PURPOSE
Suprachoroidal Injection (SCI) via a Microinjector is an investigational ocular injection procedure developed to provide high, compartmentalized, bioavailable drug concentrations to posterior tissues via the suprachoroidal space (SCS). This analysis evaluates safety of SCIs in Phase 2 and 3 clinical trials involving a proprietary suspension of triamcinolone acetonide (CLS-TA).

METHODS
• Data analyzed from 8 clinical trials involving 3 disease states:
  - Noninfectious uveitis (NIU)
  - Diabetic macular edema (DME)
  - Retinal vein occlusion (RVO)

• SCI Group: Received 1+ SCI with CLS-TA 4 mg
  • as monotherapy or with intravitreal (IVT) anti-VEGF
  • Control Group: Patients who received IVT anti-VEGF and sham SCI injections

• Procedure-related ocular serious adverse events (SAEs) assessed included lens injury, suprachoroidal or vitreous hemorrhage, retinal tear, retinal detachment, endophthalmitis, and reduced visual acuity

RESULTS
SCI Group: 621 patients received one or more SCI
• There were no SAEs involving lens injury, suprachoroidal hemorrhage, endophthalmitis, or retinal tear, either alone as monotherapy or in conjunction with an IVT
• Three patients experienced 3 SAEs of interest in the study eye; all events were deemed unrelated to treatment by a masked Investigator
  • NIU patient: 1 NIU patient experienced Retinal detachment 2 months post SCI in a different quadrant
  • RVO patients: 2 RVO combination therapy patients experienced reduced vision

Control Group: 449 patients received IVT + sham SCI
• Three RVO patients experienced 3 SAEs of interest, all deemed unrelated to treatment by a masked Investigator
  • RVO patients: 1 patient experienced a retinal detachment, 1 patient experienced a vitreous hemorrhage and 1 patient experienced endophthalmitis

CONCLUSION
The safety profile of the suprachoroidal injection procedure with a microinjector is not meaningfully different than the IVT procedure within the 8 clinical trials assessed involving NIU, DME and RVO.

SOURCES
1. Chen et al. [2020]. Published in TVST. DOI: 10.1167/tvst.9.11.27

Financial Disclosures
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CH: Clearside Biomedical, Inc. (E, S)

F = Financial Support, E = Consultant, S = Employee, S = Shareholder

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Safety of Suprachoroidal Injection Procedure via Microinjector across Three Retinal Disorders
Visual acuity reduced

SUPRACHOROIDAL INJECTION PROCEDURE VIA MICROINJECTOR IN THE CLINIC
Scan QR code to view:

SRS Microinjector®

Hold the syringe perpendicular to the ocular surface, and insert the needle. Ensure fine contact with hub of the needle and the conjunctiva, creating a seal on the outer surface. Gently press on the white plunger handle and slowly inject over 30 seconds. Suprachoroidal injection with a Microinjector involves three key procedural steps:

1. perpendicular positioning of the microinjector, (2) contact with and compression on the globe, (3) slow injection once loss of resistance is established. Two free needle-lengths are available for use in the procedure.

SCI + IVT

Serious Adverse Events

NIU

DME

RVO

Across All Disease States

<table>
<thead>
<tr>
<th>Serious Adverse Events</th>
<th>TOTAL SCI (monotherapy)</th>
<th>SCI (monotherapy)</th>
<th>SCI + IVT Total SCI</th>
<th>SCI + IVT Total SCI</th>
<th>SCI + IVT Total SCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at risk, N</td>
<td>156</td>
<td>10</td>
<td>46</td>
<td>56</td>
<td>414</td>
</tr>
<tr>
<td>Patients with ≥1 event</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Intraocular pressure</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Visual acuity reduced</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Vitreous hemorrhage</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

| Total                  | 0 (0.0)                 | 0 (0.0)          | 0 (0.0)             | 0 (0.0)             | 1 (0.2)             |

IN THE CLINIC

NOTE: Investigational procedure performed in a clinical trial

NOTE: Safety of suprachoroidal injection procedure performed in a clinical trial involving a proprietary suspension of triamcinolone acetonide (CLS-TA).
Method for Post Hoc Analysis

• Suprachoroidal Injection (SCI) data analyzed from 8 clinical trials involving 3 diseases

<table>
<thead>
<tr>
<th>Noninfectious Uveitis (NIU)</th>
<th>Diabetic Macular Edema (DME)</th>
<th>Retinal Vein Occlusion (RVO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOGWOOD (NCT02255032)</td>
<td>HULK (NCT02949024)</td>
<td>TANZANITE (NCT02303184)</td>
</tr>
<tr>
<td>PEACHTREE (NCT02595398)</td>
<td>TYBEE (NCT03126786)</td>
<td>SAPPHIRE (NCT02980874)</td>
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<tr>
<td>AZALEA (NCT03097315)</td>
<td></td>
<td>TOPAZ (NCT03203447)</td>
</tr>
</tbody>
</table>

• SCI Group: Received 1+ SCI with CLS-TA 4 mg
  • as monotherapy or with intravitreal (IVT) anti-VEGF

• Control Group: Patients who received IVT anti-VEGF and sham SCI injections

• Procedure-related ocular serious adverse events (SAEs) assessed included lens injury, suprachoroidal or vitreous hemorrhage, retinal tear, retinal detachment, endophthalmitis, and reduced visual acuity
Suprachoroidal Injection with a Microinjector is performed as in office procedure

SCIs involve three key procedural steps:
1. perpendicular positioning of the microinjector,
2. contact with and compression on the globe,
3. a slow injection once loss of resistance is established.

Two free needle lengths are available for use in the procedure. ¹

Investigator uses two hands to perform the suprachoroidal injection.
- The primary hand controls pressure on the study eye and the orientation of the device.
- The second hand slowly administers the injection into the SCS.

¹ Scan QR code to view suprachoroidal injection procedure
Results: Serious Adverse Events (SAEs)

SCI Group (N=621 patients; 1,274 SCI)
• No SAEs involving lens injury, suprachoroidal hemorrhage, endophthalmitis, retinal tears in any patient receiving ≥1 SCI
• 3 SAEs of interest, all deemed “not related” by masked investigator
  • NIU: Retinal detachment (n=1), occurred 8 weeks post-injection in different quadrant than SCI
  • RVO: reduced vision (n=2)

Control (IVT + sham SCI, N=449 patients)
• 3 SAEs of interest, all deemed “not related” by masked investigator
  • RVO: retinal detachment, vitreous hemorrhage, endophthalmitis
## Serious Adverse Events in Study Eye

<table>
<thead>
<tr>
<th>Serious Adverse Events</th>
<th>NIU</th>
<th>DME</th>
<th>RVO</th>
<th>Across All Disease States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Patients with ≥1 event</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Intraocular pressure increased</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Visual acuity reduced</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Vitreous haemorrhage</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**Note on endophthalmitis & suprachoroidal hemorrhage:**

The true risks associated with intraocular injections of the vision-threatening SAEs of endophthalmitis and suprachoroidal hemorrhage, neither of which were reported in this study, is unknown, but is likely lower than 0.25%. The 1,274 SCI reported in this analysis, administered as monotherapy or in conjunction with an IVT anti-VEGF, provided a 95% chance of at least one case of a SAE being reported if the true rate of occurrence of the SAE was 0.24%.
Conclusion

• The safety profile of the suprachoroidal injection procedure with a microinjector is not clinically meaningfully different than the IVT injection procedure within the 8 clinical trials assessed involving 1,274 suprachoroidal injections in NIU, DME and RVO.