Overview

1. Evaluation of full-field electroretinogram changes after ocriplasmin injection in a substudy of symptomatic vitreomacular adhesion subjects from the OASIS trial

   TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0095 / 3.45 -5.30 PM

2. The OASIS MP-1 substudy: characterization of the effect of ocriplasmin on microperimetry parameters

   MO. May 2, 2016: Vitreomacular Interface Disorders - Presentation Room 6C / 11 am – 12.45 PM

3. ORBIT: A phase IV clinical study - lessons learned from patient selection criteria for ocriplasmin intravitreal injection

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4. Ocriplasmin in a porcine model for PVD induction

   TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0087 / 3.45 -5.30 PM

5. Preclinical insights into ocriplasmin safety and mechanism of action

   TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0089 / 3.45 -5.30 PM

6. Repeated injections of ocriplasmin in the Göttingen mini-pig

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7. The ocriplasmin for vitreomacular traction intravitreal injection decisions (OVIID-I) trial: full study results

   TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0090 / 3.45 -5.30 PM

8. Macula Society Collaborative Retrospective Study of Ocriplasmin for Vitreomacular Traction

   MO. May 2, 2016: Vitreomacular Interface Disorders - Presentation Room 6C / 11 am – 12.45 PM
9. **Ocriplasmin for vitreo-macular traction: a Wide-Field OCT Study**
   
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10. **Pharmacologic Closure Rate of Full Thickness Macular Hole with Ocriplasmin—1 year follow-up data**
    
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11. **Real-life experience after intravitreal ocriplasmin for vitreomacular traction and macular hole**
    
    TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0119 / 3.45 -5.30 PM

12. **Safety and Efficacy of Intravitreal Ocriplasmin in Diabetic Macular Edema with Vitreomacular Adhesion**
    
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13. **Acute Ocriplasmin Retinopathy (AOR): Electroretinographic (ERG), SD-OCT and clinical features of 6-months monitoring**
    
    TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0093 / 3.45 -5.30 PM

14. **Clinical results of Ocriplasmin versus C\textsubscript{3}F\textsubscript{8} gas for symptomatic Vitreomacular Traction Syndrome**
    
    TUE. May 3, 2016: Vitreoretinal Interface Disease - Posterboard # C0094 / 3.45 -5.30 PM

15. **Comparison of Three Non-surgical Treatments for Vitreomacular Traction (VMT)**
    
    MO. May 2, 2016: Vitreomacular Interface Disorders - Presentation Room 6C / 11 am – 12.45 PM
Detail

1. Evaluation of full-field electroretinogram changes after ocriplasmin injection in a substudy of symptomatic vitreomacular adhesion subjects from the OASIS trial

Posterboard #: C0095

Abstract Number: 4050 - C0095

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Purpose: Ocriplasmin has been associated in case reports with abnormal full-field electroretinograms (ffERG) and multifocal ERGs in patients with symptomatic vitreomacular adhesion (VMA). However, no study has evaluated symptomatic VMA and ffERGs after ocriplasmin injection in a randomized, prospective study for up to 2 years. OASIS is a Phase IIIb trial designed to assess long-term outcomes in subjects with symptomatic VMA. A ffERG substudy was designed to evaluate the relationship of ERG changes with anatomic and visual outcomes for up to 24 months after a single injection of ocriplasmin 0.125 mg.

Methods: The ERG subset included postinjection ERG data from 61 subjects (40 from the ocriplasmin group and 21 from the sham group). ERGs were recorded from both eyes at each visit (every 3 months) for a 2-year follow-up period and evaluated by a masked ERG expert. Abnormal ERG changes were defined as those greater than 40% from baseline starting at Day 7 or Day 28 (acute change).

Results: The incidence of abnormal ERG changes was higher in the ocriplasmin group (16/40, 40.0%) than in the sham group (1/21, 4.8%). Most (13/16, 81.3%) ERG changes resolved in the ocriplasmin group and 1/1 (100%) returned to normal in the sham group. Reversal of an ERG after ocriplasmin injection has not previously been reported in a large, randomized, prospective study. A review of ERG cases (those that severely diminished and then reversed) along with optical coherence tomography will be presented. Three patients who did not recover at 2 years will also be discussed. The rate of VMA resolution was higher among ocriplasmin-treated subjects with abnormal ERGs than in those with normal ERGs. Best-corrected visual acuity (BCVA) did not correlate with ERG changes. In the ocriplasmin group, 15/16 patients with ERG changes had improved BCVA by the end of the study. A mechanism will be proposed to account for these findings.

Conclusions: The majority of ERG changes in subjects treated with ocriplasmin were normal, and the majority of those that were abnormal reversed to normal. The likelihood of VMA resolution was greater
in subjects with acute ERG changes than in those without. There was no correlation found between BCVA and ERG changes.

2. The OASIS MP-1 substudy: characterization of the effect of ocriplasmin on microperimetry parameters

**Abstract Number:** 1807

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**Purpose:** The MP-1 substudy of the larger OASIS trial evaluated the effects of ocriplasmin and vitreomacular traction (VMT)/symptomatic vitreomacular adhesion resolution on visual fixation and macular sensitivity using microperimetry.

**Methods:** A total of 220 subjects were randomized into the OASIS study, from which 27 were enrolled into the MP-1 substudy (19 ocriplasmin, 8 sham). The substudy was conducted at 3 sites with protocol-specified microperimetry instruments. Fixation-related data included location, degree of eccentricity, and quantitative fixation stability (eg, bivariate contour ellipse area). Retinal sensitivity-related data included the number of normally functioning and scotomatous points and mean sensitivity within various macular grid regions.

**Results:** Baseline (BL) characteristics of the MP-1 subset were largely similar to the OASIS study. The mean distance of the preferred fixation locus to the anatomic center decreased slightly after ocriplasmin injection from 1.32 degrees at BL to 1.11 degrees at Day (D) 7, returning to BL levels (1.28 degrees) by D28, compared to the sham group (1.19, 1.43, and 1.75 degrees at BL, D7, D28, respectively). This distance was identified as a predictor of VMT resolution (P=0.023). In the ocriplasmin group, the median relative scotoma increased postinjection from 1.0 at BL to 6.0 at D7 before recovering to 1.0 at Month (M) 6, whereas more scotomas were detected in the sham group over time (3.5, 4.0, and 5.0 at BL, D7, and M6, respectively). Mean bivariate contour ellipse area decreased slightly after ocriplasmin injection, from 5.98 degrees squared at BL to 4.26 degrees squared at D7 and 5.38 degrees squared at D28, compared to sham (7.73, 7.41, and 8.85 degrees squared at BL, D7, and D28, respectively). Subjects with VMT resolution at D28 had lower bivariate contour area and less relative scotoma at BL than those without. Of the visual function parameters, correlations were strongest for contrast sensitivity followed by best-corrected visual acuity, with no anatomical correlations.

**Conclusions:** Despite the small sample size, the MP-1 substudy suggests that in the ocriplasmin group, fixation and sensitivity parameters tended to be better than in the sham group over time. Although
sensitivity seemed to decrease from D7 to D28 (with more relative scotomatous points) in the ocriplasmin group, it recovered subsequently.

3. **ORBIT: A phase IV clinical study - lessons learned from patient selection criteria for ocriplasmin intravitreal injection**

**Posterboard #: C0108**

**Abstract Number:** 4063 - C0108

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**Purpose:** The goal of the Phase IV ORBIT study is to prospectively and systematically collect real-world data on clinical efficacy and safety outcomes in symptomatic vitreomacular adhesion (VMA) patients treated with ocriplasmin according to standard of care in US retina clinics. Another objective of the study is to further define patient criteria that will improve clinical outcomes compared to those from the Phase III MIVI-TRUST trial results.

**Methods:** ORBIT is a multicenter, prospective, observational Phase IV study that has enrolled 542 patients across 90 clinical sites. Patients are enrolled at the time of a single injection of ocriplasmin 0.125 µg and followed for up to 12 months. Treatment decisions, including the frequency and timing of patient visits after injection, are at the discretion of the treating physician following standard of care and are not mandated by the study design. Clinical effectiveness and safety data are entered in electronic case report forms based on investigator assessments. Images taken by spectral-domain optical coherence tomography are uploaded to a central reading center for independent review.
Results: Here we present the complete patient baseline data and the efficacy results up to 6 months follow-up according to various patient characteristics. Pharmacological VMA resolution at 1 week, 1 month, and 6 months will be reported according to key baseline characteristics: adhesion size, lens status, injection position, presence of full-thickness macular hole, and presence of an epiretinal membrane. Final 6-month efficacy data, as well as safety reports, will be presented.

Conclusions: Data collected from the ORBIT study will provide a real-world efficacy and safety profile of ocriplasmin, better characterize postinjection patient experiences, and help identify patients who may respond best to ocriplasmin therapy. The results presented here will further characterize appropriate patient selection for ocriplasmin treatment compared to the patient characteristics identified from the Phase III MIVI-TRUST studies, including injection position which will be the first time this data is reported.
4. Ocriplasmin in a porcine model for PVD induction

**Posterboard #:** C0087

**Abstract Number:** 4042 - C0087

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**Purpose:** To better understand the activity profile of ocriplasmin at the inner limiting membrane (ILM), we evaluated the pharmacological activity in the pig model for induction of Posterior Vitreous Detachment (PVD).

**Methods:** To validate the model, thirteen farm pigs were injected mid-vitreally with ocriplasmin (96µg per eye, 29µg/mL vitreous assuming a vitreous volume of 3.3mL; injection volume 100µL) or vehicle in the contralateral eye. Following treatment, eyes were examined weekly by SD-OCT to assess for a PVD for up to 6 weeks. There were 4 volume scans averaging 48 frames per image. These scans were focused nasally, temporally, and superior to the optic nerve. Enucleated eyes were processed for detailed histopathological analysis.

**Results:** A single administration of 96µg ocriplasmin resulted in a time-dependent induction of PVD. PVD was observed from Week 2 onwards (82% eyes at Week 8) in the ocriplasmin treated eyes and from Week 5 onwards (8% eyes at Week 8) in the eyes which had received vehicle. Subretinal lucencies (SRLs) were observed upon ocriplasmin treatment. Although the SRL incidence was high (85% one week post administration), the SRL volume was relatively small; 0.062±0.012mm³ (avg±SEM). Incidence and volume diminished by Week 2, disappearing completely from Week 3 onwards. SRLs were not observed in vehicle treated eyes. Hyper-reflective spots in the vitreous were observed in both ocriplasmin and vehicle treated eyes, reaching a maximum incidence of 46% and 8% for ocriplasmin and vehicle, respectively. All hyper-reflective spots had resolved by Week 3. Hematoxylin and Eosin staining did not reveal structural changes in the retina upon treatment. Immunohistochemical stains for the ILM components collagen IV, laminin and fibronectin demonstrated the specific activity of ocriplasmin on these matrix proteins by cleaving the ILM into 2 separate layers, one remaining attached to the ILM, the other associated with the PVD interface. No significant distribution changes were observed for these stains in the retina itself.

**Conclusions:** This validated pig PVD model demonstrated the ability of ocriplasmin to time-dependently induce PVD. The observed side effects such as SRLs and hyper-reflective spots proved to be transient (up to Week 3). Specific activity of ocriplasmin at the ILM could be demonstrated.
5. Preclinical insights into ocriplasmin safety and mechanism of action

**Posterboard #:** C0089

**Abstract Number:** 4044 - C0089

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**Purpose:** The purpose of this study was to gain insight into the safety and mechanism of action of ocriplasmin, a protease used for treatment of vitreomacular traction. To achieve this, we evaluated retina and vitreous tissues from a porcine model of ocriplasmin-induced Posterior Vitreous Detachment (PVD) as well as cell-based models.

**Methods:** Porcine eyes were injected intravitreally with ocriplasmin (96μg per eye, equivalent to 125μg in human) or vehicle. At several time points (up to 6 weeks) post injection, animals were sacrificed and vitreoretinal tissues were studied: retinal morphology, distribution of extracellular matrix proteins as well as number of microglial cells were histologically examined. The presence of an inflammatory response was assessed by multiplex profiling of 14 inflammatory markers in the vitreous. The effect of ocriplasmin on blood-retinal-barrier permeability was assessed using an *in vitro* electrical resistance (TEER) assay.

**Results:** Retinal morphology was not affected by vehicle or ocriplasmin at any of the investigated time points. Extracellular matrix components clearly delineated the PVD structures at the internal limiting membrane and no significant distribution changes were observed in the retina. No evidence for a major acute inflammatory response was found. Although histology indicated a minor increase of the macrophage-specific marker Iba1 in ocriplasmin treated eyes, cytokine profiling indicated no significant difference between vehicle and ocriplasmin treated eyes. A minor and transient inflammatory response related to injection in general was observed. We observed that only high doses of ocriplasmin could modulate permeability of *in vitro* retinal barrier models, all changes being cell specific and fully reversible after 48 hours.

**Conclusions:** A number of the transient observations on OCT (lucencies, inclusions) that have been observed in patients treated with ocriplasmin can be mimicked in a porcine model of PVD. Closer examination of the involved tissues did not indicate an underlying acute inflammatory response, neither did we observe signs of toxicity or extracellular matrix rearrangement specific to ocriplasmin. *In vitro* observations indicate that retinal barrier permeability can only be affected by high local doses of active ocriplasmin, and even then the effects are rapidly reversible.
6. Repeated injections of ocriplasmin in the Göttingen mini-pig

Posterboard #: C0088

Abstract Number: 4043 - C0088

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Purpose: The purpose of this study was to determine the safety of up to six consecutive injections of ocriplasmin in the mini-pig.

Methods: To assess the safety of 2, 3 and 6 ocriplasmin injections 4 weeks apart, a GLP toxicity study was performed in Göttingen mini-pigs. Each group consisted of 3 males and 3 females. The experimental eye received ocriplasmin at a dose of 63μg/eye (29μg/mL assuming a vitreous volume of 2mL). The vehicle was given to the contralateral eye which acted as a control. Fifty microliters were injected mid vitreous with a 30G, ½” needle. Animals were subjected to ophthalmic toxicology screening consisting of funduscopic and biomicroscopic (slit lamp) examination (mydriatic and non-mydriatic) and tonometry. In addition a monthly full-field ERG was performed. Enucleated eyes were processed for detailed histopathological analysis at the Charles River Laboratories in Montreal.

Results: The eyes receiving two or three ocriplasmin injections had no ERG abnormalities or evidence of retinal toxicity and were indistinguishable from control eyes. In the group receiving up to 6 injections, lens subluxation, recorded as a very small aphakic crescent in the superotemporal lens quadrant, was noted in 4/6 eyes following the 5th injection. Damage to the lens zonules is the primary etiology for lens subluxation. After 6 administrations, microscopic findings of minimal mononuclear cell infiltration (vitreous, 4/6 eyes; injection site, 2/6 eyes; iris/ciliary body, 2/6 eyes) were noted. No signs of inflammation or lens subluxation were observed in the control eyes. There were no ocriplasmin-related changes in intraocular pressure after up to six doses. Analysis of the a- and b-wave did not reveal any changes in response amplitude or latency at any interval evaluated during the course of the study both in the treated and control eyes.

Conclusions: Administration of ocriplasmin at 4-week intervals for up to 4 doses (3 months) was well tolerated in Göttingen mini-pigs at 63 μg/eye/injection; after 5 or 6 doses, minimal lens subluxation was present in 4/6 eyes.
7. **The ocriplasmin for vitreomacular traction intravitreal injection decisions (OVIID-I) trial: full study results**

**Posterboard #:** C0090 - **Abstract Number:** 4045 - C0090

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**Purpose:** OVIID-I is a Phase IV, multicenter, prospective, single-arm, open-label, interventional study designed to observe the anatomical and functional outcomes of a single injection of ocriplasmin over a 6-month follow-up period in patients with vitreomacular traction (VMT)/symptomatic vitreomacular adhesion (VMA) with focal VMT (≤1500 µm), absence of epiretinal membrane, and macular hole (MH) of ≤400 µm.

**Methods:** Key optical coherence tomography (OCT) inclusion/exclusion criteria were assessed by central reading center (CRC). Patients were followed for up to 6 study visits at the clinical site. A screening/baseline visit was followed by Visit 1, at which subjects received a single intravitreal injection of ocriplasmin 0.125 mg in a 0.1 mL volume as per the country’s product label. Subsequent to Visit 1, patients attended 4 postinjection visits at Day 7, Day 28, Day 90, and Day 180. The primary efficacy endpoint was nonsurgical VMT resolution at Day 28, as determined by CRC spectral-domain OCT. A key secondary endpoint was the proportion of patients with MH closure at Days 28, 90, and 180.

**Results:** A total of 628 patients from 11 countries were enrolled. Among 468 patients treated, 466 were included in the full analysis set. The mean age was 72 years, 344 were female (73.8%), and 442 were Caucasian (94.8%). At baseline, 35 patients (7.5%) had VMT with small MH (≤250 µm), and 51 patients (10.9%) had VMT with medium MH (250-400 µm). The overall proportion of patients with nonsurgical VMT resolution at Day 28 was 47.4%. For patients with VMT without MH at baseline, the proportion with VMT resolution at Day 28 was 43.4%. The overall proportion of nonsurgical closure of MH at Day 28 was 39.5%. Nonsurgical closure of MH was greater (57.1%) in patients with small MH (≤250 µm) at baseline. No new safety signals or trends were observed that would alter the known safety profile of ocriplasmin.

**Conclusions:** OVIID-I is a CRC-supported study conducted to observe the anatomical and functional outcomes in VMT/symptomatic VMA patients treated with ocriplasmin over a 6-month period. Results from this study suggest appropriate patient selection confirmed by CRC may increase the likelihood of success after treatment with ocriplasmin.
8. Macula Society Collaborative Retrospective Study of Ocriplasmin for Vitreomacular Traction

Abstract Number: 1805

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**Purpose:** To assess anatomic and visual outcomes of ocriplasmin for treatment of vitreomacular traction (VMT).

**Methods:** Macula Society members were surveyed online to retrospectively collect data on patients receiving ocriplasmin for VMT. Clinical findings, optical coherence tomography (OCT) parameters, change in visual acuity, and adverse events were collected online using standardized forms.

**Results:** There were 223 eyes (223 patients) with VMT. Macular hole (MH) was present at baseline in 79 eyes (35%); MH size was < 400 µ in 64 of 77 (83%) eyes with data available on hole size. VMT adherence was focal (<1500 µ) in 192 of 202 (95%) eyes with available data. Follow-up ranged from 1 day (1 eye) to 18 months. VMT resolved in 44% of eyes by 1 week, 50% of eyes by 1 month, 58% of eyes by 12 weeks and 74% of eyes at the final visit. Pars plana vitrectomy (PPVx) was performed in 6% by 1 month, 15% by 12 weeks and 29% by the last follow-up. MH closure without PPVx occurred in 16% by 1 week, 35% by 4 weeks, 40% at 12 weeks and 40% at the final visit. There was no association between rate of closure and hole size. Including PPVx, MH closure occurred in 67/79 eyes (85%) by the last visit. Mean change between baseline and final visual acuities was -0.14 logMAR; 15% of eyes lost ≥ 2 lines and 39% gained ≥ 2 lines. Scleral buckling with PPVx was performed in 1 eye and cataract extraction in 10 eyes (4%). Complications included photopsias (35 eyes, 16%), dimness of vision (35 eyes, 16%), decreased color vision (23 eyes, 10%), MH development (11 eyes, 7.6%), macular RPE atrophy (6 eyes, 2.7%), retinal detachment (4 eyes, 1.8%) and retinal tear (2 eyes, 0.9%). Diminished ERG was found in 9 eyes, 8 of which had MH. No cases of endophthalmitis were reported.

**Conclusions:** Ocriplasmin results in release of VMT in 45% of eyes and closure of macular holes in 40% without PPVx with stable or improved visual acuity in 85% eyes. Adverse events were not infrequent but mostly not serious.
9. Ocriplasmin for vitreo-macular traction: a Wide-Field OCT Study

**Posterboard #:** C0092 - **Abstract Number:** 4047 - C0092

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**Disclosure Block:** Chiara Preziosa, None; Isabella D’Agostino, None; Ugo Nava, None; Stefano Erba, None; Matteo G. Cereda, None; Novartis (Code F (Financial Support) ); Bayer (Code C (Consultant) ); Carl Zeiss Meditec (Code F (Financial Support) ); Genentech (Code C (Consultant) ); Heidelberg Engineering (Code C (Consultant) ); Novartis (Code C (Consultant) ); Ocular Instruments (Code P (Patent) ); OPTOS (Code C (Consultant) ); Quantel Medical (Code F (Financial Support) ); Roche (Code C (Consultant) )

**Purpose:** To evaluate the baseline features and the changes of vitreo-retinal adhesion (VRA) and retinal outer layers outside the macula in patients that underwent an intravitreal Ocriplasmin injection (Jetrea, ThromboGenics USA, Alcon/Novartis EU). To study the relation between vitreous detachment and the attenuation of retinal outer segment signal.

**Methods:** A retrospective case series of 13 patients treated with intravitreal Ocriplasmin injection, ten with vitreo-macular traction (VMT) and three with macular hole (MH). Each eye has been scanned in 5 different locations, 3 horizontal B-scan (central, temporal and nasal) and 2 vertical B-scan (superior and inferior) using the 55° Wide Field OCT lens (HRA Spectralis, Heidelberg Engineering, Heidelberg, Germany).

**Results:** A complete protocol of 5 scans was available for all the patients at baseline and 1 week, 1 month, 3 and 6 months post injection. At baseline all patients presented a vitreous-papillary adhesion (VPA), one patient had vitreous adherence nasally only and one patient had vitreous detached temporally only. The signal of outer segment was normal in all patients. After Ocriplasmin injection VMT resolved in 10 patients (76%), 3 of them presented a complete posterior vitreous detachment (PVD). 7 patients showed an attenuation of photoreceptor outer segments (54%) that involved all quadrants: in particular 6 of them with VMT resolution and 1 with non PVD and no VMT resolution. In 3 patients with VMT resolution the attenuation involved also areas with no PVD. Shallow, peripheral sub-retinal detachment was visible in 3 patients: all these 3 patients had attenuation of photoreceptor outer segment, 2 patients had a complete PVD and 1 had no PVD and no VMT resolution. In all the patients attenuation of the outer segment as shallow sub-retinal detachment resolved during the follow-up.

**Conclusions:** VMT are characterized by shallow vitreous detachment around the fovea always associated to a VPA. Rarely an initial peripheral vitreous detachment is visible. Intravitreal Ocriplasmin injection induces resolution of VMT and rarely a release of a VPA and a complete PVD. It can also induce and acute panretinopathy not related to vitreous detachment, characterized by an attenuation of
photoreceptor outer segments layers involving all the retina area and shallow peripheral sub-retinal detachment.

10. Pharmacologic Closure Rate of Full Thickness Macular Hole with Ocriplasmin—1 year follow-up data

Posterboard #: C0091

Abstract Number: 4046 - C0091

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Purpose: To analyze a single center’s experience with ocriplasmin for pharmacologic full-thickness macular hole (FTMH) closure associated with vitreomacular traction (VMT).

Methods: Single center retrospective study of 34 eyes that received intravitreal ocriplasmin for symptomatic FTMH with VMT. VMT release, FTMH closure, visual acuity changes, and anatomical characteristics on spectral domain optical coherence tomography (SD-OCT) were analyzed.

Results: All eyes injected with ocriplasmin had focal VMT, and 32/34 (94%) had small (<250 microns) macular holes. Nonsurgical closure of FTMH was achieved in 12/34 (35%) eyes, and 21/34 (62%) eyes had VMT release. On average, eyes achieved pharmacologic FTMH closure within 20 days (range 4-32 days, with one occurring at 76 days) and pharmacologic VMT release within 16 days (range 3-76 days). Subsequent vitrectomy was performed in 21/22 (95%) eyes at an average of 50 days (range 12-182 days) after receiving ocriplasmin. Mean logMAR best-corrected visual acuity (BCVA) improved from 0.89 (20/155) at baseline to 0.40 (20/50) at final follow-up (p<0.001, mean 13.6 months follow-up). Overall average FTMH diameter in eyes that did not experience pharmacologic closure did not vary significantly from time of injection (293 um) to 1 month follow-up (318 um). Ellipsoid changes occurred in 16/34 eyes (47%), resolving in all eyes at an average of 35 days (range 3-76 days). One eye had pharmacologic closure of FTMH, but then reopened after 2 years. At final follow-up (mean 13.6 months), 30/34 (88%) of patients experienced an increase of two or more lines of vision, while 25/34 (74%) experienced an increase in three or more lines of vision. Out of 34 patients, none experienced a decline in two or more lines of vision at time of final follow-up.

Conclusions: In clinical practice, ocriplasmin achieved VMT release in 62% of treated eyes, with a 35% closure rate for FTMH. All 34 patients in this series experienced stability or improvement in vision at final follow-up, and ocriplasmin was not associated with widening of FTMH. There were no cases of permanent visual loss in this series.
11. Real-life experience after intravitreal ocriplasmin for vitreomacular traction and macular hole

**Posterboard #:** C0119

**Abstract Number:** 4074 - C0119

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**Purpose:** Pars plana vitrectomy has been considered the gold for vitreomacular traction (VMT) and macular hole (MH) treatment. Pharmacologic vitreolysis is gaining interest, as ocriplasmin has been approved for VMT and MH therapy. The purpose of this study was to evaluate prospectively the anatomical and functional results after ocriplasmin injection in patients with VMT or MH, providing the real-life experience of three centers.

**Methods:** 24 patients with VMT (17 with VMT alone and 7 with MH) were treated with a single ocriplasmin injection and followed-up at baseline, day 7, 28 and the last examination of the follow-up for each patient (mean±SD: 64.2±24.4 days, range: 40-145 days). Best-corrected visual acuity (BCVA) and spectral domain-optical coherence tomography (SD-OCT) were performed for patients’ assessment, while various complications were recorded and analysed. At baseline, univariate analysis was also performed to examine the potential predictive factors for VMT release.

**Results:** 66.7% of patients presented VMT release at the end of the follow-up, while 28.6% exhibited MH closure. Baseline positive predictive factors for VMT release were young age, female sex, phakic lens status, increased vitreofoveal angle, V-shaped and loose vitreomacular adhesion, thin vitreous strands at the adhesion site and absence of epiretinal membrane. Enlargement of pre-existing MH and formation of lamellar MH were observed in one and four cases respectively and remained till the end of the follow-up. Ellipsoid zone disruption and subretinal fluid development became evident 7 days after injection in four cases. Formation of cystoid macular edema, not evident at baseline, was noticed in three cases at day 28 after injection. Mild adverse events, like vitreous floaters, photopsias, eye pain and foreign body sensation, were noticed at day 7 and resolved till the end of the follow-up.

**Conclusions:** Our study demonstrated a VMT release rate of 66.7%. Apart from the known baseline factors that influence the VMT release after ocriplasmin injection, the size of vitreofoveal angle, the V-shaped and loose vitreomacular adhesion, and the thin vitreous strands at the adhesion site could additionally affect the outcome of VMT release. In addition, we studied when the VMT release and concomitant events happen and for how long the induced complications lasted.
12. Safety and Efficacy of Intravitreal Ocriplasmin in Diabetic Macular Edema with Vitreomacular Adhesion

Posterboard #: C0056

Abstract Number: 3256 - C0056

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Purpose: To evaluate the safety and preliminary efficacy of 125µg of a single intravitreal injection of ocriplasmin in patients with diabetic macular edema (DME) and focal or loose broad vitreomacular adhesion/traction (VMA/VMT).

Methods: Interventional, single center observational case series of 11 eyes of 9 patients who received intravitreal ocriplasmin for DME with VMA/VMT. Adjunct treatment, when required, with laser and intravitreal injections of corticosteroids and/or antiangiogenic before or after the injection of ocriplasmin were also performed. The primary endpoint was resolution of vitreomacular adhesion at 1 month post intervention. The secondary endpoints included VMA release or decrease size of VMA over time, total posterior vitreous detachment (PVD), macular edema, best corrected visual acuity (BCVA) changes from baseline and number of anti-vascular endothelial growth factor (VEGF) injections.

Results: 11 eyes of 9 patients were treated with an intravitreal injection of ocriplasmin. The mean follow-up was 128 days (range between 81 and 223). Of the 9 patients, with an average age of 69 years, 64% are male and 55% of the cases are phakic. The mean BCVA pre-injection was 20/50 (ETDRS Scale). Non-proliferative diabetic retinopathy was present in 82% of the eyes. There was history of intravitreal injections (anti-angiogenic and/or steroids) in 82% of cases and 100% laser therapy. The average time of vitreo-macular traction was 11 months. The average measure of traction was 878µm (minimum 128µm and maximum values of 2765µm) and an epiretinal membrane was found on OCT in 9% of the cases. Floaters and/or photopsias were described in 45% of patients in the first days after the injection. The release of the TVM occurred in 64% of cases and PVD in 45.5%. There was an increase of BCVA in 82% of cases (p<0.05). The mean macular thickness decreased from 311.2µm pre-injection to 291.1µm (p=0.041).

Conclusions: The intravitreal injection of ocriplasmin in DME associated with VMT seems to be a safe and well tolerated procedure and an effective treatment with a significant improvement in visual acuity and macular edema. The anatomical-functional preliminary results suggest that this approach could be a therapeutic alternative in the DME with VMT, being the patient’s selection and the timing of injection crucial for a successful treatment.
13. Acute Ocriplasmin Retinopathy (AOR): Electroretinographic (ERG), SD-OCT and clinical features of 6-months monitoring

**Posterboard #:** C0093

**Abstract Number:** 4048 - C0093

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**Purpose:** To report ERG, SD-OCT and clinical features of 6-months monitoring a patient with AOR

**Methods:** Recently few reports notified visual acuity (VA) loss, dyschromatopsia, visual field (VF) constriction, pupillary abnormalities, loss of outer retinal signals on OCT and reduced ERG responses after intravitreal ocriplasmin injection. Safety profile of the registration trial (Phase 3 MIVI-III) suggested adverse events (AE) to be related to injection procedure and vitreolysis, explaining loss of VA with subretinal serous fluid accumulation (median recovery to baseline within 2 weeks, resolution of dyschromatopsias within 3 months). We present a course of AOR over 6 months with severe changes in function (VA, VF, ERG) and retinal structure.

**Results:** A 74-year-old woman presented to our clinic with loss of VA to hand motion, shimmering photopsias, floaters and dyschromatopsia in the right eye one day after intravitreal ocriplasmin injection. Preoperative VA was 0.32 Snellen chart in the treated eye. On day 1, SD-OCT showed resolution of the VMT, but new neurosensory serous retinal detachment (NSD). Outer retinal layers (ORL) showed severe disruption of the ellipsoid zone, which partially recovered with VA improvement to baseline at week 5 and to 0.5 at month 6. At week 5 and month 6 NSD had resolved, the ellipsoid zone showed structural recovery. VF testing (Goldmann) at day 1 showed severe constriction of all isopters which gradually recovered by week 5, but central relative scotoma persisted by month 6 (Fig.1). Full-field ERG initially showed severe reduction of scotopic and photopic responses and an electronegative ERG, suggesting postreceptoral dysfunction and decreased photoreceptor activity (Fig.2).

**Conclusions:** In our patient AOR lead to severe VA loss and dyschromatopsia, the recovery of which took longer than described in the registration trial (MIVI-III). Severe VF constriction and loss of full-field ERG responses showed a generalized retinopathy not mentioned as AE in the trial. Animal studies relate the acute toxic effect to the separation and disruption of laminin and fibronectin in the ORL. Further studies are necessary to fully understand the impact of ocriplasmin on long term visual outcome. Postoperative monitoring of VF and in cases with severe visual loss ERG is recommended.
14. Clinical results of Ocriplasmin versus C₃F₈ gas for symptomatic Vitreomacular Traction Syndrome

Posterboard #: C0094

Abstract Number: 4049 - C0094

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Purpose: Until recently, vitrectomy surgery was the preferred treatment for vitreomacular traction (VMT), but due to its potential complications, it is normally only performed once there is clinically significant loss of vision. It can also be costly and invasive for patients. As an alternative, intravitreal therapy can be used – ocriplasmin (Jetrea®) has recently been licenced for use in VMT and small macular holes, but is costly, and intravitreal gas injection can also be used. The purpose of this retrospective comparative case review is to evaluate the resolution rate of VMT after receiving either ocriplasmin or Perfluoropropane (C₃F₈ gas).

Methods: This review retrospectively analysed 20 medical records from patients with diagnosed VMT using spectral-domain optical coherence tomography (sdOCT) that underwent intravitreal injections of either Jetrea (n=10) or C₃F₈ gas (n=10). All treatments were administered by the same surgeon. Patients either received 0.125 mg of Jetrea as per the package guidelines or an injection of 0.3 mL of C₃F₈ gas. The primary outcome measure was release of VMT on sdOCT at one month after treatment. Secondary outcomes included central subfield thickness after treatment, change in visual acuity and any side effects/complications.

Results: 50% had resolution of vitreomacular traction on sdOCT by one month after Jetrea injection compared to 80% of patients treated with C₃F₈ gas. Mean visual acuity at one month improved by a mean of +10.3 letters following ocriplasmin compared to only +0.4 letters after C₃F₈ gas, probably representing persistence of the gas bubble. Consistent with this, central subfield thickness on sdOCT decreased by an average of 39 microns after injection in patients that received gas compared to only 4.9 microns in the group of patients that received ocriplasmin. No patients developed retinal tears or detachment.

Conclusions: C₃F₈ gas proved to be of similar effectiveness to Ocriplasmin in our small study, providing effective release of VMT. This study suggests that C₃F₈ gas could provide a cost effective and readily available alternative treatment for patients and that a larger prospective trial would be worthwhile to establish its use in the standard treatment pathway for VMT.
**15. Comparison of Three Non-surgical Treatments for Vitreomacular Traction (VMT)**

**Abstract Number:** 1806

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**Purpose:** Evaluate the efficacy and safety of C3F8 gas, SF6 gas, and intravitreal ocriplasmin (IVO) for the treatment of symptomatic VMT. Furthermore, dynamic optical coherence tomography (OCT) microstructural changes were evaluated to better predict successful release of VMT with gas (pneumatic vitreolysis).

**Methods:** 113 consecutive patients with VMT were treated with one of three interventions: 54 patients received IVO, 32 patients received C3F8 gas injection, and 27 patients received SF6 gas injection. Patients receiving gas were given 0.25 cc of 100% gas (for both C3F8 and SF6). All injections were performed using aseptic technique in a clinic setting. Mean follow up was greater than 6 months. VMT release rates, visual acuity (VA), tonometry, and outer retinal band (ORB) changes on OCT were retrospectively reviewed. For the two gas groups (C3F8 and SF6), dynamic OCT movements were carefully reviewed. Specifically, patients were evaluated with back and forth horizontal and vertical micro-movements (voluntary saccades) on live OCT imaging to characterize the VMT adhesion as either 'taut' or 'mobile'. VMT release rates within the two gas groups were reviewed to determine if taut versus mobile VMT had a higher degree of successful release.

**Results:** VMT release rate at final follow up was 84% (27/32) with C3F8 gas, 56% (15/27) with SF6 gas, and 48% (26/54) with ocriplasmin [SF6 versus ocriplasmin: p=0.53, C3F8 versus ocriplasmin: p<0.01, C3F8 versus SF6: p=0.01]. Thus, C3F8 was superior to both SF6 and IVO; while SF6 performed similarly to IVO. VA improved slightly in all groups, with no significant change in tonometry. ORB changes were noted more frequently in IVO versus either gas combined (p<0.05). No retinal breaks occurred in this series and no vitreous hemorrhages occurred. 'Mobile' VMT on dynamic (live) OCT released more frequently than 'taut' VMT (p<0.05) with gas.

**Conclusions:** C3F8 gas injection showed superior VMT release rates to both IVO and SF6. Minimal ORB changes were noted with C3F8 and SF6 compared to IVO.

To our knowledge, the 113 eyes included in this review represent by far the largest series to date regarding the comparison of two types of gases and ocriplasmin for VMT. This series shows highly positive results regarding the use of intravitreal gas for VMT, especially C3F8. Furthermore, by evaluating baseline dynamic (live) OCT characteristics of VMT, predictability of successful VMT release can be enhanced. **END**