

## **Topical Ophthalmic Pazopanib Therapy for Exudative Age-Related Macular Degeneration**

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Pazopanib is a receptor tyrosine kinase inhibitor that targets the VEGF, PDGF, and c-kit receptors and demonstrates potent anti-angiogenic activity in standard bioassays. With topical ophthalmic dosing, distribution studies strongly suggest a conjunctival/scleral route to the choroid and retina, and significant activity is seen in preclinical models of choroidal neovascularization. In a phase IIa proof-of-concept study, 70 subjects with active exudative AMD received one of three pazopanib eyedrop dosing regimens in the study eye for 28 days. For the overall study group, no significant change from baseline in central retinal lesion thickness (primary endpoint) was observed at day 29. A statistically significant increase in BCVA from baseline was seen in the highest dose (5 mg/ml TID) treatment arm. Preliminary analysis showed a potential pharmacogenetic association between *CFH* Y402H genotypes and treatment efficacy. In patients with the low risk (TT) genotype, a statistically significant treatment effect was seen for both central retinal thickness and BCVA. No apparent safety signals were identified that would preclude further investigation of this novel treatment approach.