Individualized Ranibizumab Treatment in Patients With RVO Leads to Visual Acuity Outcomes Consistent With a Monthly Dosing Regimen

- W. Lloyd Clark, MD
- Pin-wen Wang, PhD
- Zdenka Haskova, MD, PhD
- Carlos Quezada, MD

OBJECTIVE To evaluate visual acuity (VA) outcomes at month (M) 15 in patients (pts) with BRVO and CRVO in the individualized ranibizumab (RBZ) PRN dosing arm according to the number of RBZ injections (inj).

PURPOSE Individualized as needed (PRN) dosing helps to maximize treatment benefit while minimizing treatment burden. In SHORE, PRN dosing of RBZ was shown to be as effective as monthly (QM) dosing for the treatment of macular edema (ME) secondary to RVO. This new retrospective analysis of SHORE data shows best-corrected VA (BCVA) outcomes stratified by the number of RBZ inj received post randomization.

METHODS SHORE was a 15-month, phase IV, randomized study that evaluated QM versus PRN dosing of RBZ in 202 pts with branch RVO (n=115) and central RVO (n=87). Pts received 7 monthly RBZ 0.5 mg inj from M0-6. Between M7 and M14, pts continued to receive QM RBZ inj until the first month at which pre-specified VA and spectral-domain OCT stability criteria were met. Pts were then randomized to continue QM RBZ (n=85) or switched to PRN dosing (n=86). Pts who were never randomized (did not meet stability criteria or dropped out prior to M14) continued on QM RBZ while they

remained in the study (n=31). VA outcomes by RBZ inj number were retrospectively analyzed in PRN pts herein.

RESULTS BCVA gains from baseline at M15 were consistent in pts in the PRN arm with pts in the QM arm (+21.0 vs +18.7 letters), and there was no significant difference in the slope of change in BCVA between these arms from M7 to M15 (P=0.509). In the PRN arm, 80.2% (69/86) of pts were randomized by M8. The average number of RBZ inj post randomization in these pts was 3.2. Within this population, 24.6% of pts received 0-1 RBZ inj post randomization, 52.2% received 2-4 RBZ inj, and 23.2% received ≥5 RBZ inj. At M15 in the PRN arm, pts randomized by M8 who received fewer RBZ inj post randomization had a greater improvement from baseline in BCVA compared with pts who received a greater number of RBZ inj following randomization (+27.3, +19.5, and +19.3 letters in pts who received 0-1, 2-4, and ≥5 RBZ inj post randomization, respectively). PRN pts randomized by M8 who achieved 20/40 or better vision at M15 received fewer RBZ inj post randomization compared with pts who did not (3.0 vs 3.9 inj).

CONCLUSION In SHORE, after achieving disease stability with QM RBZ inj, individualized RBZ resulted in the majority of pts maintaining significant VA gains, similar to QM RBZ. In the PRN arm, BCVA gains at M15 were highest in pts who received the fewest RBZ inj. These data show the heterogeneous response to RBZ and support individualized dosing for RVO to reduce treatment burden while maintaining efficacy.

TAKE HOME MESSAGE Disease-stability-driven treatment with RBZ is a practical approach for treating macular edema secondary to RVO that can help to ensure maximal treatment benefit while minimizing treatment burden.

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

Baseline OCT Predictors in Macular Edema Due to BRVO: MARVEL Report No.3

- Raja Narayanan, MD, MBA
- Jay Chhablani, MD
- Bhavik Panchal, MBBS
- Michael W. Stewart, MD
- Rajeev Reddy Pappuru, MS

OBJECTIVE To describe the baseline OCT features that predict final visual acuity after anti-VEG treatment in branch retinal vein occlusion

PURPOSE To evaluate optical coherence tomography (OCT) parameters as predictor of visual acuity in eyes in macular edema (ME) secondary to branch retinal vein occlusion (BRVO) in a randomized controlled trial comparing efficacy and safety of intravitreal (IVT) ranibizumab (RBZ) versus bevacizumab (BVZ)

METHODS Seventy-five participants with ME secondary to BRVO were randomized RBZ (37) or BVZ (38). Both patients and investigators were masked to the study drug assignment. Patients were followed-up monthly and received additional injections in the first 6 months if there was fluid on OCT. Several OCT parameters at baseline, including retinal cysts, inner retinal reflectivity, central subfield thickness, macular volume, integrity of outer retinal structures, hyperrefletive spots in inner retina; were correlated with visual acuity gain and number of anti-VEGF injections required through one year using multivariate regression model.

RESULTS At 12 months, eyes with OCT thickness more than 500 microns gained 21.2 letters versus eyes with OCT thickness less than 500 microns who gained 16.1 letters. However, eyes with greater than 500 microns thickness at baseline received more injections (3.4) compared to those with less than 500 microns thickness (2.9). Eyes with hyper-reflective dots and ganglion cell cysts had less gain in vision compared to those

without them (p<0.01). Eyes with disrupted outer retinal structures had poor baseline and final visual acuity, but this was not correlated with gain in visual acuity. Presence of retinal nerve fiber layer reflectivity and subretinal fluid was not correlated with gain in visual acuity.

CONCLUSION Outer retinal hyper-reflective dots, ganglion cell cysts and central macular thickness were correlated with gain in visual acuity. Outer retinal structure integrity was correlated with absolute visual acuity, but was not correlated with gain in visual acuity.

TAKE HOME MESSAGE Central macular thickness, ganglion cell cysts and outer retinal reflective dots predict gain in visual acuity after anti-VEGF injections in BRVO.

	Present	Absent	P-value
	RNFL reflectivity		
Gain in VA	16.45	17.63	0.83
	Hyper-reflective dots		
Gain in VA	13.97	19.93	0.02
	GCL cysts		
Gain in VA	9.8	18.9	0.003
	Neurosensory detachment		
Gain in VA	15.76	18.02	0.38
	IS/OS integrity (100%)		
Gain in VA	13.72	13.18	0.9

	OCT<500 (48)	OCT>500 (27)	p-value
Baseline BCVA	56.76	51.37	0.04
Final VA 12m	72.04	71.77	0.91
Gain in VA 6m	15.16	19.7	0.06
Gain in VA 12m	16.08	21.19	0.04
CST reduction	131.5	292.7	0.0001
No. of injections	2.91	3.4	0.14

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

Selective Retina Therapy for Chronic Central Serous Chorioretinopathy

- Young Jung Roh, MD
- Young gun Park, MD
- Ralf Brinkmann, PhD

OBJECTIVE Selective retina therapy can be a useful treatment option for chronic central serous chorioretinopathy.

PURPOSE Selective retina therapy (SRT) can target retinal pigment epithelium without damaging photoreceptor cells. We report the efficacy and safety of SRT in the treatment of chronic central serous chorioretinopathy (CSC).

METHODS In this retrospective cohort study, a total of 36 eyes in 36 patients with chronic CSC for more than 3 months was recruited. All eyes were subjected to SRT laser treatment and followed up after 1,2,3 and 6 months. Following evaluation of test spots at temporal arcades, SRT (Q-switched Nd-YLF laser; wavelength, 527 nm, pulse duration, 1.7 μs) was applied to the surrounding area of leakage observed on fluorescein angiogram and/or pigment epithelial detachment. The outcome measures were a change in best-corrected visual acuity (BCVA) and a change in maximum macular thickness (MMT) measured by optical coherence tomography. SRT was repeated according to the retreatment criteria.

RESULTS The average age of the patients was 49.5 years; twenty-eight were males and eight were females. The mean values of BCVA(LogMAR) measured 3 and 6 months after laser treatment were 0.65±0.28 and 0.64±0.29 respectively, in comparison to 0.55±0.24 before laser treatment (P=0.010, 0.002). The mean MMT before laser was 318.66±100.98 μm, in comparison to 269.12±75.74 and 259.04±68.63 μm after 3 and 6 months respectively (P=0.048, 0.025). Eighteen patients (50 %) needed re-treatment after 2 months.

CONCLUSION SRT treatment targeting the surrounding area of leakage point showed favorable visual and structural outcomes in chronic CSC patients. There was no evidence of retinal damage induced by SRT treatment.

TAKE HOME MESSAGE Selective retina therapy can be a useful treatment option for chronic central serous chorioretinopathy.

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

Intravitreal Aflibercept for Previously Treated Macular Edema Associated With Central Retinal Vein Occlusions: 1 Year Results From the NEWTON Study

- Rahul N. Khurana, MD
- Alok Shawn Bansal, MD
- Louis K. Chang, MD, PhD
- James D. Palmer, MD
- Mark R. Wieland, MD

OBJECTIVE To determine whether aflibercept has a longer duration for cystoid macular edema in non-ischemic central retinal vein occlusions previously treated with ranibizumab or bevacizumab.

PURPOSE Even though anti-VEGF therapy is effective for cystoid macular edema (CME) associated with central retinal vein occlusions, the treatment is chronic and the duration of ranibizumab and bevacizumab is limited. The purpose of this study is to determine whether aflibercept can extend the CME free interval in patients who developed recurrences of CME after ranibizumab or bevacizumab treatment.

METHODS This is a phase 4, prospective, single arm interventional study. Twenty patients with non-ischemic CRVOs previously treated with ranibizumab or bevacizumab were switched to aflibercept. The inclusion criteria included treatment for at least 6 months with 3 initial loading doses, and evidence of recurrence of edema when extended beyond 4 weeks with either ranibizumab or bevacizumab. Aflibercept was administered with a “Treat and Extend” dosing regimen. Injection frequencies were

extended 2 weeks if there were no signs of disease activity on OCT or change in visual acuity.

RESULTS Twenty patients had an average duration of a CRVO for 22 months (range 7-90) and averaged an anti-VEGF treatment every six weeks. These patients received a mean of 15 treatments (range 5-47) of ranibizumab or bevacizumab for CME secondary to non-ischemic CRVOs. Among the 17 patients who completed one year of follow up, 94% of patients had a greater CME-free interval with aflibercept treatment. The CME-free interval increased from 5.7 weeks to 9.6 weeks when switched to aflibercept ($p<0.01$). There was an average increase of 28 days (0-63) in the CME-free interval with aflibercept. There was an improvement in vision (+7 ETDRS letters, $p=0.04$) and decreased retinal thickness (122 μm, $p=0.02$) with aflibercept treatment. There were 0 cases of endolphthalmitis or inflammation in 147 injections in the first year. One patient developed a combined macular hole and retinal detachment that was unrelated to the treatment.

CONCLUSION In patients previously treated with ranibizumab or bevacizumab for CME due to non-ischemic CRVOs, aflibercept increases the CME free interval. This may help minimize the treatment burden in patients with chronic CME from non-ischemic CRVOs.

TAKE HOME MESSAGE Aflibercept has a longer duration for cystoid macular edema in non-ischemic central retinal vein occlusions previously treated with ranibizumab or bevacizumab.

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

Evaluation of Macular Vascular Abnormalities Identified With Optical Coherence Tomography Angiography in Patients With Various Sickle Cell Genotypes

- Adrienne W. Scott, MD
- Mongkol Tadarati, MD
- Katia Delalibera Pacheco, MD
- Ian C. Han, MD

OBJECTIVE To describe types and frequencies of macular vascular abnormalities as identified by optical coherence tomography angiography (OCT-A) in a cohort of patients with various sickle cell genotypes

PURPOSE We recently reported that OCT-A can detect areas of abnormal vascular flow that correspond to retinal thinning seen on SD-OCT in sickle cell disease patients. This study evaluates the types and frequencies of macular vascular abnormalities seen by OCT-A in a large, consecutive case series of patients with various sickle cell genotypes.

METHODS This is an IRB-approved, single center, prospective, observational study. 42 consecutive patients with sickle cell disease seen in the investigators' (AWS, ICH) clinics were included via informed consent. Patients with other known retinal vascular disease (e.g. diabetic retinopathy) or inadequate view for OCT-A were excluded. Macular OCT-A scans were obtained using Avanti RTVue XR (Optovue Inc, Fremont, CA). Images were analyzed for vascular abnormalities, including foveal avascular zone irregularities and

areas of decreased flow. The frequency of these findings was calculated, stratified by sickle cell genotype, and correlated to clinical stage of sickle cell retinopathy.

RESULTS OCT-A images of 80 eyes (41 right, 39 left) from 42 patients were obtained. Of these, 70 eyes (36 right, 34 left) had image quality acceptable for analysis. Mean age was 34 years, and 54.8% (23/42) were female. Sickle cell genotypes included 25 patients with SS (59.5%), 13 with SC (31.0%), 3 with β-thalassemia (7.1%), and 1 with sickle trait (2.4%). Discrete areas of decreased flow, in the superficial or deep plexus or both, were noted in 37.1% of eyes (26/70) overall. When stratified by genotype, these areas were commonly-observed in both SS (17/44 eyes, 38.6%) and SC patients (8/20 eyes, 40.0%). When stratified by presence of proliferative sickle cell retinopathy (Goldberg staging), decreased flow was seen in 47.1% of eyes (16/34) with proliferative retinopathy versus 30.6% of eyes (11/36) without. When further stratified by Goldberg stages, decreased flow was seen in 52.4% of eyes (11/21) Stage 3 and above, versus 32.7% of eyes (16/49) Stage 2 or below.

CONCLUSION Areas of abnormal vascular flow within the macula are commonly detected by OCT-A in patients with various sickle cell genotypes. These areas may be seen at any stage of retinopathy but are more common in eyes with peripheral neovascularization (Stage 3 and above). Further study is needed to elucidate the clinical significance of these findings and their relationship to systemic disease.

TAKE HOME MESSAGE OCT-A can detect areas of abnormal macular vascular flow in sickle cell disease patients. These areas are common overall and seen more frequently in eyes with peripheral neovascularization.

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