Suprachoroidal CLS-TA Plus Aflibercept Compared with Aflibercept Monotherapy for DME: 
Selected Secondary Results of the Randomized Phase 2 TYBEE Trial

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Disclosures

• Financial Disclosures
  - Consultant: Boehringer Ingelheim, ThromboGenics, Genentech, Astellas, Allergan, Novartis, Alimera, Allegro

• Study Disclosures
  - This study includes research conducted on human subjects. Institutional Review Board approval was obtained prior to study initiation
Undertreatment may be one reason for worse outcomes in the “real-world”

12 Month analysis: number of injections

12 Month analysis: number of letters

TYBEE: Phase 2, Double-Masked, 6-Month DME Trial

Illustration of CLS-TA Suprachoroidal Delivery

Suprachoroidal Space (SCS)

Randomized (N=71)

- Aflibercept PRN Re-Tx Criteria
  1. CST ≥ 340 μm
  2. BCVA > 5 letters & CST > 50 μm v. last visit
  3. BCVA > 9 letters from best measurement & CST > 50 μm v. last visit

(N=36)

CLS-TA + aflibercept
Day 0

PRN aflibercept
Wk 4

PRN aflibercept
Wk 8

CLS-TA + aflibercept
Wk 12

PRN aflibercept
Wk 16

PRN aflibercept
Wk 20

Wk 24

(N=35)

Day 0

Wk 4 aflibercept

Wk 8 aflibercept

Wk 12 aflibercept

Wk 16 aflibercept

Wk 20 aflibercept

Wk 24 aflibercept

Primary Endpoint

- Sham CLS-TA injections were administered to the aflibercept arm at Day 0 and Wk12.
- Sham aflibercept injections were administered to the combination arm at Wk4 and Wk8

CLS-TA: 4mg triamcinolone acetonide (0.1 mL of 40 mg/mL suspension) delivered into suprachoroidal space. Aflibercept: 2 mg/0.05 mL

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TYBEE Endpoints

Mean Change in BCVA

Baseline BCVA: Aflibercept: 58; Combination 56

Number of Treatment Visits

Baseline BCVA: Aflibercept: 58; Combination 56
Analysis: Disorganization of the Inner Retinal layers (DRIL)

- Disorganization of the inner retinal 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 area and maximum extent measurement

DRIL Area = Total Retina – Inner Retina

DRIL area map from volume scans

Retinal thickness map

DRIL area map

DRIL area = 2.39 mm²

Similar Improvement in Area and Maximum Extent of DRIL

**Area of DRIL (mm²)**

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<tr>
<th></th>
<th>Aflibercept</th>
<th>Combination</th>
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<td>p</td>
<td>0.349</td>
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**Maximum Extent of DRIL (µm)**

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Conclusion

- Combination aflibercept & suprachoroidal CLS-TA vs aflibercept monotherapy at Wk24:
  - Similar BCVA change
  - Improved OCT CST change in the combination group
  - Similar DRSS change
  - **Similar DRIL change (maximum extent and area)**
  - Fewer treatment visits in combination group (2.8 vs 4.7 mean treatment visits)
- DRIL is a biomarker that should be evaluated in future DME clinical trials