IOP Following Administration of Suprachoroidal Triamcinolone Acetonide Suspension (CLS-TA): Results from the Phase 3 PEACHTREE Clinical Trial for Uveitis

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Disclosures

- Allergan
- Aerie
- Allegro
- Genentech
- Regeneron
- Novartis
- Santen
- Clearside
- Guidepoint
- Apelis
- Optos
- Mallinckrodt
- Spark
- Eyepoint
The Suprachoroidal Space: Targeted & Compartmentalized Delivery
The Suprachoroidal Space: Targeted & Compartmentalized Delivery

Chart scales differ – Note relative differences
PEACHTREE: Phase 3, Randomized, Controlled, Double-Masked, Multicenter Trial

**Primary Endpoint:** Proportion of subjects with change from baseline ≥15 letters in BCVA at Week 24

**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

**Control Arm:** Sham injection procedure

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

**Enrollment**

- **N=96**

**Evaluation period – 6 months**

**RESCUE CRITERIA**

- BCVA: ↓ 10+ letters
- CST: \( \leq \) ↑ 100+ µm or 20% (whichever is lower)
- ↑ 1.5+ inflammation level
- Investigators’ medical judgement

**N=64**

- Sham

- Sham
Key Inclusion and Exclusion Criteria

Inclusion
• Diagnosis of macular edema with central subfield thickness $\geq 300$ microns
• Noninfectious uveitis of any associated diagnosis/etiology
• Any anatomic location: anterior, intermediate, posterior and panuveitis
• Visual acuity: 20/800 to 20/40 ($\geq 5$ to $\leq 70$ ETDRS letters)

Exclusion
• Any active ocular disease or infection in the study eye other than uveitis
• Intraocular pressure $>22$ mmHg or uncontrolled glaucoma; subjects $\leq 22$ 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
Baseline Subject Characteristics Similar Between 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>50.40 (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
## Baseline Subject Characteristics: IOP and Glaucoma

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<thead>
<tr>
<th>Characteristic</th>
<th>CLS-TA N=96</th>
<th>Control N=64</th>
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<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Any Medical History Related to Glaucoma or IOP</td>
<td>21 (21.9)</td>
<td>14 (21.9)</td>
</tr>
<tr>
<td>Angle closure glaucoma</td>
<td>0 (0)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>10 (10.4)</td>
<td>4 (6.3)</td>
</tr>
<tr>
<td>Glaucomatous optic disc atrophy</td>
<td>1 (1.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Intraocular pressure increased</td>
<td>2 (2.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>5 (5.2)</td>
<td>7 (10.9)</td>
</tr>
<tr>
<td>Open Angle Glaucoma</td>
<td>1 (1.0)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Trabeculectomy</td>
<td>1 (1.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Uveitic glaucoma</td>
<td>1 (1.0)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>≥ 1 IOP lowering medication</td>
<td>5 (5.2)</td>
<td>2 (3.1)</td>
</tr>
</tbody>
</table>
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.

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

$p<0.001$ for comparison
Mean Change in BCVA

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

Mean change from baseline in BCVA at Week 24

- **CLS-TA (N=96)**: 13.8
- **Control (N=64)**: 3.0

*p*<0.001 for comparison

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

BCVA, best corrected visual acuity.
Mean Change in Central Subfield Thickness

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

Intention-to-treat population; last observation carried forward imputation.
BSL, baseline mean value; CST, central subfield retinal thickness.
Kaplan–Meier Analysis: Time to Rescue

13% of the patients in the CLS-TA arm and 72% in the control arm required rescue therapy.

Intention-to-treat population
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

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<table>
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<tr>
<th>IOP-Related Events</th>
<th>CLS-TA 4.0 mg</th>
<th>Control</th>
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<tbody>
<tr>
<td></td>
<td>N = 96</td>
<td>N = 64</td>
</tr>
<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>
"Elevated IOP" includes (a) increased IOP, (b) ocular hypertension, and (c) glaucoma.

AE, adverse event; IOP, intraocular pressure.

Why are IOP AEs higher in the control group?
- 46/64 (72%) control patients received rescue therapy
- All 10 patients with IOP AEs received local corticosteroids as rescue therapy

n=11/96

n=10/64
Rescue Therapy Rates: CLS-TA (n=13) vs. Control (n=46)

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

*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 medication used per investigator discretion.
Mean IOP through Week 24

- Baseline
- Week 4
- Week 8
- Week 12
- Week 16
- Week 20
- Week 24

CLS-TA

Control
Sub-Analysis of IOP in PEACHTREE

Purpose: Characterize IOP in CLS-TA and control groups, in patients that were rescued versus those not rescued

Method: Analyze IOP AEs for the clinically relevant endpoints of \( \geq 30 \text{ mmHg IOP at any visit} \) and \( \geq 1 \text{ IOP lowering medication} \)

Four (4) subgroups analyzed:

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<td>CLS-TA</td>
<td>n=83/96 (86.5%)</td>
<td>n=13/96 (13.5%)</td>
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<td>n=18/64 (28.1%)</td>
<td>n=46/64 (71.9%)</td>
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$\geq 30$ mmHg IOP at any visit through 24-weeks

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- CLS-TA: $4.8\%$ not rescued, $10.9\%$ rescued
- Control: $28.1\%$ not rescued, $71.8\%$ rescued
≥ 1 IOP lowering medication* through 24-weeks

*IOP lowering medications administered for 30 days or more
IOP rates:
CLS-TA patients not rescued (n=83) vs. rescued (n=13)

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≥ 30 mmHg at any visit through Week 24
- CLS-TA: 15.4%
- Control: 7.2%

≥ 1 IOP lowering medication
- CLS-TA: 4.8%
- Control: 7.7%
IOP rates: Control patients not rescued (n=18) vs. rescued (n=46)

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- ≥ 30 mmHg at any visit through Week 24:
  - Not Rescued Control: N=5/46 (0.0%)
  - Rescued Control: N=6/46 (13.0%)

- ≥ 1 IOP lowering medication:
  - Not Rescued Control: N=5/46 (0.0%)
  - Rescued Control: N=6/46 (13.0%)
PEACHTREE: 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 noninfectious uveitis at all anatomical locations

Safety

• No SAEs attributable to CLS-TA

• Low rates of elevated IOP and cataract

• Cataract rate was similar to control arm

• No surgical intervention for an elevated IOP Adverse Event
Thank You