Top 10 Pearls From the SHORE Study: Ranibizumab Treatment for Central and Branch Retinal Vein Occlusion

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OBJECTIVE To discuss the clinically meaningful findings of the SHORE study of ranibizumab (RBZ) monthly or as needed (PRN) therapy in patients with branch or central retinal vein occlusion (RVO).

PURPOSE To review key clinically important lessons from the SHORE study in patients with branch or central RVO treated with RBZ over 15 months.

METHODS SHORE was a 15-month, phase IV, randomized study that evaluated monthly versus PRN dosing of RBZ in 202 patients (pts) with branch RVO (n=115) and central RVO (n=87). Pts received 7 monthly RBZ 0.5 mg injection (inj) from months (M) 0-6. Between M7 and M14, pts continued to receive monthly RBZ inj until the first month at which pre-specified best-corrected visual acuity (BCVA) and spectral-domain OCT stability criteria were met. Pts were then randomized to continue RBZ monthly (n=85) or switched to individualized (PRN) dosing (n=86). Pts who did not meet stability criteria or dropped out prior to M14 were not randomized and continued on monthly RBZ while they remained in the study (n=31).

RESULTS 1) There was no significant difference in BCVA outcomes at M15 between pts randomized to PRN or monthly dosing. 2) Mean number of inj in the PRN arm during the 8-month individualized dosing period was 3.7. 3) Majority of pts randomized to the PRN arm did not require monthly inj to achieve visual benefits consistent with outcomes in the monthly arm. 4) Individualized therapy led to reduced treatment burden while achieving BCVA gain maintenance, from M7 to M15. 5) The majority of pts met disease stability criteria and were randomized by M8. 6) About half of all pts

achieved ≥20/40 vision after 1 inj at M1. 7) About 40% of all pts gained ≥15 letters after 1 inj at M1. 8) About 85% of pts experienced ≥15-letter gain from baseline at any point during the study. 9) About 71–77% of randomized pts achieved ≥20/40 vision by M15. 10) BCVA gains in RBZ-treated pts were rapid and the median time to gain ≥15 letters was 63 days.

CONCLUSION In SHORE, RBZ treatment resulted in rapid and clinically relevant visual acuity improvements in branch and central RVO pts. After disease stabilization with RBZ injections, monthly or individualized dosing effectively maintained BCVA gains through M15 with a mean 3.7 inj over 8 months. Individualized dosing decreased treatment burden while achieving similar visual acuity gains to monthly therapy.

TAKE HOME MESSAGE In SHORE, after disease stabilization with monthly ranibizumab injections, monthly or individualized dosing effectively maintained best-corrected visual acuity gains through month 15.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Impact of Retinal Ischemia on Visual Acuity Outcomes Following Ranibizumab Treatment Over 24 Months in Patients With Retinal Vein Occlusion

- Michael Peter Fielden, MD, FRCS(C)

OBJECTIVE To assess the impact of retinal ischemia (with comparison of assessment criteria) on the BCVA outcomes following ranibizumab treatment over 24 months in patients with retinal vein occlusion.

PURPOSE Retinal vein occlusion (RVO) interventional studies have assessed retinal ischemia, with varying assessment criteria adopted by different studies, investigators and reading centers. Comparative data are limited. Here we report the efficacy of ranibizumab treatment and impact of retinal ischemia on best-corrected visual acuity (BCVA) outcomes over 24 months from the BRIGHTER and CRYSTAL studies.

METHODS The 24-month, phase IIIb, multicenter studies, BRIGHTER (patients with branch RVO [BRVO], randomized, NCT01599650) and CRYSTAL (patients with central RVO [CRVO], single-arm, NCT01535261) assessed the long-term efficacy and safety of an individualized stabilization criteria-driven pro-re-nata dosing regimen of ranibizumab 0.5 mg. Both studies allowed enrollment of patients with retinal ischemia at baseline, as assessed by the investigators and the Vienna central reading center (CRC). One exploratory endpoint was the mean change in BCVA from baseline to Month 24 based on investigator- and CRC-assessed baseline retinal ischemic status.

RESULTS In BRIGHTER, 25.7%/23.3%/26.1% of investigator-assessed (per investigator's own clinical decision) and 48.3%/39.9%/45.6% of CRC-assessed (capillary loss in at least one location of the centre, inner or outer subfield) BRVO eyes had retinal ischemia at baseline in the ranibizumab/ranibizumab+laser/laser groups, respectively. At month

24, there was a mean BCVA gain of >15 letters in all treatment groups for investigator-assessed ischemic/non-ischemic BRVO eyes, except for laser-monotherapy non-ischemic eyes. Comparable results were observed with CRC-assessed ischemic/non-ischemic BRVO eyes, where a mean BCVA gain of >13 letters was observed in all treatment groups, except for laser-monotherapy non-ischemic eyes. In CRYSTAL, investigator-/CRC-assessed ischemia was observed in 15%/30% of eyes at baseline, respectively. At Month 24, there was a mean BCVA gain of 15.0/11.5 letters for investigator-assessed and 11.1/12.9 letters for CRC-assessed ischemic/non-ischemic CRVO eyes, respectively.

CONCLUSION The BRIGHTER and CRYSTAL studies demonstrate that patients with BRVO and CRVO eyes can achieve improved BCVA gains following ranibizumab treatment over 24 months, irrespective of the presence of retinal ischemia (by either method of assessment). Analysis of severity and location of the ischemia may offer further insights into the impact of retinal ischemia on BCVA outcomes in RVO patients.

TAKE HOME MESSAGE Patients with BRVO and CRVO can achieve BCVA gains with ranibizumab treatment irrespective of the presence of retinal ischemia. This applies regardless of the criteria used to identify retinal ischemia.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

The Effect of Intravitreal Aflibercept on Perfusion Status in Patients With Retinal Vascular Disease: The ANDROID Study

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OBJECTIVE This single-center prospective study demonstrates the effect of regular anti-VEGF therapy on patients with retinal vascular disease.

PURPOSE To determine the effect of intravitreal aflibercept injections (IAI) on perfusion status in proliferative retinopathy and/or macular edema from proliferative diabetic retinopathy (PDR) and central retinal vein occlusion (CRVO).

METHODS This single center, open label, prospective study randomized eyes to either monthly IAI for 12 months or to 6 monthly IAI followed by IAI every 2 months. Patients in this latter group could be treated monthly if they met pre-defined re-treatment criteria. Wide-field fluorescein angiography was obtained using the Optos 200Tx at baseline, and months 3, 6, and 12. The Digital Angiography Reading Center (DARC) and Boston Imaging Reading Center (BIRC) each measured peripheral non-perfusion in a masked fashion. Secondary outcomes included change in best-corrected ETDRS vision and change in central subfoveal thickness (CST).

RESULTS Twenty-four patients were enrolled. Fifteen eyes had PDR, 8 had CRVO, and 1 had a hemi RVO. The average total area of peripheral non-perfusion at baseline (155.5mm^2, n = 22) improved to 92.9mm^2 at 3 months (p = 0.055, n = 20), 60.7mm^2 at 6 months (p = 0.004, n = 21), and 44.5mm^2 at 12 months (p = 0.007, n = 18). Grading

was performed by two different reading centers, each with their own distinct method. At 1 year, 15 eyes (83%) had improved peripheral perfusion, while 3 worsened (17%). Visual acuity improved from 59.8 ETDRS letters (20/63) to 69 letters (20/40, p = 0.0003). The baseline CST of 395µ improved to 295µ (p = 0.006). Results were consistent amongst patients with PDR and CRVO as well as the two different regimens. There were no APTC events, nor were there any serious adverse events. Thirteen patients had a follow-up FA at 18 months, 6 months after formal study conclusion—these results will be presented.

CONCLUSION This small prospective study provides evidence that peripheral capillary non-perfusion in patients with PDR and CRVO may improve following treatment with IAI. The durability of this effect in 13 of 24 patients following prn therapy will add additional insight as to the benefit of this treatment. Further large-scale studies are required to explore this finding.

TAKE HOME MESSAGE Regular anti-VEGF therapy may improve perfusion status in patients with retinal vascular disease.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board