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

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Yeh:

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Hall & Ciulla: Clearside Biomedical, Inc. (Employee & Shareholder)
PEACHTREE: Phase 3, Randomized, Controlled, Double-Masked, Multicenter Trial

**RESCUE CRITERIA**

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

**CLS-TA:** Proprietary triamcinolone acetonide for suprachoroidal injection
The Suprachoroidal Space (SCS)
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 uveitis at enrollment
Primary Endpoint: Subjects gaining ≥15 BCVA letters from baseline at Week 24, %

<table>
<thead>
<tr>
<th></th>
<th>CLS-TA (N=96)</th>
<th>Control (N=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent patients</td>
<td>46.9%</td>
<td>15.6%</td>
</tr>
<tr>
<td>n</td>
<td>45</td>
<td>10</td>
</tr>
</tbody>
</table>

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

One serious ocular AE
- Retinal detachment 8 weeks after CLS-TA, in different quadrant from injection
- Deemed unrelated to study drug by the investigator

No cases of endophthalmitis or choroidal detachment

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

<table>
<thead>
<tr>
<th>IOP-Related Events Not Temporally Associated with the Injection Procedure</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>

Safety population; includes patients in the control group who received rescue medication

*Based on elevated intraocular pressure adverse reactions
**Rescue Therapy Rates: CLS-TA (13.5%) vs. Control (71.8%)**

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

<table>
<thead>
<tr>
<th>Type of Rescue Therapy</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>15.2%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Topical Steroid</td>
<td>30.8%</td>
<td>15.2%</td>
</tr>
<tr>
<td>Systemic Steroid</td>
<td>15.4%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Topical NSAID</td>
<td>7.7%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

*Rescue medications classified by most targeted type of therapy used during study, were: Intravitreal Corticosteroid > Periocular corticosteroid > Topical Corticosteroid > Systemic Corticosteroid > Topical NSAID

**Post-Hoc Analysis.**
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

- Unrescued CLS-TA (N=83) 51.9%
- Rescued Control (N=46) 37.0%

p=0.115

Mean BCVA by Week

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

At Week 24:
CST reduction* in
Unrescued CLS-TA subjects = 174.0 µm
Rescued control subjects = 148.5 µm

(95% CI for difference -88.2 to -2.0 µm, P=0.040)

*Subjects who completed the study with gradable images
## Safety and Adverse Events

<table>
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<tr>
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<th>Unrescued CLS-TA</th>
<th>Rescued Control</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>
Conclusion

• CLS-TA subjects vs. Rescued control subjects:
  – Significantly greater reduction in CST
  – Trended towards greater BCVA improvement
  – Lower incidence of IOP elevation and cataract

• Post hoc analysis represents a “real world” mix of rescue treatments, with limitations in terms of sample size and variable rescue treatment