Suprachoroidal Delivery of Small Molecule Suspensions and Nanoparticles

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Purpose:
The small molecule suspension triamcinolone acetonide delivered via suprachoroidal injection has demonstrated signs of efficacy and safety in preclinical models. Those results were corroborated in Phase 3 clinical trials for noninfectious uveitis. This study evaluated the suprachoroidal space (SCS) as a delivery pathway for other small molecule and nanoparticles suspensions.

Methods:
Agents were tested in rabbit eyes for pharmacokinetic (PK) effect and ocular distribution, including compartmentalization and durability. Agents tested suprachoroidally included small molecule suspensions of a tyrosine kinase inhibitor (TKI), complement inhibitor and DNA nanoparticles (DNPs).

Results:
In animal studies, suprachoroidal (SC) delivery of small molecule suspensions of a TKI and complement inhibitor demonstrated greater concentration of those agents in the retinal pigment epithelium (RPE)/sclera/choroid/retina than in anterior segment tissues. At 3 months, concentration of TKI and complement inhibitor in the RPE-sclera-choroid levels remained well above (>1000x) the relevant IC50 levels. The durability of posterior segment levels was greater than 3 months. Preclinical studies demonstrate signs of efficacy with TKI in neovascularization models. In a rabbit model, DNPs delivered suprachoroidally demonstrated similar activity of a marker gene as DNPs delivered subretinally.

Conclusions:
Suprachoroidal delivery may provide an office based method to target pharmacologic agents to the RPE, sclera, choroid and retina while minimizing exposure to other ocular tissues, such as the lens and the cornea. Small molecule suspensions demonstrate prolonged therapeutic levels with the potential for sustained release and high bioavailability, while showing compartmentalization, potentially minimizing adverse effects, such as cataract formation or corneal toxicity. Additionally, suprachoroidal administration of DNA nanoparticles may be as effective as subretinal administration. These attributes correlated to outcomes for corticosteroids, as demonstrated across multiple clinical trials. Further study with TKI and complement inhibitor suspensions, as well as nanoparticles, are warranted to fully investigate the potential efficacy and safety of this drug delivery method.