In Vivo Assessment of Everads Novel Suprachoroidal Injector for Delivery of AAV5-GFP to the Macular RPE in Non-Human Primates

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EVERADS THERAPY

Introduction

While suprachoroidal delivery of therapeutics is emerging as a clinically effective drug administration route for posterior eye diseases, it has proven difficult to access reliably, safely, and efficiently, particularly when targeting the macula.
Everads has developed a novel, non-surgical suprachoroidal delivery system utilizing a unique, non-sharp tissue separator that, by way of tangential blunt dissection, opens a channel between the sclera and the choroid enabling optimized delivery (Figures 1,2). Everads' Injector is currently being evaluated in a clinical setting (NCT06314217).
This study assesses the performance of the Everads Injector in non-human primates (NHPs) injected with AAV5-GFP, focusing on its ability to reach the posterior segment.

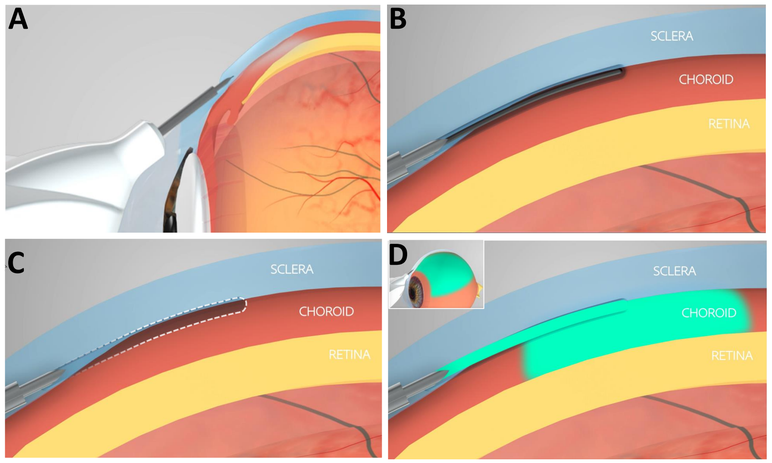


Figure 2: (A) Tangential insertion of Injector's bevel into sclera, with sleeve stopper controlling entry depth, (B) Non-sharp tissue separator extended to create path into suprachoroidal space, (C) Separator retracts, leaving a channel to choroid, (D) Therapeutic agent injected, and distributes throughout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

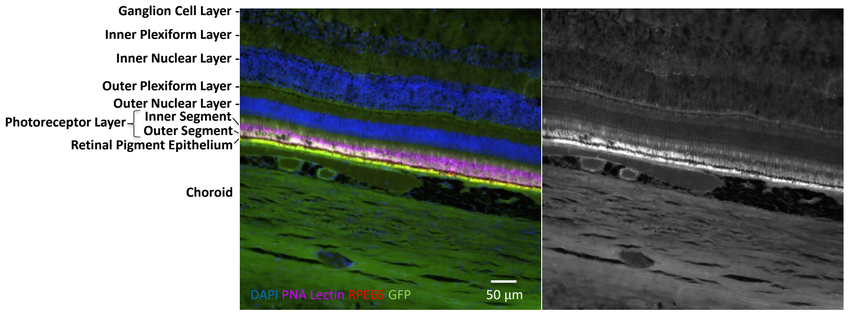
Methods

Six NHPs received bilateral (OU) AAV5-GFP injections at doses of $1.5x10^{11}$ or $7.5x10^{11}$ vg/eye delivered in a volume of 150 µL using the Everads Injector. The procedure lasted 30-45 seconds. Post-injection evaluations included intraocular pressure (IOP) measurement, slit lamp exam, OCT, and color fundus imaging. Fluorescence imaging at baseline and days 14, 28, 56, and 84 assessed in vivo GFP expression. On day 85, animals were sacrificed, and immunofluorescence on cryosections was analyzed. GFP localization and intensity were assessed using a semi-quantitative scoring system for each retinal layer at five positions within each eye: central fovea, peripheral fovea, central macula (excluding fovea), peripheral macula, peripheral retina (nasal).

Figure 1: Everads' Suprachoroidal Injector

Results

Suprachoroidal dosing yielded robust, widespread GFP expression predominantly within the RPE across the entire posterior segment including at the macula (figure 4).
No procedure-related adverse events were observed; there were no signs of retinal detachment, edema, vasculitis, or other major ocular complications. Ocular inflammation, as assessed by slit lamp biomicroscopy, ranged from absent to mild over the course of the study. Retinal morphology remained within normal limits. Retinal thickness and volume as seen on OCT remained stable for all treated eyes over the course of the study. Physical examination was normal for all animals, and all animals were found to be in good health throughout the study.



Section Level	GCL	IPL	INL	OPL	ONL	IS	OS	RPE	C	ONH	S
Peripheral-Nasal											
Macula Peripheral											
Macula Central											
Fovea Peripheral											
Fovea Central											

Undetected — High

Figure 4: Immunohistochemical staining of ocular cryosections demonstrating bright GFP expression within the retinal pigment epithelium (RPE) and outer segment (OS) photoreceptor layers in the macular region.
Semi-quantitative analysis of GFP expression demonstrates the strongest GFP signal in the RPE of the central macula. GFP signal was consistently observed in the RPE and OS in all sections evaluated. In some sections, GFP was occasionally observed in the ganglion cell layer (GCL), inner segment (IS) photoreceptor layer and the choroid (C).

Conclusions

Suprachoroidal delivery of AAV5-GFP using the Everads Injector was well-tolerated, yielding robust, widespread GFP expression predominantly within the RPE across the entire retina. No significant procedure-related adverse events were noted, and only transient inflammation was observed. This study highlights the Everads Injector's safety and effectiveness, and supports its use for delivering AAV-based gene therapies to the posterior segment and macula.

Financial Disclosures
K Mano Tamir is an employee of Everads. M Mangelus and Y Barak are consultants to Everads. Both Y Barak and K Mano Tamir hold stock options in Everads. M Lawrence is an employee of Virscio

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