Durability of Suprachoroidal Triamcinolone Acetonide in Combination with Afibbercept in the Management of Retinal Vein Occlusion: 9-Month Analysis of the TANZANITE Phase 2 Trial and Extension Study

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Disclosures

• Financial
  – Consultant - Allergan, Alimera, Bayer, Clearside Biomedical, DORC, Genentech, ONL Therapeutics, Regeneron
  – Speaker - Allergan, Regeneron
  – Research Support – Acucela, Alcon/Novartis, Alimera, Allergan, Apellis, Clearside Biomedical, DORC, DRCR.Net, Genentech/Roche, Iconic, Ophthotech, Regeneron/Bayer, Thrombogenics, Tyrogenex

• Human Subjects
  – This study is Institutional Review Board approved
Retinal Venous Occlusive Disease

Prevalence 1.5% > 75 years
FDA-Approved: ME Secondary to RVO

Block VEGF

Ranibizumab

Aflibercept

Dexamethasone
FDA-Approved: ME Secondary to RVO

Block VEGF

Aflibercept

Ranibizumab

Affect a multitude of transcriptional cascades

Inflammation

Vascular leakage

Angiogenesis

Corticosteroids

Dexamethasone
Suprachoroidal Delivery of Corticosteroids

- Maximize drug levels in retina
- Minimize drug levels in AC
- Potential to
  - Reduce cataract acceleration
  - Reduce incidence of increased IOP
Microneedle
Specifically for Suprachoroidal Delivery of Preservative Free Triamcinolone Acetonide (CLS-TA)

CLS-TA: Non-preserved, terminally sterilized, aqueous suspension of triamcinolone acetonide administered as a single injection of 4 mg in 0.1mL
TANZANITE
Phase 2

- 46 Patients
  - CST ≥ 310 µm
  - 20/40-20/400

- Months 1, 2 & 3:
  Determine eligibility for re-treatment
  - IR or SRF + CST ≥ 340 µm
  - Decrease BCVA ≥10 letters vs previous visit
  - Decrease BCVA ≥10 letters from best prior + increase CST 50 µm
TANZANITE: Endpoints

• Primary
  – Number of protocol determined aflibercept retreatments through Month 3

• Secondary
  – Mean improvements in best corrected visual acuity at Months 1, 2 and 3
  – Mean reductions in macular edema at Months 1, 2 and 3

• Safety
  – Incidence of treatment emergent adverse events and serious adverse events
  – Incidence of changes in safety parameters including: IOP, slit lamp bio-microscopy, indirect ophthalmoscopy, imaging parameters and vital signs
VA gains greater in the combination arm (CLS-TA + aflibercept) compared to the monotherapy arm (aflibercept)

Baseline: 49 ETDRS letters in each arm

Bars are standard error of the mean; * only month 2 showed p<0.05
TANZANITE Primary Endpoint

Number of Aflibercept Retreatments

14 fewer aflibercept retreatments in combination arm vs monotherapy arm

61% reduction in the requirement for additional intravitreal aflibercept injections
TANZANITE: *Retreatment by Subjects*

Did not meet criteria for aflibercept retreatment

- 78% (18/23) in combination arm
- 30% (7/23) in the control
TANZANITE Extension Study

CLS 1003-202

• Non-interventional & retrospective
• Assess the durability of suprachoroidal CLS-TA in combination with intravitreal aflibercept following completion of TANZANITE
TANZANITE Extension Study

Eligibility and Methods

• Patients who completed TANZANITE & did not receive re-treatment during TANZANITE
• Patients managed according to treating physician’s discretion without a prospective protocol
• Records were obtained retrospectively
• **Main efficacy outcome:** time to first RVO re-treatment
• Other outcomes: VA, CRT & Safety assessments
TANZANITE Extension
Enrollment & Re-Treatment

97% (31/32) eligible patients captured in Extension Study. Mean follow-up time: 247 days (range 1 – 587 days)

Combination (n=20)
3 (15%) re-treated
- 2: aflibercept
- 1: bevacizumab
- 1: unknown agent

Monotherapy (n=11)
6 (55%) re-treated
- 4: aflibercept
- 1: bevacizumab
- 1: unknown agent

Combination = CLS-TA + aflibercept. Monotherapy = aflibercept
TANZANITE + Extension

Time To and Need for First Re-Treatment

• Mean time to first re-treatment among patients (n=25) who received re-treatment
  – Combination: 108 days (26%; n=6)
  – Monotherapy: 68 days (83%; n=21)

• Greater proportion of combination patients never received re-treatment
  – Combination: 74% (n=17/23)
  – Monotherapy: 17% (n=4/23)

Combination = CLS-TA + aflibercept. Monotherapy = aflibercept
### TANZANITE

- **Combination Arm (SEM):**
  - Months 1: 15.6 (2.8)
  - Months 2: 20.1 (3.2)
  - Months 3: 18.6 (3.3)
  - Months 4-6: 11.6 (5.8)
  - Months 7-9: 8.3 (9.8)
  - Months 10-12: 8.2 (7.7)

- **Aflibercept Arm (SEM):**
  - Months 1: 9.3 (2.5)
  - Months 2: 13.5 (3.5)
  - Months 3: 12.0 (3.4)
  - Months 4-6: 9.9 (3.2)
  - Months 7-9: 11.1 (6.3)
  - Months 10-12: 7.4 (7.2)

<table>
<thead>
<tr>
<th>Months</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4-6</th>
<th>7-9</th>
<th>10-12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combination Arm (SEM)</strong></td>
<td>15.6 (2.8)</td>
<td>20.1 (3.2)</td>
<td>18.6 (3.3)</td>
<td>11.6 (5.8)</td>
<td>8.3 (9.8)</td>
<td>8.2 (7.7)</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>13</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td><strong>Aflibercept Arm (SEM)</strong></td>
<td>9.3 (2.5)</td>
<td>13.5 (3.5)</td>
<td>12.0 (3.4)</td>
<td>9.9 (3.2)</td>
<td>11.1 (6.3)</td>
<td>7.4 (7.2)</td>
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<tr>
<td><strong>n</strong></td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>9</td>
<td>7</td>
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</tbody>
</table>
Change in CRT

### Central Retinal Thickness

<table>
<thead>
<tr>
<th>Months</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4-6</th>
<th>7-9</th>
<th>10-12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combination Arm (SEM)</strong></td>
<td>-468 (60)</td>
<td>-481 (62)</td>
<td>-466 (58)</td>
<td>-471 (87)</td>
<td>-627 (102)</td>
<td>-431 (120)</td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>12</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td><strong>Aflibercept Arm (SEM)</strong></td>
<td>-467 (93)</td>
<td>-488 (94)</td>
<td>-381 (56)</td>
<td>-400 (71)</td>
<td>-377 (110)</td>
<td>-391 (86)</td>
</tr>
<tr>
<td>n</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>9</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

**TANZANITE**

**Extension Study**
## TANZANITE Safety: Ocular Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Aflibercept N=23 n (%)</th>
<th>Combination N=23 n (%)</th>
<th>Total N=46 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total # of adverse events</td>
<td>12</td>
<td>28</td>
<td>40</td>
</tr>
<tr>
<td>Cataract</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>AC Inflammation</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>1 (4.3)</td>
<td>2 (8.7)</td>
<td>3 (6.5)</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>1 (4.3)</td>
<td>0</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Corneal edema</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Eye pain</td>
<td>1 (4.3)</td>
<td>8 (34.8)</td>
<td>19 (19.6)</td>
</tr>
<tr>
<td>Lacrimation increased</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Macular fibrosis</td>
<td>1 (4.3)</td>
<td>0</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Ocular discomfort</td>
<td>2 (8.7)</td>
<td>0</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>0</td>
<td>2 (8.7)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Optic disc vascular disorder</td>
<td>1 (4.3)</td>
<td>0</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Optic nerve disorder</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Punctate keratitis</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Retinal degeneration</td>
<td>1 (4.3)</td>
<td>0</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Retinal hemorrhage</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>1 (4.3)</td>
<td>0</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Visual acuity reduced</td>
<td>2 (8.7)</td>
<td>0</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Vitreous floaters</td>
<td>0</td>
<td>1 (4.3)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>IOP increased</td>
<td>0</td>
<td>2 (8.7)</td>
<td>2 (4.3)</td>
</tr>
</tbody>
</table>
TANZANITE + Extension Study

Conclusions

• The combination of suprachoroidal preservative free triamcinolone acetonide (CLS-TA) with intravitreal aflibercept may increase the durability of treatment effect when managing eyes with ME secondary to RVO

• Additional Trials of CLS-TA in Retinal Vascular Diseases Ongoing
  – RVO
    • SAPPHIRE Phase III
  – DME
    • HULK Phase I/II
    • TYBEE Phase II