Retina Roundup
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Risk of inflammation, retinal vasculitis and retinal occlusion-related events with brolucizumab: post-hoc review of HAWK and HARRIER

Monés J, Srivastava SK, Jaffe GJ, Tadayoni R, Albini TA, Kaiser PK

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ABSTRACT

Objective: An independent Safety Review Committee (SRC; supported by Novartis Pharma AG [Basel, Switzerland]) analyzed investigator-reported cases of intraocular inflammation (IOI), endophthalmitis and retinal arterial occlusion in the phase 3 HAWK and HARRIER trials of brolucizumab versus aflibercept in neovascular age-related macular degeneration (nAMD).

Design: A post-hoc analysis of a subset of data from two 2-year, double-masked, multicenter, active-controlled randomized phase 3 trials (NCT02307682, NCT02434328).

Participants: Patients (N=1817) with untreated, active choroidal neovascularization due to AMD in the study eye were randomized and treated in HAWK/HARRIER. The SRC reviewed data from cases of investigator-reported IOI (60/1088 brolucizumab-treated eyes; 8/729 aflibercept-treated eyes).

Methods: The SRC received details and images (color fundus photography, fluorescein angiography and optical coherence tomography) for all investigator-determined cases of IOI, retinal arterial occlusion and endophthalmitis. Cases were reviewed in detail by ≥2 readers, then adjudicated by the SRC as a group.

Main outcome measures: Within this subset of patients: incidence of IOI, signs and incidence of retinal vasculitis and/or retinal vascular occlusion, and visual acuity loss; time since first brolucizumab injection to IOI event onset;

frequency of visual acuity loss following brolucizumab injection by time of first IOI event onset.

Results: Fifty brolucizumab-treated eyes were considered to have definite/probable drug-related events within the spectrum of IOI, retinal vasculitis and/or vascular occlusion. Based on these cases, incidence of definite/probable IOI was 4.6% (IOI + vasculitis, 3.3%; IOI + vasculitis + occlusion, 2.1%). There were 8 cases (incidence 0.74%) of at least moderate visual acuity loss (≥15 ETDRS letters) in eyes with IOI; 7 were in eyes with IOI + vasculitis + occlusion. Of the 8 cases, 5 experienced their first IOI-related event within 3 months of the first brolucizumab injection (increasing to 7/8 within 6 months). Incidence of IOI in aflibercept-treated eyes was 1.1%, with at least moderate visual acuity loss in 0.14%.

Conclusions: This analysis of IOI cases following brolucizumab injection identified signs of retinal vasculitis with or without retinal vascular occlusion, and an associated risk of visual acuity loss. The findings will help physicians to evaluate the risks and benefits of brolucizumab treatment for nAMD.

Phenotyping of retinal neovascularization in ischemic retinal vein occlusion using wide field OCT angiography

Huemer J, Khalid H, Wagner SK, Nicholson L, Fu DJ, Sim DA

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ABSTRACT

Background/objectives: Abnormal retinal neovascularization caused by ischemic retinal vein occlusion (RVO) is a frequent cause of visually significant vitreous hemorrhage. The early detection of new vessels may be challenging and often requires the use of invasive tests such as fundus fluorescein angiography (FA). We demonstrate the use of wide-field optical coherence tomography angiography (WF-OCTA) in the detection and characterization of neovascularization secondary to ischemic RVO.

Subjects/methods: We conducted a retrospective observational case series of patients diagnosed with ischemic RVO between August 2018 and March 2019, who underwent WF-SS-OCTA imaging (PLEX Elite 9000, Carl Zeiss Meditec). We performed real-life montage imaging, covering the involved area and compared the findings of WF-SS-OCTA to standard clinical examination and when available, ultrawide-field fluorescein angiography (UWF-FA, Optos 200TX).

Results: In the included 39 eyes with ischemic RVO, neovascularization elsewhere (NVE) was encountered in 16 of 39 eyes (41%) on WF-OCTA and were characterized as sea-fan type vessels and nodular type vessels, based on their appearance and localization. NVE was identified in 4/39 eyes on standard clinical examination, equating to a detection rate of 10.3%. All were of a sea-fan morphology. In one case, NVE found on WF-OCTA was not observed on UWF-FA, which was a nodular type. Neovascularization of the disc (NVD) was detected in one eye.

Conclusions: WF-OCTA may become a useful noninvasive tool in the detection of neovascularization in patients with ischemic RVO. Furthermore, the characterization of different morphologies of neovascularization detected by WF-OCTA could be of clinical relevance.

Retinal Fluid Volatility Associated with Interval Tolerance and Visual Outcomes in Diabetic Macular Edema in the VISTA Phase III Trial

Ehlers JP, Uchida A, Sevgi DD, Hu M, Reed K, Berliner A

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ABSTRACT

Purpose: To describe longitudinal retinal fluid dynamics on spectral domain OCT and to identify imaging biomarkers that predict the worsening of DME with interval extension during anti-vascular endothelial growth factor (VEGF) therapy.

Design: A post hoc sub-analysis of phase III, VISTA-DME study.

Methods: Eyes received either intravitreal aflibercept injection 2 mg every 4 weeks (2q4) or every 8 weeks after 5 initial monthly injections (2q8), and eyes imaged with the Cirrus HD-OCT system were included. The macular cube was analyzed for 10 time-points from baseline through week 100. Retinal OCT images were evaluated using a novel software platform to extract retinal fluid features for calculation of volumetric fluid parameters, including the retinal fluid index (RFI): the percentage of retinal volume that was occupied by intraretinal fluid.

Results: Fifty-five eyes were included in the 2q4 group, and 58 eyes were included in the 2q8 group. Early RFI volatility with a central macular RFI increase by ≥5 points from week 4 to 8 (P = .004, odds ratio [OR] 31.3, 95% confidence interval [CI] 3.0 to 329) and cumulative RFI volatility with an aggregate increase in macular RFI by ≥10 points from those timepoints with increased RFI between baseline to week 20, P = .005, OR 10.2, 95% CI 2.1 to 51.3) were both significant predictors for the worsening of DME and visual acuity when the treatment interval was extended to 8 weeks in the 2q8 group.

Conclusions: Early fluid dynamics as measured by (1) early RFI volatility and (2) cumulative RFI instability with aggregate increased RFI were associated with intolerance of interval extension.

Traumatic retinal detachment in patients with self-injurious behavior: an international multicenter study

Rossin EJ, Tsui I, Wong SC, Hou KK, Prakhunhungsit S, Blair MP, Shapiro MJ

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ABSTRACT

Purpose: To describe the clinical characteristics, surgical outcomes and management recommendations in patients with traumatic rhegmatogenous retinal detachment (RRD) due to self-injurious behavior (SIB).

Design: International, multicenter, retrospective, interventional case series.

Participants: Patients with SIB from 23 centers with RRD in at least one eye.

Methods: Clinical histories, pre-operative assessment, surgical details, post-operative management, behavioral intervention and follow-up examination were reviewed.

Main outcome measures: The rate of single surgery anatomic success (SSAS) was the primary outcome. Other outcomes included new RRD in formerly attached eyes, final retinal reattachment and final visual acuity.

Results: A total of 107 eyes with RRDs were included from 78 patients. Fifty-four percent of patients had bilateral RRD or phthisis bulbi in the fellow eye at final follow-up. The mean age at presentation was 15.7 ±11.4 years and 73.1% were male. The most common systemic diagnoses related to SIB were autism spectrum disorder (35.9%), trisomy 21 (21.8%), cognitive impairment (12.8%) and cerebral palsy (12.8%). The most common behaviors were face hitting (74.4%), eye rubbing (25.6%) and head banging (16.7%). The average follow-up time was 3.3±2.8 years, and surgical outcomes for operable eyes were restricted to patients with at least 3 months of followup (81 eyes). Primary initial surgeries were vitrectomy alone (33.3%), primary scleral buckle (SB)

(25.9%) and vitrectomy with SB (39.7%), and 5 prophylactic SBs were placed. Twenty-three eyes (21.5%) with RRDs were deemed inoperable. The single surgery anatomic success rate (SSAS) was 23.1% without tamponade (37.2% if including silicone oil), and final reattachment was attained in 80% (36.3% without silicone oil tamponade). Funnel-configured RRD (P=0.006) and the presence of grade C proliferative vitreoretinopathy (P=0.002) predicted RRDs that were more likely to fail reattachment (P=0.04 and P=0.05, respectively, if restricting to the 64 patients with ≥12 months followup). The use of a SB predicted final attachment rate during the initial surgery (P=0.005) or at any surgery (p=0.008; P=0.012 and 0.002, respectively, if restricting to patients with ≥12 months followup). Anatomic reattachment correlated with better visual acuity (P<0.001).

Conclusions: RRD from SIB poses therapeutic challenges due to limited patient cooperation, bilateral involvement, chronic RRDs, and ongoing trauma in a vulnerable and neglected patient population. The surgical success rates in this study were some of the lowest in the modern retinal detachment literature. The use of a SB may result in better outcomes, and visual function can be restored in some patients.

Choroidal vascular changes after encircling scleral buckling for rhegmatogenous retinal detachment

Bernabei F, Pellegrini M, Taroni L, Roda M, Toschi PG, Schiavi C

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ABSTRACT

Background/objectives: There is an ongoing debate on whether encircling scleral buckling (SB) procedure for the treatment of rhegmatogenous retinal detachment (RRD) may cause an impairment in choroidal blood flow. The aim of this study was to compare choroidal vascularity index (CVI) and subfoveal choroidal thickness (CT) between eyes that had undergone encircling SB with unoperated fellow eyes (FEs).

Subjects/methods: Thirty patients treated with encircling SB for unilateral RRD were included. Demographic and clinical characteristics as well as enhanced depth imaging-optical coherence tomography scans were retrospectively collected. Images were binarised using ImageJ software, total choroidal area along with luminal and stromal area (respectively, TCA, LA and SA) were segmented and the CVI was computed as the ratio of LA/TCA. In addition, CT was evaluated.

Results: The mean follow-up interval between surgery and examination was 25.5 ± 16.8 months. Choroidal thickness, TCA, LA and SA were significantly increased in the operated eyes compared to FEs (respectively, 271.7 ± 78.0 µm vs. 238.5 ± 83.4, P = 0.001; 1.804 ± 0.491 mm2 vs. 1.616 ± 0.496, P = 0.001; 1.199 ± 0.333 mm2 vs. 1.067 ± 0.337, P < 0.001 and 0.605 ± 0.171 mm2 vs. 0.550 ± 0.171, P = 0.001). Conversely, CVI did not significantly differ between the two groups (66.4 ± 3.6 vs. 65.9 ± 3.2, P = 0.490).

Conclusions: In conclusion, eyes treated with encircling SB for RRD presented increased LA, SA and CT compared with FEs, but showed no difference in CVI.

Neurodevelopmental Outcomes After Bevacizumab Treatment for Retinopathy of Prematurity-A Meta-Analysis

Tsai CY, Yeh PT, Tsao PT, Ella Chung YC, Chang YS, Lai TT

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ABSTRACT

Objective: To evaluate neurodevelopmental outcomes after intravitreal bevacizumab (IVB) in retinopathy of prematurity (ROP) infants compared to those not exposed to IVB.

Clinical relevance: The primary concern regarding IVB treatment of ROP is the potential systemic side effects, especially the risk of causing severe neurodevelopmental impairment (sNDI). Results regarding neurodevelopmental outcomes after IVB are conflicting.

Methods: We conducted a meta-analyses and searched PubMed, Embase, and Web of Science for related publications from inception to March 12, 2020. The eligibility criteria were as follows: comparative studies of ROP patients that (1) included IVB as a treatment arm; (2) included a control group without bevacizumab treatment; and (3) reported on at least one neurodevelopmental outcome, such as sNDI, Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) composition scores, or cerebral palsy (CP). The Newcastle-Ottawa Scale was employed for risk-of-bias assessment. The primary outcome was sNDI, with the odds ratio (OR) calculated. Secondary outcomes were mean differences (MDs) for cognitive, language, and motor scores (Bayley-III) and OR for CP. The quality of evidence was assessed using the GRADE approach.

Results: Eight studies, namely 6 including laser-controlled ROP infants and 2 including ROP infants not requiring treatment, were included. The weighted OR for sNDI in the IVB group was 1.39 (95% confidence interval [CI]: 0.98 to 1.97). The weighted MDs were -2.10 (95% CI: -4.94 to 0.74), -1.32 (95% CI: -4.65 to 1.99), and -3.66 (95% CI: -6.79 to -0.54) for cognitive, language, and

motor scores in Bayley-III, respectively. The OR for CP was 1.20 (95% CI: 0.56 to 2.55). No differences were observed between the preset subgroups comprising laser-controlled ROP infants and ROP infants not requiring treatment. The current quality of evidence was rated as low (sNDI and all Bayley-III scores) to very low (CP).

Conclusion: sNDI risk was not increased in ROP patients after IVB treatment. Bayley-III scores were similar in the IVB and control groups, except for a minor difference in motor performance. These findings suggest that the risk of additional sNDI after IVB treatment is low. Randomized trials are warranted to provide a higher quality of evidence.

Autologous full-thickness retinal transplant for refractory large macular holes

Rojas-Juárez S, Cisneros-Cortés J, Ramirez-Estudillo A, Velez-Montoya R

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ABSTRACT

Background: Despite the constant refinement of techniques and surgical aids, extremely large and refractory macular holes continue to have poor surgical outcomes with the current standard of care. The objective of the present study is to assess the anatomical and functional outcomes, as well as the structural change through time, of the optical coherence tomography of patients with refractory macular holes treated with a full-thickness autologous retinal transplant.

Methods: Prospective, case series. We include patients with a clinical diagnosis of refractory macular holes with a minimum diameter of at least 500 µm. All the patients had a comprehensive ophthalmological examination, which included a best-corrected visual acuity assessment, fundus examination, and optical coherence analysis. All the patients underwent a 23-gauge pars plana vitrectomy with a full-thickness retinal transplant and silicone oil tamponade (5000 cs<). Follow-up was done at 1, 3, 6, and 12 months. Statistical analysis was done with a test for repeated measurements and Bonferroni correction, with an alpha value of 0.05 for statistical significance and a Mann-Whitney U test for nonparametric continuous variables.

Results: We enrolled 13 eyes from 13 patients (mean age: 67.15 years) with refractory macular holes, with a mean base diameter of 1615.38 ± 689.19 µm and a minimum diameter of 964.08 ± 709.77 µm. The closure rate after 12 months of follow-up was 76.92%. Six patients with a closed macular hole at the end of the follow-up had complete recovery of the myoid/ellipsoid layer. The remaining showed a 44.9% reduction of the initial gap. Most patients formed a pseudofovea and normalization of the internal retinal layers. Despite a positive trend toward visual recovery (p = 0.034), after the correction of the alpha value, the change lost its statistical significance. During follow-up, one patient

developed mild proliferative vitreoretinopathy and epiretinal membrane without anatomical or functional consequences.

Conclusions: An autologous full-thickness retinal transplant may improve the anatomical and structural outcome of patients with refractory macular holes. The full safety profile of this new technique is still unknown. More studies are needed in order to assess functional changes through time.

Compiled by : Dr. Ritesh Chainani, Aravind Eye Hospital, Chennai