


Presentation Abstract

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Abstract Title: **SAVE (Superdose AntiVEgf) Trial - 2.0-mg Intravitreal Ranibizumab For Recalcitrant Neovascular Age-related Macular Degeneration**

Presentation Start/End Time: Monday, May 02, 2011, 2:30 PM - 2:45 PM

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Reviewing Code: 109 age-related macular degeneration: limited randomized clinical trial - RE

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Keywords: 412 age-related macular degeneration; 466 clinical (human) or epidemiologic studies: treatment/prevention assessment/controlled clinical trials

Abstract Body: **Purpose:** Many patients with neovascular AMD have persistent edema on OCT or fluorescein leakage despite monthly anti-VEGF intravitreal injections. As the MARINA and ANCHOR trials both demonstrated a dose-response curve favoring 0.5 mg ranibizumab over 0.3 mg ranibizumab dosing, this study was designed to test whether a higher dose of ranibizumab might lead to further anatomic and visual acuity improvements.
Methods: In this Phase I-II multicenter open label controlled clinical trial, 50 patients with recalcitrant neovascular AMD (defined as having leakage on SD OCT despite monthly 0.5 mg ranibizumab injections) were treated with 2.0 mg ranibizumab injections monthly for 3 loading doses followed by randomization to either 4 week (Cohort A) or 6 week (Cohort B) follow-up exams. All patients in the follow-up period received a “capped PRN” treatment with 2.0 mg ranibizumab injections mandated at each quarterly visit and 2.0 mg ranibizumab PRN injections given at

follow-up visits (treatment given if any evidence of CNVM activity on OCT, FFA, or clinical exam). At every visit, all patients had ETDRS 4 meter refractions, clinical exam, Stratus OCT, Cirrus HD OCT, and Spectralis OCT.

Results: 50 patients with evidence of fluid on OCT (intraretinal, subretinal, or sub-RPE) were enrolled. Patients had (on average) 26.8 ranibizumab injections prior to enrollment and 10.5 injections in the preceding 12 months. Mean refracted VA was 68.8 ETDRS letters at baseline and mean central subfield was 414 microns. Anatomically, mean OCT central subfield thickness improvement from baseline in microns was: -53.3 at day 7, -36.8 at month one, and -39.6 at month two. Mean visual acuity gain (ETDRS) over baseline was 4.3 letters at day 7, 4.8 letters at month 1, and 6.6 letters by month 2. Upon randomization to different follow-up intervals, cohorts A and B had OCT improvement from baseline of -45.1 and -27.9 microns at month 5 and -40.7 and -5.2 microns at month 8, respectively. Visual acuity gains in cohort A were 4.5 and 4.8 letters at months 5 and 8; at the same intervals, cohort B gained 2.6 and 3.8 letters. No serious ocular adverse events have been observed in any subject, but two patients had myocardial infarctions.

Conclusions: 2.0 mg ranibizumab intravitreal injections led to anatomic improvements and visual acuity gains even in patients with persistent fluid on a regimen of monthly 0.5 mg ranibizumab injections. This data supports the rationale behind the phase III HARBOR 2.0 mg ranibizumab trial and implies that some patients with neovascular AMD may require a higher dose of ranibizumab than is commercially available.

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Clinical Trial: <http://www.clinicaltrials.gov>, NCT01025232