Targeted Drug Delivery Within the Eye Through the Suprachoroidal Space

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To the Editor,

ALTHOUGH DRUG DELIVERY targeted to the eye is in widespread use, targeting drug delivery within the eye has received less attention. Indeed, topical eye drops generally target the anterior segment and intravitreal injections target the posterior segment, but diseases are usually more localized within these regions of the eye. Better targeting to the sites of therapeutic action within the eye may play a role in increasing efficacy while reducing side effects.

Suprachoroidal administration is an emerging investigational route for the treatment of ophthalmic diseases that enables targeting sites of therapeutic drug action within the eye (Fig. 1).¹ Drug administration in this manner, between the choroid and sclera, offers the unique capability of targeting a formulation to disease sites in the choroid and adjacent retina. When a formulation is injected, the choroid and sclera separate to form the suprachoroidal space (SCS), allowing the formulation to spread circumferentially around the eye. Recent work has shown the ability to further localize drug delivery near the posterior pole, adjacent to the ciliary body and other locations within the SCS using novel formulations and delivery methods.² The resulting targeted delivery of the drug to specific sites within the eye could improve management of diseases such as uveitis, retinal vein occlusion (RVO), age-related macular degeneration, glaucoma, and others.

In animal studies, solutions, suspensions, and even gel formulations have been administered through the SCS. In addition, we have developed microneedles as a nonsurgical method of SCS delivery performed in both animals and humans. These microneedles are designed to penetrate perpendicularly across the sclera, stopping at the base of the sclera, where fluid injection can open the SCS.³

Clearside Biomedical is conducting clinical trials to evaluate treatment via suprachoroidal delivery of its proprietary formulation of triamcinolone acetonide (TA) in humans. In phase 1/2 and phase 2 clinical trials in noninfectious uveitis, patients have experienced reductions in macular edema and improvements in visual acuity.⁴ A phase 3 trial in noninfectious uveitis is currently ongoing and enrolling patients. Recently, in a phase 2 trial in RVO, subjects receiving an initial treatment of suprachoroidal TA concomitantly with intravitreal aflibercept required 60% fewer additional injections of aflibercept than those receiving an initial treatment of in-

travitreal aflibercept alone during a 3-month trial period. Furthermore, subjects who received the concomitant treatment of TA plus aflibercept on average gained more letters in best corrected visual acuity than aflibercept monotherapy (ie, 19 letters vs. 11 letters, respectively, at the end of the 3-month trial period). There were no treatment-related serious adverse

FIG. 1. Suprachoroidal injection using a microneedle. (A) Histological section demonstrating injection of fluorescent nanoparticles (orange) into the suprachoroidal space of a pig eye. (B) Clearside Biomedical's SCSTM microinjector for suprachoroidal injection.

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events reported in these trials and the treatment was generally well tolerated.⁵

The growing arsenal of drugs to treat posterior-segment indications provides great promise to patients with blinding eye diseases. However, conventional intravitreal injection, which floods the posterior segment with drug, may not be the best route of administration in many cases. Targeting delivery to sites of therapeutic action through the SCS, especially when administered with a microneedle and coupled with novel formulations, may increase drug effectiveness and reduce side effects, thereby improving therapy of ocular diseases.

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Author Disclosure Statement

The potential conflict of interest has been disclosed and is overseen by Georgia Institute of Technology and Emory University.

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