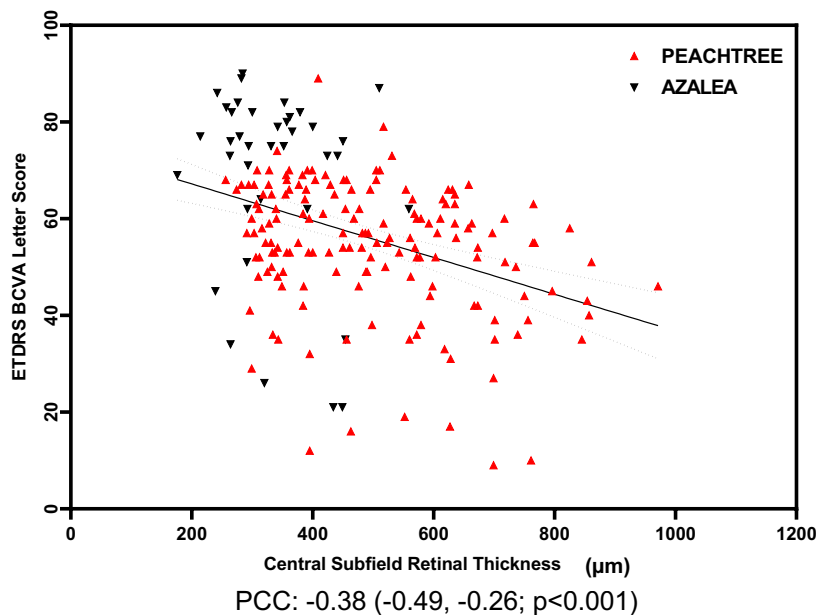
- Post hoc analysis of 198 eyes with NIU enrolled in two phase 3, 24 week clinical trials with CLS-TA (triamcinolone acetonide injectable suspension)^{1, 2}.
- Assessed relationships between BCVA and
 - **Ellipsoid zone (EZ)** integrity
 - Presence and location of **cystoid spaces**
 - Presence and location of **subretinal fluid (SRF)**
- Correlation analyses performed to describe the relationship at baseline, and change from baseline at 24 weeks.
- A longitudinal treatment-response analysis modeled the temporal relationship between change in BCVA and CST.

1. Yeh S, Khurana RN, Shah M, et al. Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis: Phase 3 Randomized Trial. *Ophthalmology*. 2020;127(7):948-955. doi:10.1016/j.ophtha.2020.01.006

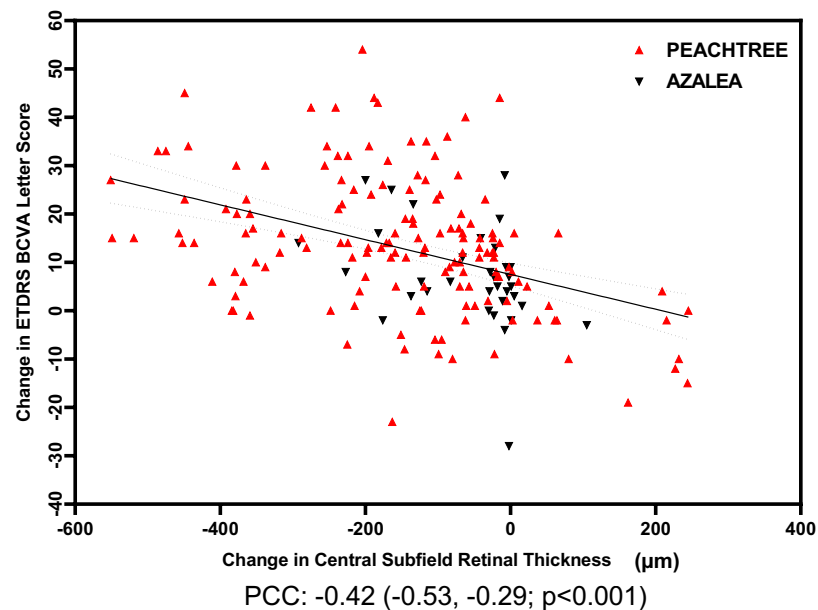
2. Henry CR, Shah M, Barakat MR, et al. Suprachoroidal CLS-TA for non-infectious uveitis: an open-label, safety trial (AZALEA) [published online ahead of print, 2021 Feb 5]. *Br J Ophthalmol*. 2021;bjophthalmol-2020-318019. doi:10.1136/bjophthalmol-2020-318019

Moderate Relationships Between BCVA and CST

Baseline



Change from Baseline at Week 24

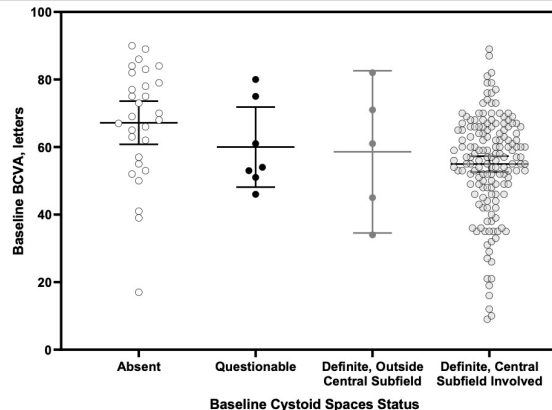
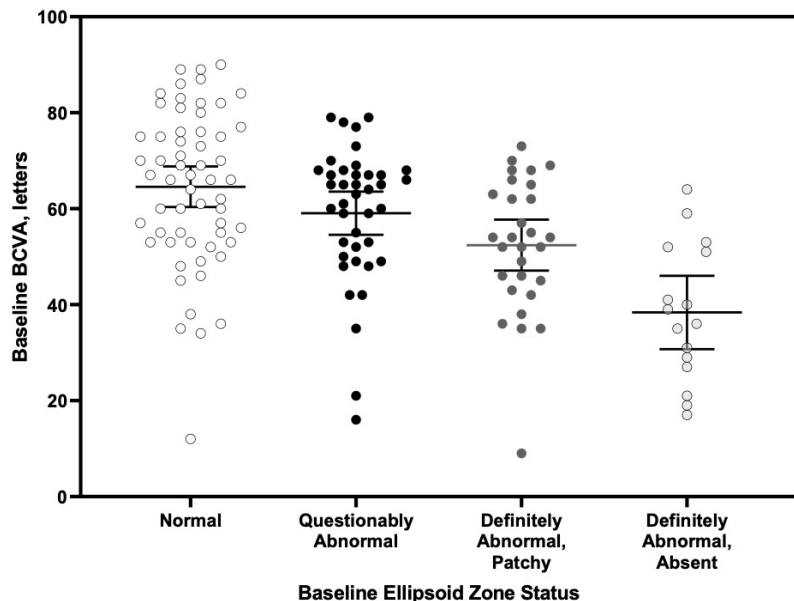


PCC: Pearson Correlation Coefficient

Ciulla TA, Kapik B, Grewal DS, Ip MS. Visual Acuity in Retinal Vein Occlusion-, Diabetic-, and Uveitic Macular Edema: Central Subfield Thickness and Ellipsoid Zone Analysis [published online ahead of print, 2020 Oct 29]. *Ophthalmol Retina*. 2020;S2468-6530(20)30429-2. doi:10.1016/j.oret.2020.10.016

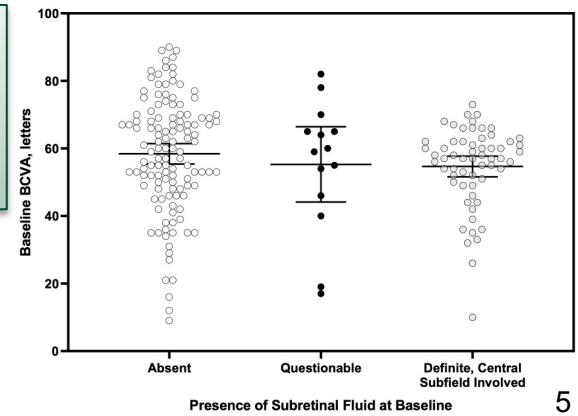
Relationship between Baseline BCVA and EZ, Cystoid Spaces, SRF at Baseline

Baseline BCVA v. Baseline EZ:
 Mean BCVA *statistically significantly*
 worsened with each EZ grade



Baseline BCVA v. Baseline Cystoid Spaces:
 Differences between grades and BCVA not statistically significant

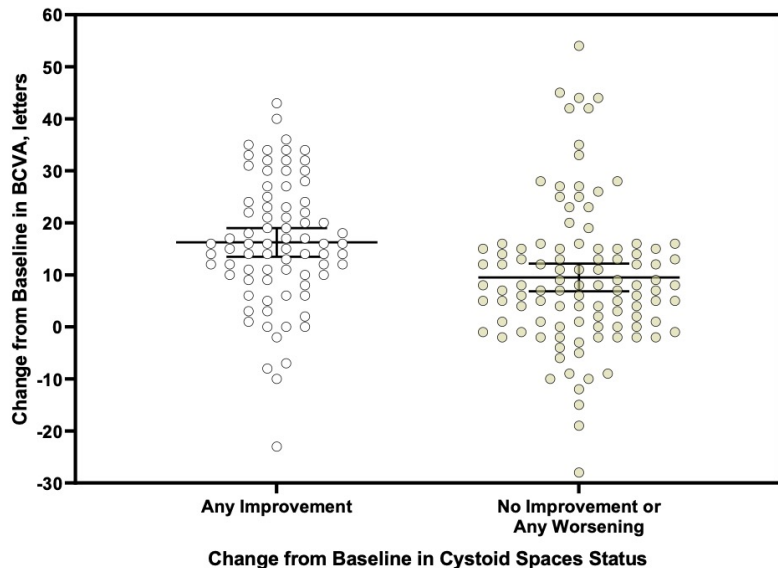
Baseline BCVA v. Baseline SRF:
 Differences between grades and BCVA not statistically significant



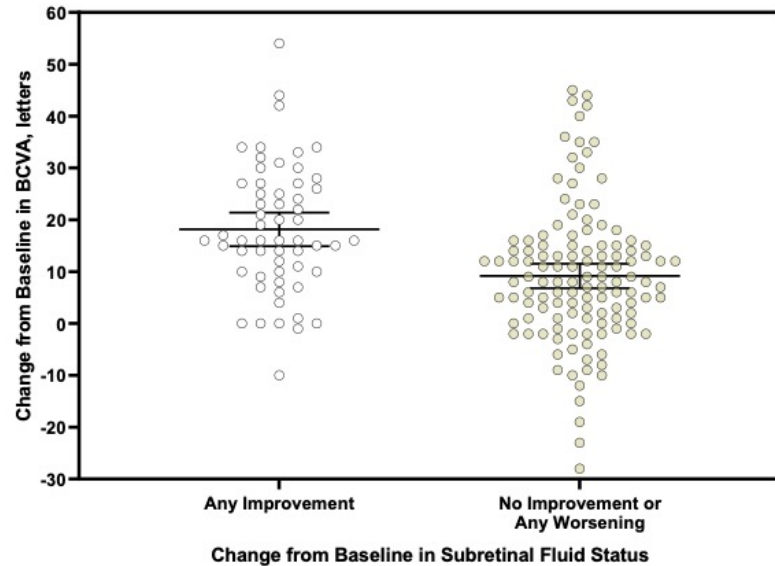
All pair-wise comparisons to 'Definitely abnormal (absent)' group were statistically significant ($p \leq 0.034$) after adjustment for multiple comparisons

Relationship between Change in BCVA and Change in Cystoid Space & SRF Status

Change in BCVA v. Change in Cystoid Spaces
at Week 24



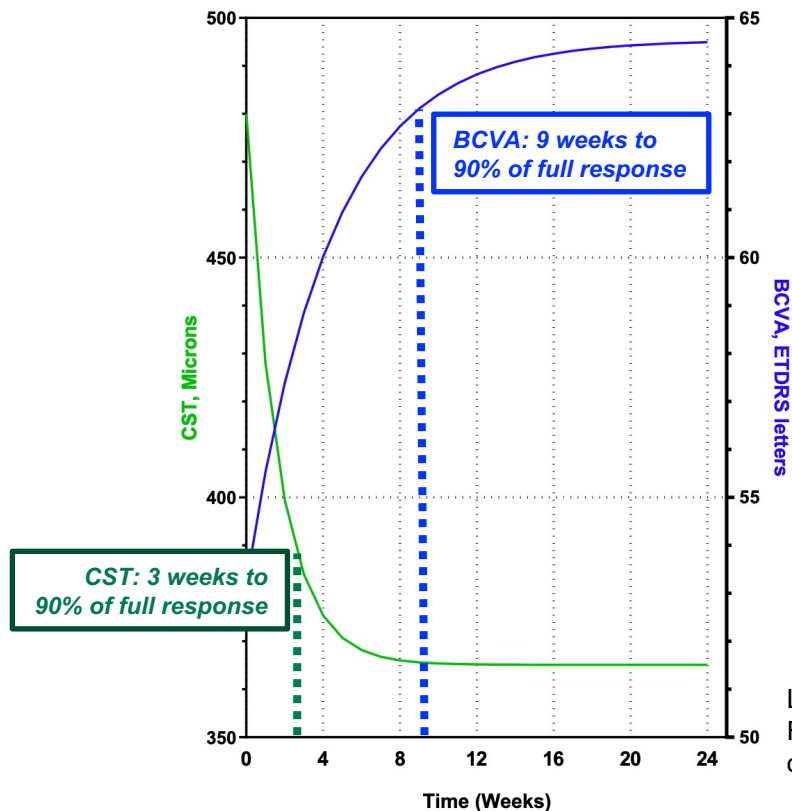
Change in BCVA v. Change SRF
at Week 24



Eyes that showed any improvement in cystoid spaces and/or SRF showed a significantly greater improvement in BCVA ($P < 0.001$ for both)

Longitudinal modeling showed more rapid response for CST

Typical BCVA and CST Response from CLS-TA



Longitudinal modeling showed that the **frame of response was more rapid for CST than BCVA.**

- **CST required approximately 3 weeks** to reach over 90% of full response
- **BCVA required approximately 9 weeks** to reach the same magnitude of response.

Longitudinal non-linear mixed effects model based on methods according to the US FDA guidance for determining population pharmacokinetics and the EU guidance on reporting population pharmacokinetic analysis results.

Conclusion

- In NIU-ME, normal EZ, center involved cystoid spaces, and SRF at baseline predict improved therapeutic response.
- Anatomic response may precede visual response in uveitic macular edema by one month or more.
- These analyses have received favorable review at the American Journal of Ophthalmology.