Aflibercept Improves Outcome in Eyes with Poor Vision from Neovascular Age Related Macular Degeneration

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Neovacular age-related macular degeneration (nAMD) is treated by intravitreal injections of either ranibizumab, bevacizumab or aflibercept, resulting in stabilization of vision in over 90% of eyes and significant improvement in approximately a third.(Seguin-Greenstein et al. 2016) Studies have attempted to identify subgroups of nAMD patients that might benefit more from one agent or another, based on baseline retinal thickness, visual acuity or genetic factors, but no advantage has been reported.(Chang et al. 2014) We examined the effect of treatment with aflibercept on best corrected visual acuity (BCVA) and central retinal thickness (CRT) according to BCVA at the time of treatment switch, in nAMD eyes previously treated with ranibizumab.

All eyes had been initially treated for at least 12 months with ranibizumab according to a *pro-re-nata* (PRN) protocol with monthly clinic visits. Ranibizumab treatment failure was determined as persistent intraretinal or subretinal fluid. Following the switch to aflibercept (baseline) eyes were treated with three loading injections, every four weeks, followed by additional injections, one every eight weeks. BCVA, measured as ETDRS letters, and CRT were recorded at every follow-up visit. We examined the change in BCVA and CRT during the last 12 months of treatment with ranibizumab as well as during the first 6 months of treatment with aflibercept.

128 eyes of 122 patients were switched from ranibizumab to aflibercept and included in the study. The mean age at baseline was 81±0.75 years and the mean length of time eyes were treated with ranibizumab was 25.5±1.2 months with an average of 13.5±0.7 injections. For the entire cohort, BCVA at baseline was 20/100 (49.9±2.4 letters) and remained stable at four (20/100, 47.6±2.6 letters, p=0.63) and six months (20/100, 47.8±2.6 letters, p=0.5, Figure 1A). CRT at baseline was 336.5±11.4µm, improving at four months (297.7±10.9µm, p<0.001) and remaining stable at six months (295.0±12.0µm, p=0.006, Figure 1B).

Examining the change in BCVA, we found that in eyes with a baseline BCVA of >20/200, visual acuity improved during the last 12 months of treatment with ranibizumab (+3.6±1.2

letters, p=0.001, average BCVA 44.6±0.8 letters), but following the switch this improvement was lost and by four months they had lost on average -2.0±1.1 letters (p=0.005, average BCVA 42.8±1.0 letters), remaining stable at 6 months (-2.6±1.1 letters, p=0.001, average BCVA 42.02±1.11 letters). Conversely, in eyes with a baseline BCVA ≤20/200, visual acuity reduced during the last 12 month sof ranibizumab treatment (-2.1±1.3 letters, p=0.017, average BCVA 19.6±1.2 letters), but increased at four months (+0.9±0.9, p=0.027, average BCVA 20.4±1.4 letters) and continued at six months following the switch (+1.1±1.0, p=0.017, average BCVA 20.4±1.5, Figure 1A).

Our findings suggest that there may be a difference in response to treatment with aflibercept based on eyes BCVA at time of switch. While these changes in vision should be regarded as quite modest, the difference in response trends still suggests the entire group of nAMD patients may not be homogenous in regards to response to treatment and that groups of patients will respond in a variable manner to the different drugs. This also supports other studies that have demonstrated that eyes with vision below 20/200 tend to enjoy a greater effect from anti-VEGF treatment.(Muniraju et al. 2013) Because our patients were treated with ranibizumab using a PRN protocol, these results might not reflect changes in BCVA if they were being treated on a monthly basis. However, all our patients were treated using the same protocol and the difference in response may still reflect a variable reaction. It is possible that in unresponsive patients, switching to a higher frequency of aflibercept injections would result in a more favorable outcome. (Arcinue et al. 2015) Whereas, all our patients demonstrated a reduction in CRT following conversion, the visual function did not change accordingly, suggesting that in patients with continued visual deterioration despite anatomical stability, changing agents may be advised to achieve maximal therapeutic effect.

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Figure legends

Figure 1- Change in best corrected visual acuity and central retinal thickness before and following conversion to aflibercept.

(A) Change in best corrected visual acuity. (B) Change in central retinal thickness. Following conversion there was a reduction in CRT in all patients. *= p value<0.05. BCVA= best corrected visual acuity, CRT= central retinal thickness, ETDRS= early treatment diabetic retinopathy study. Solid line- all patients; Dashed line- patients with BCVA at baseline ≤ 20/200; Dotted line- patients with BCVA at baseline>20/200.

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