Retina Roundup

September 2023

1. Ophthalmol Retina. 2023 Jul;7(7):573-585S

RANDOMIZED PHASE IIB STUDY OF BRIMONIDINE DRUG DELIVERY SYSTEM GENERATION 2 FOR GEOGRAPHIC ATROPHY IN AGE-RELATED MACULAR DEGENERATION

William R. Freeman, MD , Francesco Bandello, MD, Eric Souied, MD, PhD, Kimmie Kim, PhD, Francisco J. López, MD, PhD

ABSTRACT

PURPOSE : To evaluate the safety and efficacy of repeat injections of Brimonidine Drug Delivery System (Brimo DDS) Generation 2 (Gen 2) containing 400-µg brimonidine in patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

DESIGN : A phase IIb, randomized, multicenter, double-masked, sham-controlled, 30-month study (BEACON).

PARTICIPANTS : Patients diagnosed with GA secondary to AMD and multifocal lesions with total area of > 1.25 mm2 and ≤ 18 mm2 in the study eye.

METHODS : Enrolled patients were randomized to treatment with intravitreal injections of 400-µg Brimo DDS (n = 154) or sham procedure (n = 156) in the study eye every 3 months from day 1 to month 21.

MAIN OUTCOME MEASURES : The primary efficacy endpoint was GA lesion area change from baseline in the study eye, assessed with fundus autofluorescence imaging, at month 24.

RESULTS : The study was terminated early, at the time of the planned interim analysis, because of a slow GA progression rate (~ 1.6 mm2/year) in the enrolled population. Least squares mean (standard error) GA area change from baseline at month 24 (primary endpoint) was 3.24 (0.13) mm2 with Brimo DDS (n = 84) versus 3.48 (0.13) mm2 with sham (n = 91), a reduction of 0.25 mm2 (7%) with Brimo DDS compared with sham (P = 0.150). At month 30, GA area change from baseline was 4.09 (0.15) mm2 with Brimo DDS (n = 49) versus 4.52 (0.15) mm2 with sham (n = 46), a reduction of 0.43 mm2 (10%) with Brimo DDS compared with

sham (P = 0.033). Exploratory analysis showed numerically smaller loss over time in retinal sensitivity assessed with scotopic microperimetry with Brimo DDS than with sham (P = 0.053 at month 24).

Treatment-related adverse events were usually related to the injection procedure. No implant accumulation was observed.

CONCLUSIONS : Multiple intravitreal administrations of Brimo DDS (Gen 2) were well tolerated. The primary efficacy endpoint at 24 months was not met, but there was a numeric trend for reduction in GA progression at 24 months compared with sham treatment. The study was terminated early because of the lower-than-expected GA progression rate in the sham/control group.

PMID: 36906177

DOI: 10.1016/j.oret.2023.03.001

2. Ophthalmol Retina. 2023 Jun;7(6):480-488.

A COMPARISON OF OCULAR COMPLICATIONS AFTER 0.7 MG DEXAMETHASONE IMPLANT VERSUS 2 MG OF INTRAVITREAL TRIAMCINOLONE IN VITRECTOMIZED EYES

Taku Wakabayashi, MD, PhD, Catherine K. Liu, BS, Hannah E. Anderson, BS, Jason Hsu, MD, Sunir J. Garg, MD, Marc J. Spirn, MD

ABSTRACT

OBJECTIVE : To compare the rates of complications in eyes that received a dexamethasone (DEX) implant (0.7 mg) or intravitreal triamcinolone (IVT) (2 mg) to treat postvitrectomy macular edema (ME).

DESIGN : Retrospective, comparative, case series.

SUBJECTS : A total of 148 eyes (147 patients); 75 eyes (75 patients) in the DEX group and 73 eyes (72 patients) in the IVT group.

METHODS : The medical records of patients who received an intravitreal DEX 0.7 mg (Ozurdex) or triamcinolone (2 mg) (Triesence) for postvitrectomy ME between July 2014 and December 2021 with a minimum follow-up of 3 months were reviewed. Ocular hypotony and ocular hypertension were defined as intraocular pressure of < 6 mmHg and > 24 mmHg, respectively.

MAIN OUTCOME MEASURES : The rates of complications.

RESULTS : The follow-up duration was 2.5 ± 1.6 years, with no significant difference between the groups (P = 0.398). The rate of transient ocular hypotony per eye and per injection was significantly higher in the DEX group (10 eyes [13%], 30 of 443 injections [7%]) compared with the IVT group (2 eyes [3%], 2 of 262 injections [0.8%]) (P = 0.039 and < 0.001, respectively). Mean visual acuity significantly decreased at the time of ocular hypotony (P = 0.031), but returned to preinjection level after resolution of the hypotony after a median of 12

days. The incidence of ocular hypertension was higher in the DEX group (23 eyes [31%]) than the IVT group (16 eyes [22%]), but this was not statistically significant (P = 0.307). Ocular hypertension was controlled with observation or topical medication. There were no between-group differences in the incidence of vitreous hemorrhage (DEX, 3 eyes [4%]; IVT, 1 eye [1%]; P = 0.632) or rhegmatogenous retinal detachment (DEX, 3 eyes [4%]; IVT, 0 eyes [0%]; P = 0.253). Four eyes (5%) experienced migration of the DEX implant into the anterior chamber. No eye developed endophthalmitis.

CONCLUSION : The incidence of ocular hypotony, which causes transient visual impairment, was significantly higher in vitrectomized eyes treated with DEX compared with eyes treated with IVT. Injections other than the inferotemporal quadrant or rotating injection sites may be recommended.

PMID: 36572383

DOI: 10.1016/j.oret.2022.12.009

3. Ophthalmol Retina. 2023 Jul;7(7):586-592.

NASCENT GEOGRAPHIC ATROPHY AS A PREDICTOR OF TYPE 3 MACULAR NEOVASCULARIZATION DEVELOPMENT

Riccardo Sacconi, MD, PhD, David Sarraf, MD, SriniVas R. Sadda, MD, Francesco Bandello, MD, Anat Loewenstein, MD, Giuseppe Querques, MD, PhD

ABSTRACT

PURPOSE : To investigate the association of nascent geographic atrophy (GA) preceding the development of exudative type 3 macular neovascularization (MNV) in patients with age-related macular degeneration (AMD).

DESIGN : Retrospective longitudinal study.

PARTICIPANTS : Patients with AMD diagnosed with treatment-naive exudative type 3 MNV in 1 or both eyes were evaluated. Inclusion criteria included serial tracked structural OCT examinations for ≥ 2 years before the detection of exudative type 3 MNV.

METHODS : Clinical characteristics and retinal imaging, including structural OCT at baseline and at each follow-up examination, were analyzed. Eyes showing the presence of nascent GA during the follow-up were selected for analysis of prevalence, and clinical characteristics at the site of subsequent type 3 MNV development.

MAIN OUTCOME MEASURES : Description of the prevalence and clinical characteristics of nascent GA at the site of subsequent type 3 MNV development.

RESULTS : Overall, 97 eyes affected by type 3 MNV meeting inclusion criteria were analyzed. Of 97 eyes (71 patients), 22 eyes of 21 patients (mean age 82 ± 9 years) showed nascent GA preceding exudative type 3 MNV. The observed prevalence of nascent GA preceding exudative type 3 MNV was 22.7% (95% confidence interval, 14.4%–31.0%). Exudative type 3 MNV developed a mean of 9 ± 6 months after detection of nascent GA. The presence of reticular pseudodrusen in the study eye did not

significantly influence the timing of exudative type 3 MNV development after the observation of nascent GA ($P > 0.1$ in all analyses). Reduced best-corrected visual acuity was recorded at the exudative type 3 stage in comparison with the nascent GA stage ($P = 0.003$).

CONCLUSIONS : As nascent GA may precede the development of exudative type 3 MNV, the detection of nascent GA in eyes with AMD may warrant closer surveillance to identify early exudative type 3 MNV warranting treatment.

PMID: 36736896

DOI: 10.1016/j.oret.2023.01.019

4. Ophthalmol Retina. 2023 Jun;7(6):468-479.

VISUAL AND ANATOMIC OUTCOMES OF SUPRACHOROIDAL HEMORRHAGE - A SYSTEMATIC REVIEW AND META-ANALYSIS

Tianyu Liu, MD , Ayman G. Elnahry, MD, PhD, Zujaja Tauqeer, MD, DPhil, Yinxi Yu, MS, Gui-Shuang Ying, PhD, Benjamin J. Kim, MD

ABSTRACT

TOPIC : To characterize the presentation, management, and outcomes of suprachoroidal hemorrhage (SCH).

CLINICAL RELEVANCE : Suprachoroidal hemorrhage is a potentially devastating condition but there is no high-quality evidence for the prognosis or management of SCH.

METHODS : We performed a systematic review and meta-analysis of peer-reviewed studies of SCH published in PubMed, EMBASE, Web of Science, or Google Scholar between January 1, 1990, and September 1, 2022. The protocol was prospectively registered on the Open Science Framework (https://osf.io/69v3q/). Random-effects models were used to calculate the pooled estimate and 95% confidence intervals (CIs) for visual acuity (VA) and anatomic outcomes. Univariable and multivariable random-effects meta-regressions were performed to determine factors associated with VA outcomes and anatomic success, defined as the retina attached at the last follow-up.

RESULTS : Sixty-eight studies comprising 1246 eyes of 1245 patients were included, with mean (standard deviation [SD]) follow-up of 14.0 (9.4) months. The pooled estimate (95% CI) for mean change in logarithm of the minimum angle of resolution (logMAR) VA from baseline to the last follow-up was −0.98 (−1.22 to −0.74) (I2 = 88.4%), with 72.0% (63.5%–80.5%) (I2 = 74.3%) achieving VA improvement of ≥ 0.3 logMAR (3-line improvement in ETDRS VA), 39.6% (32.5%–46.7%) (I2 = 83.2%) achieving final VA of 1.0 logMAR (Snellen equivalent 20/200) or better, and 75.5% (68.4%–82.7%) (I2 = 74.7%) achieving anatomic success. Studies with predominantly nonspontaneous SCH and greater percent of eyes receiving systemic steroids were

associated with greater improvement in logMAR VA, a greater proportion of eyes with VA improvement ≥ 0.3 logMAR, and greater proportion of eyes achieving anatomic success (all $P < 0.05$ univariable meta-regression). Studies with greater percent of eyes treated surgically were associated with greater proportion of eyes with VA improvement of ≥ 0.3 logMAR in ($P < 0.05$, univariable and multivariable analysis). The mean (SD) quality score across studies was 13.9 (2.3) out of 24, and outcomes were of very low certainty of evidence.

CONCLUSION : Although limited by heterogeneous observational studies, published reports of SCH indicate that most eyes with SCH experience some degree of VA improvement and anatomic success. However, final VA outcomes remain poor, with most cases resulting in severe visual impairment or blindness.

PMID: 36858317

DOI: 10.1016/j.oret.2023.02.011

5. Graefes Arch Clin Exp Ophthalmol. 2023 Aug 11.

RELATIONSHIP BETWEEN THE DISTRIBUTION OF INTRA-RETINAL HYPER-REFLECTIVE FOCI AND THE PROGRESSION OF INTERMEDIATE AGE-RELATED MACULAR DEGENERATION

Verma A, Corradetti G, He Y, Nittala MG, Nassisi M, Velaga SB, Haines JL, Pericak-Vance MA, Stambolian D , Sadda SR, Doheny Eye Institute, Pasadena, CA, USA.

ABSTRACT

PURPOSE : To assess the relationship between the distribution of intra-retinal hyper-reflective foci (IHRF) on optical coherence tomography (OCT) and progression of intermediate age-related macular degeneration (iAMD) over 2 years.

METHODS : Cirrus OCT volumes of the macula of subjects enrolled in the Amish Eye Study with 2 years of follow-up were evaluated for the presence of iAMD and IHRF at baseline. The IHRF were counted in a series of 5 sequential en face slabs from outer to inner retina. The number of IHRF in each slab at baseline and the change in IHRF from baseline to year 2 were correlated with progression to late AMD at 2 years.

RESULTS : Among 120 eyes from 71 patients with iAMD, 52 eyes (43.3%) of 42 patients had evidence of both iAMD and IHRF at baseline. Twenty-three eyes (19.0%) showed progression to late AMD after 2 years. The total IHRF count increased from 243 at baseline to 604 at 2 years, with a significant increase in the IHRF number in each slab, except for the innermost slab 5 which had no IHRF at baseline or follow-up. The IHRF count increased from 121 to 340 in eyes that showed progression to late AMD. The presence of IHRF in the outermost retinal slabs 1 and 2 was independently associated with a significant risk of progression to late AMD. A greater increase in IHRF count over 2 years in these same slabs 1 and 2 was also associated with a higher risk of conversion to late AMD.

CONCLUSIONS : The risk of progression to late AMD appears to be significantly associated with the distribution and extent of IHRF in the outermost retinal layers. This observation may point to significant

pathophysiologic differences of IHRF in inner versus outer layers of the retina.

PMID: 37566303

DOI: 10.1007/s00417-023-06180-4