Safety of Suprachoroidal Injection Procedure via Microinjector across Three Retinal Disorders

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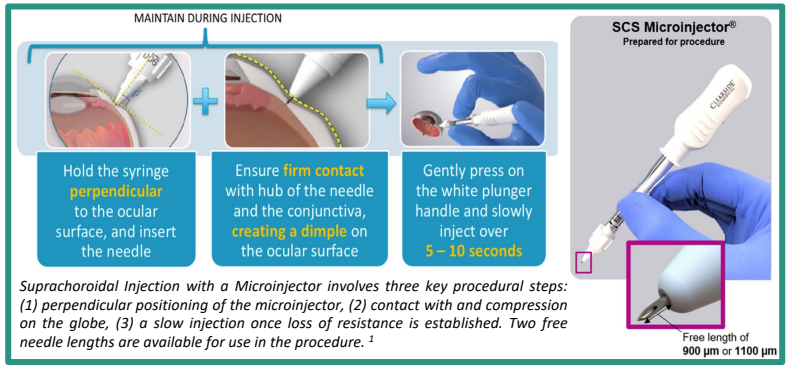
PURPOSE

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).



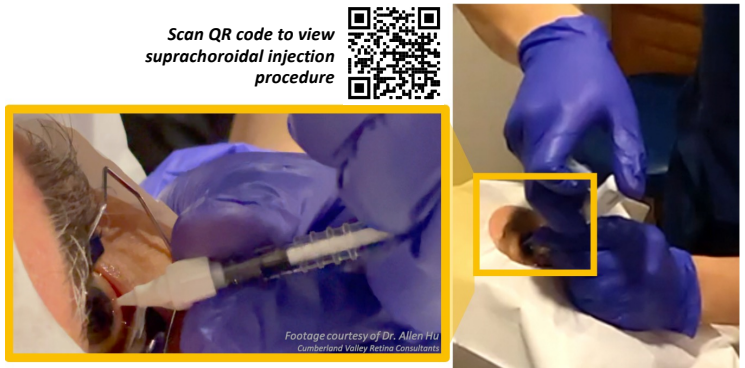
Suprachoroidal Injection with a Microinjector involves three key procedural steps: (1) perpendicular positioning of the microinjector, (2) contact with and compression on the globe, (3) a slow injection once loss of resistance is established. Two free needle lengths are available for use in the procedure. [1]

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

SUPRACHOROIDAL INJECTION PROCEDURE VIA MICROINJECTOR IN THE CLINIC

Scan QR code to view suprachoroidal injection procedure



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

NOTE: Investigational procedure performed in a clinical trial

SERIOUS ADVERSE EVENTS IN STUDY EYE

	NIU	DME			RVO	Across All Disease States	
Serious Adverse Events	TOTAL SCI (monotherapy)	SCI (monotherapy)	SCI + IVT	Total SCI	SCI + IVT	TOTAL SCI (monotherapy)	Total IVT+ SCI Sham
Patients at risk, N	156	10	46	56	414	626	449
Patients with ≥1 event	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	6 (1.0)	4 (0.9)
Endophthalmitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Intraocular pressure increased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	3 (0.5)	0 (0.0)
Retinal detachment	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
Visual acuity reduced	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.3)	0 (0.0)
Vitreous haemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

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

NOTE: The true risks associated with intraocular injections of endophthalmitis and suprachoroidal hemorrhage is likely lower than 0.25%. The 1,274 SCI reported in this analysis 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 meaningfully different than the IVT procedure within the 8 clinical trials assessed involving NIU, DME and RVO.

SOURCES

1. Chen-rei Wan, Barry Kapik, Charles C. Wykoff, Christopher R. Henry, Mark R. Barakat, Milan Shah, Rafael V. Andino, Thomas A. Ciulla; Clinical Characterization of Suprachoroidal Injection Procedure Utilizing a Microinjector across Three Retinal Disorders. *Trans. Vis. Sci. Tech.* 2020;9(11):27. doi: https://doi.org/10.1167/tvst.9.11.27.

Financial Disclosures

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

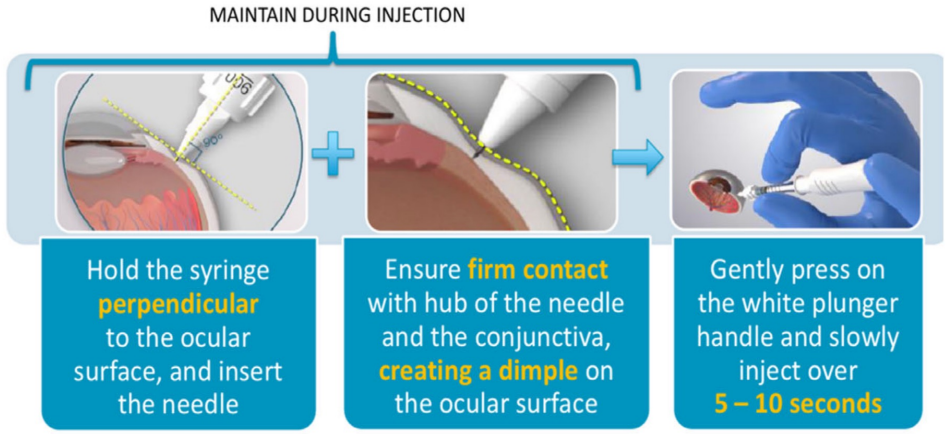
Method for Post Hoc Analysis

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

Noninfectious Uveitis (NIU)	Diabetic Macular Edema (DME)	Retinal Vein Occlusion (RVO)
DOGWOOD (NCT02255032) PEACHTREE (NCT02595398) AZALEA (NCT03097315)	HULK (NCT02949024) TYBEE (NCT03126786)	TANZANITE (NCT02303184) SAPPHIRE (NCT02980874) TOPAZ (NCT03203447)

- 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,
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Two free needle lengths are available for use in the procedure. [1]

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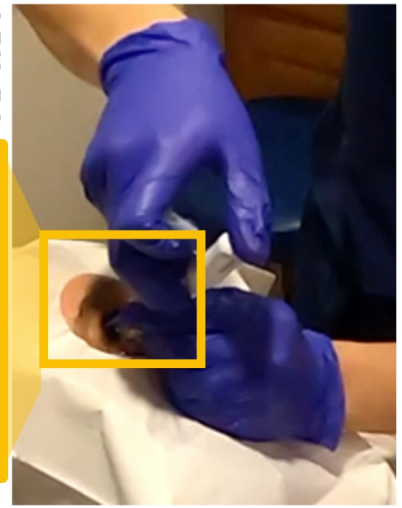

Results: Serious Adverse Events (SAEs)

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

	NIU	DME			RVO	Across All Disease States	
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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.