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Macula Society Collaborative Retrospective Study of Ocriplasmin for Symptomatic Vitreomacular Adhesion

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Purpose: To assess anatomic and visual outcomes of ocriplasmin use for symptomatic vitreomacular adhesion (VMA).

Design: Retrospective chart review.

Methods: Macula Society members were surveyed online to collect data on ocriplasmin for symptomatic VMA. Clinical and optical coherence tomography data were collected using standardized data entry forms.

Results: There were 208 patients (208 eyes) with symptomatic VMA followed at least 3 weeks after receiving ocriplasmin. At baseline, VMA was focal (<1500 μm) in 179 eyes (86%), broad in 9 eyes (4%), and not reported in 20 eyes (10%). A full-thickness macular hole (MH) was present in 75 eyes (36%); size was <400 μm in 62 eyes (82%). Baseline mean visual acuity was approximately 20/63. Of the 204 eyes with ≥12 weeks follow-up, pars plana vitrectomy (PPVx) was performed in 12 (6%) by 4 weeks, 31 (15%) by 12 weeks, and 64 (31%) by the last visit. VMA had resolved by 12 weeks with ocriplasmin alone in 83 of 191 eyes (43%) by week 12 and in 148 of 200 eyes (74%) by the last visit, including eyes undergoing PPVx. Among eyes with a baseline MH, closure was achieved with ocriplasmin alone in 10 of 65 (15%) by 1 week, 26 of 74 (35%) by 4 weeks, and 30 of 75 (40%) at the last visit. Mean change in visual acuity at the last visit compared with baseline was −0.06±0.40 logarithm of the minimum angle of resolution (logMAR) (modest vision improvement) ($P = 0.03$). At the last visit, visual acuity improved by ≥2 lines in 69 eyes (35%) and by ≥3 lines in 54 eyes (27%). Visual acuity decreased ≥2 lines in 35 eyes (18%) and by 3 lines in 27 eyes (14%) at the final visit. Complications included photopsias (15%), dimness of vision (14%), decreased color vision (10%), MH development (5%), macular retinal pigment epithelium atrophy (2.7%), retinal detachment (1.9%), and retinal tear (1.4%). No endophthalmitis cases were reported.

Conclusions: Physician-reported outcomes on ocriplasmin use confirmed VMA release in 45% and closure of MH in 40% of eyes without PPVx. Visual acuity decreased in approximately 20% of eyes. Adverse events were not infrequent and suggest caution when considering ocriplasmin use. *Ophthalmology Retina 2017;■:1–8 © 2017 by the American Academy of Ophthalmology*

Pharmacologic vitreolysis is a theoretically attractive option for the management of vitreoretinal tractional interface disorders. Ocriplasmin (Jetrea, ThromboGenics, Iselin, NJ) is a recombinant protease that cleaves fibronectin and laminin. Ocriplasmin was approved by the Food and Drug Administration for pharmacologic vitreolysis following the demonstration of efficacy in the pivotal licensing clinical trials in which a single intravitreal injection of ocriplasmin (125 μg) was compared with a placebo (saline).[1] Vitreomacular adhesion (VMA) resolved in 26.5% of treated and in 10.1% of placebo-treated eyes. In addition, nonsurgical closure of macular holes (MHs) was achieved in 40.6%, vs. 10.6% of placebo-treated eyes.

In the years after approval of ocriplasmin for symptomatic VMA, various reports[2–4] have emerged with varied results as compared with the MIVI-TRUST study.[1] Furthermore, concerns have arisen with respect to the safety of ocriplasmin. The present study was performed primarily to ascertain anatomic and safety outcomes following Food and Drug Administration approval of ocriplasmin when used in a clinical setting for treatment of symptomatic VMA.

Methods

Members of the Macula Society were approached to participate in an online retrospective study of patients treated with ocriplasmin for symptomatic VMA. Participating members provided information for each eligible patient in their practice; the study was online and data collection was open for 6 months (November 20, 2014 to May 18, 2015). Patients with symptomatic VMA, with or without MH, and who received intravitreal ocriplasmin and had not undergone any other recent (within 3 months) treatments were eligible. The data consisted of demographics, visual acuity, extent of VMA, presence or absence of MH, and spectral-domain optical coherence tomography findings from before treatment and after ocriplasmin

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Table 1. Rates of Vitreomacular Adhesion Release

	VMA Release (From Injection Alone)		VMA Release (Including Release for Injection or PPVx)	
	N (%)	*95% CI*	*N (%)*	*95% CI*
Overall				
VMA release by 1 week	70/161 (44%)	36%–51%	70/161 (44%)	36%–51%
VMA release by 4 weeks	85/190 (45%)	38%–52%	94/190 (51%)	42%–57%
VMA release at final visit	90/200 (45%)	38%–52%	148/200 (74%)	68%–80%
	N (%)	*P Value**	*N (%)*	*P Value**
Baseline adhesion type				
VMA release by 1 week		0.14		0.14
Baseline: broad adhesion	1/8 (13%)		1/8 (13%)	
Baseline: focal adhesion	65/149 (44%)		65/149 (44%)	
VMA release by 4 weeks		0.04		0.03
Baseline: broad adhesion	1/9 (11%)		1/9 (11%)	
Baseline: focal adhesion	81/173 (47%)		88/173 (51%)	
VMA release at final visit				
Baseline: broad adhesion	4/9 (44%)	1.0	6/9 (67%)	0.70
Baseline: focal adhesion	82/179 (46%)		132/179 (74%)	
Baseline retinal flap				
VMA release by 1 week		0.002		0.002
Baseline flap: absent	46/125 (37%)		46/125 (37%)	
Baseline flap: present	24/36 (67%)		24/36 (67%)	
VMA release by 4 weeks		0.02		0.002
Baseline flap: absent	58/146 (40%)		63/146 (43%)	
Baseline flap: present	27/44 (61%)		31/44 (70%)	
VMA release at final visit		0.50		0.007
Baseline flap: absent	67/154 (44%)		107/154 (69%)	
Baseline flap: present	23/46 (50%)		41/46 (89%)	
Baseline macular hole				
VMA release by 1 week		0.02		0.02
Baseline hole: absent	35/97 (36%)		35/97 (36%)	
Baseline hole: present	35/64 (55%)		35/64 (55%)	
VMA release by 4 weeks		0.007		0.002
Baseline hole: absent	43/117 (37%)		47/117 (40%)	
Baseline hole: present	42/73 (58%)		47/73 (64%)	
VMA release at final visit		0.31		0.01
Baseline hole: absent	60/125 (48%)		85/125 (68%)	
Baseline hole: present	30/75 (40%)		63/75 (84%)	

CI = confidence interval; PPVx = pars plana vitrectomy; VMA = vitreomacular adhesion.
*Fisher exact test.

treatment. Data entry was accomplished through the Macula Society website using specifically designed web-based forms. Data on adverse events and additional ocular procedures that might have been needed after treatment also were included and no limit was placed on the length of follow-up. No personal identifiers were entered; the website merely required the investigator to use the initials for each patient whose data were entered. Institutional review board approval (IRB) was obtained from the Western IRB for all participating Macula Society members. In addition, if deemed necessary, investigators from institutions requiring local IRB approval obtained permission to provide data to this study.

Point estimates and 95% confidence intervals (CI) are reported for main outcomes using *t* test for continuous outcomes and the binomial proportion for categorical outcomes. Fisher exact test was used to compare baseline factors for each categorical outcome. At each time point, only available data were used to calculate percentages. Although baseline data are available on 223 participants, only data pertaining to the 208 participants with at least 4 weeks of follow-up are included in the remainder of this report. SAS software version 9.4 (SAS Institute, Cary, NC) was used for all analyses.

Results

The dataset consisted of information captured on 208 eyes of 208 patients from 31 investigators. There was 1 investigator with 54 participants (26%) and 1 with 42 participants (20%); no other investigator had more than 15 participants (outcome rates were similar with and without the high-recruiting sites; data not shown). There were more women (143 women, 69%) than men. Most of the patients were non-Hispanic white (175, 84%). African Americans (19, 9%), Asians (7, 3%), and Hispanics (7, 3%) comprised the remainder of the patients. Fifty-two participants (25%) had diabetes.

All patients enrolled had symptomatic VMA. The VMA was reported as focal (<1500 μm) in 179 eyes (86%), broad (≥1500 μm) in 9 eyes (4.5%), and not reported in 20 eyes (10%). At baseline, 75 eyes (36%) had a full-thickness MH and 41 eyes (20%) had a lamellar hole. The full-thickness MH size was smaller than 250 μm in 31 eyes (41%), 250 to 399 μm in 31 eyes (41%), 400 μm or more in 12 eyes (16%), and unavailable in 1 eye (1%). A retinal flap (retinal tissue overhanging 1 edge of an MH) was reported in 31 (41%) of the eyes with MH. Mean baseline visual acuity was approximately 20/63.