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

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Thank You to the PEACHTREE Investigators!

USA

India

Israel
Macular Edema Due to Noninfectious Uveitis

Uveitis and Macular Edema

• Macular edema (ME) is the leading cause of vision impairment and vision loss in uveitis
• ME is common
  – 40% to 60% of intermediate, posterior and panuveitis
  – 20% anterior

Therapeutic options for ME

• Local periocular and intravitreal corticosteroids
• Systemic corticosteroids and steroid-sparing medications
Suprachoroidal Injection for Posterior Segment Disease

• Novel technique for suprachoroidal injection
  – 30G needle approx. 1000 microns in length
  – Proprietary microinjector syringe

• Laboratory data: Suprachoroidal vs. intravitreal injection
  – Higher bioavailability in the choroid, RPE, and retina
  – Lower exposure to the anterior segment
  – Potential for improved efficacy and safety
**Primary endpoint**: Proportion of subjects in each arm gaining ≥15 ETDRS letters in BCVA from baseline at week 24

• 3:2 randomization of suprachoroidally injected CLS-TA (N=96) vs. sham procedure (N=64)
Key Inclusion and Exclusion Criteria

Inclusion
• Non-infectious uveitis of any associated diagnosis/etiology
• Any anatomic location: anterior, intermediate, posterior and panuveitis
• Diagnosis of macular edema with central subfield thickness >300 microns
• Visual acuity: ≥5 and ≤70 ETDRS letters; 20/40 to 20/800
• Patients could have active or controlled disease at enrollment

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

ETDRS: Early treatment of diabetic retinopathy study
IOP: intraocular pressure
Baseline Demographic Characteristics Were Similar Between Treatment Groups

<table>
<thead>
<tr>
<th>Characteristic</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>
<td></td>
</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>50.4 (14.2)</td>
<td>50.0 (15.1)</td>
<td>50.2 (14.5)</td>
</tr>
</tbody>
</table>
Baseline Ocular Characteristics Were Similar Between Treatment Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CLS-TA N=96</th>
<th>Control N=64</th>
<th>Overall N=160</th>
</tr>
</thead>
<tbody>
<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>CRT, study eye (μm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>479.8 (149.7)</td>
<td>518.0 (150.0)</td>
<td>495 (150.5)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>456 (256-857)</td>
<td>517 (274-861)</td>
<td>481 (256-861)</td>
</tr>
<tr>
<td>Uveitis anatomic location, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>27 (28.1)</td>
<td>14 (21.9)</td>
<td>41 (25.6)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>34 (35.4)</td>
<td>23 (35.9)</td>
<td>57 (35.6)</td>
</tr>
<tr>
<td>Posterior</td>
<td>22 (22.9)</td>
<td>13 (20.3)</td>
<td>35 (21.9)</td>
</tr>
<tr>
<td>Panuveitis</td>
<td>28 (29.2)</td>
<td>24 (37.5)</td>
<td>52 (32.5)</td>
</tr>
</tbody>
</table>
PEACHTREE Met Its Primary Efficacy Endpoint: Visual Acuity Gain $\geq 15$ ETDRS Letters from Baseline

Subjects gaining $\geq 15$ ETDRS letters from baseline, %

\[ p < 0.001 \text{ for comparison} \]

- **CLS-TA (N=96)**: 46.9%
  - n=45

- **Control (N=64)**: 15.6%
  - n=10

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

Mean change at week 24 from baseline in BCVA in ETDRS letters read

\[ p < 0.001 \] for comparison

Mean change at each visit from baseline in BCVA in ETDRS letters read

- CLS-TA
- Control

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.
% Subjects Reading ≥70 ETDRS Letters (20/40 or Better) by Treatment Arm

Intention-to-treat population; LOCF imputation.
Mean Change in Central Subfield Thickness

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

Mean change from baseline at week 24 in central subfield thickness (µm)

CLS-TA (N=96)

Control (N=64)

-17.9

Mean change at each visit from baseline in central subfield thickness (µm)

CLS-TA

Control

Observation (week)

p<0.001 for comparison

Intention-to-treat population; LOCF imputation.

CST, central subfield retinal thickness.
Resolution of Macular Edema, CST <300 μm

Improvement in CLS-TA group at Week 4, Maintained through Week 24

Intention-to-treat population; LOCF imputation.
Less than 300 microns by SD-OCT
CST, central subfield retinal thickness.
Over 85% of the patients in the CLS-TA arm did not require rescue therapy.
Safety

Patient Retention
• 97% of patients completed the study

Serious Adverse Events
• There were no deaths in the study
• Three serious adverse events none considered to be treatment-related; none led to study discontinuation
Ocular Adverse Events: Study Eye

<table>
<thead>
<tr>
<th>Adverse Events, n (%)</th>
<th>CLS-TA 4.0 mg</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of ocular adverse events</td>
<td>122</td>
<td>54</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>
<tr>
<td>Serious ocular AEs</td>
<td>1 (1.0)</td>
<td>0</td>
</tr>
<tr>
<td>Treatment-related serious AEs</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Number of subjects with ≥1 eye disorder</td>
<td>41 (42.7)</td>
<td>34 (53.1)</td>
</tr>
</tbody>
</table>
## Ocular Adverse Events in ≥5% of Subjects

<table>
<thead>
<tr>
<th>Adverse Events, n (%)</th>
<th>CLS-TA 4.0 mg N=96</th>
<th>Control N=64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>7 (7.3)</td>
<td>4 (6.3)</td>
</tr>
<tr>
<td>Cystoid macular edema</td>
<td>0</td>
<td>11 (17.2)</td>
</tr>
<tr>
<td>Eye pain: time of procedure</td>
<td>12 (12.5)</td>
<td>3 (4.7)</td>
</tr>
<tr>
<td>Eye pain: any time post procedure</td>
<td>6 (6.3)</td>
<td>0</td>
</tr>
<tr>
<td>Elevated IOP: time of procedure</td>
<td>8 (8.3)</td>
<td>0</td>
</tr>
<tr>
<td>Elevated IOP: corticosteroid-related</td>
<td>11 (11.5)</td>
<td>(10) 15.6*</td>
</tr>
<tr>
<td>Uveitis</td>
<td>2 (2.1)</td>
<td>7 (10.9)</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>5 (5.2)</td>
<td>1 (1.6)</td>
</tr>
</tbody>
</table>

*All IOP-related events in the control group occurred after rescue local corticosteroid administration.*
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 AE of cataract-related surgeries in this trial.

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

Efficacy

- Suprachoroidal CLS-TA met the primary study endpoint, with a significantly greater proportion of subjects vs. control with ≥15 ETDRS BCVA gain at 6 months
- CLS-TA improved macular edema in uveitis patients by OCT criteria
- Vast majority of patients in CLS-TA arm did not require rescue therapy during study

Safety

- Favorable safety profile overall with no SAEs attributable to suprachoroidal CLS-TA
- Low rates of elevated IOP and cataract
THANK YOU