A Novel Suprachoroidal Delivery Technology: Results from a First-in-Human Pilot Study – Cohort 1

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Purpose

Suprachoroidal delivery represents a promising frontier for treating posterior segment ocular pathologies. However, safe, efficient, and consistent access to the suprachoroidal space (SCS) remains a challenge. The Everads Injector is a novel, non-surgical device utilizing a non-sharp tissue separator which, via tangential blunt dissection, opens a channel from the sclera to the choroid to access the SCS (figure 1). Previously reported data using this injector in non-human primates and rabbits demonstrated rapid delivery to the posterior segment and macula[1,2]. This study (NCT06314217) evaluates the safety and performance of the Everads Injector when delivering triamcinolone acetonide (TA) in patients with Diabetic Macular Edema (DME).

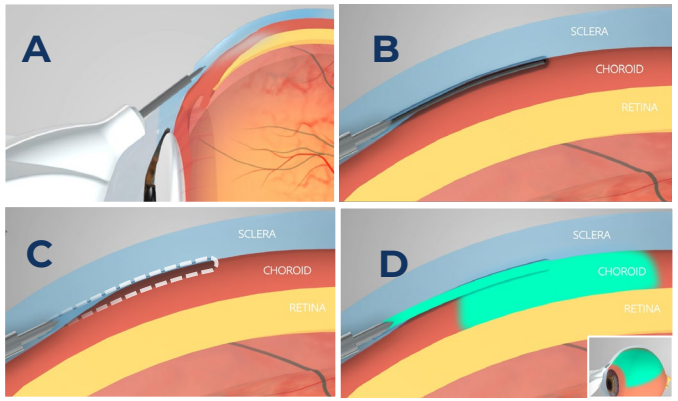


Figure 1: SCS delivery using the Everads Injector.
(A) Tangential insertion of Injector's bevel into sclera, with a sleeve stopper controlling entry depth, (B) Non-sharp tissue separator extended to create path into the SCS, (C) Separator retracts, leaving a channel to the SCS, (D) Therapeutic agent injected, and distributes throughout the posterior segment.

Methods

Three patients with DME who did not respond to standard intravitreal (IVT) treatments and met the inclusion and exclusion criteria for the first cohort, were screened and enrolled after providing signed informed consent. The study eyes were determined according to predefined eligibility criteria, including ETDRS BCVA letter score worse than 35 (Snellen equivalent of 20/200 imperial or 6/60 metric). Each patient received a single injection into the SCS of 4 mg of TA (Intracinol, Farmigea Ophthalmics) in a volume of 100 µl, using the Everads Injector. All injections were performed by the Principal Investigator (PI) in an office setting, undaer topical anesthesia without the need for an assistant to perform the injection. Thermal imaging was used to confirm injection into the SCS during the procedure. Following the injection, study eyes were assessed by indirect ophthalmoscopy and imaged with EDI-OCT. Intraocular pressure (IOP) was evaluated 30±10 minutes post-injection. Post-injection adverse events (AEs) were assessed. Within 1-hour post-injection, ophthalmic examinations were performed including: ETDRS BCVA, SD-OCT, fundus photography and slit-lamp biomicroscopy. Following the injection visit, subjects underwent four follow-up visits on Days 3, 14, 28, and 42.

Figure 2: Everads' Suprachoroidal Injector

References

1. Rotenstreich et al.2023
2. Sher et al. 2021

Results

Successful suprachoroidal delivery of TA was achieved in all three patients, confirmed by real-time thermal imaging which showed a rapid posterior flow of the drug. The injection was well tolerated in all patients; none of the patients reported experiencing pain. No serious adverse events (SAEs) were observed. Two patients exhibited mild subconjunctival hemorrhage in the treated eye immediately following the injection, which resolved spontaneously without any treatment and did not lead to any complications. Both events were classified as adverse device effects (ADEs), assessed by the PI to be mild in intensity. IOP was assessed at screening, baseline (pre-injection), post-injection and at all on-site follow up visits. In all three patients IOP was stable and remained within normal range throughout the study. Central macular thickness (CMT) and BCVA remained stable for all patients over the course of the study.

Conclusions

These results from the 1st cohort of patients in this first-in-human study using the Everads Injector demonstrates the safety, feasibility and tolerability of the injector for the delivery of TA into the SCS in an office setting and with topical anesthesia alone. Furthermore, this study highlights the advantage of utilizing real-time thermal imaging to confirm successful delivery into the SCS. Recruitment of patients into the second cohort is ongoing.

Financial Disclosures
YB is a consultant to Everads and holds stock options in the company. YR is a shareholder in Everads. AA, ABH, and MM are consultants to Everads. KMT is an employee of Everads and holds stock options the company.

Everads Injector – Suprachoroidal Delivery

Watch video here

MATERIALS & METHODS

Injection Procedure

- Standard 1mL luer lock syringe was filled with TA, and inserted into the injector, followed by priming
- Needle tip of Everads Injector (Figures 1,3) was placed ~4 mm posterior to limbus.
- Initial entry was done at an angle at 20°-30° followed by tangential advancement of the needle up to sleeve stopper, creating scleral tunnel.
- The tissue separator was extended and retracted to open channel to choroid via blunt dissection of scleral and choroidal tissues. (figure 3)
- Triamcinolone acetonide was then injected by depressing the syringe plunger.
- Following injection, a cotton tip applicator was placed over the injection site, and the injector was removed and discarded.

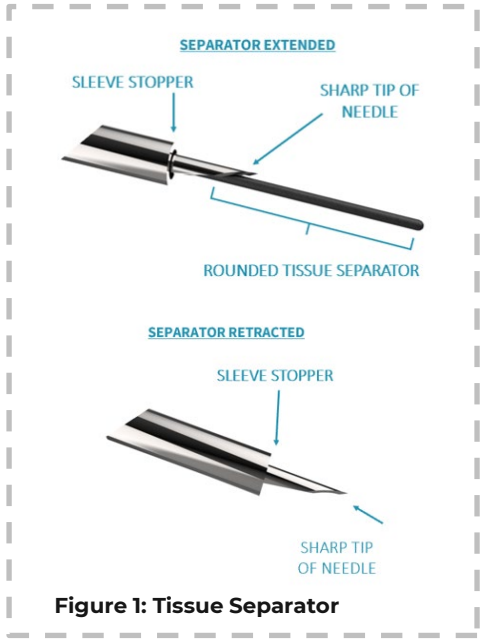


Figure 1: Tissue Separator

Figure 3: Everads' Injector

Assessments

- During injection, thermal imaging was used to visualize the injection into the SCS
- Following injection, study eyes were assessed by indirect ophthalmoscopy and imaged with EDI-OCT.
- Intraocular pressure (IOP) and adverse events (AEs) were assessed post-injection.
- Within 1-hour post-injection, ophthalmic examinations were performed including: ETDRS BCVA, SD-OCT, fundus photography and slit-lamp biomicroscopy.
- Following the injection visit, subjects underwent four follow-up visits on Days 3, 14, 28, and 42.

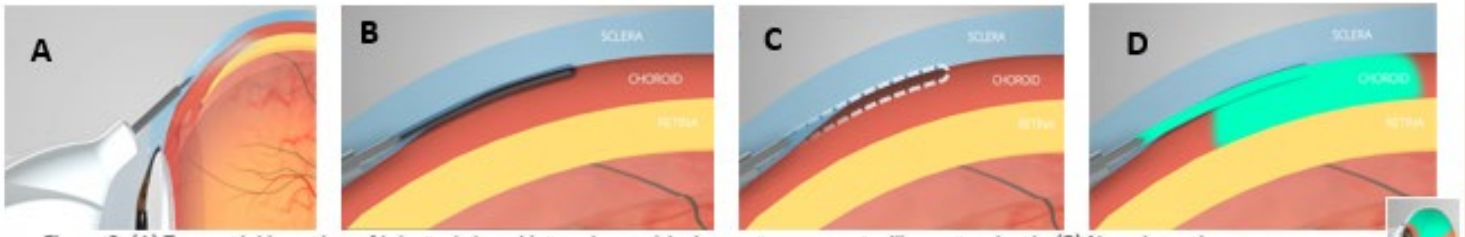
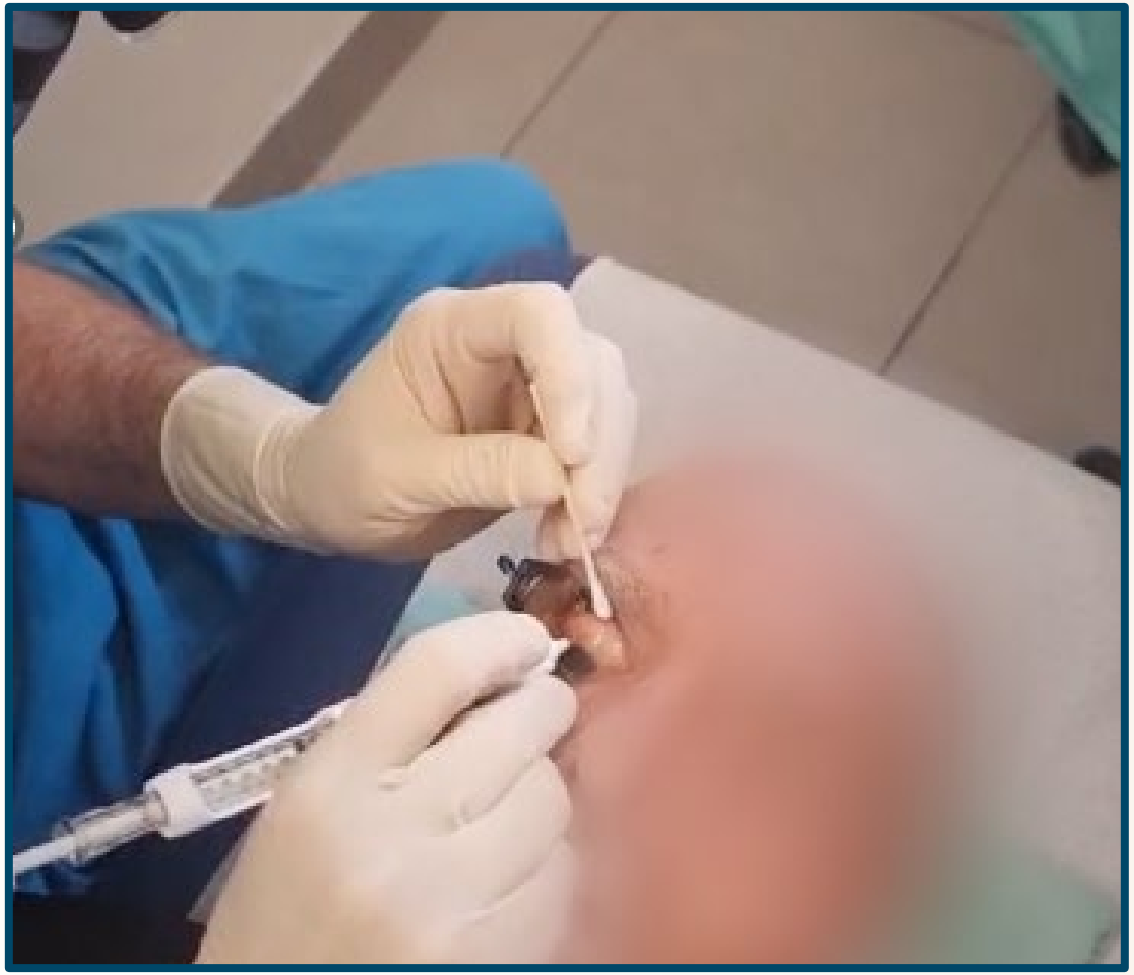
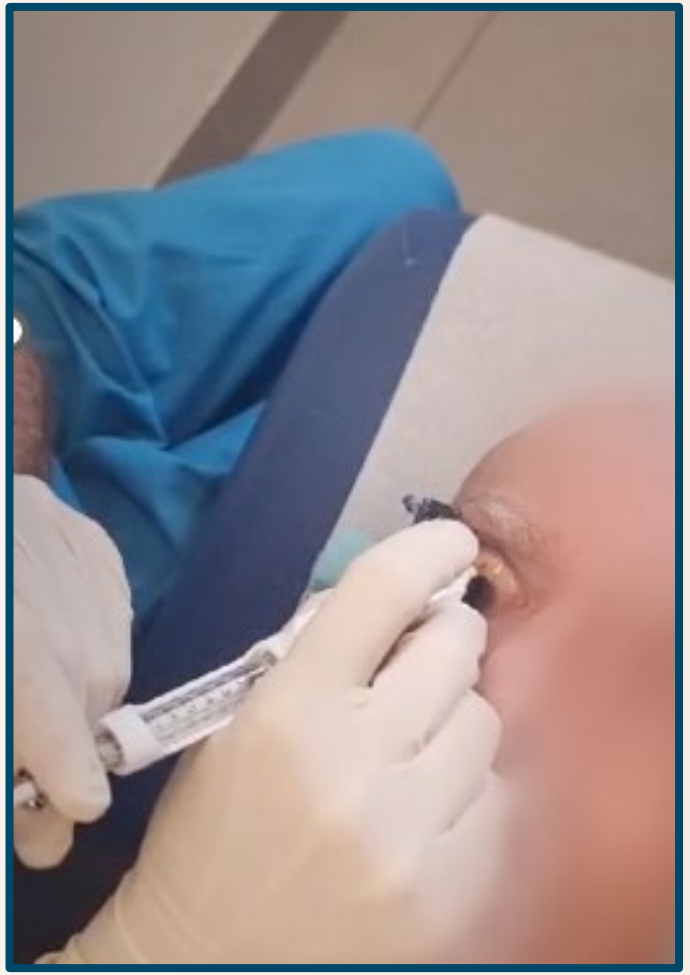


Figure 2: (A) Tangential insertion of Injector's bevel into sclera, with sleeve stopper controlling entry depth, (B) Non-sharp tissue separator extended to create path into suprachoroidal space, (C) Separator retracts, leaving a channel to choroid, (D) Therapeutic agent injected, and distributes throughout the posterior segment.

Quick office-based procedure under topical anesthetic



Insertion of needle bevel of the Injector and extension/retraction of tissue separator by pushing the separator button



Depression of the plunger of the syringe to inject the triamcinolone acetonide. 100µL was injected over 5-7 seconds. Total procedure time was ~40 seconds.

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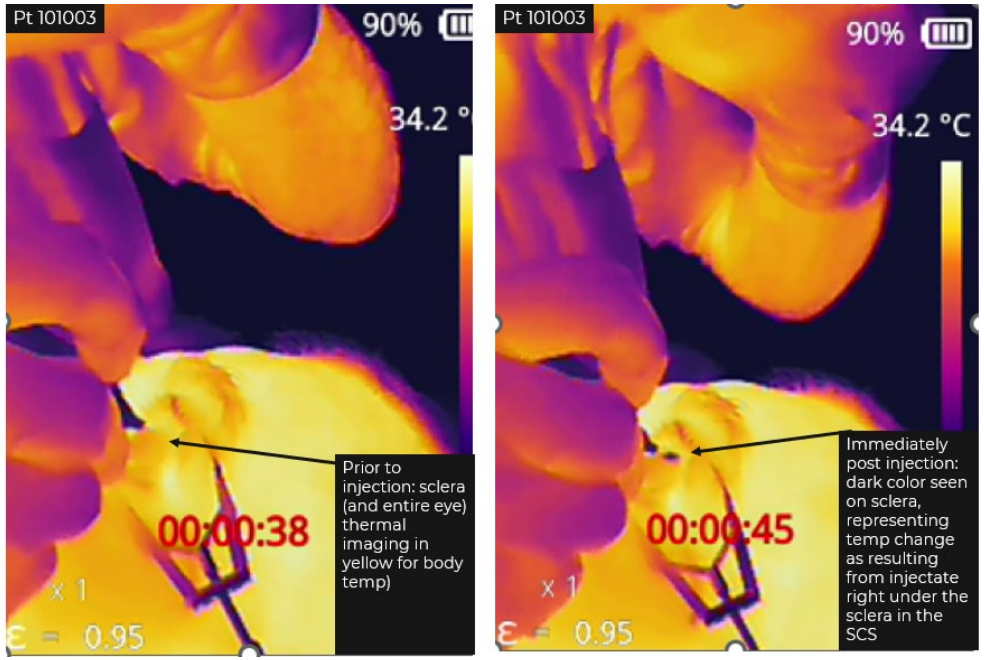
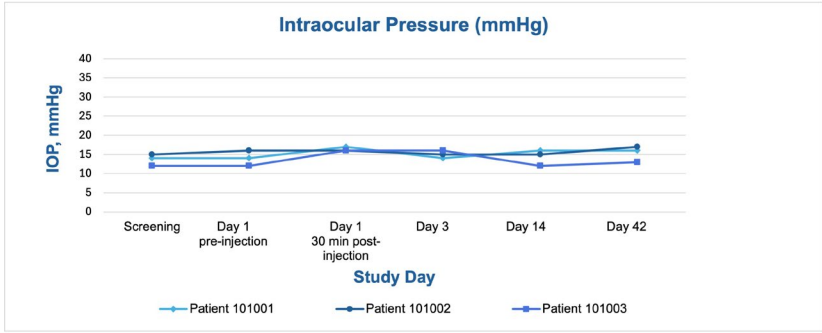
RESULTS

- Successful suprachoroidal delivery of TA was achieved in all three patients.
- The injection was well tolerated in all patients.
- No serious adverse events (SAEs) were observed.
- Two patients exhibited mild subconjunctival hemorrhage in the treated eye immediately following injection, which resolved spontaneously without any treatment and did not lead to any complications.



Suprachoroidal delivery confirmed using real-time thermal imaging.

- In all three patients, IOP was stable and remained within normal range throughout the study.
- Central macular thickness (CMT) and BCVA remained stable for all patients over the course of the study.



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CONCLUSIONS

- These results from the 1st cohort of patients in this first-in-human study using the Everads Injector demonstrates the safety, feasibility and tolerability of the injector for the delivery of TA into the SCS in an office setting.
- The anesthesia used for the study was limited to topical anaesthetic.
- This study also highlights the advantage of utilizing real-time thermal imaging to confirm successful delivery into the SCS.
- Following the evaluation of the results from this 1st Cohort by the ethics committee, this study was cleared to continue recruitment, which is ongoing.

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