Post Hoc Analysis of Suprachoroidal CLS-TA versus Rescue Therapies for Uveitic Macular Edema: Safety and Visual Function

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Disclosure

- ES: Abbvie, Clearside Biomedical, EyeGate, EyePoint, Eyevensys, Gilead (research support and consultant);
- BK: Clearside Biomedical: Employee & Shareholder
- TC: Clearside Biomedical: Employee & Shareholder
PEACHTREE: Phase 3, Randomized, Controlled, Double-Masked, Multicenter Trial

**Primary Endpoint:** Proportion of patients with an improvement from baseline ≥15 letters in BCVA at Week 24

**Rescue Criteria:**
- BCVA: ↓ 10+ letters
- CST: ↑ 100+ µm or 20% (whichever is lower)
- Inflammation level: ↑ 1.5+ or 3+ to 4+
- Investigators’ medical judgement

**Enrollment**
- Suprachoroidal CLS-TA
  - N=96
  - Day 0, Wk 4, Wk 8, Wk 12, Wk 16, Wk 20, Wk 24
  - Active Arm: Suprachoroidal injection of 4 mg CLS-TA

**Control Arm:** Sham injection procedure
- N=64
  - Day 0, Wk 4, Wk 8, Wk 12, Wk 16, Wk 20, Wk 24
  - Sham

**Evaluation period – 6 months**
The Suprachoroidal Space

*Targeted and Compartmentalized Delivery*
Key Inclusion and Exclusion Criteria

Inclusion

• Diagnosis of macular edema with central subfield thickness ≥300 microns on SD-OCT
• Noninfectious uveitis of any associated diagnosis/etiology
• Any anatomic location: anterior, intermediate, posterior and panuveitis
• Visual acuity: 20/800 to 20/40 (≥5 to ≤70 ETDRS letters)

Exclusion

• Any active ocular disease or infection in the study eye other than uveitis
• Intraocular pressure >22 mmHg or uncontrolled glaucoma; patients ≤22 mmHg could be on up to 2 IOP-lowering medications

Subjects could have active or controlled disease at enrollment
PEACHTREE: Met Primary Efficacy Endpoint

Primary Endpoint: Subjects gaining ≥15 BCVA letters from baseline at Week 24, %

Intention-to-treat population; Last Observation Carried Forward imputation. The p-value is based on a Cochran-Mantel-Haenszel test for general association between treatment and response with stratification by country.
## Safety

<table>
<thead>
<tr>
<th>IOP-Related Events</th>
<th>CLS-TA N = 96</th>
<th>Control N = 64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated IOP adverse events</td>
<td>11 (11.5%)</td>
<td>10 (15.6%)</td>
</tr>
<tr>
<td>IOP elevation ≥10 mmHg change from baseline at any visit*</td>
<td>9 (9.4%)</td>
<td>7 (10.9%)</td>
</tr>
<tr>
<td>IOP elevation ≥30 mmHg absolute reading at any post baseline visit*</td>
<td>5 (5.2%)</td>
<td>4 (6.3%)</td>
</tr>
<tr>
<td>Given any additional IOP-lowering medication</td>
<td>7 (7.3%)</td>
<td>6 (9.4%)</td>
</tr>
<tr>
<td>Any surgical intervention for an elevated IOP Adverse Event</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**One serious ocular AE**
- Retinal detachment 8 weeks after CLS-TA, in different quadrant
- Determined to be unrelated to study drug by the Investigator

**Cataract:** 7.3% (7/96) in the CLS-TA arm vs. 6.3% (4/64) in the sham arm

*Safety population; includes patients in the control group who received rescue medication
*Based on elevated intraocular pressure adverse reactions
Rescue Therapy Rates: CLS-TA (n=13) vs. Control (n=46)

Most Targeted (Localized) Subsequent Medication*
Used Rates, CLS-TA vs. Control

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>CLS-TA</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVT Steroid</td>
<td>46.2%</td>
<td>63.0%</td>
</tr>
<tr>
<td>Periocular Steroid</td>
<td>0.0%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Topical Steroid</td>
<td>15.2%</td>
<td>30.8%</td>
</tr>
<tr>
<td>Systemic Steroid</td>
<td>4.3%</td>
<td>15.4%</td>
</tr>
<tr>
<td>Topical NSAID</td>
<td>7.7%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

*Rescue medications hierarchically ranked: Intravitreal Corticosteroid > Periocular corticosteroid > Topical Corticosteroid > Systemic Corticosteroid > Topical NSAID

Post-Hoc Analysis. Rescue medication used per investigator discretion.
Sub-Analysis by Rescue Status in PEACHTREE

**Purpose:** To compare outcomes between CLS-TA and real-world rescue therapies

**Methods:** VA and safety in unrescued CLS-TA versus rescued control group

Two (2) subgroups analyzed:

<table>
<thead>
<tr>
<th></th>
<th>Unrescued</th>
<th>Rescued</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLS-TA</td>
<td>n=83/96 (86.5%)</td>
<td>n=13/96 (13.5%)</td>
</tr>
<tr>
<td>Control</td>
<td>n=18/64 (28.1%)</td>
<td>n=46/64 (71.9%)</td>
</tr>
</tbody>
</table>
Visual acuity in unrescued CLS-TA: Greater mean BCVA and more 3 line gainers at week 24

≥ 15 Letter Improvement from Baseline in BCVA at Week 24

Mean BCVA by Week

Difference at Week 24
4.5 letters, p=0.080
A significantly greater mean reduction in CST was observed for unrescued CLS-TA subjects versus rescued control subjects.

At Week 24, the unrescued CLS-TA subjects who completed the study with gradable images showed a 174.0 µm reduction, compared to a 148.5 µm reduction in the rescued control subjects (95% CI for difference -88.2 to -2.0 µm, $P = 0.040$).
Safety: Treatment Emergent Adverse Events (TEAE)

<table>
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<tr>
<th></th>
<th>Unrescued CLS-TA</th>
<th>Rescued Control</th>
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<tbody>
<tr>
<td>% of subjects with ≥1 TEAE</td>
<td>48.2%</td>
<td>63.0%</td>
</tr>
<tr>
<td>AEs related to elevated IOP</td>
<td>10.8%</td>
<td>21.7%</td>
</tr>
<tr>
<td>Incidence of Cataract</td>
<td>4.8%</td>
<td>8.7%</td>
</tr>
<tr>
<td>IOP-related surgical interventions</td>
<td>none</td>
<td>none</td>
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Conclusion

- This post hoc analysis corroborates the pre-specified endpoints of the PEACHTREE study
  - Unrescued CLS-TA subjects experienced significantly greater reduction in CST than rescued subjects in the control group
  - Unrescued CLS-TA subjects tended towards greater improvement in BCVA compared with rescued control subjects
  - Suprachoroidally administered CLS-TA appeared associated with a lower incidence of IOP-related safety findings.

- This post hoc analysis represents a “real world” mix of rescue treatments, with expected limitations in terms of sample size, treatment type, etc.