

Overview Preclinical and Clinical Data Presented at ARVO 2017 Baltimore Convention Center in Baltimore, May 7 - 11, 2017

Sunday, May 7, 2017 – Exhibit / Poster Hall – Program #/Board # Range: 212–262/B0243–B0293

1. One year retrospective analysis of ocriplasmin for the treatment of symptomatic vitreomacular traction

filofteia Tacea, Leonidas Makris, Ahmed Kamal. Ophthalmology, Aintree University Hospital, Liverpool, United Kingdom.

Program Number: 224 *Poster Board* Number: B0255
Presentation Time: 8:30 AM–10:15 AM

Purpose:

To evaluate the efficacy and safety of a single intravitreal injection of ocriplasmin in symptomatic patients with vitreomacular traction (VMT).

Methods:

Retrospective analysis of all patients with symptomatic metamorphopsia, micro-scotomas and deterioration of vision secondary to VMT, confirmed with Spectral Domain Optical Coherence Tomography (SD-OCT). Patients received a single injection of ocriplasmin (JETREA[®]). LogMAR visual acuity, measurement of intraocular pressure (IOP) and SD-OCT were recorded at their first follow-up at 1 month, at 3 months and at the final follow-up visit at 12 months.

Results:

Thirty-three patients (10 males and 23 females) and a total of 35 eyes were included in our study. Fifteen out of 35 eyes (42.8%) experienced complete release of the VMT. One out of three eyes with a small full thickness macular hole (33.3%) closed post-injection. One eye developed partial thickness macular hole with spontaneous closure at 3 months, after a successful VMT release. Mean visual acuity improved by 6.2 logMAR letters and central macular thickness decreased by an average of 55µm in this group of 15 eyes that achieved VMT release. Twelve out of these 15 eyes (80%) also experienced improvement of symptoms. Despite a successful VMT release in three eyes, there was no improvement in their visual symptoms. The safety review showed that visual symptoms such as vitreous floaters and photopsia were common early after ocriplasmin injection, but rapidly resolved afterwards.

Conclusions: Intravitreal ocriplasmin in carefully selected patients is a promising and safe treatment option for VMT in symptomatic patients and it could represent a viable alternative to pars plana vitrectomy.

Commercial Relationships: *filofteia Tacea*; *Leonidas Makris*, None; *Ahmed Kamal*, None

2. Cost effectiveness of Intravitreal Ocriplasmin for vitreomacular adhesion and macular hole

Kapil G. Kapoor^{1, 2}, *Tayab Waseem*¹, *Colin Reinhart*². ¹Research, Wagner Macula & Retina Center, Virginia Beach, VA; ²Ophthalmology, Eastern Virginia Medical School, Virginia Beach, VA.

Program Number: 237 Poster Board Number: B0268

Presentation Time: 8:30 AM–10:15 AM

Purpose:

Intravitreal ocriplasmin (IVO) has altered the therapeutic landscape for vitreomacular interface pathology. Recent studies have demonstrated improving success rates and this highlights the question of the cost effectiveness of IVO compared to the current standard of care - pars plana vitrectomy (PPV). The purpose of this study is to provide a new patient pool to evaluate cost efficacy of IVO for vitreomacular adhesion (VMA) and macular hole (MH).

Methods:

A retrospective single center, multiple physician, IRB approved study was done of 247 patients with VMA and MH over 15 months. Clinical charts and imaging were cross referenced with billing records and total treatment cost was determined. Patients were divided into three groups: Group 1 – VMA and MH treated by PPV, Group 2 – VMA and MH treated by IVO, Group 3 – VMA treated by IVO.

Results: Initial interventional success rates were 98% (Group 1), 55.6% (Group 2), 67.7% (Group 3). Secondary success rates were 66.6% (Group 1), 81.8% (Group 2), 90% (Group 3). Cost of PPV at our institution was \$6,538 and IVO cost was \$3480. Quality-adjusted life years (QALY) calculation (based on average life expectancy of 14.3 years from mean patient age of 71.2 years) demonstrated an average of 2.5 lines of vision saved from successful treatment. Using a cohort-based computer model the treatment decision tree demonstrated Group 1 patients had a cost per line of \$2,654.39, cost per line-year saved of \$185.62, and cost per QALY of \$6,187. Group 2 treatment was more cost effective with a cost per line of \$2,456.25, cost per line year saved of \$171.77, and cost per QALY of \$5,726.

The difference in cost effectiveness showed IVO was more cost effective than PPV as an initial intervention, with a difference in cost per line of \$198.14, cost per line-year saved of \$13.85, and cost per QALY of \$461. Group 3 was cost effective with increased success rates for initial and secondary procedures.

Conclusions:

IVO is a cost-effective intervention for VMA and MH with appropriate patient selection. The success rate of IVO in our patient population was greater than previously published rates, which may reflect more optimal patient selection. The success rates likely impacted the weighted probability model of cost efficacy and further research targeting optimizing success rates of IVO will be beneficial to optimize the cost efficacy of this therapeutic intervention.

Commercial Relationships: **Kapil G. Kapoor**, None; **Tayab Waseem**, None; **Colin Reinhart**, None

Monday, May 8, 2017 – Hall G – Paper presentation 11:15 AM–11:30 AM

3. Evaluation of Visual Acuity and Acute Retinal Changes Following Intravitreal Injection of Ocriplasmin

Author Block: *Dhruvesh Patel*¹, *Amar Shah*², *Andrew Melchioris*³, *David G. Miller*³

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Disclosure Block: Dhruvesh Patel, None; Amar Shah, None; Andrew Melchioris, None; David G. Miller, None

Purpose: To quantify the impact of ocriplasmin injection on visual acuity and evaluate its toxicity as manifested on optical coherence tomography (OCT).

Methods: A 1-year retrospective chart analysis was conducted on 66 eyes with symptomatic vitreomacular traction (VMT) that received 125µg intravitreal injection of ocriplasmin. Each patient underwent complete ocular assessment, including baseline OCT, prior to treatment. Follow-up data were assessed at approximately 1-week, 1-month, 3-month, 6-month and 1 year intervals post-injection. Primary outcome was development of ellipsoid zone degradation at any interval. Secondary outcomes included changes in visual acuity (VA), resolution of VMT at 1 month, closure of macular hole, and development of subretinal fluid. Snellen VAs were converted to ETDRS letters scores to stratify patients into groups ranging from greatly improved ($\geq +15$) to severely worse (≤ -15) from baseline VA.

Results: Fifteen of 66 eyes (22.7%) were noted to have ellipsoid zone degradation. Of these, 13 had resolution of degradation over a period of 3-9 weeks, with 2 eyes having persistent degradation. Visual acuity was documented for 62 patients 1 month post-injection. Twenty-one (33.9%) eyes were classified as worse or severely worse, whereas 24 (38.7%) were improved or greatly improved. At 6 months, 7/51 remained severely worse. Thirty-six of 66 eyes (54.5%) had complete resolution of VMT within 1 month of injection. Fifteen patients underwent PPV for persistent or worsening VMT. Nine of the 19 eyes with macular holes had resolution. Five of the 19 eyes had surgical closure of the macular hole. Subretinal fluid developed in 8 eyes post-injection, with complete resolution noted in 6 eyes over a period of 3-6 weeks.

Conclusions: Greater than 1 in 5 patients experienced ellipsoid zone degradation, suggesting a potential unintended toxicity of ocriplasmin to retinal tissue. Other findings include diminished visual acuities in 33.9% and 28.8% of patients at 1 month and 3 months, respectively. Despite resolution of VMT in over half our patients, this benefit must be weighed heavily against the significant presence of clinical risks.

Tuesday, May 9, 2017 – Exhibit / Poster Hall – Program #/Board # Range: 212–262/B0243–B0293

4. Does intravitreal Ocriplasmin degrade intraretinal extracellular matrix molecules?

Posterboard #: B0318

Abstract Number: 3693 - B0318

Author Block: Declan C. Murphy¹, Majed Felembam¹, Nicola Hunt¹, Stuart N. Baker¹, Majlinda Lako¹, David Steel¹

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Disclosure Block: Declan C. Murphy, None; Majed Felembam, None; Nicola Hunt, None; Stuart N. Baker, None; Majlinda Lako, None; David Steel, None

Purpose: Ocriplasmin (OCP), a recombinant truncated form of plasmin, is a non-specific protease which results in vitreoretinal (VR) separation in a proportion of patients with vitreomacular traction thought to be by its action on extracellular matrix (ECM) molecules at the VR interface. Outer-retinal complications such as photoreceptor dysfunction have been reported after OCP and hypothesized to result from off target effects. We carried out an experimental study to investigate the effect of OCP on a variety of retinal ECM molecules in primate eyes.

Methods: Six eyes of rhesus *macaque* primates were enucleated immediately post mortem after intracardiac perfusion with phosphate buffered saline. Two eyes were injected with 62.5 mcg of OCP with a 30g needle in the mid vitreous cavity, then immediately placed in carboxy perfused aCSF for 24hrs at room temperature before fixation in 4% paraformaldehyde (PFA) with removal of the anterior segment (OCP treated group). Four control eyes were used: Two eyes were placed into carboxy perfused artificial cerebrospinal fluid (aCSF) for 24 hours before PFA fixation (Control aCSF). Two further eyes underwent PFA perfusion and were immediately placed in PFA after enucleation (Control fixed). All eyes were wax embedded and horizontally sectioned at 7-8µm through the macula. Immunohistochemistry with quantification using Image J software was performed to detect and quantify the following: Panlaminin, Laminin5, Laminin chains α 4 and γ 3, Fibronectin and Collagen IV. Antibody levels were compared across the 10 retinal layers from Bruchs membrane to the ILM using two way ANOVA with the two control groups compared to the OCP treated group

Results: The control aCSF globes had well preserved retinal anatomy compared to the control fixed globes with an attached vitreous. There was vitreomacular separation over the macula in the OCP treated eyes suggesting that a therapeutic dose had been given. Fibronectin and panlaminin had highest expression in the ILM in the OCP treated group ($P=0.0055$ and 0.0150 respectively) (Figure 1 showing panlaminin results). There were no other significant differences in expression levels.

Conclusions: There was no evidence for any outer retinal effect of OCP or higher specificity to any of the laminin subtypes with the dose of OCP administered. The high levels of laminin and fibronectin in the ILM despite vitreoretinal separation in the OCP group was unexpected.

5. Ocriplasmin for the treatment of vitreomacular traction with or without macular hole – predictors of success

Janine Lenk, Egbert Matthé, Lutz E. Pillunat, Dirk Sandner. Ophthalmology, University of Dresden, Dresden, Germany.

Program Number: 3696 Poster Board Number: B0321

Presentation Time: 3:45 PM–5:30 PM

Purpose: Vitreomacular traction (VMT) means an abnormal adhesion between vitreous cortex and retina, especially in the fovea, which might even result in macular holes. In symptomatic cases patients mainly complain about metamorphopsias and decreased visual acuity. Since 2013, Ocriplasmin (Jetrea[®]) has been approved for treatment of symptomatic vitreomacular traction with or without macular holes ($\leq 400 \mu\text{m}$).

Methods: We retrospectively examined 23 eyes of 21 patients who underwent intravitreal ocriplasmin treatment for symptomatic vitreomacular traction with or without macular holes. Best corrected visual acuity (BCVA) and central retinal thickness (CRT) were measured before and after treatment. We investigated the different morphologic appearance of VMT. Statistical analysis was performed using SPSS: t-test for paired samples was used. Multivariate Regression was used in order to investigate predictors for successful resolution (age, lense status, gender, size of VMT).

Results: Vitreomacular traction was resolved in 8 out of 23 eyes (34,8%). 2 out of 4 macular holes closed during treatment. The average BCVA was 0.39 ± 0.25 logMAR at baseline and $0,41 \pm 0,24$ logMAR at the first follow-up visit after injection ($P=0,613$). The average CRT was $453,3 \pm 172,7 \mu\text{m}$ at baseline and decreased slightly to $412,0 \pm 212 \mu\text{m}$ ($P=0.124$). Regarding predictors for successful VMT-resolution, younger patients were more likely to have complete resolution of vitreomacular traction than older patients ($P= 0.05$). Furthermore, patients who reported chromatopsia had more VMT resolution than did those without. A high dome-shape morphology of VMT seems to be a disadvantage compared to a flat, punctuated adhesion.

Conclusions: Intravitreal injection of Ocriplasmin seems to be a useful tool in patients with symptomatic vitreomacular traction. A critical patient selection is important to raise chances for successful treatment.

Commercial Relationships: Janine Lenk, None; Egbert Matthé, None; Lutz E. Pillunat, None; Dirk Sandner, None

6. Full-Thickness Macular Hole (FTMH) and Vitreomacular Traction (VMT): Comparison of visual results in patients receiving pars plana vitrectomy (PPV) for FTMH in one eye and ocriplasmin in the contralateral eye

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Program Number: 3697

Poster Board Number: B0322

Presentation Time: 3:45 PM–5:30 PM

Purpose: To determine if there is a difference in Best Corrected Visual Acuity (BCVA) in patients with VMT in one eye and a FTMH in the other. The eye with the FTMH received PPV while that with traction only, without a FTMH, received ocriplasmin.

Methods: Nine patients received a single injection of 0.125mg ocriplasmin (for traction alone) or PPV (for FTMH) to initially treat this condition. After the first eye was treated, with one of the two treatment options and was stable, the second eye was treated with the opposite modality. The interval between treatments averaged 4.6 months. All patients were female with ages ranging from 60 to 78 years. Three eyes were phakic OU and 6 eyes were pseudophakic OU. There were two different study sites and two surgeons (VG, AK) who performed the PPV and administered the injections. BCVA was measured at baseline (BL), 3 months, 6 months and in some patients up to two years. The mean follow up was 14 months. The order of treatment was not randomized. The eye with the worst BCVA at BL was treated first. Seven patients had PPV first while two patients had ocriplasmin as the initial treatment.

Results: Patients in both groups had successful anatomical resolution. None of the ocriplasmin patients required subsequent PPV for VMT release. Patients who received ocriplasmin had a mean BCVA at BL of 20/61 and a final visual acuity of 20/34. In the PPV group the mean BL visual acuity was 20/156 and at study end it was 20/53. There were no statistical differences in final BCVA between these two groups. There were no differences with respect to lens status or patient age. There were no sex differences since all were female.

Conclusions: Patients with VMT in one eye and a history of FTMH in the fellow eye who underwent PPV for FTMH benefit from early ocriplasmin treatment and could avoid the development of a FTMH in the other eye and thus a second PPV.

Commercial Relationships: **Greggory Gahn**, None; **Arshad M. Khanani**, ThromboGenics (C); **Victor H. Gonzalez**, ThromboGenics (C); **Joseph I. Markoff**; **Hamzah Khalaf**, None

7. Safety and Efficacy of Intravitreal Ocriplasmin in Diabetic Macular Edema with Vitreomacular Adhesion – results of a guided intravitreal injection method

João Coelho^{1, 2}, *Bernardete Pessoa*¹, *Nuno A. Correia*¹, *João Melo Beirão*^{1, 3}, *Angelina Meireles*^{1, 3}.
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Program Number: 3700 **Poster Board Number:** B0325

Presentation Time: 3:45 PM–5:30 PM

Purpose: To evaluate the safety and efficacy of a single intravitreal injection of ocriplasmin (125µg), or up to two injections, in patients with diabetic macular edema (DME) and focal or loose broad vitreomacular adhesion/traction (VMA) with the purpose of VMA release without the need of vitrectomy. We also analysed the results of a guided intravitreal injection method of ocriplasmin (125µg) proximal to VMA.

Methods: Single centre observational case series of 24 consecutive eyes of 18 patients who received intravitreal ocriplasmin for DME with VMA. Adjunct treatment, when required, with laser and intravitreal injections of corticosteroids and/or antiangiogenic were performed. Minimum follow-up of one month after ocriplasmin injection was defined. The primary endpoint was the resolution of VMA during the follow-up. The secondary endpoints included the maximal central macular thickness (MCMT) and best corrected visual acuity (BCVA) changes from baseline and the effect on the number of intravitreal injections (corticosteroids or antiangiogenic).

Results: The mean follow-up was 294±157 days. Of the 18 patients, with an average age of 68 years, 55,5% are male and 58% of the eyes are phakic. The mean measure of the adhesion was 665µm (ranging from 128µm to 2115µm). The release of the VMA occurred in 66,7% of cases. VMA resolution of 100% (7 eyes) was achieved with the guided injection method and 52,9% with the unguided method, $p<0,05$. After ocriplasmin the mean BCVA improved from 69.0 (EDTRS, early diabetic treatment retinopathy study, letters) to a maximum BCVA during follow-up of 79.6 letters ($p=0,001$). Mean MCMT improved from 374.6µm at baseline to 342.1µm during the follow up ($p<0,001$). There was a significant reduction in the number of intravitreal injections after ocriplasmin in the eyes with VMA release ($p=0,005$) with no reduction in eyes without VMA release. The side effects with both techniques were mild and transitory.

Conclusions: This treatment approach in DME associated with VMA seems to be safe and effective with a significant improvement in visual acuity and macular edema being the patient's selection and the timing of injection crucial for a successful treatment. The preliminary results of the guided injection method of ocriplasmin are favourable with resolution of the VMA being achieved in all cases.

Commercial Relationships: João Coelho, None; Bernardete Pessoa, None; Nuno A. Correia, None; João Melo Beirão, None; Angelina Meireles, None

8. ORBIT: A Phase IV Clinical Study – Efficacy and Safety Outcomes From Ocriplasmin Intravitreal Injection

Brian C. Joondeph^{1, 2}, *Arshad M. Khanani*³, *Jay S. Duker*^{4, 5}, *David S. Boyer*^{6, 7}, *Jeffrey Heier*⁸, *Peter K. Kaiser*⁹, *Mathew W. MacCumber*^{10, 11}, *Dante J. Pieramici*^{12, 13}. ¹Colorado Retina Associates, PC, Denver, CO; ²Rocky Vista University College of Osteopathic Medicine, Parker, CO; ³Sierra Eye Associates, Reno, NV; ⁴New England Eye, Boston, MA; ⁵Tufts University School of Medicine, Boston, MA; ⁶Retina-Vitreous Associates Medical Group, Los Angeles, CA; ⁷University of Southern California/Keck School of Medicine, Los Angeles, CA; ⁸Ophthalmic Consultants of Boston, Boston, MA; ⁹Cole Eye Institute, Cleveland, OH; ¹⁰Illinois Retina Associates, Chicago, IL; ¹¹Rush University Medical Center, Chicago, IL; ¹²California Retina Consultants, Santa Barbara, CA; ¹³California Retina Research Foundation, Santa Barbara, CA.

Program Number: 3703 Poster Board Number: B0328

Presentation Time: 3:45 PM–5:30 PM

Purpose: The Phase 4 ORBIT Study (NCT02079883) was designed to observe the clinical outcomes and safety of patients receiving ocriplasmin in a real-world setting for the treatment of symptomatic VMA/VMT.

Methods: ORBIT, a large, multicenter, prospective, observational study enrolled 539 patients across 90 retina clinics throughout the US. Patients were ≥18 years, diagnosed with symptomatic VMA/VMT and treated with ocriplasmin at the physician's discretion in a manner consistent with the US product label. Data were collected at Baseline visit (BL - day of 2.5 mg/mL ocriplasmin injection, per standard of care) and postinjection visits (at the discretion of the treating physician), and entered into electronic case report forms, based on investigators' assessment. Spectral-domain optical coherence tomography (SD-OCT) images were uploaded to the central reading center (CRC) for independent review. Clinical outcome measures and safety parameters were collected for up to 12 months postinjection.

Results: Demographics were similar between those with VMA/VMT at BL (n=480) (per CRC) compared to all treated subjects (n=539); however, 10.9% (480/539) of all subjects did not have VMA/VMT based on the assessment of the CRC. Overall pharmacologic VMA/VMT resolution at Month 1 was 45.8% (220/480). Pharmacological VMA/VMT resolution improved over time to a rate of 59.0% (283/480) at Month 12. The FTMH closure rate was 30.5% (36/118) at Month 1 and 32.2% (38/118) at Month 12. Patients had a low rate of adverse drug reactions: 13.5% (73/539) experienced photopsia, 9.6% (52/539) vitreous floaters, and 6.7% (36/539) had reduced visual acuity. Serious adverse drug reactions were also low.

Conclusions: Overall VMA/VMT resolution at 1 month was higher than the MIVI-TRUST results (45.8% in ORBIT compared to 26.5% in MIVI-TRUST), demonstrating the importance of patient selection. No new safety signals were identified.

9. Improvement in baseline amplitude of the scotopic b-wave after release of vitreomacular traction (VMT): Further substudy analysis from the OASIS trial (1)

Joseph I. Markoff^{1, 2}, *David G. Birch*³, *Petra Kozma*⁴, *Robert Sergott*^{1, 2}. ¹Visual Physiology, Wills Eye Hospital, Philadelphia, Moorestown, NJ; ²Thomas Jefferson Medical College, Philadelphia, PA; ³Retina Foundation of the Southwest, Dallas, TX; ⁴ThromboGenics NV, Leuven, Belgium.

Program Number: 3704 **Poster Board Number:** B0329

Presentation Time: 3:45 PM–5:30 PM

Purpose: 1. To compare the scotopic b-wave in those ocriplasmin treated patients who had a pharmacological VMT release to those who did not
2. To propose a mechanism to account for the data

Methods: Full-field ERGs were recorded from both eyes in a subset of patients participating in the OASIS study (1) at baseline (BL), Day 7, Day 28 and every 3 months thereafter until Month 24. The ERGs were evaluated by a masked expert. The scotopic b-wave was analyzed in 20 patients who received 0.125 mg of ocriplasmin and did not have a vitrectomy. This group was further sub-divided into those that exhibited VMT release and those that did not. This study compared amplitudes at BL to those at last visit.

Results: Of the 20 patients, 7 (35%) showed VMT release on OCT at anytime. All 7 had an increase or minimal change in their scotopic b-wave amplitude between BL and last visit, with an average increase of 24% (CI: 1% to 47%). Thirteen (65%) had no VMT release on OCT and most showed a decrease or no change in this potential compared to BL, with an average decrease of 22% (CI: -1% to -44%). The difference between the two groups was statistically significant ($p < 0.006$ using two tailed t-test).

Conclusions: Thirty five percent of patients with VMT had BL scotopic ERG amplitudes that increased after VMT release following ocriplasmin administration. Ocriplasmin patients who did not release showed a decrease in their scotopic b-wave from BL to last visit. These data are consistent with a panretinal abnormality that is present at BL in certain patients as a result of mechanical traction extending beyond the macula. VMT release seems to result in improved current flow in photoreceptors.

Commercial Relationships: **Joseph I. Markoff**, ThromboGenics (C); **David G. Birch**, ThromboGenics (C); **Petra Kozma**, ThromboGenics (E); **Robert Sergott**, ThromboGenics (C)

Clinical Trial: NCT01429441

Wednesday, May 10, 2017 – Exhibit / Poster Hall – Program #/Board # Range: 5000–5024/B0418–B0442

10. Post-hoc analysis of ellipsoid zone changes beyond the central subfield (CS) in symptomatic vitreomacular adhesion (VMA) subjects from the OASIS trial

Srinivas R. Sadda^{2, 1}, *Muneeswar G. Nittala*². ¹Ophthalmology, University of California - Los Angeles, Los Angeles, CA; ²Doheny Image Reading Center, Doheny Eye Institute, Los Angeles, CA.

Program Number: 5020 Poster Board Number: B0438

Presentation Time: 3:45 PM–5:30 PM

Purpose: OASIS is a Phase IIIb trial (NCT01429441) assessing long-term outcomes in subjects with VMA. The pre-specified OCT analysis in OASIS only evaluated the ellipsoid zone (EZ) in the central 1mm, but this region was affected by VMA and/or macular hole (MH) in most subjects at baseline. The purpose of this post-hoc analysis is to evaluate the EZ over time outside the central 1mm.

Methods: A masked post-hoc analysis of OCT images was performed at the Doheny Image Reading Center from subjects enrolled in the MP-1 and ERG substudies of the OASIS trial. The status of the EZ band was assessed in 3 different macular regions: the CS (≤ 1 mm diameter, covering the same region previously analysed), the Parafoveal Area (PAA) (> 1 mm - ≤ 3 mm) and the Perifoveal Area (PEA) (> 3 mm - ≤ 6 mm). The EZ band was rated as normal/intact, abnormal but continuous, discontinuous/disrupted, or absent at all available visits from baseline (BL) (pre-treatment) to final follow-up.

Results: In the ocriplasmin group, at BL 28.8% (17/59) of subjects had a normal EZ in CS, 96.6% (57/59) in PAA, and 98.3% (58/59) in PEA, compared to 31.0% (9/29), 89.7% (26/29), and 100.0%, respectively in the sham group. The disruption of the EZ in the CS corresponded to vitreomacular interface (VMI) abnormalities in this region (e.g. MH). At Day 7, the proportion of subjects with normal EZ in the ocriplasmin group were 20.3% (12/59), 86.4% (51/59), and 89.8% (53/59) for CS, PAA and PEA, and in the sham group were 32.1% (9/28), 89.3% (25/28) and 100% (28/28), respectively. These EZ alterations in the ocriplasmin group appeared to normalize by Month 3. At Month 24, the proportion of subjects with normal EZ in the ocriplasmin group were 82.8% (24/29), 93.1% (27/29), and 93.1% (27/29) for CS, PAA and PEA, and in the sham group were 40.0% (2/5), 80.0% (4/5) and 100.0%, respectively.

Conclusions: The pattern of EZ alteration appears to depend on the retinal region. While the status of the EZ in the CS correlated with VMI disease, the more peripheral EZ (especially the PEA) was less influenced by VMI abnormalities, allowing assessment of a likely direct drug effect. Although transient disruption of PAA and PEA EZ was observed at Day 7, there was recovery over subsequent follow-up, mirroring the previously reported microperimetric and electrophysiologic findings.

Commercial Relationships: **Srinivas R. Sadda**, Optos (C), Carl Zeiss Meditec (F), Genentech (C), Centervue (C), Optos (F), Thrombogenics (C), Topcon (R), Allergan (C), Iconic (C); **Muneeswar G. Nittala**, None

Clinical Trial: NCT01429441

Wednesday, May 10, 2017 – Presentation Diabetic Retinopathy - Ballroom 1: 11.30 – 11:45 AM

11. Neutralization of placental growth factor as a novel treatment option in diabetic retinopathy

Tine Van Bergen¹, Tjing-Tjing Hu¹, Isabelle Etienne¹, Geert E. Reyns¹, Lieve Moons², Jean H.M. Feyen¹

¹ThromboGenics NV, Gaston Geenslaan 1, 3001 Heverlee, Belgium and ² Neural Circuit Development and Regeneration Research Group, Department of Biology, KU Leuven, Leuven, Belgium

Purpose: Anti-vascular endothelial growth factor (VEGF) therapy has shown a significant improvement in visual acuity in patients with diabetic retinopathy (DR), however treatment response can be variable and might be associated with potential side effects. In this study, inhibition of placental growth factor (PIGF) was explored as a possible alternative therapy for DR by investigating its effect on different hallmarks of DR in various experimental murine models.

Methods: The *in vivo* efficacy of the anti-PIGF antibody (5D11D4; 0.77 – 5.4 µg/eye) was tested in diabetic streptozotocin (STZ; n=15-30/group) and Akimba mouse models (n=20-27/group) and in the laser-induced mouse model of choroidal neovascularization (CNV; n=10-20/group). Intravitreal (IVT) administration of the anti-PIGF antibody was compared to anti-VEGFR-2 antibody (DC101; 3.1 - 6.2µg/eye), VEGF-Trap (aflibercept; 2.4 -20 µg/eye), triamcinolone acetonide (TAAC; 40 µg/eye) and PBS as negative control. Vascular leakage was investigated by FITC-labelled bovine serum albumin perfusion or by fluorescein angiography. Immunohistological stainings were performed to check for neurodegeneration (Brn3a), inflammation (CD45, F4/80) and fibrosis (collagen type 1a and Sirius Red).

Results: In the diabetic STZ and Akimba models, repeated IVT administration of 5D11D4 reduced vascular leakage with $34 \pm 14\%$ and $22 \pm 13\%$ ($P < 0.05$), respectively. This effect was equally efficacious as DC101 treatment in STZ mice ($P = 0.43$). 5D11D4 treatment did not alter retinal ganglion cell (RGC) density, whereas DC101 significantly reduced RGC density with $20 \pm 6\%$ ($P = 0.04$). In the CNV model, 5D11D4 injection dose-dependently reduced inflammation and fibrosis, as compared to PBS treatment ($P < 0.05$). Equimolar administration of 5D11D4, aflibercept and TAAC decreased leukocyte and macrophage infiltration with $45 \pm 5\%$ ($P < 0.001$), whereas DC101 had no effect on the inflammatory response ($P = 0.96$). Administration of 5D11D4 and TAAC similarly reduced collagen I and total collagen deposition with $40 \pm 5\%$ and $35 \pm 8\%$ ($P < 0.001$), while no effect was observed after equimolar DC101 ($P = 0.82$) nor aflibercept administration ($P = 0.66$).

Conclusions: The neutralization of PIGF showed equal efficacy compared to VEGF inhibition on the process of vascular leakage, but differentiates itself by also reducing inflammation and fibrosis, without triggering a neurodegenerative response.

Financial disclosure: ThromboGenics NV.

12. Longitudinal Ellipsoid Zone Mapping following Intravitreal Ocriplasmin in the ORBIT Trial

Posterboard #: B0790 - **Abstract Number:** 5990 - B0790

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Purpose: To quantitatively evaluate the longitudinal ellipsoid zone (EZ) alterations following intravitreal ocriplasmin in a prospective, observational phase 4 clinical trial.

Methods: The ORBIT study is a phase 4 observational clinical study examining the real-world use of intravitreal ocriplasmin. This study was a sub-analysis of imaging features following ocriplasmin injection. Inclusion criteria included the following: (1) available SD-OCT scans at baseline (BL) and week 1. (2) Available SD-OCT at month 1, month 3, or month 6. Exclusion criteria included: (1) SD-OCT scans of limited quality for segmentation analysis, (2) lack of macular cube scan, and (3) significant macular pathology (other than vitreomacular interface disease) resulting in anatomic alterations (e.g., drusen). Macular cube scans were imported into a novel EZ mapping platform utilizing a previously validated and reported software platform. Quantitative assessments for EZ alterations were assessed.

Results: Fifty-five subjects were included in this analysis. Final visit was assessed based on the latest available SD-OCT which included month 1 (n = 22), month 3 (16), and month 6 (17). The average total macular EZ-RPE volume was 1.12 mm³ at BL, which decreased to 0.89 mm³ at week 1 and recovered to 94% of BL value at final visit. *En face* EZ atrophy increased from an average of 2.9% at BL to 14.9% at week 1, and improved to 6.8% at final visit. *En face* EZ attenuation (< 20 micron thickness) increased from an average of 5.1% at BL to 29.4% at week 1, and recovered to 11.7% at final visit. At final follow-up, 3 of 55 subjects were defined as outliers (i.e., 2 standard deviations above the mean) and did not appear to experience EZ recovery with persistent *en face* EZ atrophy > 20% and *en face* EZ attenuation >30% map area.

Conclusions: Intravitreal ocriplasmin resulted in EZ attenuation that is noted at 1-week. Generally, these changes were transient and predominantly recovered between month 1 and month 6 following therapy. Three of 55 subjects were noted to have significant persistent EZ attenuation. Additional research is needed to further evaluate the overall impact of these anatomic outcomes with functional features.