Suprachoroidally Injected CLS-TA Results in Rapid and Sustained Resolution of Macular Edema in a Majority of Patients

Results of DOGWOOD, PEACHTREE, and AZALEA Studies

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Disclosures

• Consultant or Speaker’s Bureau
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Purpose

To conduct a post-hoc evaluation of resolution of macular edema following suprachoroidally injected CLS-TA across 3 prospective, multicenter, clinical trials in patients with noninfectious uveitis

• Macular edema is the most common cause of vision impairment in patients with uveitis\(^1\)

• Corticosteroids are a sensible choice to treat this condition as inflammatory cytokines result in a dysfunctional blood-retinal barrier that results in accumulation of fluid\(^2\)

• The cumulative effect of chronic uveitis and the recurrence or persistence of macular edema can result in permanent tissue damage and irreversible vision loss\(^3\)

1. Rothova 1996
2. Lardenoye 2006
3. Durrani 2004
Mechanisms for Local Corticosteroid Administration

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\(^1\)
  – 1–5% develop a significant IOP elevation requiring IOP lowering surgery\(^2\)

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
  – Comparable efficacy is found with as little as 1/10\(^{th}\) of intravitreal steroid dose

Suprachoroidal Administration for Treatment of Noninfectious Uveitis

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

• Novel technique developed for suprachoroidal injection utilizing a proprietary microinjector syringe device
  – 30g needle approximately 1000 µm in length

• Proposed benefits of suprachoroidal corticosteroid
  – Efficacy advantages due to high bioavailability
  – Longer duration of effect
  – Fewer side effects as TA substantially spares anterior structures

In three distinct trials using suprachoridal CLS-TA to treat ME secondary to noninfectious uveitis, consistent efficacy was observed with a reasonable safety profile
Suprachoroidal Corticosteroid Noninfectious Uveitis Trials

- **DOGWOOD- Phase 2 Trial**
  - 8 weeks / 22 Patients

- **PEACHTREE- Phase 3**
  - 24 weeks / 160 Patients

- **AZALEA- Phase 3 Trial**
  - 24 weeks / 38 Patients

- A single SC injection of CLS-TA was given at baseline in each study. No additional medication was administered through week 12.

- In **PEACHTREE** and **AZALEA** that ran 24 weeks, a second protocol mandated SC injection of CLS-TA was given at week 12. No additional medication was administered from week 12 through week 24.
DOGWOOD, PEACHTREE, and AZALEA Studies

- Reduction in retinal thickness in patients with ME secondary to uveitis was evaluated following suprachoroidal injection of 4 mg of CLS-TA
  - For this post-hoc analysis, resolution was defined as a retinal thickness <300 microns by SD-OCT

- Patients were evaluated for the presence of intraretinal and subretinal fluid every 4 weeks through week 24
## Demographics

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>DOGWOOD N = 16</th>
<th>PEACHTREE N = 160</th>
<th>AZALEA N = 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years Mean (SD)</td>
<td></td>
<td>51.8 (20.2)</td>
<td>50.2 (14.5)</td>
<td>56.3 (14.5)</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td>50%</td>
<td>55%</td>
<td>60%</td>
</tr>
<tr>
<td>Duration of uveitis in months Mean (SD)</td>
<td></td>
<td>69 (81)</td>
<td>37 (51)</td>
<td>32 (35)</td>
</tr>
<tr>
<td>CST in µm Mean (SD)</td>
<td></td>
<td>537 (128.8)</td>
<td>499 (156)</td>
<td>399 (64.9)</td>
</tr>
<tr>
<td>ETDRS letters read Mean (SD)</td>
<td></td>
<td>60.5 (13.4)</td>
<td>54.2 (13.5)</td>
<td>65.7 (21.7)</td>
</tr>
</tbody>
</table>
Resolution in a Majority of Patients is Observed Rapidly

Percentage of patients with resolution of macular edema at **week 4**
(individual study data and combined data)

Data are consistent across the three studies, showing that approximately 50% of patients are below 300 microns in retinal thickness at 4 weeks.
Reduction in Retinal Thickness to <300 µm at Week 4

Percentage of patients with resolution of macular edema at **week 4**

The effect of suprachoroidal CLS-TA on CST appears to be rapid.
Reduction in Retinal Thickness to <300 µm at Week 8

Percentage of patients with resolution of macular edema at **week 8**

The effect of suprachoroidal CLS-TA on CST appears to be sustained through week 8 with no additional CLS-TA administered.

CST: central subfield retinal thickness
PEACHTREE and AZALEA Trials were 24 Weeks Long

• A protocol mandated second injection of CLS-TA was administered at week 12 only in PEACHTREE and AZALEA
  – Injection was administered despite over 50% of the patients in these trials showing resolution of ME and having improved vision at this time point

• After the 2nd CLS-TA injection at week 12, no additional CLS-TA was administered to these patients through week 24
Reduction in Retinal Thickness to <300 μm at Week 12

The effect of suprachoroidal CLS-TA on CST appears to be sustained through week 12 with no additional CLS-TA administered.

CST: central subfield retinal thickness
Reduction in Retinal Thickness to <300 µm at Week 24

Percentage of patients with resolution of macular edema at **week 24**

The effect of suprachoroidal CLS-TA on CST appears to be sustained between weeks 12 and 24 with no additional CLS-TA administered.
The rapid reduction in retinal thickness in a majority of patients, first observed at week 4, is sustained at each observation through 24 weeks.
Similar to the reductions in retinal thickness, improvements in BCVA are rapid and sustained through week 24.
Key Findings

• Use of CLS-TA to treat macular edema secondary to noninfectious uveitis results in a rapid (by week 4) reduction in retinal thickness
  – Resolution observed in over 50% of subjects following a single suprachoroidal injection

• Rapid resolution is sustained in a majority of patients through week 12 with no additional CLS-TA (or other treatment) administered

• A protocol mandated second injection of CLS-TA was administered at week 12 in two of the studies, PEACHTREE and AZALEA
  – Evaluation of the data show that over 50% of the patients in each of these trials showed resolution of ME and improved vision at this time point prior to the second injection
  – Data observed through Week 24 reveal a majority of patients continued to show macular edema resolution and did not require additional treatment

• Vision improvements are consistent with ME reduction results- approximately 10 ETDRS letters gained from baseline observed at week 24