Suprachoroidal CLS-TA Improves Visual Acuity and Macular Edema in Noninfectious Uveitis: Results of the Phase 3 PEACHTREE Study

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42nd Annual Macula Society Meeting
Bonita Springs, FL
February 13-16, 2019
Financial Disclosures

• Clearside Biomedical, Inc. (Consultant)
• Santen (Consultant)
• AGTC (Consultant)
• Research to Prevent Blindness (Grant)
• Marcus Foundation Combating Childhood Illness Seed Funding (Grant)
Thank You to the PEACHTREE Investigators!
Macular Edema Due to Noninfectious Uveitis

- Macular edema (ME) is the leading cause of vision impairment and vision loss in uveitis\(^1\)
- Commonly observed across anatomic subtypes of uveitis
  - 34-66% of intermediate, posterior, panuveitis
  - 11% of anterior uveitis
- Macular edema may persist despite adequate control of inflammation

• **Favorable drug concentrations:** Retina, RPE, choroid >> Anterior segment
• Potential for uveitic macular edema with fewer side effects
• Primary endpoint: Proportion of subjects gaining ≥15 ETDRS letters in BCVA at week 24
• 3:2 randomization of suprachoroidal CLS-TA vs. sham procedure
Key Inclusion and Exclusion Criteria

**Inclusion**
- Macular edema with central subfield thickness ≥300 microns
- Noninfectious uveitis of any associated diagnosis/etiology
- Any anatomic location: anterior, intermediate, posterior and panuveitis
- Disease activity: Active or controlled inflammation
- Visual acuity: 20/800 to 20/40 (≥5 to ≤70 ETDRS letters)

**Exclusion**
- Any ocular disease or active infection in the study eye other than uveitis
- Intraocular pressure >22 mmHg or uncontrolled glaucoma
- Subjects ≤22 mmHg could be on up to 2 IOP-lowering medications
Baseline Subjects Characteristics - Similar Between Treatment Groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CLS-TA N=96</th>
<th>Control N=64</th>
<th>Overall N=160</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>42 (43.8)</td>
<td>30 (46.9)</td>
<td>72 (45.0)</td>
</tr>
<tr>
<td>Female</td>
<td>54 (56.3)</td>
<td>34 (53.1)</td>
<td>88 (55.0)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>50.40 (14.2)</td>
<td>50.0 (15.1)</td>
<td>50.2 (14.5)</td>
</tr>
<tr>
<td>BCVA, study eye (ETDRS letters)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>54.7 (13.9)</td>
<td>53.5 (12.9)</td>
<td>54.2 (13.5)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>57 (9 – 89)</td>
<td>54 (12-79)</td>
<td>56 (9-89)</td>
</tr>
<tr>
<td>CST, study eye (μm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>480.9 (153.2)</td>
<td>525.4 (158.1)</td>
<td>498.7 (156.3)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>453.0 (256-857)</td>
<td>518.5 (274-971)</td>
<td>481.5 (256-971)</td>
</tr>
</tbody>
</table>

CST: central subfield thickness; ETDRS: Early Treatment Diabetic Retinopathy Study
All Anatomic Subtypes Enrolled

CLS-TA (N=96)
- Panuveitis: 29.2%
  - Anterior: 28.1%
  - Posterior: 22.9%
  - Intermediate: 35.4%

Control (N=64)
- Panuveitis: 37.5%
  - Anterior: 21.9%
  - Posterior: 20.3%
  - Intermediate: 35.9%

Overall (N=160)
- Panuveitis: 32.5%
  - Anterior: 25.6%
  - Posterior: 21.9%
  - Intermediate: 35.6%
PEACHTREE Met Its Primary Efficacy Endpoint

Subjects gaining ≥15 ETDRS letters from baseline, %

\( p < 0.001 \) for comparison

![Bar chart showing subjects gaining ≥15 ETDRS letters from baseline]

- **Subjects gaining ≥15 ETDRS letters from baseline, %**
  - **CLS-TA (N=96):** 46.9%
  - **Control (N=64):** 15.6%

Intention-to-treat population; LOCF imputation.

The \( p \)-value is based on a CMH Cochran-Mantel-Haenszel test for general association between treatment and response with stratification by country.

ETDRS, Early treatment diabetic retinopathy study; LOCF, last observation carried forward.
Mean Change in BCVA

*Improvement From as Early as Week 4 Through Week 24 in the CLS-TA Arm*

Intention-to-treat population; LOCF imputation.
t-test. Differences between the CLS-TA and control arms were significant at each visit.

BCVA, best corrected visual acuity.
BCVA Mean Change from Baseline by Anatomic Location

**Anterior**

- Visit Week 0: 2.6
- Visit Week 4: 1.2
- Visit Week 8: 2.2
- Visit Week 12: 5.4
- Visit Week 16: 4.5
- Visit Week 20: 2.9
- Mean change in BCVA: 9.0

**Intermediate**

- Visit Week 0: 1.5
- Visit Week 4: 2.5
- Visit Week 8: 3.1
- Visit Week 12: 5.5
- Visit Week 16: 7.2
- Visit Week 20: 6.7
- Mean change in BCVA: 11.2

**Posterior**

- Visit Week 0: 10.4
- Visit Week 4: 15.8
- Visit Week 8: 16.5
- Visit Week 12: 18.2
- Visit Week 16: 16.4
- Visit Week 20: 15.6
- Mean change in BCVA: 10.9

**Panuveitis**

- Visit Week 0: -0.9
- Visit Week 4: -1.4
- Visit Week 8: -2.0
- Visit Week 12: -1.8
- Visit Week 16: -2.5
- Visit Week 20: -1.6
- Mean change in BCVA: 8.6
Mean Change in Central Subfield Thickness

*Improvement From as Early as Week 4 through Week 24 in CLS-TA Arm*

Intention-to-treat population; LOCF imputation.

CST, central subfield retinal thickness.
Mean Change from Baseline in CST by Anatomic Location

**Anterior**

Mean Change in Central Subfield Thickness (µm)

Visit Week

-15.1 -16.0 -6.8 -12.0 -19.5 -38.9

-103.8 -126.0 -115.8 -126.5 -132.7 -106.8

\( p = 0.229 \)

**Intermediate**

Mean Change in Central Subfield Thickness (µm)

Visit Week

-19.7 -47.6 -29.8 -36.7 -28.7 -40.2

-167.3 -173.4 -180.7 -182.7 -172.9 -155.1

\( p = 0.013 \)

**Posterior**

Mean Change in Central Subfield Thickness (µm)

Visit Week

11.5 -6.3 6.1 20.0 -22.2 -19.1

-148.0 -152.1 -120.0 -178.4 -165.6 -153.8

\( p = 0.021 \)

**Panuveitis**

Mean Change in Central Subfield Thickness (µm)

Visit Week

-19.1 -19.3 -15.4 -12.5 3.3 -6.2

-150.8 -113.1 -123.3 -170.2 -176.6 -164.3

\( p = 0.002 \)
Anterior Chamber and Vitreous Inflammation: % Subjects with Resolution, Week 24

P<0.001 for all comparisons (AC Cell, AC Flare, Vitreous Haze)
Kaplan-Meier Analysis: Time to Rescue

13% of the patients in the CLS-TA arm and 72% in the control arm required rescue therapy.
MAGNOLIA: Prospective, Non-interventional, Masked, Observational 24-week Extension Trial

- To be eligible for MAGNOLIA, subjects must have completed PEACHTREE and NOT have received rescue medication.
- Primary Endpoint: Time to rescue therapy relative to Day 0 of PEACHTREE.

Rescue criteria:
- Loss of 10 letters
- CST > 320 μm
- ↑ of 100 μm or ↑ 20% CST
- Investigator discretion
Kaplan-Meier: Time to First Rescue – Primary Endpoint

- 50% of CLS-TA subjects did not receive any additional medication through Week 48
- 9 months from last CLS-TA dose
Safety

Serious AEs
• No deaths
• Three SAEs in CLS-TA arm: none considered treatment-related
  • Two non-ocular (sialoadenitis, lumbar vertebral fracture)
  • One ocular (retinal detachment approximately 8 weeks after injection)

<table>
<thead>
<tr>
<th>Ocular AEs, Study Eye</th>
<th>CLS-TA 4.0 mg</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=96</td>
<td>N=64</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Number of subjects with ≥1 ocular AEs</td>
<td>49 (51.0)</td>
<td>37 (57.8)</td>
</tr>
<tr>
<td>Treatment-related ocular AEs</td>
<td>29 (30.2)</td>
<td>8 (12.5)</td>
</tr>
</tbody>
</table>

Ocular AEs
• AEs occurring in >5% subjects in the CLS-TA arm included: elevated IOP, eye pain, cataract
Elevated IOP Adverse Events

“Elevated IOP” includes (a) increased IOP, (b) ocular hypertension, and (c) glaucoma.

AE, adverse event; IOP, intraocular pressure.
Cataract Adverse Events

- New or worsening cataracts occurred with similar frequency in the CLS-TA and control groups.
- No cataract-related surgeries in this trial.

“Cataract” includes (a) cataract, (b) cataract subcapsular, and (c) cataract nuclear.
PEACHTREE Study: Take Home Points

Efficacy

• Primary endpoint was met, with ~47% of patients gaining ≥15 ETDRS letters
• Suprachoroidally injected CLS-TA significantly improved vision and macular edema in uveitis at all anatomical locations
• Anterior segment and vitreous inflammation resolved in the majority of CLS-TA patients

Safety

• Low rates of elevated IOP and cataract
• No SAEs attributed to CLS-TA
THANK YOU