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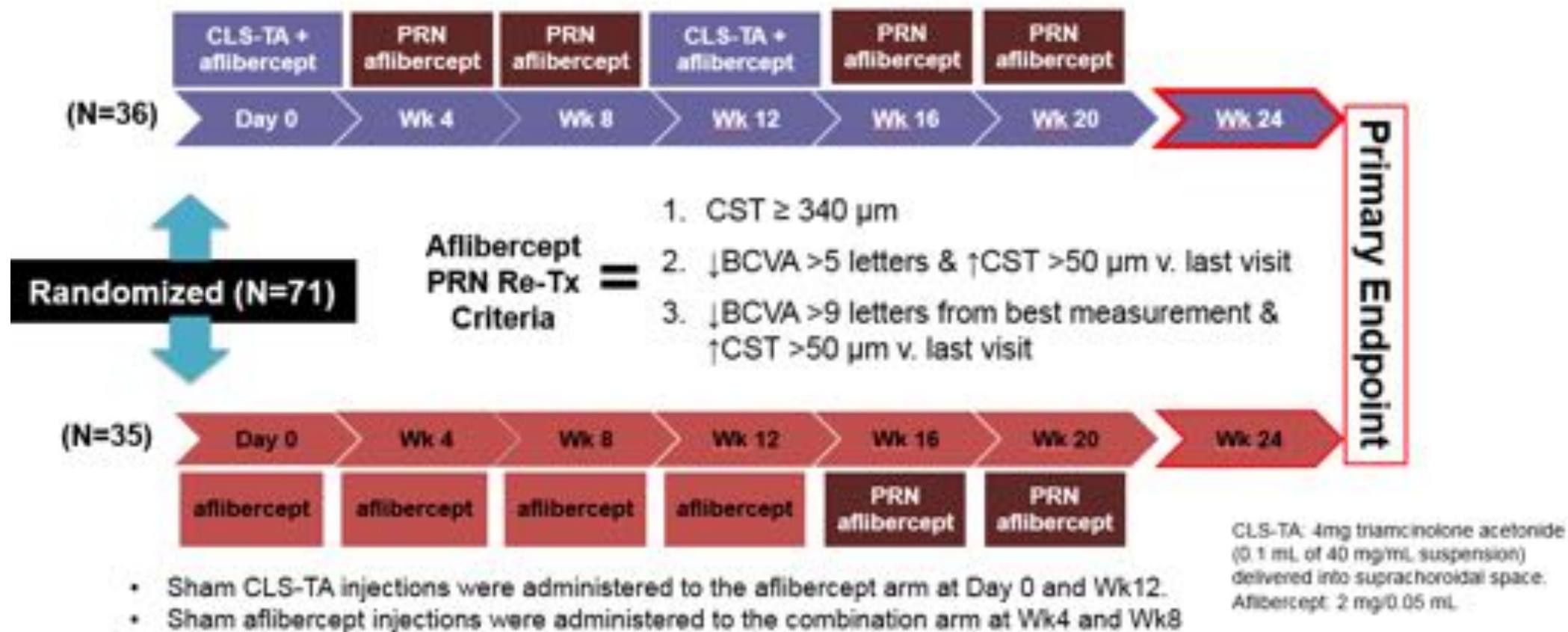
# **Suprachoroidal CLS-TA Plus Aflibercept Compared with Aflibercept Monotherapy for DME: *Analysis of OCT Biomarkers in the Randomized Phase 2 TYBEE Trial***

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# Disclosures

- Consultant: Boehringer Ingelheim, Thrombogenics, Quark, Omeros, Genentech, Allergan, Novartis, Amgen, Astellas, Alimera
- Research Support: Novartis, Genentech, Clearside, Biogen
- Study Disclosures
  - This study includes research conducted on human subjects. Institutional Review Board approval was obtained prior to study initiation

# TYBEE Phase 2 Double-Masked 6-Month DME Trial



# Analysis of Additional Anatomical Outcomes When Comparing Combination Treatment vs. Aflibercept Monotherapy

- ***Disorganization of the Retinal Inner Layers (DRIL)***
- Choroidal Vasculature Index (CVI)

## Analysis: Disorganization of the Retinal Inner Layers (DRIL)

- Disorganization of the retinal inner layers was defined where 1 or more boundaries between the following layers are not separately identifiable:
  - ganglion cell layer and inner plexiform layer complex
  - inner plexiform layer complex and inner nuclear layer
  - inner nuclear layer and outer plexiform layer
- Performed maximum extent and novel area measurement

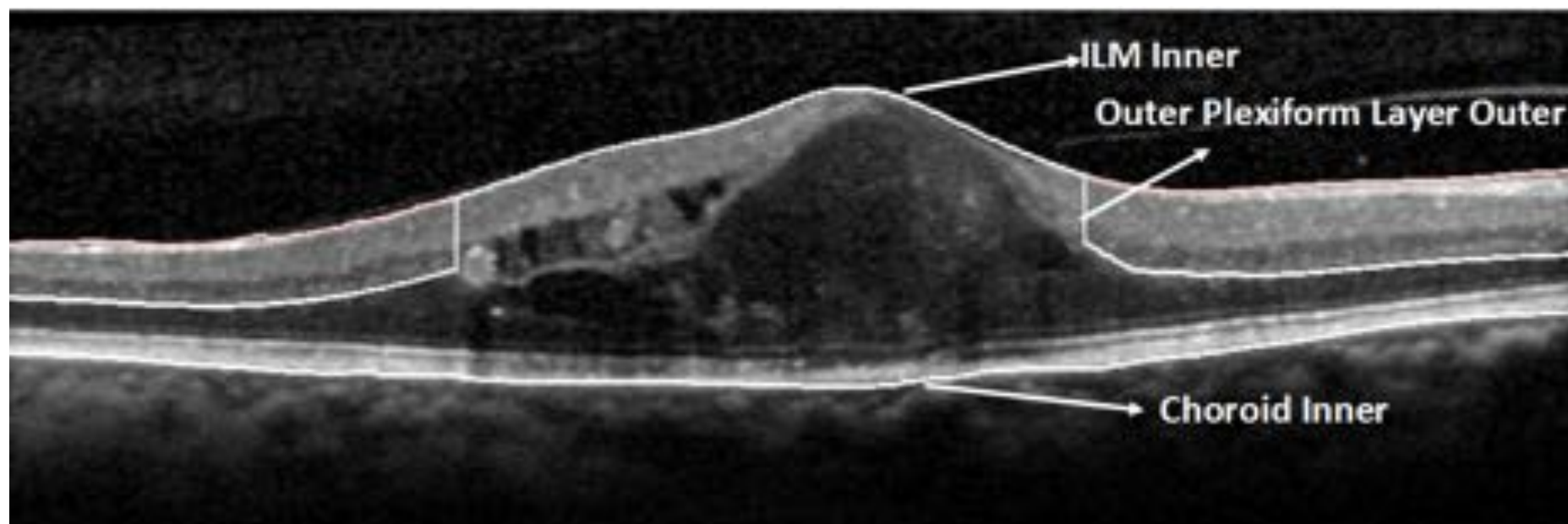
Sun, et al. JAMA Ophthalmol. 2014;132(11):1309-1316.

Radwan, et al. JAMA Ophthalmol. 2015;133(7):820-825.

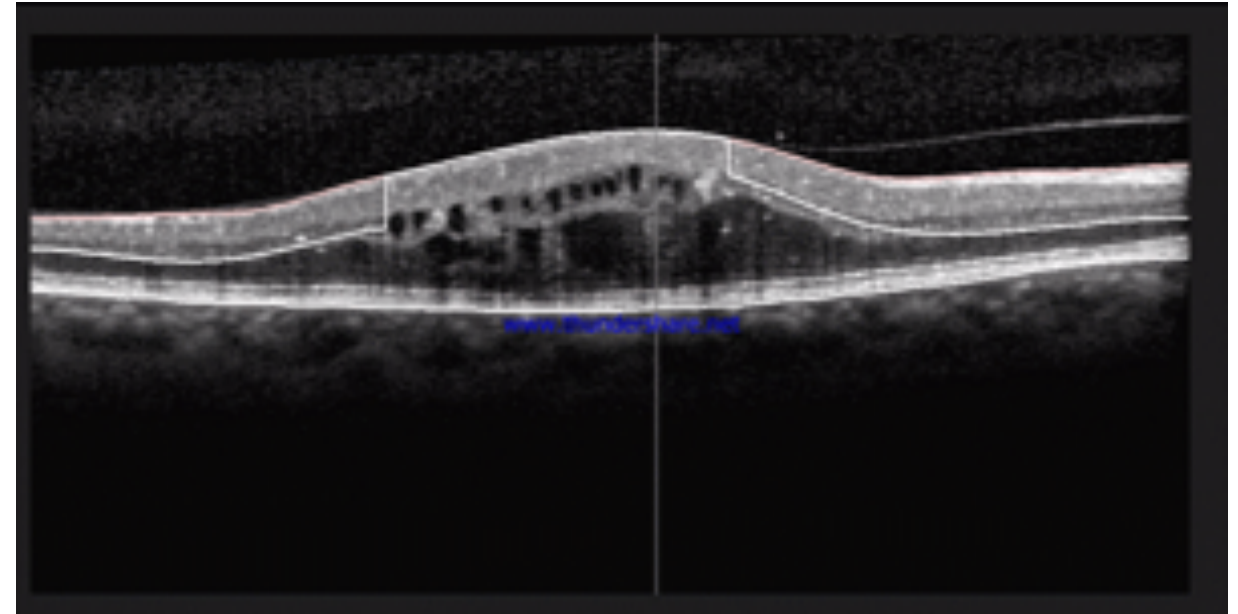
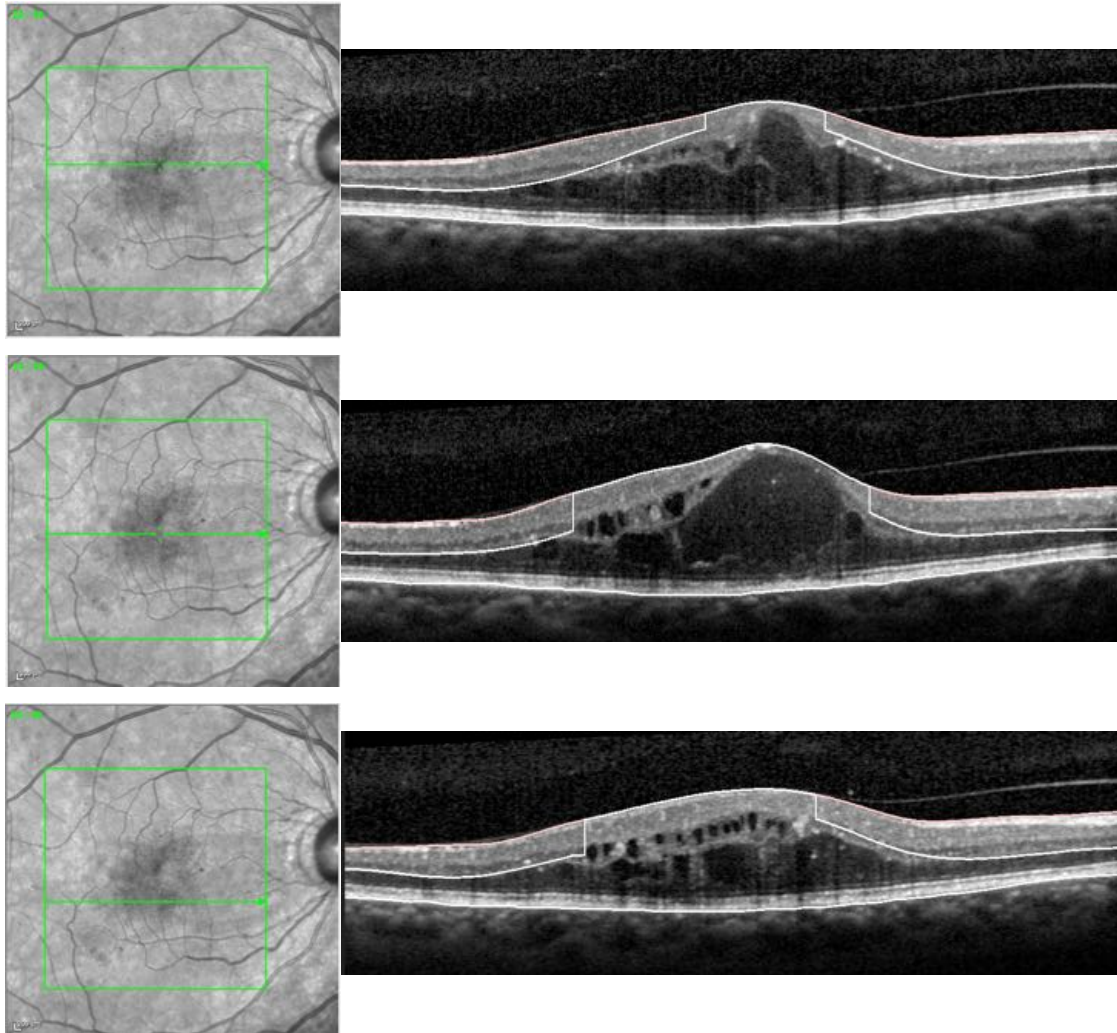
Babiuch, et al. JAMA Ophthalmol. 2019;137(1):38-46.

# DRIL Maximum Extent Illustration

- Manual delineation of DRIL using OCTOR



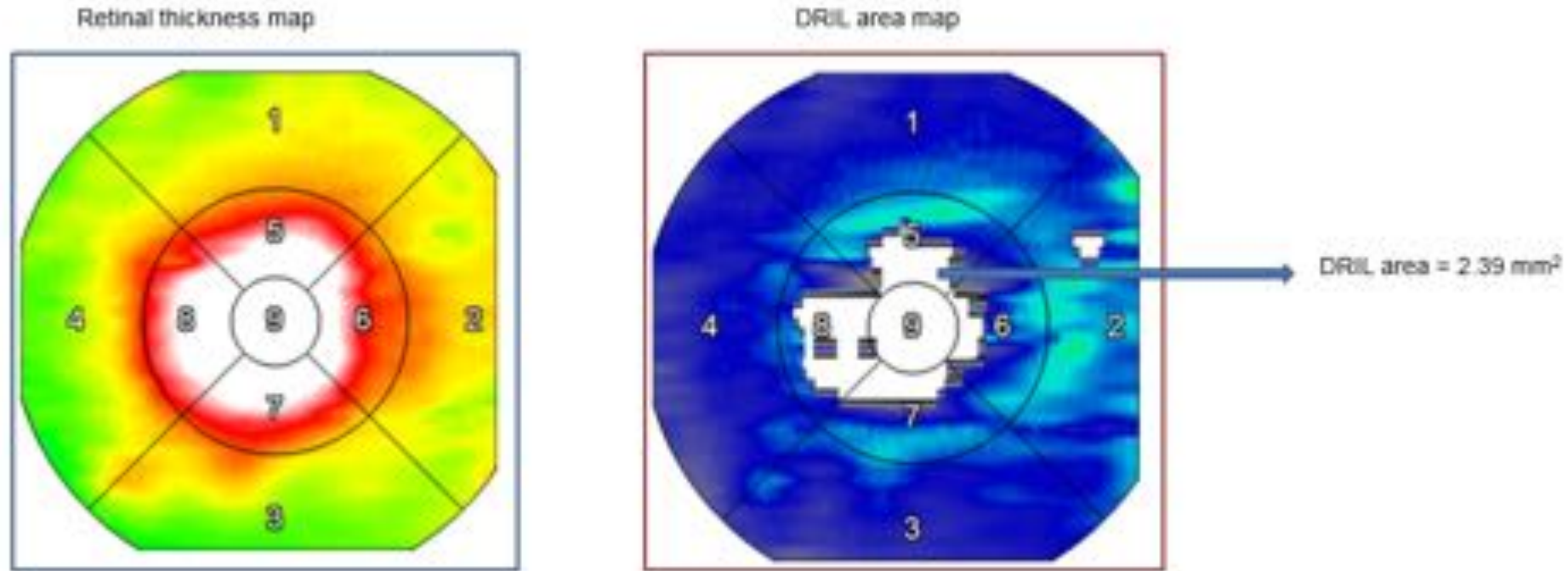
# *En Face* Projection for DRIL Area



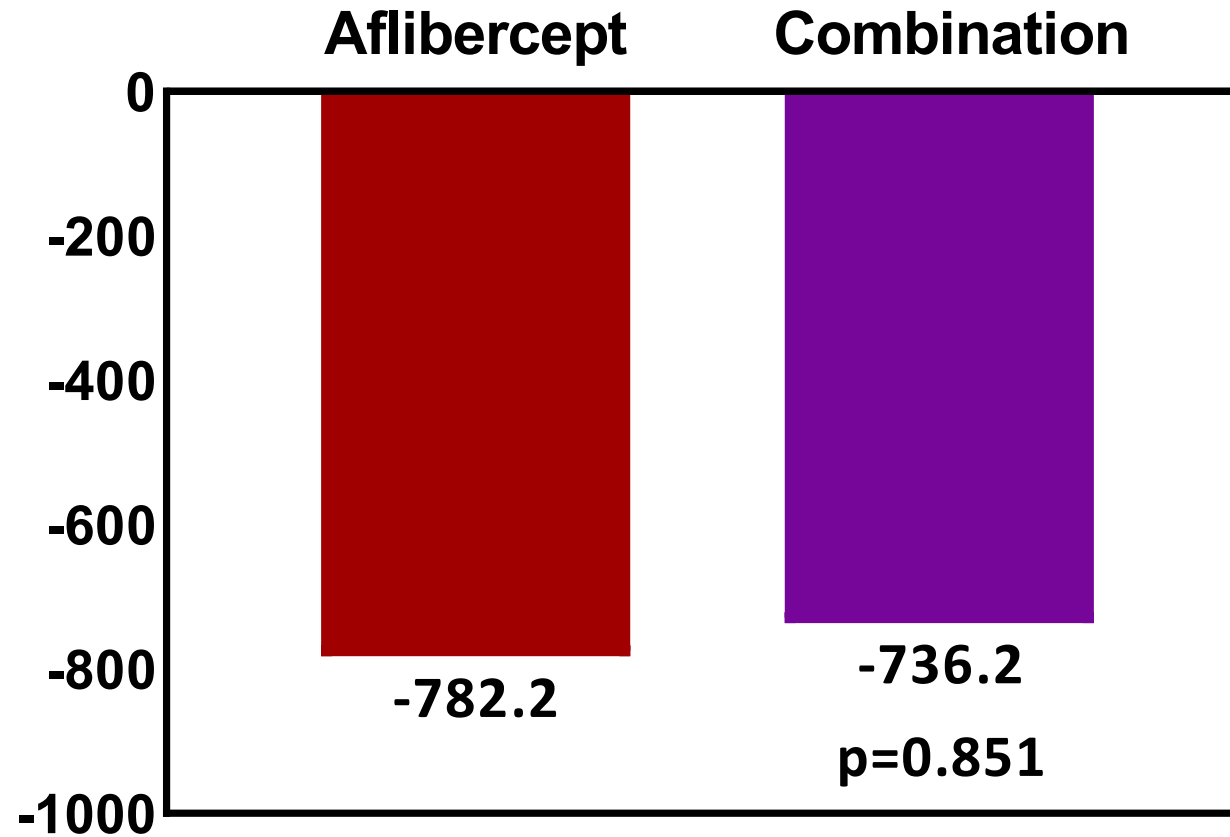


# DRIL area map from volume scans

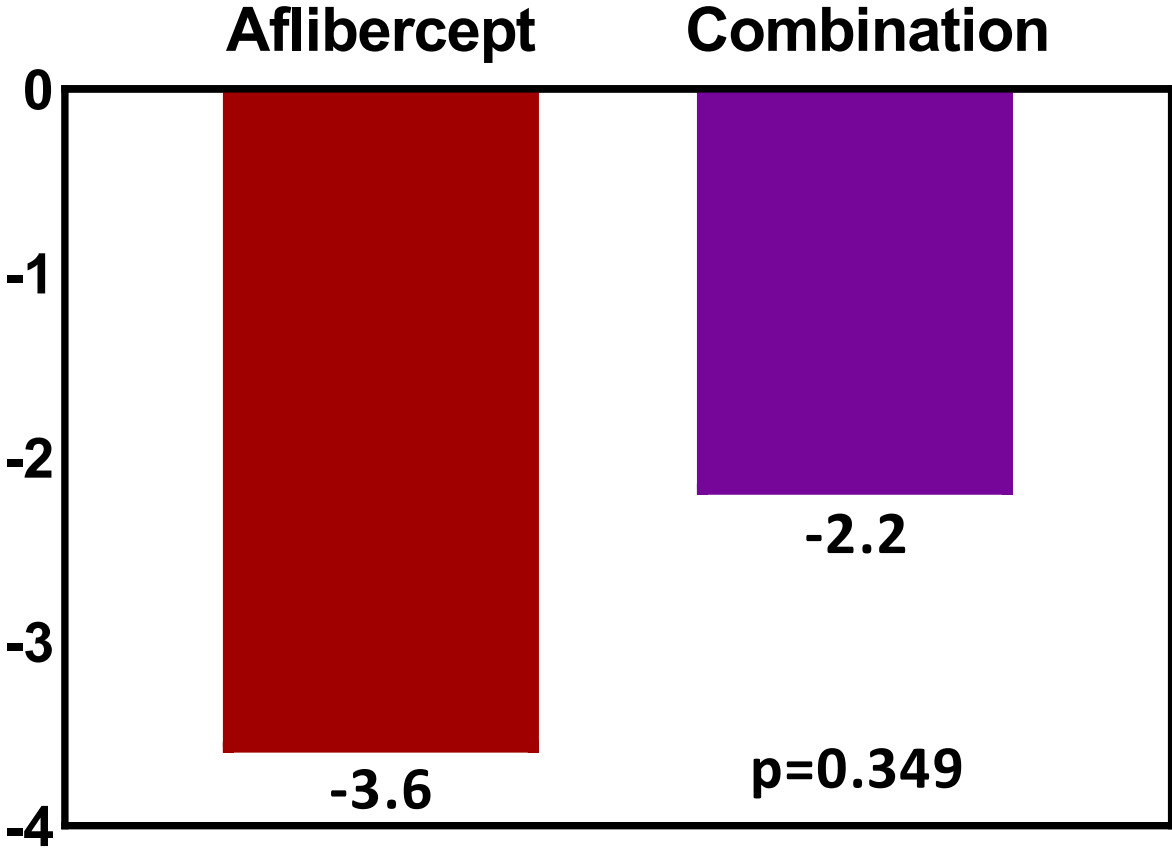
DRIL area = Total retinal area – intact inner retinal area



# Similar improvement in maximum extent of DRIL ( $\mu\text{m}$ )



# Similar improvement in area of DRIL (mm<sup>2</sup>)



# Analysis of Additional Anatomical Outcomes When Comparing Combination Treatment vs. Aflibercept Monotherapy

- Disorganization of the Retinal Inner Layers (DRIL)
- ***Choroidal Vasculature Index (CVI)***

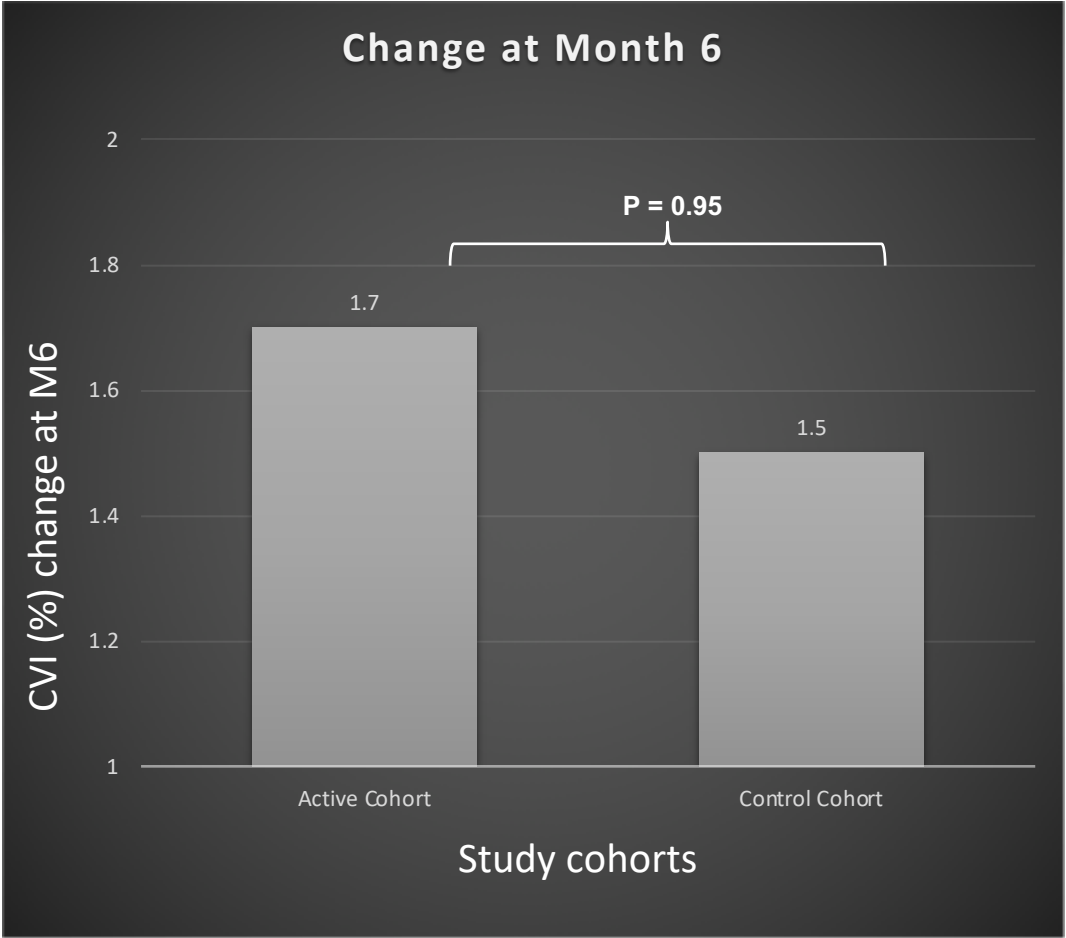
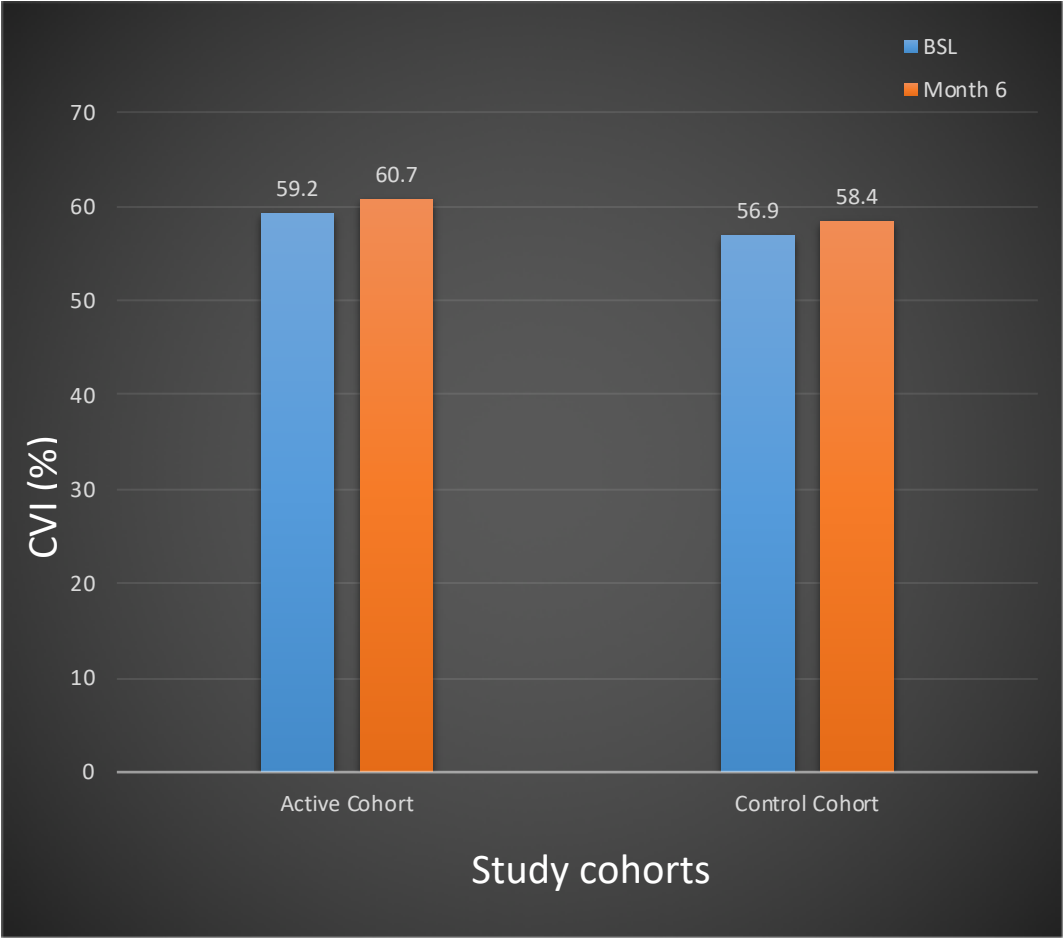
# Choroidal vascularity index (CVI)

Binarized choroidal luminal area (dark pixels) and stromal area (bright pixels)

$CVI = LA / \text{Total Choroidal Area}$



# CVI between study cohorts at baseline and Month 6; change at month 6



# Multivariate analysis

Summary of Multiple Regression Analysis of the Change from Baseline in Best Corrected Visual Acuity at Week 24 (ITT Population)

Variable	Parameter Estimate	Standard Error	95% Confidence Interval	P-value
Baseline BCVA	0.626	0.1359	(0.353, 0.898)	<0.001
Baseline CST	-0.053	0.0234	(-0.100, -0.006)	0.028
Baseline FCSRT	0.049	0.0195	(0.010, 0.088)	0.016
Baseline Area of DRIL	0.230	0.1847	(-0.142, 0.600)	0.185

BCVA = best corrected visual acuity, CST = central subfield retinal thickness, FCSRT = foveal center subfield retinal thickness, DRIL = disorganization of the retinal inner layer. Analysis performed using regression model using a forward selection technique and a 0.25 significance level for entry into the final model.

# Conclusion

- Combination aflibercept & suprachoroidal CLS-TA vs aflibercept monotherapy at Wk24:
  - Similar DRIL improvement (maximum extent)
  - Similar DRIL improvement (area)
  - Similar CVI (no change)
- **Of the novel OCT biomarkers we evaluated in this analysis, only area of DRIL was found to be predictive for VA at week 24 (multivariate analysis)**
- Area of DRIL is a biomarker that should be considered for evaluation in future DME clinical trials





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