OCT Anatomic and Temporal Biomarkers in Uveitic Macular Edema

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Financial Disclosures

- DG: EyePoint (C), Allergan (C)
- BK: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment);Clearside Biomedical, Inc.:Code I (Personal Financial Interest)
- TC: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment);Clearside Biomedical, Inc.:Code I (Personal Financial Interest)

Background

- There is limited information on longitudinal structure-functional correlations in Uveitic Macular Edema.

- In clinical practice, physicians often base treatment decisions on both BCVA and OCT assessment.

- This study assessed these relationships, focusing on baseline anatomic features with potential prognostic value for visual response.

1.Stone T, American Society of Retina Specialists Preferences and Trends Survey. 2015.

Methods

- Post hoc analysis of 198 eyes with NIU enrolled in two phase 3, 24 week clinical trials.

- Assessed relationships between BCVA and
  - Ellipsoid zone (EZ) integrity
  - Presence and location of cystoid spaces
 - Presence and location of subretinal fluid (SRF)

Methods

- Correlation analyses were performed to describe the relationship at baseline, and between change from baseline.

- A longitudinal treatment-response analysis modeled the temporal relationship between change in BCVA and CST.

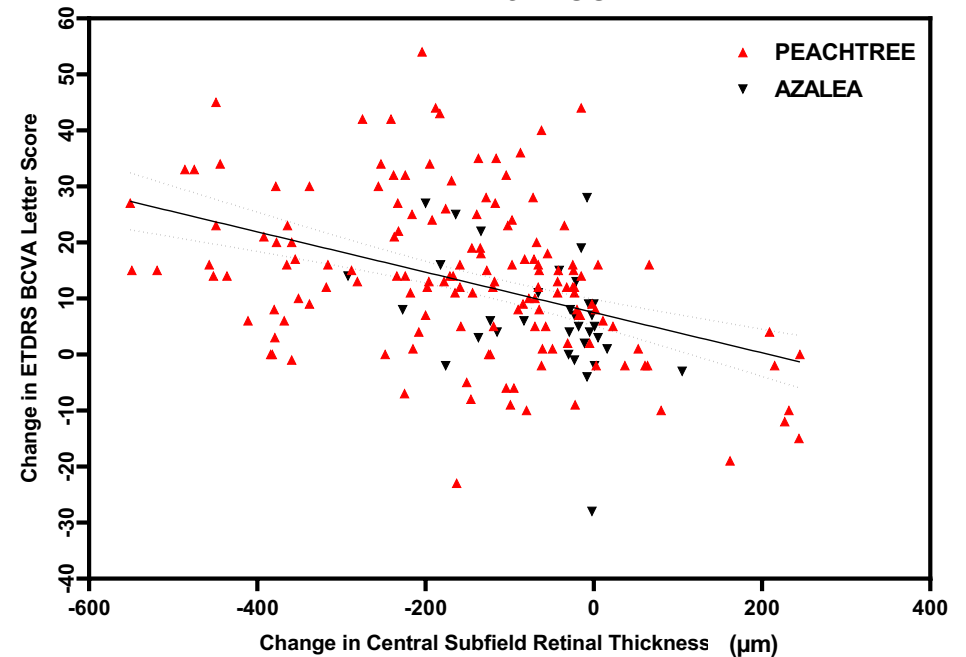- An early CST anatomic response was assessed for BCVA prognosis.

Moderate Relationships Between BCVA and CST

Baseline: BCVA v. CST
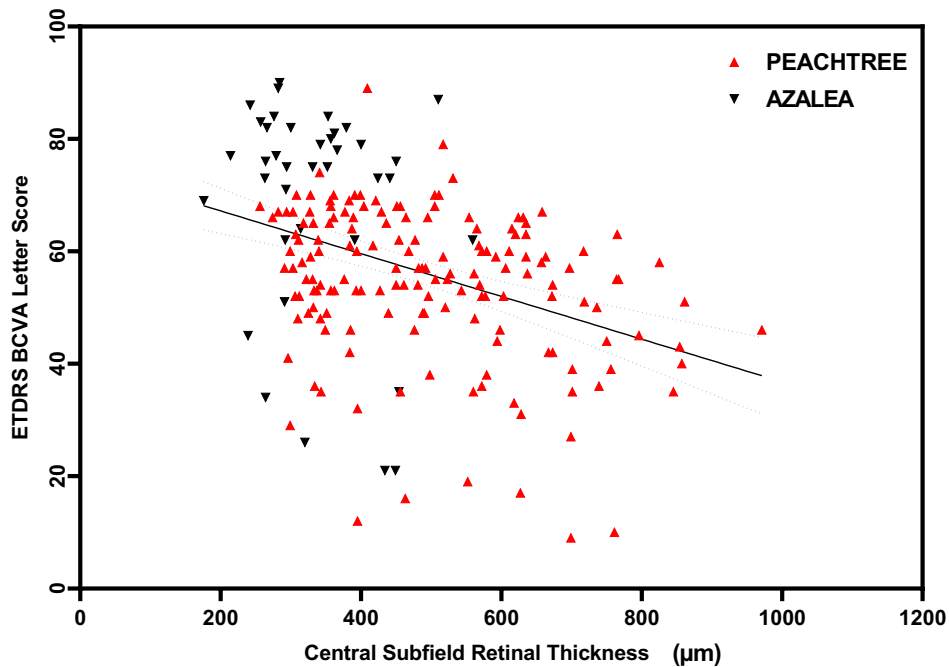
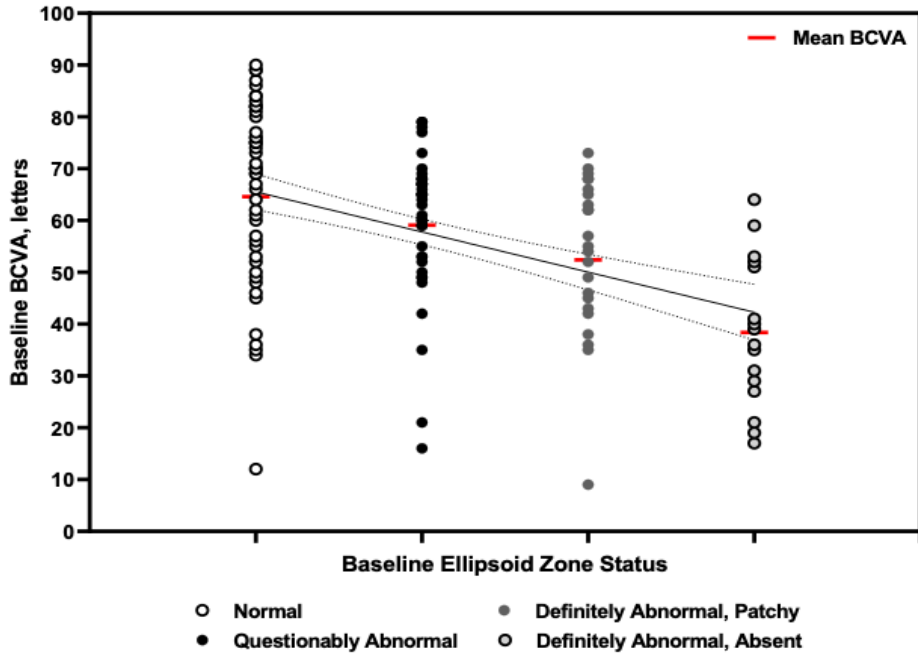**Change from Baseline: BCVA v. CST, At Week 24**

PCC: -0.38 (-0.49, -0.26; p<0.001)

PCC: -0.42 (-0.53, -0.29; p<0.001)

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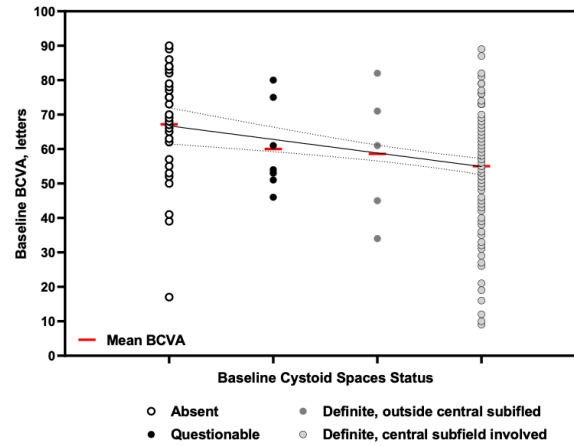
Relationship between Baseline BCVA and EZ, Cystoid Spaces, SRF at Baseline

Baseline BCVA v. Baseline EZ:
Mean BCVA *statistically significantly* worsened with each EZ grade (p ≤ 0.050)

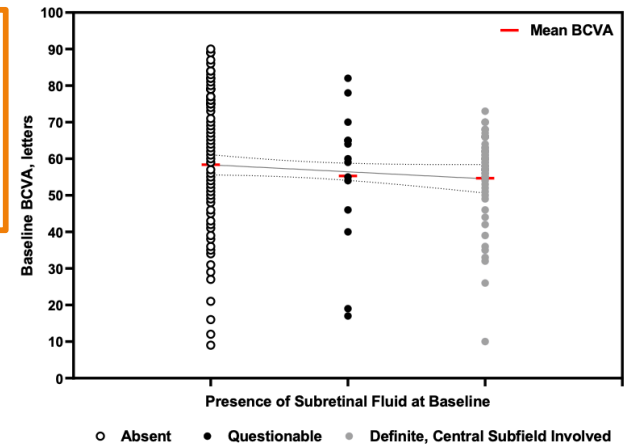**Baseline BCVA v. Baseline Cystoid Spaces:**
Differences between grades and BCVA not statistically significant

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

Baseline BCVA, letters — Baseline Ellipsoid Zone Status
— Mean BCVA
○ Normal   ● Definitely Abnormal, Patchy
● Questionably Abnormal   ◎ Definitely Abnormal, Absent

Baseline BCVA, letters — Baseline Cystoid Spaces Status
— Mean BCVA
○ Absent   ● Definite, outside central subfield
● Questionable   ● Definite, central subfield involved

Baseline BCVA, letters — Presence of Subretinal Fluid at Baseline
— Mean BCVA
○ Absent   ● Questionable   ● Definite, Central Subfield Involved

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

Relationship between Change in BCVA and Ellipsoid Zone Status at Baseline

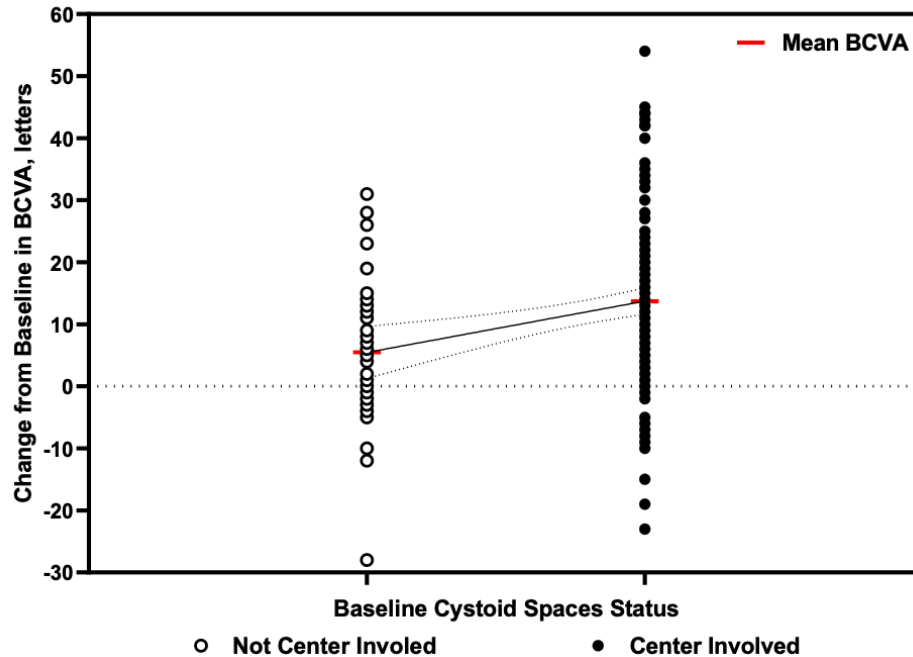**Change in BCVA (Wk 24) v. Baseline EZ Status**
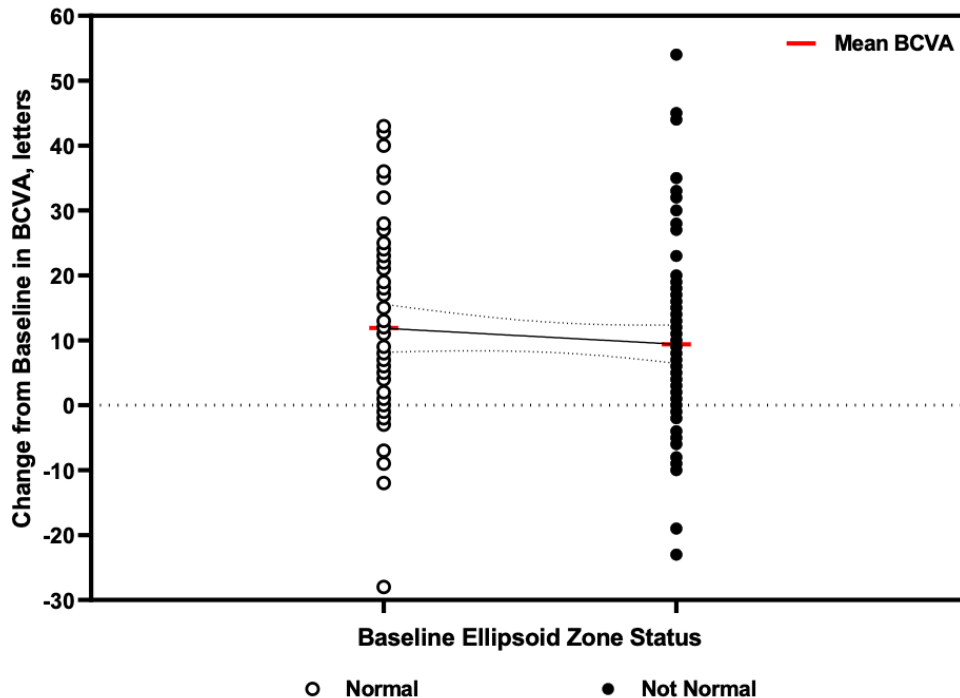
- **Eyes with normal EZ** at baseline experienced a **greater improvement in BCVA** versus eyes with EZ considered not normal
  - 11.9 letters vs. 9.4 letters, *P = 0.006*

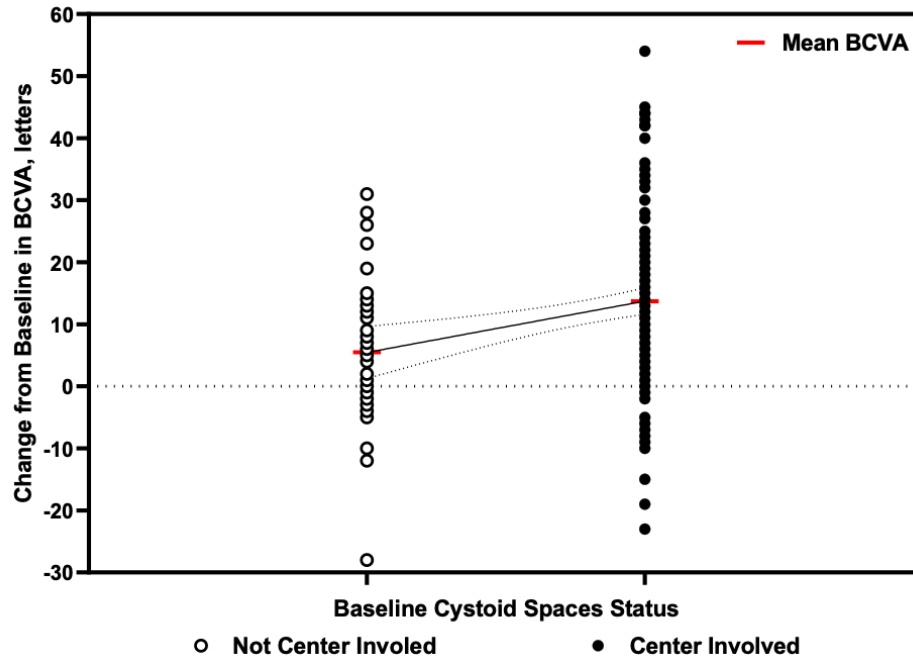# Relationship between Change in BCVA and Cystoid Spaces at Baseline

Change in BCVA (Wk 24) v. Baseline Cystoid Spaces Status

- **Eyes without center involved cystoid spaces** at baseline showed **less improvement at 24 weeks** versus eyes with center-involvement
  - 5.5 letters vs 13.7 letters; *P = 0.012*

Relationship between Change in BCVA and Sub-Retinal Fluid Status at Baseline
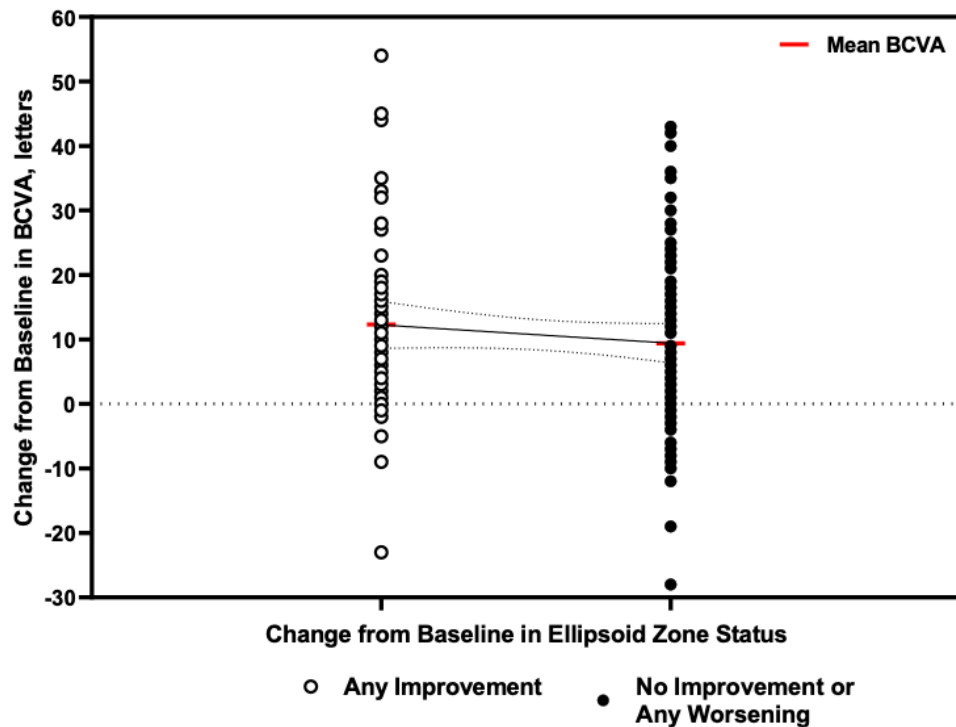
Change in BCVA (Wk 24) v. Baseline SRF Status

- **Eyes without central SRF** at baseline showed **less improvement at 24 weeks** versus eyes with center-involvement
    - 9.5 letters vs 17.2 letters; *P < 0.001*

Relationship between Change in BCVA and Change in Ellipsoid Zone Status
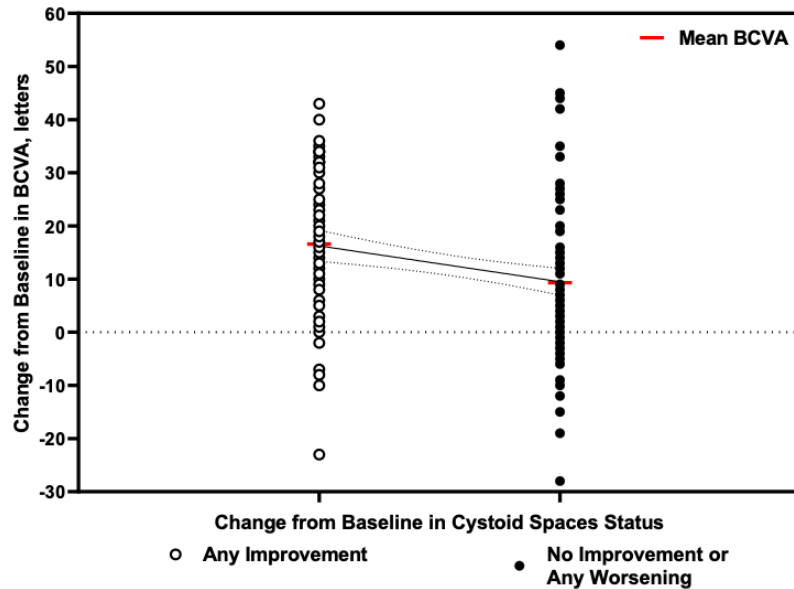
Change in BCVA v. Change in EZ
at Week 24

- Eyes showing any improvement in EZ status at week 24 experienced a mean change from baseline in BCVA that was numerically greater, versus eyes that did not show any change from baseline or who worsened
  - Not statistically significant (11.4 letters vs. 10.0 letters; *P = 0.512*).

Relationship between Change in BCVA and Change in Cystoid Space & Sub-Retinal Fluid Status

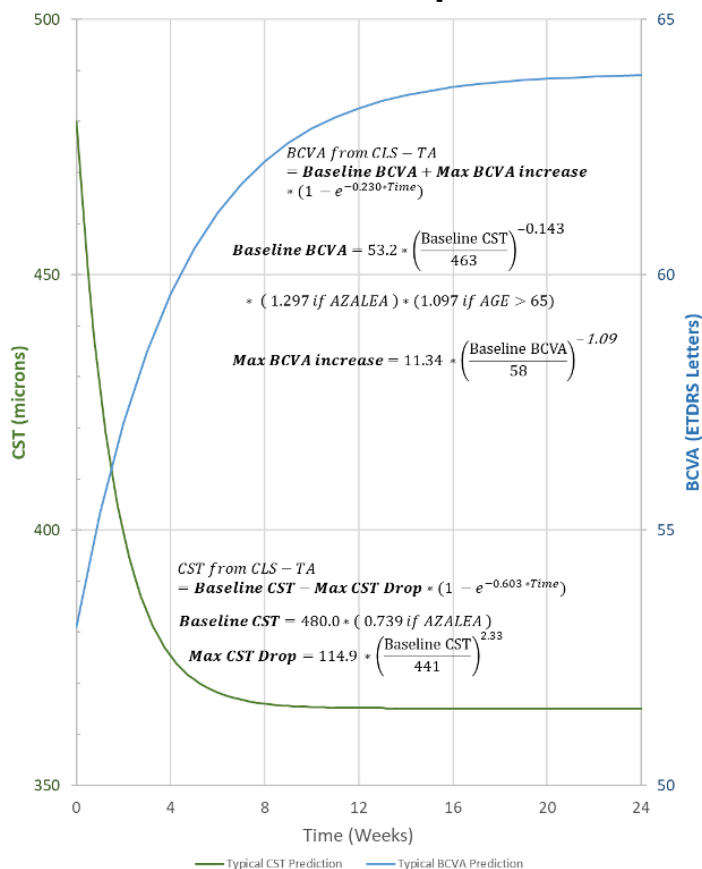**Change in BCVA v. Change in Cystoid Spaces**
at Week 24

Change in BCVA v. Change SRF
at Week 24
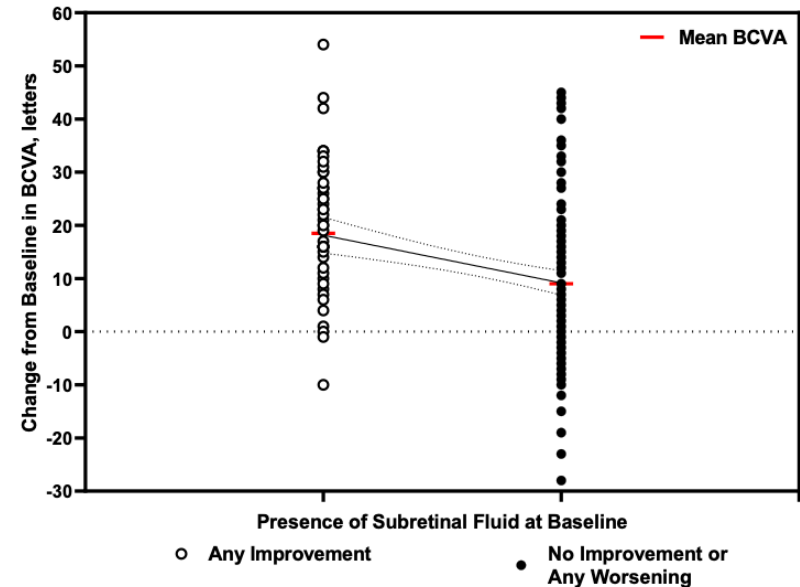
- Eyes that **showed any improvement in cystoid spaces and/or SRF** showed a **significantly greater improvement in BCVA (***P < 0.001 for both***)**

Longitudinal modeling showed more rapid response for CST

Typical BCVA and CST Response from CLS-TA

Chart equations:

$$BCVA\ from\ CLS-TA = Baseline\ BCVA + Max\ BCVA\ increase * (1 - e^{-0.230*Time})$$

$$Baseline\ BCVA = 53.2 * \left(\frac{Baseline\ CST}{463}\right)^{-0.143}$$

$$* (1.297\ if\ AZALEA) * (1.097\ if\ AGE > 65)$$

$$Max\ BCVA\ increase = 11.34 * \left(\frac{Baseline\ BCVA}{58}\right)^{-1.09}$$

$$CST\ from\ CLS-TA = Baseline\ CST - Max\ CST\ Drop * (1 - e^{-0.603*Time})$$

$$Baseline\ CST = 480.0 * (0.739\ if\ AZALEA)$$

$$Max\ CST\ Drop = 114.9 * \left(\frac{Baseline\ CST}{441}\right)^{2.33}$$

Y-axis left: CST (microns); Y-axis right: BCVA (ETDRS Letters); X-axis: Time (Weeks)

Legend: —— Typical CST Prediction —— Typical BCVA Prediction

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

- Clinically relevant relationships between BCVA and OCT anatomic and temporal features.

- Anatomic response may precede visual response in uveitic macular edema.

- Anatomic features described herein account for a minority of BCVA variation.