Clinical Trial Results From Patients With Macular Edema Due to Noninfectious Uveitis

Treated with 4.0 mg of triamcinolone acetonide using a suprachoroidal injection

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Financial Disclosures

• Research Grants and Consultant
  – Santen
  – Allergan
Key Take Home Points

• Novel microinjector syringe allows for office based delivery of therapy to the suprachoroidal space

• Injection of triamcinolone to suprachoroidal space was well tolerated and produced significant reductions in macular edema at 2 months
  – Significant improvements in BCVA
  – Reduction in other signs of uveitis
    • Anterior chamber cell
    • Vitreous haze

• Suggests that suprachoroidal injection of steroid provided efficacy in this study population
Suprachoroidal Injection in Development

• Potentially useful approach for the treatment of ocular conditions affecting the posterior segment of the eye

• Novel technique
  – 30G needle (1000 micron in length)
  – Proprietary microinjector syringe

• Proposed benefits
  – High bio availability in target tissues
  – Sparing anterior segment might result in fewer ocular side effects
  – Potential for longer duration

2. Noronha G. Using suprachoroidal administration as an approach to treat noninfectious uveitis – from concept through clinical data. ISOPT 2015 Clinical Conference proceedings. Published March 2016
Novel Microinjector Provides Access Through the Suprachoroidal Space to the Choroid and Retina
Phase 2 Clinical Study

Noninfectious disease etiologies

All anatomic locations included
- Anterior
- Intermediate
- Posterior
- Panuveitis

Macular edema
Phase 2 Study Design

This study was powered only for the 4.0 mg dose

4.0 mg Suprachoroidal CLS-TA: 0.8 mg Suprachoroidal CLS-TA; 4:1

High Dose Arm
4.0 mg Suprachoroidal injection of CLS-TA on Day 1

Day -10
Screening

Day 1
2 month study

Month 1
Month 2

Low Dose Arm
0.8 mg Suprachoroidal injection of CLS-TA on Day 1

Day 1

Month 1
Month 2

20 patients; 4:1 randomization

Primary Endpoint: Mean change in central retinal thickness

Single suprachoroidal injection of triamcinolone to the study eye
Subjects were followed for 2 months
## Phase 2 Study

Protocol Design: Target 20 (16:4) subjects - Actually Randomized: 22 (17:5)

<table>
<thead>
<tr>
<th>TOTAL NUMBER OF SUBJECTS</th>
<th>CLS-TA 4.0 mg N=17</th>
<th>CLS-TA 0.8 mg N=5</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>RANDOMIZED</td>
<td>17</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>COMPLETED</td>
<td>17</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>DISCONTINUED</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SAFETY</td>
<td>17</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>INTENT-TO-TREAT</td>
<td>17</td>
<td>5</td>
<td>22</td>
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</table>
## Study Demographics

<table>
<thead>
<tr>
<th></th>
<th>CLS-TA 4.0 mg N=17</th>
<th>CLS-TA 0.8 mg N=5</th>
<th>TOTAL N=22</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE (YEAR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEAN</td>
<td>52.2</td>
<td>51.8</td>
<td>52.1</td>
</tr>
<tr>
<td>MEDIAN</td>
<td>50.0</td>
<td>53.0</td>
<td>53.0</td>
</tr>
<tr>
<td>MIN, MAX</td>
<td>20, 83</td>
<td>24, 69</td>
<td>20, 83</td>
</tr>
<tr>
<td><strong>SEX n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALE</td>
<td>9 (52.9)</td>
<td>1 (20.0)</td>
<td>10 (45.5)</td>
</tr>
<tr>
<td>FEMALE</td>
<td>8 (47.1)</td>
<td>4 (80.0)</td>
<td>12 (54.5)</td>
</tr>
<tr>
<td><strong>RACE n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BLACK OR AFRICAN AMERICAN</td>
<td>2 (11.8)</td>
<td>2 (40.0)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>WHITE</td>
<td>15 (88.2)</td>
<td>3 (60.0)</td>
<td>18 (81.8)</td>
</tr>
</tbody>
</table>
Geographic Location of Uveitis: 4.0 mg Triamcinolone Group

- Anterior: 9 (53%)
- Intermediate: 2 (12%)
- Posterior: 1 (6%)
- Pan: 5 (29%)

CLS1001-201 Table 16.2.4-2.3 16 Dec 2015
Primary Endpoint: Central Subfield Thickness

Intent-to-treat (ITT) population: 4.0 mg dose N=16

<table>
<thead>
<tr>
<th>Month</th>
<th>Mean change in retinal thickness</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 1</td>
<td>-135</td>
<td>0.0056</td>
</tr>
<tr>
<td>Month 2</td>
<td>-164</td>
<td>0.0017</td>
</tr>
</tbody>
</table>

1 CST is the central retinal thickness measured using optical coherence tomography (OCT)

Mean baseline = 526 µm
# Secondary End Points: Macular Edema Reduction

- Subjects with a ≥ 20% reduction in CST
- Subjects with CST <310 microns

<table>
<thead>
<tr>
<th>Visit</th>
<th>CST information</th>
<th>4.0 mg (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Month 1</strong></td>
<td>Subjects with ≥ 20% reduction in CST</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Subjects with CST &lt;310 microns</td>
<td>9</td>
</tr>
<tr>
<td><strong>Month 2</strong></td>
<td>Subjects with ≥ 20% reduction in CST</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Subjects with CST &lt;310 microns</td>
<td>9</td>
</tr>
</tbody>
</table>
Change in Best Corrected Visual Acuity
Secondary Endpoint

ITT population; N=17

<table>
<thead>
<tr>
<th>Month</th>
<th>BCVA letters read change from baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 1</td>
<td>7.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Month 2</td>
<td>9.2</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Mean baseline = 60 letters
Anterior Cell Grade Change: Baseline to Month 2

<table>
<thead>
<tr>
<th>Cell Grade</th>
<th>Baseline</th>
<th>Month 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>0</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

Numbers indicate number of patients

Trend towards less ocular inflammation
Vitreous Haze Score Change: Baseline to Month 2

Vitreous haze change

Numbers indicate number of patients

Trend towards less ocular inflammation
Safety

• 1 Serious systemic adverse event in the study: atrial fibrillation
  – Occurred in the 4.0 mg group
  – Not related to study treatment

• No adverse events (AEs) that led to discontinuation

• 4 subjects received additional treatment (2 on 4 mg, 2 on 0.8 mg)

• No serious ocular adverse events

• No corticosteroid related increases in intraocular pressure (IOP)
No patient showed steroid related increases in IOP in either trial. No IOP lowering medication was required or used.
Summary

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• Phase 3 clinical trial is ongoing
Acknowledgments

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