Safety and Visual Function of Suprachoroidal CLS-TA versus Real World Rescue Therapies for Macular Edema associated with Noninfectious Uveitis: A Post-hoc Analysis

Pouya Dayani, MD\textsuperscript{1}
Colette Hall, MD\textsuperscript{2}
Thomas A. Ciulla, MD, MBA\textsuperscript{2}
1. Retina-Vitreous Associates Medical Group
2. Clearside Biomedical, Inc.

Financial Disclosures
PD: Alimera, Eyepoint, Novartis, Regeneron
CH, TC: Clearside Biomedical, Employee & Shareholder

The Retina Society
54\textsuperscript{th} Annual Scientific Meeting
September 29 – October 2, 2021
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

**Suprachoroidal CLS-TA**

- **Day 0**
- **Wk 4**
- **Wk 8**
- **Wk 12**
- **Wk 16**
- **Wk 20**
- **Wk 24**

**Active Arm:** Suprachoroidal injection of 4 mg CLS-TA

**Sham**

**Control Arm: Sham procedure**

- **Day 0**
- **Wk 4**
- **Wk 8**
- **Wk 12**
- **Wk 16**
- **Wk 20**
- **Wk 24**

**Enrollment**

- N=96
- N=64

**Evaluation period – 6 months**
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 disease at enrollment

ETDRS: Early Treatment Diabetic Retinopathy Study
IOP: intraocular pressure
Primary Endpoint: Subjects gaining ≥15 BCVA letters from baseline at Week 24, %

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLS-TA (N=96)</td>
<td>46.9%</td>
</tr>
<tr>
<td>Control (N=64)</td>
<td>15.6%</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
- 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

<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>

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>Medication</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>17.4%</td>
<td>15.4%</td>
</tr>
<tr>
<td>Topical Steroid</td>
<td>30.8%</td>
<td>15.2%</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 classified by most targeted type of therapy used during study, where:
Intravitreal Corticosteroid > Periocular corticosteroid > Topical Corticosteroid > Systemic Corticosteroid > Topical NSAID

Post-Hoc Analysis.

- Rescue criteria was standardized
- Type of rescue used was at Investigators’ 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

- At least 15 letter improvement from baseline in BCVA at Week 24

![Chart showing percentage of patients with at least 15 letter improvement from baseline in BCVA at Week 24.](chart)

- Mean BCVA by Week

![Graph showing mean BCVA by week.](graph)
A 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)

*in subjects who completed the study with gradable images
## Safety: Treatment Emergent Adverse Events (TEAE)

|                                  | Unrescued CLS-TA  
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 83</td>
<td></td>
</tr>
<tr>
<td>% of subjects with ≥1 TEAE</td>
<td>48.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>63.0%</td>
<td></td>
</tr>
<tr>
<td>AEs related to elevated IOP</td>
<td>10.8%</td>
<td></td>
</tr>
<tr>
<td>Incidence of Cataract</td>
<td>4.8%</td>
<td></td>
</tr>
<tr>
<td>IOP-related surgical interventions</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td></td>
<td>none</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 46</td>
<td></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

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