Suprachoroidal Administration of Triamcinolone Acetonide

Combined Results of Phase 1/2 and Phase 2 Clinical Studies

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Disclosures

• Consultant or Speaker’s Bureau
  – Clearside Biomedical, Ocular Therapeutix, Janssen, Alcon, Allergan, Bayer, OD-OS, Spark, Takeda, Leica, Alimera Sciences, and Regeneron
Uveitis

Commonly treated with corticosteroids and/or immunosuppressive agents

- Macular edema (ME) is the most common cause of vision loss
  - 40% to 60% of intermediate, pan-, and posterior uveitis
  - 20% anterior uveitis

ME associated with uveitis is treated almost exclusively with local administration of corticosteroid

- Commonly used steroids include dexamethasone, fluocinolone, and triamcinolone acetonide (TA)
- TA has been demonstrated to reduce the complications of uveitis, including ME, and improve visual outcomes

1. Lardenoye CWTA et al. *Ophthalmology*. 2006;113(8):1446
Mechanisms for Local Administration of Corticosteroids

Challenges exist with all current methods to locally administer steroids

- **Incomplete delivery**
- **Inconsistent delivery**
  - Uncertain concentration of TA suspensions in syringe when preparing drug
  - Amount of drug diffusing to retina and choroid is uncertain
- **Side effect profile: IOP elevation and cataract formation**
  - 35–39% develop a moderate IOP elevation with TA
  - 1–5% develop a significant IOP elevation requiring IOP lowering surgery

Suprachoroidal administration is a novel treatment approach for the eye

- In preclinical animal models, drug administered suprachoroidally had high posterior tissue bioavailability
  - Drug distributes preferentially to the choroid and retina
  - Drug level in the anterior segment is minimal
  - Favorable efficacy is found with as little as 1/10th of intravitreal steroid dose

Suprachoroidal injection could become a useful approach for the treatment of ocular conditions affecting the posterior segment of the eye.

- Novel technique exists for suprachoroidal injection of drug utilizing a proprietary micro-injector syringe device
  - 30g needle approximately 1000 µm in length

- Proposed benefits
  - Efficacy advantages due to high bioavailability
  - Longer duration of effect
  - Fewer side effects as TA kept away from anterior structures

In Phase 1/2 and Phase 2 trials, consistent efficacy was observed, with a favorable safety profile, in patients with ME associated with uveitis.
**Background: Phase 1/2 Study in Noninfectious Uveitis**

**Open label, multi-center study**

- Subjects with noninfectious uveitis, and
  - Vitreous haze ≥1.5 or macular edema >310 μm on SD-OCT
  - BCVA +1.0 logMAR or better (20/200 Snellen equivalent) by ETDRS
- Single suprachoroidal injection of TA
  - Subjects were to be observed for 26 weeks post treatment
  - 8 subjects* received a single unilateral suprachoroidal injection of TA and followed for 26 wks

*of 11 total subjects
<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Age in years, median (min, max)</td>
<td>60 (42, 78)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>4 (36)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Uveitis classification for the study eye</td>
<td></td>
</tr>
<tr>
<td>Anterior plus intermediate uveitis</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Intermediate uveitis</td>
<td>2 (18)</td>
</tr>
<tr>
<td>Pan-uveitis</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Intraocular pressure in mmHg, median (min, max)</td>
<td>14 (10, 19)</td>
</tr>
<tr>
<td>BCVA (ETDRS) base logMAR score median (min, max)</td>
<td>0.50 (0.0, 1.0)</td>
</tr>
<tr>
<td>Central subfield thickness in microns, median (min, max)</td>
<td>469 (227, 825)</td>
</tr>
</tbody>
</table>
Phase 1/2 Study – Change in Visual Acuity from Baseline

Improvement in BCVA

<table>
<thead>
<tr>
<th>Improvement in BCVA</th>
<th>Week 4 N=7 n (%)</th>
<th>Week 8 N=8 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10 letters</td>
<td>5 (71)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>≥15 letters</td>
<td>2 (29)</td>
<td>5 (63)</td>
</tr>
</tbody>
</table>

CHANGE FROM BASELINE

<table>
<thead>
<tr>
<th>Change from baseline in letters read</th>
<th>MONTH 1</th>
<th>MONTH 2</th>
<th>MONTH 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 5</td>
<td>11</td>
<td>13</td>
<td>13.5</td>
</tr>
<tr>
<td>5 - 10</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 - 15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Phase 1/2 Study – Change in Retinal Thickness from Baseline

**Mean Reduction in Retinal Thickness**

<table>
<thead>
<tr>
<th>Week</th>
<th>Reduction in Retinal Thickness (µm)</th>
<th>Post-treatment observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk1</td>
<td>-123</td>
<td>n=7</td>
</tr>
<tr>
<td>Wk2</td>
<td>-127</td>
<td>n=6</td>
</tr>
<tr>
<td>Wk4</td>
<td>-152</td>
<td>n=7</td>
</tr>
<tr>
<td>Wk8</td>
<td>-154</td>
<td>n=6</td>
</tr>
<tr>
<td>Wk12</td>
<td>-110</td>
<td>n=5</td>
</tr>
<tr>
<td>Wk16</td>
<td>-76</td>
<td>n=4</td>
</tr>
<tr>
<td>Wk20</td>
<td>-132</td>
<td>n=3</td>
</tr>
<tr>
<td>Wk26</td>
<td>-107</td>
<td></td>
</tr>
</tbody>
</table>

**Reduction in Macular Edema**

<table>
<thead>
<tr>
<th>Reduction in Macular Edema</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥20%</td>
<td>N=7</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
</tr>
<tr>
<td></td>
<td>4 (57%)</td>
</tr>
</tbody>
</table>
Phase 1/2 Study – Changes in IOP

Normal IOP is below 22 mmHg
Safety Overview from Phase 1/2 Trial

38 total events
• Most mild to moderate (89%)

• 8 systemic AEs
  – 1 serious systemic AE, pulmonary embolism
    • Patient with known history of pulmonary embolism
  – None related to study treatment

• 21 ocular AEs
  – Most common ocular AE was eye pain which was attributed to procedure
  – 1 serious ocular AE, retina neovascularization
    • Due to progression of underlying disease
    • Not related to study drug
Combined Efficacy from Phase 1/2 and Phase 2

Change in BCVA from Baseline (N=25)

<table>
<thead>
<tr>
<th>Improvement in BCVA</th>
<th>MONTH 1 N=24 n (%)</th>
<th>MONTH 2 N=25 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10 letters</td>
<td>12 (50)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>≥15 letters</td>
<td>6 (25)</td>
<td>10 (40)</td>
</tr>
</tbody>
</table>
Combined Efficacy from Phase 1/2 and Phase 2

Mean change from baseline in retinal thickness

MONTH 1

MONTH 2

Mean change from baseline in retinal thickness (µm)

-200

-150

-100

-50

0

-150

-160
Combined Safety Overview from Phase 1/2 and Phase 2 Trials

- 43 ocular AEs
  - 21 from the Phase 1/2 and 22 from the Phase 2
  - No serious ocular AEs related to study drug
  - Most common ocular AE was eye pain which was attributed to procedure
    - 5 from Phase 1/2 and 4 from Phase 2
  - Two incidents (one in each study) of punctate keratitis
  - Single incidents of conjunctival hemorrhage, conjunctival edema, dry eye, eye irritation, ocular discomfort, eyelid margin crusting, retinal ischemia, and retinal neovascularization

- 2 systemic AEs, both serious
  - Pulmonary embolism and atrial fibrillation, one from each study
  - Neither related to study drug
Combined IOP Changes From Phase 1/2 and Phase 2

- Normal IOP is below 22 mmHg
- Elevated IOP: >30 mmHg or a relative increase of >10 mmHg
- No patient experienced steroid related IOP rise in either clinical trial
- No IOP lowering medication was required in any patient
Study data demonstrated proof of concept that suprachoroidal administration is a new approach with the potential for treating macular edema associated with non-infectious uveitis

- Findings include improvements in visual acuity and reductions in CRT
- Lack of steroid induced IOP rise in these two clinical studies suggests that the ocular distribution of the drug spared the anterior segment

These Phase 1/2 and Phase 2 clinical data support the belief that drug delivery to the suprachoroidal space can be a novel treatment approach for various posterior segment diseases