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High fat-high fructose diet triggered metabolic syndrome and retinal neovascular complications in the rat

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Sunday, May 01, 2016 1:30 PM–3:15 PM

Exhibit/Poster Hall Poster Session

Program #/Board # Range: 510–553/A0147–A0190

Organizing Section: Retina

Program Number: 510 **Poster Board Number:** A0147

Presentation Time: 1:30 PM–3:15 PM

Treat-and-Extend Regimen using Ranibizumab for Polypoidal Choroidal Vasculopathy: One Year Results

Seok Jae Lee, Kang Yeun Pak, Sung Who Park, Ik Soo Byon, Ji Eun E. Lee. Pusan national university hospital, Busan, Korea (the Republic of).

Purpose: Clinical efficacy of treat-and-extend regimen (TER) has been reported in patients with exudative age-related macular degeneration. However, the clinical outcomes of a TER to treat polypoidal choroidal vasculopathy (PCV) have not yet been reported. We performed *retrospective review study* to investigate the efficacy of TER using ranibizumab to treat PCV.

Methods: We retrospectively reviewed the medical records of patients with PCV who had been treated using a TER for 1 year. Primary outcome was the proportion of eyes that did not lose ≥ 3 best-corrected visual acuity (BCVA) lines. Secondary outcomes included BCVA, central subfield macular thickness (CSMT), the number of intravitreal injections, the number of recurrences, and the maximal treatment interval without recurrence.

Results: The mean visual acuity improved from 0.69 ± 0.49 logMAR at baseline to 0.42 ± 0.37 logMAR at 3 months ($P = 0.001$), 0.40 ± 0.39 logMAR at 6 months ($P = 0.001$) and 0.33 ± 0.32 logMAR at 12 months ($P < 0.001$). The mean CSMT improved from 324.3 ± 90.7 μm at baseline to 236.4 ± 43.1 μm at 3 months ($P < 0.001$), 238.7 ± 77.6 μm at 6 months ($P = 0.001$), and 266.2 ± 99.3 μm at 12 months ($P = 0.011$). None of the subjects lost ≥ 3 lines, and 12 eyes (52.2%) gained ≥ 3 lines. The mean number of intravitreal injections was 7.4. The mean maximal treatment interval was 8.6 weeks. After the loading phase, 7 eyes (30.4%) showed no recurrence at treatment interval of 12 weeks. Six eyes (26.1%) demonstrated persistent disease activity for 12 months.

Conclusions: The TER effectively improved visual acuity in PCV while reducing the number of injections required.

Commercial Relationships: Seok Jae Lee, None; Kang Yeun Pak, None; Sung Who Park, None; Ik Soo Byon, None; Ji Eun E. Lee, None

Program Number: 511 **Poster Board Number:** A0148

Presentation Time: 1:30 PM–3:15 PM

Short-term efficacy of intravitreal aflibercept depending on subtypes of polypoidal choroidal vasculopathy: polypoidal choroidal neovascularization or idiopathic choroidal vasculopathy

Min Sagong, Seongyong Jeong, Moohyun Kim, Sooncheol Cha, JunHyuk Son. Surgery/Ophthalmology, Yeungnam University College of Medicine, Daegu, Korea (the Republic of).

Purpose: To compare the short-term treatment efficacy of intravitreal injection of aflibercept between polypoidal choroidal neovascularization (CNV) and idiopathic polypoidal choroidal vasculopathy (PCV).

Methods: Twenty nine patients (29 eyes) with treatment-naive subfoveal PCV were enrolled prospectively. All subjects were classified into two subtypes (type 1 polypoidal CNV: 16 eyes and type 2 idiopathic PCV: 13 eyes) based on the presence or the absence of both of a feeder and a draining vessels on indocyanine green angiography. All patients received intravitreal injection of aflibercept

(2.0 mg) at baseline and months 1, 2 and 4. Primary outcome was polyp regression rate after 3 monthly loading injections. Changes of largest polyp diameter, best corrected visual acuity (BCVA), central macular thickness (CMT), largest pigment epithelium detachment (PED) height and subfoveal choroidal thickness (CT) were evaluated at each monthly follow-up for 6 months.

Results: Complete polyp regression rate was significantly higher in type 1 than type 2 PCV after 3 monthly injections (81% vs 30%, $P=0.020$). Type 1 PCV showed better visual improvement at month 3 with higher frequency of dry macula than type 2 PCV (-0.34 vs -0.08 LogMAR, $P=0.050$). There was no significant difference between two groups in the frequency of dry macula and changes of largest polyp diameter, largest PED height, and CMT at month 6. Although subfoveal CT was significantly decreased with injections in both types of PCV, type 2 PCV with thicker choroid at baseline showed more decrease than type 1 PCV (-19.6 vs -43.5 μm , $P=0.032$) at month 3.

Conclusions: Our study demonstrated a difference in early treatment response with aflibercept between two types of PCV. Type 1 polypoidal CNV showed better visual improvement with higher rate of polyp regression than type 2 idiopathic PCV.

Commercial Relationships: Min Sagong, None; Seongyong Jeong, None; Moohyun Kim, None; Sooncheol Cha, None; JunHyuk Son, None

Clinical Trial: NCT02597855

Program Number: 512 **Poster Board Number:** A0149

Presentation Time: 1:30 PM–3:15 PM

Intravitreal Aflibercept Injections in the Management of Treatment Refractory Polypoidal Choroidal Vasculopathy

Laurence S. Lim¹, Wei Yan Ng², Ian Yeo¹, Ranjana Mathur¹, Gemmy Cheung¹, Tien Yin Wong¹. ¹Vitreo-retinal, Singapore National Eye Center, Singapore, Singapore; ²Singapore National Eye Center, Somga[pre, Singapore.

Purpose: To determine if eyes with polypoidal choroidal vasculopathy (PCV) unresponsive to intravitreal ranibizumab or bevacizumab injections would benefit from conversion to aflibercept.

Methods: This retrospective case series included 40 eyes of 37 patients with PCV unresponsive to ranibizumab and/or bevacizumab injections and who were subsequently converted to aflibercept.

All patients had persistent exudation despite at least 3 consecutive monthly intra-vitreous bevacizumab or ranibizumab injections. Visual outcomes and spectral domain optical coherence tomography (OCT) changes were analysed.

Results: The mean age of the subjects was 65.7 ± 8.7 years, 21 (57%) were male and all were of Asian ethnicity. The mean number of ranibizumab or bevacizumab injections before switching to aflibercept was 8.8, and the mean number of aflibercept injections after switching was 3.3. The mean follow-up was 7.0 ± 3.1 months. Of the 40 eyes, 28 (70%) had complete resolution of exudation with aflibercept treatment. Mean central foveal thickness (CFT) was 244.90 ± 120.72 μm immediately prior to the switch, decreased to 190.20 ± 104.99 μm ($p=0.004$) after one aflibercept injection, and decreased further to 189.05 ± 98.71 μm at the end of follow-up. ($p < 0.001$ compared to baseline) The mean macular cube volume also showed significant reduction from 9.72 ± 2.17 μm^3 pre-conversion to 9.01 ± 2.08 μm^3 after one aflibercept injection ($p < 0.001$), and was 8.95 ± 1.46 μm^3 at the last follow up ($p=0.014$ compared to baseline). Prior to conversion, 38 eyes (95%) had pigment epithelial detachments (PEDs). At the end of follow-up, PEDs in 3 eyes (7.9%) had resolved while 8 eyes (21.1%) had reductions in PED height. PEDs in the remaining 27 eyes (71.1%) were unchanged. Mean visual acuity was 0.72 ± 0.69 logMAR units just prior to the switch,

0.74±0.64 logMAR (p=0.06) after one aflibercept injection, and 0.72±0.63 logMAR at the end of follow-up.(p=0.12 compared to baseline)

Conclusions: Intra-vitreous aflibercept treatment appears to be effective in improving anatomical outcomes in patients with PCV refractory to bevacizumab or ranibizumab in the short term. Whether this results in long-term visual acuity gain is unclear.

Commercial Relationships: Laurence S. Lim, None; Wei Yan Ng, None; Ian Yeo, None; Ranjana Mathur, None; Gemmy Cheung, None; Tien Yin Wong, None

Program Number: 513 **Poster Board Number:** A0150

Presentation Time: 1:30 PM–3:15 PM

Effects of Aflibercept on Patients with Polypoidal Choroidal Vasculopathy: One-year results of VAULT Study

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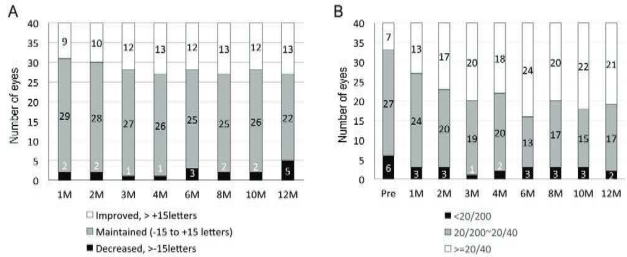
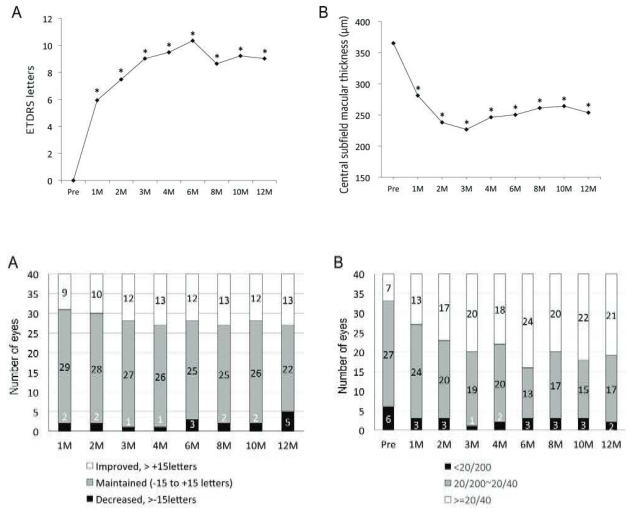
Purpose: To investigate efficacy of aflibercept for treatment naïve PCV.

Methods: A prospective, single-arm, interventional case series. Three doses of initial monthly intravitreal aflibercept 2.0 mg injections were followed by every two month maintenance injections. At every visit, best-corrected visual acuity (BCVA) measurement using ETDRS chart, and spectral domain optical coherence tomography (OCT) were performed before the injections. Fluorescein angiography (FA) and Indocyanine green angiography (ICGA) were obtained at baseline, month 3, and month 12. Primary outcome measure was the ratio of patients who maintained visual acuity without losing 15 ETDRS letters or more at month 12. Changes in ETDRS visual acuity, macular appearance on OCT, and polypoidal lesions on ICGA were also evaluated.

Results: From 48 patients initially enrolled, 40 patients finished complete follow up and were included in the final analysis. Mean age was 67.0 years old (range; 44-84). Thirty five eyes (87.5%) did not lose visual acuity more than 15 letters at month 12. Mean ETDRS letter score showed significant improvement from 55.1 at baseline to 64.2 at month 12 (9.0 letters gain, p<0.001). Mean central macular thickness measured by OCT changed significantly from 365.2µm at baseline to 253.6µm at month 12 (p<0.001). Complete dry-up of macular was seen in 32 (76.2%), 27 (64.3%), and 24 (60.0%) eyes at month 3, 6, and 12, respectively. Reappearance or increase of fluid was noted in 14 at month 6, and 16 patients at month 12. Complete polyp regression was achieved in 27 (64.3%) and 26 eyes (66.7%), at month 3, and 12, respectively.

Conclusions: Functional and anatomical outcomes were favorable after aflibercept intravitreal injection for PCV patients. However, fluid reaccumulation and new polyp formation was seen in one-third of the patients after extending treatment interval. Bimonthly injections may be suboptimal and more frequent injections are needed

to maintain stable condition achieved by initial monthly injections in some of PCV patients.



Commercial Relationships: Hyun Woong Kim, Novartis (C), Bayer (C), Allergan (S); Joo Eun Lee; Jae Pil Shin, None; Woohyok Chang, Bayer (C), Novartis (R), Allergan (C); Yu Cheol Kim, None; Sang Joon Lee, None; In Young Chung, None; Ji Eun E. Lee, Novartis (C), Allergan (C), Bayer (C), Bayer (F)
Clinical Trial: NCT01950741

Program Number: 514 **Poster Board Number:** A0151

Presentation Time: 1:30 PM–3:15 PM

2-year results of switching to aflibercept for polypoidal choroidal vasculopathy in patients refractory to ranibizumab

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¹Centre for Ophthalmology, Osaka City Univ Grad Sch of Med, Osaka, Japan; ²Shiraniwa Hospital, Ikoma, Japan.

Purpose: The aim of this study was to examine two year outcome of intravitreal injections of aflibercept (IVA) in patients with polypoidal choroidal vasculopathy (PCV) refractory to intravitreal injections of ranibizumab (IVR).

Methods: 26 eyes of consecutive 26 patients, who had been treated previously with IVR with or without photodynamic therapy (PDT) more than one year but failed to resolve subretinal fluid (SRF), were reviewed. Loading treatment of IVA was composed of three monthly injections and additional monthly injections until disappearance of SRF on optical coherence tomography (OCT). After the resolution of SRF, IVA injections were done 1-2 month intervals based on presence or absence of SRF on OCT.

Results: The mean decimal visual acuity was 0.27±0.30 at baseline (range, -0.2-0.8), 0.18±0.29 at month 12 (p=0.028) and 0.19±0.30 at month 24 (p=0.026). Mean central foveal thickness significantly decreased from 247.8±86.3 µm (range, 136-477) at baseline to 173.2±53.4 µm (range, 76-331) at 3 months (P<0.001); the decrease was maintained until 24 months (P<0.001). Mean numbers of IVA were 8.1±1.2 (range, 6-10) and 7.5±1.8 (range, 5-10) during years 1 and years 2, respectively. No recurrence of the SRF was seen in 9 eyes (37.5%) with bimonthly IVA. In the remaining 15 eyes (62.5%), SRF recurred and subsequent 2-month or less intervals of IVA were performed to obtain dry retina. Supplementary PDT, however, was required in 3 eyes (12.5%) during the years 2 and SRF remained in 8 eyes (33.3%) at 24 months.

Conclusions: The switching to IVA for PCV refractory to IVR therapy improved or maintained the visual acuity for 2 years. However, approximately 30 % of patients were refractory to IVA and failed to resolve SRF using 2-month or less intervals of IVA.

Commercial Relationships: Takeya Kohno, None; Manabu Yamamoto, None; Akira Cho, None; Kumiko Hirayama, None; Ayako Yasui, None; Shinsuke Ataka, None; Michiko Hirabayashi, None; Kunihiko Shiraki, None

Program Number: 515 **Poster Board Number:** A0152

Presentation Time: 1:30 PM–3:15 PM

One-year outcomes with ranibizumab in treatment naïve patients with neovascular age-related macular degeneration: an interim analysis from the LUMINOUS™ study

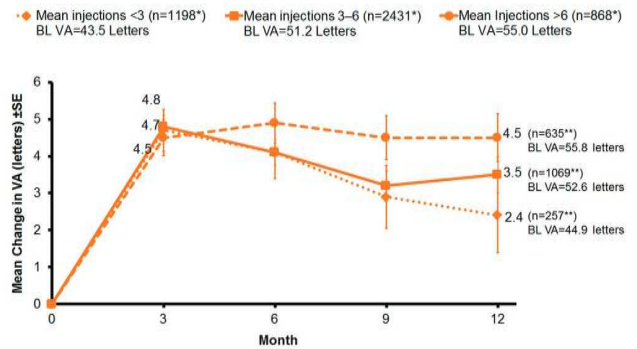
Christopher Brand¹, Sue Lacey². ¹Royal Hallamshire Hospital, Sheffield, United Kingdom; ²Novartis Pharma AG, Basel, Switzerland.

Purpose: LUMINOUS™ (NCT01318941) is an ongoing, 5-year, multicenter, global, observational study, designed to evaluate the long-term safety, effectiveness, treatment patterns, and health-related quality of life outcomes associated with ranibizumab treatment in routine clinical practice across all approved indications. Here we present baseline characteristics and visual outcomes of treatment naïve patients from a cohort of 17656 patients with neovascular age-related macular degeneration (nAMD) enrolled before March 2014 and who had the potential for 1-year follow-up, from the third interim analysis of LUMINOUS™.

Methods: Consenting adult (≥18 years) nAMD patients, who were treatment naïve or previously treated with ranibizumab or other ocular treatments were enrolled and treated as per the local label. This analysis focuses on injection patterns in the study eye of treatment naïve patients.

Results: Of the 43 countries participating in the study, the highest number of patients with nAMD were enrolled from the United Kingdom (n=7350) followed by Australia (n=1694), Canada (n=1632), Poland (n=567), and Russia (n=561). Of the total 17656 patients enrolled with nAMD, 4497 were treatment naïve. The mean age of treatment naïve patients was 75.0 years; 68.8% were Caucasian, 55.8% were female. In treatment naïve patients, at baseline, the mean visual acuity (VA) was 49.9 letters, and the mean central retinal thickness was 360.6 µm. At 1 year, the mean change in VA from baseline was 3.6 letters with a mean of 4.3 injections and 7.3 visits. The VA gains in treatment naïve patients receiving <3, 3–6, and >6 injections were 2.4 letters, 3.5 letters, and 4.5 letters, respectively (Figure). Those patients receiving >6 injections including 3 loading doses of ranibizumab within the first 90 days of treatment gained 5.3 letters at 1 year from a baseline of 55.5 letters. Safety findings in treatment naïve patients were consistent with the well-established safety profile of ranibizumab.

Conclusions: At 1 year, treatment naïve patients had substantial improvement in VA with ranibizumab treatment. Future follow-up data and country-level analyses from the LUMINOUS™ study will provide invaluable information to optimize patient outcomes with ranibizumab treatment.



Observed data set; primary treated eye; *number of patients at baseline; **number of patients who completed the 1-year follow-up
BL, baseline; SE, standard error; VA, visual acuity

VA, stratified by injection frequency at 1 year in treatment naïve patients

Commercial Relationships: Christopher Brand, Novartis Pharmaceuticals (F), Oraya (C), Allergan (F), Oraya (R), Novartis Pharmaceuticals (C), Pfizer (C), Bayer (C), Allergan (C), Pfizer (R), Novartis Pharmaceuticals (R), Alcon (F), Roche (F), Oraya (F); Sue Lacey, Novartis Pharma AG

Clinical Trial: NCT01318941

Program Number: 516 **Poster Board Number:** A0153

Presentation Time: 1:30 PM–3:15 PM

Changes in Neovascular Activity Following Continuous Anti-Vascular Endothelial Growth Factor Administration in the VIEW Studies

Darius M. Moshfeghi. Optometry and Visual Science, Byers Eye Institute at Stanford, Palo Alto, CA.

Purpose: To evaluate the presence of leakage on fluorescein angiography (FA), the status of retinal fluid on optical coherence tomography (OCT), and the changes in best-corrected visual acuity (BCVA) in the VIEW studies of patients with neovascular age-related macular degeneration (nAMD).

Methods: 2457 nAMD patients were randomized to intravitreal aflibercept injection (IAI) 2 mg q4 weeks (2q4), IAI 0.5 mg q4 weeks (0.5q4), IAI 2 mg q8 weeks after three monthly doses (2q8), or ranibizumab 0.5 mg q4 weeks (Rq4). Independent masked reading centers determined leakage status (no leakage defined as 0 mm²) and fluid status (no fluid defined as the absence of both intraretinal and subretinal fluid) at baseline, week 24 and week 52. Treatment groups were combined and four subgroups were established based on leakage and retinal fluid status: 1) both leakage and fluid present, 2) leakage present, fluid absent, 3) leakage absent, fluid present, 4) both leakage and fluid absent.

Results: At baseline, 95% of patients had both leakage and retinal fluid; 4% of patients had leakage but no fluid; 0.2% of patients had fluid but no leakage; and 0.04% of patients had neither leakage nor retinal fluid. At week 24, the corresponding percentages of patients were 28%, 23%, 14%, and 35% with a mean (standard error) BCVA gain of 7.4 (0.48), 8.6 (0.51), 8.3 (0.79) and 9.9 (0.45) letters, respectively. At week 52, the corresponding percentages of patients were 16%, 19%, 16% and 49% with a mean (standard error) BCVA gain of 9.2 (0.68), 9.6 (0.63), 8.5 (0.88) and 10.3 (0.43) letters, respectively.

Conclusions: The proportion of patients demonstrating absence of both leakage and fluid was 35% at week 24 and 49% at week

52. Gains in BCVA were observed in all subgroups, and appeared dependent on both leakage and retinal fluid status.

Commercial Relationships: Darius M. Moshfeghi, Regeneron Pharmaceuticals, LLC (C)

Clinical Trial: NCT00964795

Program Number: 517 **Poster Board Number:** A0154

Presentation Time: 1:30 PM–3:15 PM

One year visual and anatomic outcomes in eyes receiving aflibercept according to a fixed-interval dosing (Q8W) for neovascular age-related macular degeneration

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Georgios I. Agorogiannis¹, Srini Goverdhan¹, Andrew J. Lotery^{1,2}.

¹Eye Unit, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; ²Clinical and Experimental Sciences, University of Southampton, Southampton, United Kingdom.

Purpose: To investigate 1-year visual and anatomic outcomes of intravitreal aflibercept for neovascular age-related macular degeneration (nAMD) given according to a fixed-interval dosing (Q8W).

Methods: Retrospective, single-practice data analysis from an electronic medical record system. A total of 124 eyes (106 patients) with treatment-naïve nAMD receiving aflibercept every-8-weeks (Q8W) followed up for 1 year.

Results: Mean age of patients was 82 years. 66 (53%) eyes showed occult with no classic CNV, 19 (15%) eyes showed predominantly classic lesions, 30 (24%) eyes showed a retinal angiomatous proliferation (RAP) lesion, whereas 3 eyes (2%) showed drusenoid PED with subretinal fluid (SRF) and corresponding leak on fluorescein angiography. Indocyanine-green angiography revealed polypoidal choroidal vasculopathy lesions in 6 (5%) eyes. Mean LogMar best corrected visual acuity (BCVA) improved from 0.66 at baseline to 0.51 at month 11 ($P < 0.0001$). Mean central retinal thickness (CRT) decreased from 312.55 μm at baseline to 219.79 μm at month 11 ($P < 0.0001$). At month 11, 52 eyes (42%) were deemed inactive as defined by absence of intraretinal (IRF) or subretinal fluid on OCT, whereas 72 eyes (58%) remained active with the presence of SRF, IRF, intraretinal cysts, or macular haemorrhage. Mean LogMar BCVA at month 11 for the active and inactive groups was 0.52 and 0.48 respectively ($P=0.5225$). Mean CRT at month 11 for the active and inactive groups was 240.18 μm and 190.70 μm respectively ($P=0.0050$). In 51 out of the 52 wet macula eyes (96%), the main feature was the presence of SRF.

Differences were not statistically significant ($P=0.6418$) when patients were stratified by age, LogMar BCVA, the top 25% (best BCVA) when compared with the bottom 25% (worst BCVA) in terms of active/inactive disease and when the top 25% (eldest patients) were compared to the bottom 25% (youngest patients) in terms of active/inactive disease ($P=0.3411$).

Conclusions: Intravitreal aflibercept administered by Q8W fixed dosing over 1 year improved both visual acuity and macular morphology in a large number of treatment-naïve eyes with nAMD. Active lesions at month 11 do not have worse VA outcomes cf. inactive lesions. Treatment is effective irrespective of patients' age and gender.

Commercial Relationships: Osama Kanavati, None;

Hussein Almuhtaseb; Georgios I. Agorogiannis, None;

Srini Goverdhan, Bayer and Novartis (R); Andrew J. Lotery,

Bayer (R)

Program Number: 518 **Poster Board Number:** A0155

Presentation Time: 1:30 PM–3:15 PM

Evaluation of both native and pathological vascular changes occurring during the Aflibercept intravitreal injections' loading phase in treatment-naïve wet AMD patients

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Filomena Pinto¹, Leonardo Mastropasqua¹. ¹Ophthalmology

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Neuropsychological, Morphological and Movement Sciences,

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Purpose: To investigate vessel changes occurring after Aflibercept injections in treatment-naïve exudative age-related macular degeneration (AMD) patients.

Methods: Fifteen eyes of 15 patients affected by wet AMD were enrolled in the study. All the patients had a diagnosis of type 1 choroidal neovascularization (CNV) and were treated with three monthly Aflibercept intravitreal injections (IVI). Subjects were evaluated by means of Optical Coherence Tomography Angiography (OCTA) at baseline, the day after the first injection and one month after both the first and the second IVI. At last, all the patients were followed up to 2 months after the 3rd IVI. Main outcomes were: (i) superficial plexus vessel density; (ii) choroidal thickness; (iii) CNV lesion area; and (iv) CNV flow area.

Results: Foveal superficial vessel density was 29,01% (21,13 to 37,32%) at baseline and was significantly reduced as soon as 1 month after the 1st IVI (median: 20,78%; IQR: 14,75 to 23,13%; $p=0,017$). Parafoveal superficial vessel density was 47,09% (44,91 to 51,72%) at baseline and significantly decreased as soon as 1 month after the 2nd IVI (median: 44,40%; IQR: 41,59 to 49,29%; $p=0,034$). Choroidal sub-foveal thickness was 185,50 μm (140,25 to 254,25 μm) at baseline and was significantly thinned as soon as 1 month after the 1st IVI (median: 147,50 μm ; IQR: 125,50 to 192,75 μm ; $p=0,036$). CNV lesion area remained stable throughout the follow-up. Nevertheless, interestingly, CNV flow area was significantly reduced as soon as the next day the 1st IVI (median: 0,37 mm^2 and IQR: 0,27 to 0,72 mm^2 at baseline; median: 0,30 mm^2 and IQR: 0,24 to 0,64 mm^2 at 1 day after the 1st IVI; $p=0,047$).

Conclusions: Intravitreal Aflibercept injections caused a significant change in native retinal and choroidal vasculature. Moreover, the treatment did not cause a reduction in lesion area, but rather reduced the flow in the CNV. Our results give credit to the theory that, in most cases, the treatment does not lead to a reduction in the size of CNV, but rather reduces the number and the perfusion of the smallest pathological vessels.

Commercial Relationships: Enrico Borrelli, None; Lisa Toto,

None; Paolo Carpineto, None; Rodolfo Mastropasqua, None;

Luca Di Antonio, None; Michele Palmieri, None; Filomena Pinto,

None; Leonardo Mastropasqua, None

Program Number: 519 **Poster Board Number:** A0156

Presentation Time: 1:30 PM–3:15 PM

Change in Pigment Epithelial Detachment Volume and its Relationship with Subretinal Fluid and Visual Acuity in Patients with Exudative AMD after Aflibercept Switch Therapy. Post hoc analysis from the ARI2 Study

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Purpose: The ARI2 study was a multicentric, phase IIIb open label study that aimed at establishing the efficacy and safety of Aflibercept intra vitreal treatment (IVT) switch therapy for persistent pigment epithelium detachment PED. This post hoc analysis explores the correlation between modifications in PED and the presence of subretinal fluid as well as the relationship between PED and best corrected visual acuity (BCVA).

Methods: Prospective, phase IIIb, open label, multi center study. Patients had to meet the following criteria: active subfoveal choroidal neovascularization (CNV) lesions secondary to AMD, at least 12 months previous Ranibizumab injections (≥ 8 injections) and PED $> 250 \mu\text{m}$ with persisting sub retinal fluid at baseline. Patients were switched to Aflibercept, receiving 3 consecutive IVT treatments at 4 weeks intervals (primary endpoint). Patients continued to receive Aflibercept IVT at 6 weeks intervals for the remainder of the study. PED volume calculations were performed with ReVAnalyzer (ADCIS, Saint-Contest, France). Paired T-test was used to compare paired-data. Comparisons of unpaired means or medians were performed using the T-test or Mann-Whitney test (STATA v13.0, StataCorp LP, Texas, USA).

Results: Mean PED volume reduction from baseline values was statistically significant at the primary and secondary endpoints ($p < 0.0001$). There was a statistically significant correlation between reduction in PED volume and presence of subretinal fluid at the 12 week and 32 week endpoints ($p < 0.008$ and $p < 0.002$ respectively). There was no association between BCVA changes and PED volume nor any correlation between the presence sub retinal fluid and BCVA changes, either at the primary or secondary endpoints.

Conclusions: Aflibercept switch therapy seems effective at reducing PED volume in wet AMD patients previously unresponsive to Ranibizumab therapy. Reduction in PED volume was strongly correlated to the disappearance of subretinal fluid in this cohort of patients. We conclude that Aflibercept is effective in reducing neovascular activity (represented by exudation as subretinal fluid) in patients with recalcitrant PED detachments. However, no evidence of direct association between PED volume modifications and BCVA improvement was found

Commercial Relationships: Camille JUNG, None; Rocio Blanco-Garavito, None; Oudy Semoun, Bayer (C), Novartis (C); Joel Uzzan, Bayer (C), Allergan (C), Novartis (C); Florence Coscas, None; Maddalena Quaranta-El Maftouhi, None; Jose Sahel; Jean-Francois Korobelnik, None; Nathalie Puche, Novartis (R), Bayer (R); Giuseppe Querques, Bayer Schering Pharma (C), Heidelberg (C), Zeiss (C), Bausch and Lomb (C), Alimera Sciences (C), Novartis (C); Eric H. Souied, Bayer (C), Allergan (C), Novartis (C)
Clinical Trial: NCT02157077

Program Number: 520 **Poster Board Number:** A0157

Presentation Time: 1:30 PM–3:15 PM

Long term visual outcomes in ranibizumab non-responders: patients with neovascular age-related macular degeneration switched from ranibizumab to aflibercept

Farid Afshar, Emily Fletcher, Quresh Mohamed, Rob Johnston. Ophthalmology, Cheltenham General Hospital, Eastleigh, United Kingdom.

Purpose: To report visual outcomes in eyes with neovascular age-related macular degeneration (nAMD) switched from treatment with ranibizumab to aflibercept.

Methods: Data was collected prospectively using an electronic patient record system. Patients with nAMD with persistent fluid after a minimum of 5 ranibizumab injections in 6 months, in addition to 3 loading doses, were switched to aflibercept. Eyes were initially treated with a pro re nata regimen. After switching eyes had a loading phase of 3 aflibercept injections at monthly intervals and fixed injections initially at 2 month intervals followed by a treat and extend regimen, with an 18 month follow up.

Results:

Mean visual outcomes in 254 eyes. Prior to switching the visual acuity declined from a mean of 63.6 letters to 58.7 letters when switched. After 18 months of treatment with aflibercept the mean visual acuity was 55.3 letters. The mean annual rate of decline in vision with ranibizumab treatment was 3.3 letters and 2.3 letters after switching to aflibercept.

Conclusions: In this well defined group of patients with nAMD non-responsive to ranibizumab switching to aflibercept did not improve vision but may reduce treatment burden.

Commercial Relationships: Farid Afshar, None; Emily Fletcher, None; Quresh Mohamed, None; Rob Johnston, Medisoft (C)

Program Number: 521 **Poster Board Number:** A0158

Presentation Time: 1:30 PM–3:15 PM

Twelve-Month Outcomes of “Treat and Extend” aflibercept Therapy for Neovascular Age-Related Macular Degeneration

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Purpose: To report the 12-month outcomes of aflibercept therapy for treatment-naïve eyes with neovascular age-related macular degeneration (nAMD) using a treat and extend treatment regimen in routine clinical practice.

Methods: Treatment-naïve eyes that were receiving only aflibercept for nAMD under a treat and extend regime as reported by practitioners were extracted from the Fight Retinal Blindness observational registry. The primary outcome measures were change in visual acuity (VA) over 12 months and the number of injections and visits.

Results: Data from 116 eyes from 110 patients starting aflibercept therapy between November 2012 and May 2014 for nAMD with 12-month follow-up under a treat and extend regime were included in the analysis. Mean VA increased by +9.5 logMAR letters from 59.7 letters at time of first injection to 69.2 letters at 12 months. Mean VA gains predominantly occurred during the initial 6 months of treatment, increasing by +9.1 letters in the first 6 months compared

with +0.4 in the second 6 months. The proportion of eyes with VA > 20/40 increased from 34% at time of first injection to 67% after 12 months of treatment. The proportion of eyes with VA < 20/200 decreased from 16% at time of first injection to 10% after 12 months of treatment. 97% of eyes receiving treatment avoided a vision loss of ≥ 15 letters. There was an overall mean of 7.3 injections over the 12 months with 4.6 injections in the first 6 months and 2.7 in the second 6 months of treatment. The mean number of visits was 7.8 over the 12 months, 4.8 visits in the first 6 months and 3.0 in the second 6 months of treatment. An injection was received in 86% of all visits within the 12-month follow-up period.

Conclusions: These data indicate that eyes treated with aflibercept in routine clinical practice under a treat and extend regimen achieve good visual outcomes for the first 12 months while decreasing the burden of treatments and clinic visits compared to the pivotal monthly injection trials. Longer term outcomes of aflibercept treatment with this regimen are being collected.

Commercial Relationships: Daniel Barthelmes, None; Vuong Nguyen, None; Jennifer Arnold, Alcon (R), Novartis (R), Bayer (R); Ian McAllister, None; Robyn Guymer, Novartis (R), Bayer (R); Rohan Essex, None; Stephanie Young, None; Mark C. Gillies, Bayer (F), Novartis (F), Novartis (R), Bayer (R) **Support:** Supported by a grant from the Royal Australian NZ College of Ophthalmologists Eye Foundation (2007-2009) and a grant from the National Health and Medical Research Council, Australia (NHRMC 2010-1012). Daniel Barthelmes and Mark Gillies are among owners of the copyright for the software with which the data for this project was collected. The other authors state they have no conflicts of interest to declare. Mark Gillies is a Sydney Medical Foundation Fellow and is supported by an NHMRC practitioner fellowship. Daniel Barthelmes was supported by the Walter and Gertrud Siegenthaler Foundation Zurich, Switzerland, the Holcim Foundation and the Swiss National Foundation.

Program Number: 522 **Poster Board Number:** A0159

Presentation Time: 1:30 PM–3:15 PM

Aflibercept as a Second Line Therapy for Neovascular Age Related Macular Degeneration Following Initial Bevacizumab Therapy

Ori Segal^{1,2}, Liran Tiosano³, Ayala Pollack⁴, Rita Ehrlich⁵, Itamar Klemperer⁶, Yoreh Barak⁷, Nurit Mathalone⁸, Michaela Goldstein^{9,2}, Itay Chowers³. ¹Ophthalmology, Meir medical center, Tel-Aviv, Israel; ²Ophthalmology, Sackler school of medicine, Tel-Aviv University, Tel-Aviv, Israel; ³Hadassah-Hebrew University Medical Center, Jerusalem, Israel; ⁴Kaplan Medical Center, Rehovot, Israel; ⁵Rabin medical center, Petach-Tikva, Israel; ⁶Soroka Medical Center, Beer-Sheva, Israel; ⁷Rambam Medical Center, Haifa, Israel; ⁸Carmel Medical Center, Haifa, Israel; ⁹Tel-Aviv medical center, Tel-Aviv, Israel.

Purpose: Second line therapy in patients with neovascular age-related macular degeneration (nvAMD) was mostly evaluated in chronic cases following prolong usage of first line treatment. This study aims to evaluate second line aflibercept therapy in nvAMD eyes showing partial or lack of response for initial therapy with bevacizumab.

Methods: The Aflibercept as a Second Line Therapy for nvAMD in Israel (ASLI) study is a prospective, multi-center (n=8), open-label, clinical trial. Forty seven nvAMD eyes that had persistent intra retina, sub retinal, or pigment epithelium detachment following 3-9 initial bevacizumab injections. Three monthly intravitreal aflibercept (2mg) injections were administered followed by two bi-monthly injections (weeks 16 and 24), and a final examination at week 28th. According to the investigator discretion, an additional injection was given at week

20. Best corrected visual acuity (BCVA) was evaluated with an Early Treatment Diabetic Retinopathy Study (ETDRS) chart and spectral-domain optical coherence tomography (SD-OCT) was performed at each visit. Baseline and final fluorescein angiography were also performed. Change in the central sub-field macular thickness (CST) from baseline to week 28 on OCT was defined as the primary end-point. Secondary end-points included the mean change in BCVA, and structural changes in OCT and FA.

Results: Mean \pm SD patient's age was 75.2 \pm 8.9 years. The mean \pm SD number of bevacizumab injections prior to enrollment to the study was 5.5 \pm 2.1 (range 3-9). CST reduced from mean \pm SD of 409 \pm 127 microns at baseline to 345 \pm 89 microns at week 8 (n=43, p<0.05; paired T-Test). 24/47 eyes had at least 5 letters gain, while 9 lost 5 or more letters. Five eyes lost 15 letters or more and 5 gain 15 letters or more. Twenty four patients required the optional treatment at week 20.

Conclusions: Interim results from the ASLI study demonstrate decrease in CST after the first 2 aflibercept injections, and improved BCVA at the end of the study. These preliminary results suggest that intravitreal aflibercept may be effective in eyes with nvAMD that show lack or partial response to initial bevacizumab treatment.

Commercial Relationships: Ori Segal, Bayer Israel Ltd. (F); Liran Tiosano, Bayer Israel Ltd. (F); Ayala Pollack, Bayer Israel Ltd. (F); Rita Ehrlich, Bayer Israel Ltd. (F); Itamar Klemperer, Bayer Israel Ltd. (F); Yoreh Barak, Bayer Israel Ltd. (F); nurit mathalone, Bayer Israel Ltd. (F); Michaela Goldstein, Bayer Israel Ltd. (F); Itay Chowers, Bayer Israel Ltd. (F)

Support: Bayer Israel Ltd. partial funding

Clinical Trial: NCT01918878

Program Number: 523 **Poster Board Number:** A0160

Presentation Time: 1:30 PM–3:15 PM

Twelve months outcomes of ranibizumab vs. aflibercept for neovascular age-related macular degeneration: observational study data

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Purpose: To compare the 12-month outcomes of ranibizumab vs. aflibercept therapy for treatment-naïve eyes with neovascular age-related macular degeneration (nAMD) in routine clinical practice.

Methods: Eyes commencing treatment over a 10 month recruitment period (01-Dec-2013 to 30-Sep-2014) formed the study population. The primary study outcome was mean change in visual acuity (VA) over 12 months. Secondary outcomes included the proportion of eyes in which the lesion became inactive and the number of injections to first recorded grading as inactive.

Results: The study population consisted of 261 eyes of 252 patients treated at 26 practices. Accrual rates over the 10 month recruitment period were similar resulting in similar sized groups (n=131 ranibizumab and n=130 aflibercept). Demographics and clinical characteristics were similar for both groups with mean index VA of 64.2 (ranibizumab) and 62.4 (aflibercept) LogMAR letters. The only significant difference was that the ranibizumab group mean age was 3.8 years older. Group mean 12 month VA outcomes for eyes which completed the study period were similar. The treatment-by-time interaction from the longitudinal model provided no evidence for a difference between the two groups (P=0.456). Group mean VA

at 12 months were similar: 70.1 (ranibizumab) vs 68.5 (aflibercept) letters ($P=0.604$; t -test). Eyes which completed the study period had an average of 8.6 (ranibizumab) and 8.1 (aflibercept) injections ($P=0.860$, Conway-Maxwell Poisson) and an average of 10.0 (ranibizumab) and 10.1 (aflibercept) visits.

Conclusions: We found no difference in the efficacy of ranibizumab vs aflibercept for nAMD in this observational study. Further studies are warranted to determine, for example by genetic testing, whether either agent is superior for individual eyes.

Commercial Relationships: Mark C. Gillies, Bayer (F), Novartis (F), Novartis (R), Bayer (R); Richard Walton, None; Jennifer Arnold, Alcon (R), Bayer (R), Novartis (R); Rohan Essex, None; Nigel Morlet, None; Daniel Barthelmes, None

Support: Supported by a grant from the Royal Australian NZ College of Ophthalmologists Eye Foundation (2007-2009) and a grant from the National Health and Medical Research Council, Australia (NHRMC 2010-1012). Daniel Barthelmes and Mark Gillies are among owners of the copyright for the software with which the data for this project was collected. The other authors state they have no conflicts of interest to declare. Mark Gillies is a Sydney Medical Foundation Fellow and is supported by an NHMRC practitioner fellowship. Daniel Barthelmes was supported by the Walter and Gertrud Siegenthaler Foundation Zurich, Switzerland, the Holcim Foundation and the Swiss National Foundation.

Program Number: 524 **Poster Board Number:** A0161

Presentation Time: 1:30 PM–3:15 PM

Real Life Use of Aflibercept In France: observational study in Wet AMD: the RAINBOW study

OUBRAHAM-MEBROUKINE Hassiba¹, Celine Faure², Florence Coscas³, Thi Ha Chau Tran⁴, Benedicte Briand-Joulain⁵, Laurent Velasque⁶, Isabelle Aubry⁷, Michel Weber⁸, Salomon Y. Cohen⁹. ¹Cabinet Libéral Montargis, Montargis, France; ²Clinique Saint-Martin, Caen, France; ³Cabinet Odeon, Paris, France; ⁴Hopital Saint-Vincent de Paul, Lille, France; ⁵Pole de Consultation Tassigny, Angers, France; ⁶Clinique Tourny, Bordeaux, France; ⁷Centre des Arceaux, Montpellier, France; ⁸CHU Hotel-Dieu, Nantes, France; ⁹CIL, Paris, France.

Purpose: To report interim outcomes of patients having completed one year in the RAINBOW study, aiming to collect efficacy and safety data from real-life clinical practice on naïve wet Age-related Macular Degeneration (wAMD) patients treated with intravitreal aflibercept in France.

Methods: RAINBOW is an observational retrospective and prospective study initiated in January 2014 in France, aiming to enroll 600 patients over 4 years. The primary endpoint is the change in Best Corrected Visual Acuity (BCVA), measured using the ETDRS chart from baseline to 12 months. The worst eye of each patient was considered as study eye, but the second eye could also be considered for the study if treatment-naïve. A preliminary analysis was performed on 92 eyes from 84 patients having completed 1 year of follow-up (Full Analysis Set, comprising all patients/eyes having received at least one injection).

Results: The baseline BCVA is summarized in table 1. The primary endpoint results are summarized in table 2. The mean (\pm SD) number of injections at 12 months was 7.2 (\pm 2.6) in the eyes. Two patients (2.4%) experienced one serious adverse event each, one of which (stroke) was treatment-related, while the other (pneumonia) was not.

Conclusions: The interim analysis of the RAINBOW study showed significant BCVA gains at 12 months (5.9 letters with an average of 7.2 injections) in wAMD naïve patients treated under real-life conditions. No new safety signals were detected.

		Eyes FAS (N=92)
BCVA score at M0 (ETDRS ltrs)	N	92
	Mean \pm SD	60.0 (\pm 15.4)
	[min-max; median]	[20.0 – 85.0 ; 61.5]

		Eyes FAS (N=92)
Mean BCVA change from baseline to month 12 (ETDRS ltrs)	N	92
	Mean \pm SD	5.9 (\pm 11.9)
	p	<0.001

Commercial Relationships: OUBRAHAM-MEBROUKINE Hassiba, Novartis (C), Allergan (C), Bayer (C); Celine Faure, Alcon (C), Bayer (C), Novartis (C); Florence Coscas, Allergan (C), Bayer (C), Novartis (C), Roche (C); Thi Ha Chau Tran, Bayer (C), Bausch&Lomb (C), Novartis (C); Benedicte Briand-Joulain, None; Laurent Velasque, None; Isabelle Aubry, Bayer (C); Michel Weber, Alimera (C), Alcon (C), Thea (C), Allergan (C), Bayer (C), Novartis (C); Salomon Y. Cohen, Novartis (C), Allergan (C), Bayer (C), Thea (C), Alcon (C)
Support: Bayer/Regeneron
Clinical Trial: NCT02279537

Program Number: 525 **Poster Board Number:** A0162

Presentation Time: 1:30 PM–3:15 PM

Combined Cell and Gene Therapy towards the Treatment of Age-Related Macular Degeneration and Diabetic Retinopathy

Sabiha Hacibekiroglu^{1,2}, Iacovos P. Michael¹, Peter D. Westenskow⁴, Brian Ballios^{2,3}, Nikolaos Mitrousis³, Jingsheng Tuo⁵, Chi-Chao Chan⁵, Derek van der Kooy³, Molly Shoichet³, Martin Friedlander⁴, Andras Nagy^{1,2}. ¹Mount Sinai Hospital, Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada; ²Institute of Medical Science, University of Toronto, Toronto, ON, Canada; ³Donnelly Centre for Cellular and Biomolecular Research, Toronto, ON, Canada; ⁴The Scripps Research Institute, San Diego, CA; ⁵National Eye Institute, National Institutes of Health, Bethesda, MD.

Purpose: Anti-angiogenic drugs (i.e. Avastin) only temporarily repair leaky blood vessels, thus AMD and DR-patients require monthly injections. These treatments may cause side effects such as stroke, gastrointestinal perforations and hemorrhage. We hypothesized that cells transplanted into a diseased eye expressing novel, local acting anti-vascular biologics, or “VEGF Sticky-Trap”, can inhibit VEGF-dependent neovascularization (NV) in AMD and DR in a controlled and long-term manner, replacing damaged cells and avoiding any potential systemic side effects.

Methods: Cells expressing VEGF Stick-trap in an inducible manner (human RPE and mouse MSC) were generated *in vitro* and 4×10^4 cells (2×10^4 cells/ul) in 0.5%/0.5% hydrogel solution were injected subretinally (RPE; n=10) or intravitreally (MSC; n=10) of CD-1 mice. The contralateral eyes served as vehicle (hydrogel) controls (n=20). Subsequently to cell injections, half of the experimental

groups were fed a doxycycline (DOX) diet to induce transgene expression from transplanted cells. 3 weeks post cell transplantation surgery, mice were perfused with 4% PFA solution and enucleated. Eyes were either subjected for cross-sectioning or retina's were isolated and flat mounted.

Results: In previous studies we have shown, that upon intravitreal and subretinal injection with traps (10ug/eye), VEGF Sticky-Trap binds to the eye ECM. In contrast to the original VEGF- trap, developed by Regeneron, VEGF Sticky-trap was local acting and undetectable in circulation 6 hrs post eye injection. Furthermore, we have shown that VEGF Sticky-trap is able to inhibit NV in an oxygen-induced retinopathy mouse up to 74% compared to 39 and 26% in the case of VEGF-trap and vehicle (n=23, p<0.05)). VEGF Sticky-trap, expressed by generated RPE cells and MSC *in vitro*, is able to bind to ECM and trap soluble VEGF only upon DOX induction (VEGF-ELISA assay). 5% of injected cells incorporates into the eye, and expresses VEGF Sticky-trap *in vivo* only upon induction with DOX diet. In addition, VEGF Sticky-trap expressed by transplanted cells, is able to bind to eye ECM.

Conclusions: The injection of transgenic cells into the eye of CD-1 mice showed a low integration potential, but all incorporated cells were able to express VEGF Sticky-trap upon DOX induction. Next, we will determine, if incorporated cells are able to inhibit NV in mouse models of AMD and DR.

Commercial Relationships: Sabiha Hacibekiroglu;

Iacovos P. Michael, None; Peter D. Westenskow, None; Brian Ballios, None; Nikolaos Mitrousis, None; Jingsheng Tuo, None; Chi-Chao Chan, None; Derek van der Kooy, None; Molly Shoichet, None; Martin Friedlander, None; Andras Nagy, None

Support: Foundation Fighting Blindness Grant

Program Number: 526 **Poster Board Number:** A0163

Presentation Time: 1:30 PM–3:15 PM

Association of serum neutralizing antibodies with safety and efficacy outcomes in a Phase 2a trial of rAAV.sFlt-1 in the treatment of wet AMD

Elizabeth P. Rakoczy^{1,2}, Chooi-May Lai¹, Aaron Magno², Martyn French⁴, Samuel B. Barone³, Steven D. Schwartz⁵, Mark Blumenkranz⁶, Mariapia Degli-Esposti¹, Ian J. Constable¹.

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Purpose: Purpose: To explore relationship between safety and efficacy outcomes and immunological status following subretinal rAAV.sFlt-1 injection at one year post-treatment.

Methods: Subjects were randomized to receive subretinal rAAV.sFlt-1 (10E11vg, n=21) or control (n=10). All subjects were able to receive intravitreal ranibizumab (RBZ) retreatment according to protocol-driven criteria for worsening wet AMD. Ophthalmic safety, immune response to AAV2, and routine laboratory safety tests were assessed.

Results: No serious adverse events (AE) related to rAAV.sFlt-1 were observed at one year. Transient AEs were: subretinal hemorrhage, inflammation, and increased IOP. Ten of eleven phakic subjects developed post vitrectomy cataract which was treated by extraction and lens implantation. In the rAAV.sFlt-1 treated group the mean BCVA increased by +2.2 ETDRS letters and mean CPT increased by +27µm from baseline (BL). Eleven of 21 rAAV.sFlt-1 treated

subjects required ≤2 RBZ rescue injections. Of these, 10 had AAV2 neutralizing antibodies (nAb) present at BL. For these 11 subjects, mean CPT remained unchanged (BL 338µm vs 1 yr 343µm) and mean BCVA increased by +6.7 ETDRS letters. The rAAV2.sFlt-1 treated subjects requiring >2 RBZ injections (n=10) lost a mean of -2.7 ETDRS letters, while mean CPT increased by +51µm (BL 406µm vs 1 yr 456µm), and two had nAb present at BL. Controls showed a mean -9.3 ETDRS letter loss and -85µm CPT decrease (BL 418µm vs 1 yr 333µm). They received a mean of 3.6 (median=4) rescue RBZ injections compared to a mean of 3.1 (median=2) injections for the rAAV.sFlt-1 treated group. Three controls had nAbs present at BL. Of the 21 rAAV.sFlt-1 treated subjects, 5 demonstrated transient and 3 showed sustained increases in nAb titer.

Conclusions: In this phase 2a study, subretinal rAAV.sFlt-1 was well-tolerated with a favorable safety profile. At one year following rAAV.sFlt-1, a subset of subjects had encouraging signs of a response with vision gain and fewer injections received while mean foveal thickness showed minimal change. Presence of pre-existing serum neutralizing antibodies did not appear to affect clinical outcomes.

Commercial Relationships: Elizabeth P. Rakoczy, Avalanche Biotechnologies (C), Avalanche Biotechnologies (P); Chooi-May Lai, Aaron Magno, Avalanch (F); Martyn French, None; Samuel B. Barone, Avalanche Biotechnologies (I), Avalanche Biotechnologies; Steven D. Schwartz, Avalanche Biotechnologies (I); Mark Blumenkranz, Avalanche Biotechnologies (I); Mariapia Degli-Esposti, None; Ian J. Constable, Avalanche Biotechnologies (P), Avalanche Biotechnologies (F)

Clinical Trial: NCT0149805

Program Number: 527 **Poster Board Number:** A0164

Presentation Time: 1:30 PM–3:15 PM

Extended Release of anti-VEGF Biologics from Biodegradable Hydrogel Implants for the Treatment of Age Related Macular Degeneration

Gary Owens, Melissa Sandahl, Melissa Hernandez, Andres Garcia, Stuart Williams, Tomas Navratil, Rhett Schiffman. Ophthalmology, Envisia Therapeutics, Research Triangle Park, NC.

Purpose: Decreasing the frequency of intravitreal injections of standard anti-VEGF therapies by means of an extended release formulations, would not only result in reduced burden to patients but may also result in improved clinical outcomes in the treatment of age-related macular degeneration (AMD), diabetic macular edema (DME), and retinal vein occlusion (RVO). Development of such extended release therapies has proven challenging due to the limited physicochemical stability of anti-VEGF biologics. Herein, we demonstrate the ability to produce extended release intravitreal implants for the release of anti-VEGF biologics by encapsulating solid state protein microparticles in biodegradable, extended release hydrogel matrices.

Methods: Micronized solid state protein particles were embedded uniformly throughout the hydrogel implant. Hydrogels with various degradation rates were studied. *In-vitro* release rate of the biologics from the hydrogel matrix and overall duration of action was monitored in 1X PBS pH 7.4 at 37 C, using total protein assays and a VEGF ELISA. Additional physicochemical characterization of protein released over several months was performed to assess protein stability by size exclusion chromatography and bioactivity by surface plasmon resonance.

Results: *In vitro* studies demonstrate complete release of protein over several months at therapeutically relevant levels. Physicochemical characterization of ongoing *in vitro* release studies indicate that the released protein is comparable to initial starting material with respect to functionality, binding kinetics and monomer content. These data

support advancing implant formulations *in vivo* for pharmacokinetic and tolerability evaluation in non-human primates.

Conclusions: We have demonstrated the ability to formulate biodegradable intravitreal implants with tunable, reproducible release kinetics of anti-VEGF biologics. Our *in vitro* data establishes proof of concept for multi-month extended release of active anti-VEGF biologics, potentially bypassing the need for monthly intravitreal injections.

Commercial Relationships: Gary Owens, Envisia; Melissa Sandahl, envisia; Melissa Hernandez, envisia; Andres Garcia, Envisia; Stuart Williams, envisia; Tomas Navratil, Envisia; Rhett Schiffman, Envisia

Program Number: 528 **Poster Board Number:** A0165

Presentation Time: 1:30 PM–3:15 PM

A Phase III b, Multicenter Study of the Efficacy and Safety of Aflibercept Switch in Patients With Exudative AMD With Retinal Pigment Epithelium Detachment, Previously Treated With Ranibizumab Intravitreal Injections. The ARI2 Study

Rocio Blanco-Garavito¹, Camille JUNG¹, Joel Uzzan³, Florence Coscas⁴, Maddalena QUARANTA EL-MAFTOUHI⁵, Jose Sahel⁶, Jean-Francois Korobelnik⁶, Ruxandra HERA⁷, Giuseppe Querques¹, Oudy Semoun¹, Eric H. Souied¹.

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Purpose: To evaluate the safety and efficacy of Aflibercept intravitreal injections (IVT) switch therapy to induce regression in pigment epithelium detachment (PED) height on patients previously extensively treated by Ranibizumab IVT. The primary outcome measure was change in maximal PED height from baseline to 12 weeks. Secondary outcome measures include: change in maximal PED height from baseline to 32 weeks as well as change in central retinal thickness, change in best corrected visual acuity (BCVA) and change in PED volume from baseline to 12 and 32 weeks.

Methods: Prospective, phase IIIb, open label, multi center study. Patients had to meet the following criteria: active subfoveal choroidal neovascularization (CNV) lesions secondary to AMD, at least 12 months previous Ranibizumab injections (≥ 8 injections) and PED $> 250 \mu\text{m}$ with persisting sub retinal fluid at baseline. Patients were switched to Aflibercept, receiving 3 consecutive IVT treatments at 4 weeks intervals (primary endpoint). Patients continued to receive Aflibercept IVT at 6 weeks intervals for the remainder of the study. Paired T-test was used to compare paired-data. Comparisons of unpaired means or medians were performed using the T-test or Mann-Whitney test.

Results: A total of 82 patients were analyzed. Mean age at inclusion was 80.65 years. Mean reduction in maximal PED height from baseline to 12 weeks was 78.81 microns ($p < 0.0001$). At 32 weeks, reduction of maximal PED height compared to baseline was 58 microns; the statistical significance was maintained ($p < 0.0001$). Mean BCVA was 0.36, 0.34 and 0.31 logMAR, at baseline, 12 weeks and 32 weeks time points respectively (improvement in BCVA was statistically significant at 32 weeks ($p = 0.04$) but not at 12 weeks ($p < 0.05$)). Reduction in PED volume from baseline (mean = 1.33 mm^3) to week 12 (mean = 0.95 mm^3) was statistically significant ($p < 0.0001$).

Conclusions: According to the results in this study, Aflibercept switch therapy seems to be effective in reducing PED volume and height in patients not responding to Ranibizumab therapy. Visual

acuity improvement was also observed. This is the largest controlled study analyzing PED response to anti VEGF switch therapy.

Commercial Relationships: Rocio Blanco-Garavito; Camille JUNG, None; Joel Uzzan, Novartis (C), Allergan (C), Bayer (C); Florence Coscas, None; Maddalena QUARANTA EL-MAFTOUHI, None; Jose Sahel, Genesignal (C), GenSight Biologics (C), Chronolife (I), Sanofi-Fovea (C), Pixium Vision (C), Chronocam (I), Vision Medicines (C); Jean-Francois Korobelnik, None; Ruxandra HERA, Bayer (R); Giuseppe Querques, Alimera Sciences (C), Bausch and Lomb (C), Allergan (C), Novartis (C), Heidelberg (C), Bayer Schering pharma (C), Zeiss (C); Oudy Semoun, Bayer (I), Novartis (C); Eric H. Souied, Novartis (C), Allergan (C), Bayer (C)
Clinical Trial: NCT02157077

Program Number: 529 **Poster Board Number:** A0166

Presentation Time: 1:30 PM–3:15 PM

Two year results of intravitreal aflibercept injections for neovascular age-related macular degeneration using a treat and extend regimen

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Purpose: The treatment of neovascular age-related macular degeneration (nAMD) has been revolutionized by anti-vascular endothelial growth factor (VEGF) medications. However, there is no consensus on a particular standard regimen for anti-VEGF medications in nAMD. In this retrospective consecutive case series, We have evaluated 2 year outcomes for intravitreal aflibercept injections using a treat and extend regimen for these patients.

Methods: Eighteen eyes of 18 patients diagnosed with treatment-naïve nAMD were treated monthly with 2 mg aflibercept injections, for at least 3 months. Monthly injections continued until no retinal exudative changes (i.e. new subretinal hemorrhage or subretinal and/or intraretinal fluid) were observed by optical coherence tomography. If no retinal exudative changes were seen, the interval between injections was extended by 2 weeks, up to a maximum of 12 weeks during the first year or 16 weeks during the second year. If signs of exudation recurred, this interval was shortened by 2 weeks. The main outcome measures were changes in best corrected visual acuity (BCVA), central retinal thickness (CRT), and retinal exudation, the mean number of injections, and the interval between injections at 2 years.

Results: The mean BCVA (logarithm of the minimal angle of resolution, log MAR) improved significantly from 0.42 ± 0.31 at baseline to 0.21 ± 0.31 at 2 years ($p = 0.005$, paired t-test). The BCVA improved by more than 0.3 logMAR units in 8 eyes (44.4%), was unchanged in 9 eyes (50%) and worsened by more than 0.3 logMAR units in 1 eye (5.6%). The mean CRT decreased significantly from $360.4 \pm 123.2 \mu\text{m}$ at baseline to $210.6 \pm 67.1 \mu\text{m}$ at 2 years, ($p < 0.0001$, paired t - test). After 2 years, 66.7% patients (12 eyes) had no retinal exudation. The mean number of injections was 7.8 ± 1.5 in year 1 and 5.9 ± 2.6 in year 2. The mean interval between injections at 2 years was 11.2 ± 4.9 weeks.

Conclusions: The use of a treat and extend regimen for intravitreal aflibercept injections in nAMD was effective in improving BCVA, CRT, and retinal exudates for up to 2 years. The mean number of injections and mean interval between them was very variable between cases.

Commercial Relationships: Mio Hosokawa, None; Yuki Morizane, None; Shuhei Kimura, None; Mika Hosogi, None; Shinichiro Doi, None; Fumio Shiraga, None

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Presentation Time: 1:30 PM–3:15 PM

Sustained Delivery of Ranibizumab: The LADDER Trial of the Ranibizumab Port Delivery System

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Purpose: The use of anti-VEGF intravitreal (ITV) injections to treat retinal diseases including neovascular age-related macular degeneration (nAMD) is well-established. However, treatment often requires frequent ITV injections, which can be burdensome. The phase 2 LADDER trial is evaluating the Ranibizumab (RBZ) Port Delivery System (RPDS), a refillable implanted device, in patients with nAMD. The RPDS uses a diffusion-controlled drug delivery mechanism to provide sustained ITV release of RBZ between refills. LADDER follows a phase 1 open-label study of the RPDS in 20 treatment-naïve patients with nAMD, which established proof-of-concept for RPDS safety and efficacy.

Methods: LADDER is a phase 2 multicenter, randomized, interventional, active-treatment controlled clinical trial, with the primary endpoint 9 months after last patient randomization. Eligible patients have subfoveal nAMD, diagnosed within 6 months, with documented response to ITV anti-VEGF treatment. Patients are randomized 3:3:3:2 to RPDS with 1 of 3 RBZ formulations (N=60 each) or monthly ITV RBZ 0.5 mg (N=40). The RPDS is surgically implanted in the pars plana (subconjunctival), and refills are performed in the clinic using a customized refill needle that exchanges the reservoir contents with fresh drug.

Results: LADDER anticipates enrolling 220 patients at up to 55 US sites. The primary objective is to evaluate the time to the first RPDS refill according to protocol-defined refill criteria. The key secondary endpoint, change from baseline in BCVA, will be used to test the non-inferiority (NI) of each of the RPDS arms vs monthly ITV RBZ 0.5 mg using a 4 letter NI margin. Other secondary outcomes include: mean change in BCVA from baseline (BL) to Month 9, mean average change in BCVA through Month 9, mean change from BL in central foveal thickness on SD-OCT, and adverse event (AE) incidence (ocular, non-ocular, AEs of special interest).

Conclusions: Sustained delivery has the potential to reduce the treatment burden associated with anti-VEGF injections for patients and improve visual outcomes associated with under-treatment in clinical practice. LADDER is an ongoing phase 2 study evaluating dosing and functional outcomes with sustained delivery of RBZ via the RPDS.

Commercial Relationships: J.J. Hopkins, Genentech, Inc; Carl D. Regillo, Genentech, Inc (F), Genentech, Inc (C); Aaron Osborne, Genentech, Inc; Steven F. Francom, Genentech, Inc; Giulio Barteselli, Genentech, Inc
Support: Genentech, Inc., South San Francisco, CA, provided support for the study and participated in the study design; conducting the study; and data collection, management, and interpretation.
Clinical Trial: NCT02510794

Program Number: 531 **Poster Board Number:** A0168

Presentation Time: 1:30 PM–3:15 PM

Baseline characteristics and 1-year outcomes of patients with neovascular age-related macular degeneration from the real-world LUMINOUS™ study: global results vs Australian cohort

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Purpose: LUMINOUS™ (NCT01318941), the largest prospective observational trial in medical retina, is designed to evaluate the long-term safety, effectiveness, treatment patterns, and health-related quality-of-life associated with ranibizumab treatment in clinical practice across all licensed indications. Here we describe baseline characteristics and 1-year outcomes of treatment naïve patients from the global and Australian cohorts with neovascular age-related macular degeneration (nAMD), recruited before March 2014 in the LUMINOUS™ study.

Methods: Patients were treated according to the local product label, and data were analyzed based on prior treatment status of the primary treated eye (treatment naïve, prior ranibizumab treated, or other prior ocular treated). We report the results on treatment naïve patients only.

Results: A total of 17,656 patients with nAMD were recruited, including 1,694 patients from Australia. Of the global and Australian cohorts, 4497 and 227 patients, respectively, were treatment naïve. The baseline characteristics of the Australian patients were similar to the global group in terms of age and sex (Table). The mean age of the global/Australian cohorts was 75.0/79.3 years and 44.2%/44.1% were male. The global cohort had 68.8% of Caucasians whereas it was 91.2% in the Australian cohort. In the global/Australian cohorts, pigment epithelium detachment was present in 41.6%/25.6% of patients and polypoidal choroidal vasculopathy was present in 8.4%/3.1% of patients. At baseline, for global/Australian cohorts, the mean visual acuity (VA, letters) was 49.9/52.9 and the mean central retinal thickness (CRT, µm) was 360.6/300.6. At 1 year, in global/Australian cohorts, the mean change in VA was 3.6/5.3 with a mean of 4.3/7.9 ranibizumab injections and 7.3/9.4 visits. No new safety events were reported in these cohorts.

Conclusions: Overall, treatment naïve patients from the Australian cohort had higher VA and lower CRT at baseline than the global cohort. At 1 year, compared with the global cohort, better VA outcomes were achieved in the Australian cohort, with a higher mean number of injections. Safety findings were consistent with the well-established safety profile of ranibizumab. Future follow-up data from this and other cohorts will provide long-term evidence on ranibizumab treatment outcomes.

Demographics and baseline ocular characteristics

	Australian cohort	Global cohort
	Treatment naïve (N=227)	Treatment naïve (N=4497)
Demographics		
Mean age, years	79.3	75.0
Gender, Male, %	44.1	44.2
Race, Caucasian, %	91.2	68.8
Mean time since diagnosis to first ranibizumab treatment, weeks	14.6	15.6
Ocular characteristics		
Mean VA, letter score	52.9	49.9
Mean CRT, µm	300.6	360.6
Disease characteristics		
Pigment epithelium detachment, %	25.6	41.6
Polypoidal choroidal vasculopathy, %	3.1	8.4

CRT, central retinal thickness; VA, visual acuity

Commercial Relationships: Robyn H. Guymer, Bayer (C), Bayer (R), Novartis (C), Novartis (R); Wayne Macfadden, Novartis Pharma AG, Basel, Switzerland
Clinical Trial: NCT01318941

Program Number: 532 **Poster Board Number:** A0169

Presentation Time: 1:30 PM–3:15 PM

Two year visual outcome of patients with wet age related macular degeneration in a multi-office retina practice in the United States

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Purpose: A retrospective clinical study was performed to examine the real world visual outcome of patients with wet age-related macular degeneration (AMD) who underwent treatment with anti-vascular endothelial growth factor (VEGF) agents in a multi-office retina practice in the United States for at least 2 years.

Methods: Patients with the diagnosis of wet AMD, at least 2 years of follow-up and who received at least one anti-VEGF injection between January 2010 and December 2012 were included. Patients with ocular comorbidities that could affect visual acuity (VA) were excluded. The following data were collected through chart review: age; sex; treated eye; VA at baseline, 3 and 6 months, 1 and 2 years, and at last follow-up; ocular comorbidities; injection complications; phakic status; fundus findings; optical coherence tomography (OCT) findings including: central retinal thickness (CRT), subretinal/intraretinal fluid (SRF/IRF), subretinal hyperreflective material (SHRM).

Results: A preliminary analysis of the 50 eyes included in this study showed 36 females (72%) and 14 (28%) males. The mean age was 83 (median: 85, min: 61, max 96). The mean visual acuity at baseline was: 20/77; at 3 months: 20/59; at 6 months: 20/53; at 1 year: 20/72; at 2 years: 20/83. Over 2 years of therapy, a mean of 8.8 injections were received (median: 8.5, min: 1, max: 23; 6 injections during first year and 2.8 injections during the second year). No complications were reported.

Patients with baseline VA \geq 20/40 had the best mean VA at 2 years (20/52), received the least number of injections (mean: 8.2), and lost a mean of 8 letters over 2 years. Patients with baseline VA between 20/40 and 20/200 (inclusive) had a mean VA of 20/82 at 2 years with a mean of 8.7 injections and lost a mean of 2 letters. Patients with baseline VA $<$ 20/200 had a mean of 20/200 at 2 years with a mean of 10.2 injections and gained a mean of 21 letters.

Conclusions: Patients with baseline VA \geq 20/40 were at highest risk of losing vision over time but received the fewest number of injections. Patients with VA $<$ 20/200 gained the most number of letters and received the highest number of injections over 2 years; however, their final visual outcome was worse than the other 2 groups.

Commercial Relationships: Marina Gilca, None; Kourous A. Rezaei

Program Number: 533 **Poster Board Number:** A0170

Presentation Time: 1:30 PM–3:15 PM

Association of fluid recurrence with visual maintenance following the loading phase in anti-VEGF therapy for neovascular AMD

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Purpose: Parameters such as baseline (BL) vision and certain lesion characteristics correlate with visual gain during anti-vascular endothelial growth factor (VEGF) therapy for neovascular age-related macular degeneration (nAMD). However, it is also important to understand individual differences in required treatment intensity to maintain this gain, which may allow treatment regimens to be individually customized. This study examined the association

between specific courses of best corrected visual acuity (BCVA) development and fluid accumulation patterns on optical coherence tomography (OCT) after the completion of the loading phase of anti-VEGF therapy in nAMD patients.

Methods: Post-hoc analysis was performed on data from treatment-naïve nAMD patients enrolled in the EXCITE (n=353) and SUSTAIN (n=513) studies with fixed 12-weekly (q12) or PRN maintenance regimens after loading phase. Three groups were identified based on change in BCVA: 1) gain/maintain (BCVA change from BL–month M3 \geq 0 and from M3–M12 \geq -5); 2) gain/loss (BCVA from BL–M3 \geq 0 and BCVA from M3–M12 \leq -5); 3) no gain (BCVA from BL–M3 $<$ 0). Morphological parameters included presence of subretinal fluid (SRF) and intraretinal cystoid fluid (IRF). Fluid status at M4 (after the first treatment-free visit at M3) was compared between the groups.

Results: In EXCITE q12 patients (n=238), in the gain/maintain (n=98) and no gain (n=35) groups, IRF was stable after treatment discontinuation at M4 (IRF present in 14% of patients at M3 and 18% at M4; and 23% and 29%, respectively). In the gain/loss group (n=91), IRF presence increased significantly from M3 to M4 (from 13% at M3 to 37% at M4). New IRF at M4 was associated with decline in mean BCVA from M3 to M12 with this q12 regimen; increases in IRF later in the treatment period, i.e. at M5, were not associated with a BCVA decline. Loss of BCVA did not demonstrate strong associations with dynamic changes in SRF.

Conclusions: Declining BCVA after the loading phase with discontinuous anti-VEGF treatment was associated with an early increase in IRF, which suggests that patients with such fluid recurrence would likely benefit from more intensive treatment. Customizing individual treatment regimens in this manner may lessen the logistical burden which is increasingly evident in the treatment of nAMD.

Commercial Relationships: Sebastian M. Waldstein, Bayer (C), Novartis (C); Victor Chong, Quantel (C), Bayer (R), Allergan (C), Novartis (C), Allergan (F), Novartis (F); Michael Larsen, Roche (F), Novartis (F), Allergan (F), Alcon (F); James Warburton, Novartis Pharma UK; Andreas Weichselberger, Novartis/Alcon; Jonathan Wright, Novartis Pharma UK (C); Ursula Schmidt-Erfurth, Boehringer Ingelheim GmbH (C), Bayer (C), Novartis Pharma AG (C), Alcon (C)

Clinical Trial: NCT00275821

Program Number: 534 **Poster Board Number:** A0171

Presentation Time: 1:30 PM–3:15 PM

Ranibizumab in patients with neovascular age-related macular degeneration in real-world clinical settings in France: 1-year data from the LUMINOUS™ study

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Purpose: LUMINOUS™ (NCT01318941; initiated March 2011) is the largest, prospective, observational, global study in the field of medical retina. LUMINOUS™ is an ongoing 5-year study that is designed to evaluate the long-term safety, effectiveness, treatment patterns, and health-related quality of life associated with

ranibizumab (RBZ) 0.5 mg treatment across all approved indications in 30,000 patients from routine clinical practice. We present the 1-year data from the French patients included in LUMINOUS™.

Methods: Overall, 17,545 adult patients with neovascular age-related macular degeneration (nAMD) were enrolled before March 2014; of these 9125 adult nAMD patients with a potential for 1-year follow-up were enrolled before March 2013. We analyzed the baseline characteristics of nAMD patients that were enrolled in France before March 2014 and the 1-year data from the French cohort.

Results: Baseline characteristics of the French and the global nAMD cohorts are shown in Table 1. Both the French and the global cohorts had similar mean baseline visual acuity (VA; Early Treatment Diabetic Retinopathy Study [ETDRS] letter score; French/global nAMD cohorts: VA, 58.6/54.3). A higher proportion of patients in the French cohort had pigment epithelium detachment (PED) than those in the global cohort (68.0% versus 42.4%). In the global cohort, the 1-year data showed that on average treatment-naïve patients gained VA from baseline whilst those previously treated with RBZ either gained or maintained VA, with a relatively low number of injections and visits (Table 2). The 1-year data for the French cohort are expected in February 2016.

Conclusions: The French nAMD patients enrolled in the LUMINOUS™ study were slightly older and had similar baseline VA, a higher proportion had PED, and a similar proportion had non-ocular comorbidities at baseline compared with the global nAMD cohort. The 1-year follow-up data from the French cohort will provide an invaluable source of information from a diverse group of patients currently underrepresented in randomized clinical trials.

	French nAMD cohort (n=469)	Global nAMD cohort (n=17,546)
Mean (SD) age, years	80.2 (7.67)	77.4 (9.46)
Sex, male/female, %	32.4/67.6	41.6/58.4
Non-ocular comorbidities, %		
Myocardial infarction	5.5	7.3
Stroke	5.5	5.6
Other thromboembolic events	4.9	4.9
Family history of coronary artery disease	14.1	14.9
Diabetes	10.7	14.5
Hypertension	51.4	56.7
Obesity (BMI, >30 kg/m ²)	11.5	10.0

Missing data: 3.6% for French nAMD cohort and 0.7% for Global nAMD cohort
French nAMD and global nAMD cohorts include treatment-naïve and previously treated patients
BMI, body mass index; SD, standard deviation; n, number of patients; nAMD, neovascular age-related macular degeneration;

Table 1. Baseline characteristics of the French and the global nAMD patients enrolled before March 2014

	Treatment naïve (N=1628, n=706)	Previously treated (RBZ) (N=7454, n=3556)
Mean VA change (ETDRS letters)	+4.4	-1.5
Mean number of injections	4.7	4.3
Mean number of visits	7.5	7.5

ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; RBZ, ranibizumab; VA, visual acuity

Table 2. Outcomes at Year 1 of the global nAMD patients enrolled before March 2013

Commercial Relationships: Vittorio Capuano, None; OUBRAHAM-MEBROUKINE Hassiba; Benjamin Wolff, Allergan (C), Bayer (C), Novartis (C); Salomon Y. Cohen, Thea (C), Alcon (C), Novartis (C), Bayer (C), Allergan (C); Catherine P. Garcher, B+L (C), Allergan (C), Bayer (C), Novartis (C), Alcon (C), Thea (C); Jean-Francois Korobelnik, Zeiss (C), Bayer (C), Allergan (C), Thea (C), Alimera (C), Alcon (C), Novartis (C), Roche (C), Horus (C); Ramin Tadayoni, Novartis (C), Thrombogenics (C), B+L (C), Roche (C), Bayer (C), Allergan (C), Alcon (C), Zeiss (C), Genentech (C), FCI (C); Christian Delhay, None; Audrey Derveloy, Novartis; Eric H. Souied, Novartis (C), Allergan (C), Bayer (C), Thea (C)

Support: Novartis

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Program Number: 535 **Poster Board Number:** A0172

Presentation Time: 1:30 PM–3:15 PM

Intravitreal Aflibercept For Neovascular Polypoidal Choroidal Vasculopathy In A Predominantly Non-Asian Population: 1-Year Rival Trial Results

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Purpose: Evaluation of anti-VEGF therapy for polypoidal choroidal vasculopathy (PCV) has primarily occurred in Asian patients and little data exist for African-American and Caucasian populations. We performed a prospective, non-randomized clinical trial to evaluate the safety and potential efficacy of intravitreal aflibercept in the treatment of PCV-related CNV in a predominantly non-Asian population.

Methods: Open-label, prospective, unmasked, non-randomized study enrolled 20 eyes (10 treatment-naïve; 10 non-naïve) with neovascular PCV from 20 subjects. Eyes received monthly aflibercept 2.0 mg intravitreally for 3 months followed by mandatory aflibercept every 2 months for 1 year. Subjects were evaluated monthly for additional intravitreal aflibercept or rescue treatment if pre-defined criteria were met.

Results: Eighteen of 20 eyes completed 1 year follow-up. Baseline average visual acuity was 60 (20/63), 64 (20/50), and 56 (20/80) EDTRS letters in the overall, treatment-naïve, and non-naïve groups, respectively. At baseline, average OCT central subfield thickness (CST) was 280 um, 291 um, and 268 um in the overall, treatment-naïve, and non-naïve groups, respectively. Through one year, the overall, treatment-naïve, and non-naïve groups received an average of 6.2, 6.6 and 5.8 out of the 7 mandatory scheduled intravitreal aflibercept injections, respectively. Through one year, the overall, treatment-naïve, and non-naïve groups received an average of 0.65 (range 0-4), 0.5 (range 0-2), and 0.8 (range 0-4) out of a maximum of 5 additional PRN intravitreal aflibercept injections, respectively. No eyes required rescue therapy such as photodynamic therapy (PDT). At 1 year, average visual acuity was 69 letters (20/40) with an average gain of 8 letters (treatment-naïve eyes gained 11 letters; non-naïve eyes gained 5 letters). At 1 year, average OCT CST was 213 um indicating an average thinning of 69 um (treatment-naïve and non-naïve eyes thinned 78 um and 58 um, respectively). No endophthalmitis, retinal tears, detachments, vitreous hemorrhage, or arterial thrombotic events were reported.

Conclusions: This data indicates favorable visual acuity and anatomic response, as well as safety of intravitreal aflibercept monotherapy for neovascular PCV in a predominantly non-Asian population.

Commercial Relationships: Dennis M. Marcus, Genentech (C), Neurotech (F), Pfizer (F), Acucela (F), Alimera (C), Genentech (F), Del Mar (F), Alimera (F), Thrombogenics (C), Chiltern (F), Alcon (F), Allergan (F), Ophthotech (F), Thrombogenics (F), Regeneron (F), Xcovery (F), Regeneron (C); Amina Farooq, None; Heather Frazier, None; Chelsea Fechter, None; William B. Marcus; Harinderjit Singh, Genentech (F), Alcon (F), Acucela (F), Neurotech (F), Pfizer (F), Chiltern (F), Alimera (F), Xcovery (F), Thrombogenics (F), Regeneron (F), Ophthotech (F), Allergan (F), Del Mar (F)

Support: Investigator Initiated Trial Grant Support provided by Regeneron Pharmaceuticals

Clinical Trial: NCT02092532

Program Number: 536 **Poster Board Number:** A0173

Presentation Time: 1:30 PM–3:15 PM

Intravitreal aflibercept in wet age-related macular degeneration patients from Japan: 6-month outcomes of J-PMS

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Purpose: To assess the safety and effectiveness of intravitreal aflibercept injections (IAI) in wet age-related macular degeneration (wAMD) patients in Japan.

Methods: J-PMS is a postmarketing surveillance study with postapproval commitment by the Japanese authority. It is a prospective, multicenter, observational study that is monitoring 36-month outcomes following IAI treatment in routine clinical practices in Japan. Safety (primary outcome) and visual and anatomic outcomes were assessed in a planned 6-month interim analysis, which is reported here. The decision to treat (or switch) to IAI was made by the patient's own physician.

Results: 1636 wAMD patients provided safety data and 1610 patients provided efficacy data. The mean age of patients was 74.2 years, 69.8% were male, 70.6% had choroidal neovascularization (CNV), 45.0% had polypoidal choroidal vasculopathy, and 42.5% had comorbidities, including hypertension (29.3%). Most patients (58.9%) were treatment naïve and, among previously treated patients, the main reason for switching was insufficient response to other anti-vascular endothelial growth factor agents (76.4%). The mean number of IAI injections was 3.5 at 6 months. Serious adverse events (SAEs) were reported in 17 patients (1.0%). The most common ocular SAEs were vitreous hemorrhage (0.2%), retinal pigment epithelial tear (0.2%), and retinal detachment (0.2%), and the most common nonocular SAE was myocardial infarction (0.1%). The mean change in best-corrected visual acuity (BCVA) (logMAR) was -0.132 (6.6 letters) at Month 6. Vision was maintained (BCVA change >-0.3 to <0.3) or improved (BCVA change ≤-0.3) in 78.1% and 18.5% of patients at Month 6, respectively. The mean reduction in central retinal thickness was -103.8 μm at Month 6. IAI was effective in treatment-naïve and previously treated patients (Table) and across wAMD subtypes.

Conclusions: Ocular SAEs were consistent with the known safety profile of IAI. Improvements in visual and anatomic outcomes were observed in all groups. The benefits in treatment-naïve patients were comparable to VIEW.

BCVA (logMAR)	Month 0	Month 6	Mean change
All	0.456	0.324	-0.132
Treatment-naïve	0.418	0.258	-0.160
Switched	0.512	0.427	-0.085
CRT (μm)	Month 0	Month 6	Mean change
All	356.6	252.8	-103.8
Treatment-naïve	358.1	253.4	-104.7
Switched	353.8	251.3	-102.5

Commercial Relationships: R Mori, Bayer (F); M Ohji, K Takahashi, Bayer (F), Bayer (C); Tatsuro Ishibashi, Bayer (F), Bayer (C); H Migita, Bayer; T Sakaguchi, Bayer; L Inuyama, Bayer; M Yuzawa, Bayer (F), Bayer (C)

Clinical Trial: NCT01756248

Program Number: 537 **Poster Board Number:** A0174

Presentation Time: 1:30 PM–3:15 PM

Long-Term Outcomes Of Intravitreal Ranibizumab In Patients With Neovascular Age-Related Macular Degeneration. Besides Clinical Trials

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Purpose: Intravitreal ranibizumab has proven to be effective in the management of patients with neovascular age-related macular degeneration (AMD). The aim of the present study was to assess the long-term outcome of patients with neovascular AMD in the real world scenario.

Methods: Observational, retrospective, multicenter (10 sites across Spain) study to assess the clinical and demographic characteristics of patients with neovascular AMD treated with ranibizumab 0.5 mg and followed for at least 24 months. Patients were included if visual acuity (VA) was at least 20/200 within 3 months previous to data collection.

Results: A total number of 67 eyes (66 patients; mean age 78.2±6.3; women 50%) were recruited. The mean time from diagnosis of neovascular AMD was 3.1±0.8 years. Only 65.7% of cases had received a loading dose of 3 consecutive monthly injections of ranibizumab. Mean VA improved 3.7±12.0 letters at month-12; and 4.2±12.3 letters at month-24. VA improvement after loading dose (month-3) was more sustained in patients aged under 75 years, cases with less than 3 years since diagnosis and cases with less than 350 microns in central retinal thickness. Pigment epithelium detachment (PED) was more frequent in patients under 75 years of age at baseline (68.2% and 57.8%), and also after 24-month follow-up (45.5% and 33.3%).

PRN with strict monthly follow-up (43.3%; mean annual injections 4.2±1.6), and PRN without fixed follow-up criteria (43.3%; 2.7±1.3) were the most frequent strategies registered. Ranibizumab was administered to treat further recurrences in 61 of the 67 study eyes, mainly due to persistent or recurrent macular fluid (qualitative parameter) regardless of age, time since diagnosis, VA or retinal thickness. The overall mean number of injections per year since diagnosis was 3.4±1.6.

Conclusions: The present study results suggest that ranibizumab may be effective in the real world scenario in patients with neovascular AMD with VA improvement since month-3 that may remain stable at 24-month follow-up. In addition, the presence of PED was evidenced to be decreased at the end of follow-up. Younger age, shorter time since diagnosis of neovascular AMD and lower basal retinal thickness might be associated with sustained VA improvements.

Commercial Relationships: Jose juan Escobar, Novartis Pharma (F); Roberto Gallego, Beatriz Romero, Novartis Pharma

Support: Study sponsored by Novartis Pharma

Program Number: 538 **Poster Board Number:** A0175

Presentation Time: 1:30 PM–3:15 PM

Canadian Treat and Extend Analysis Trial with Ranibizumab in Patients with Neovascular AMD: Interim Analysis of the CANTREAT Study

Peter Kertes^{1,7}, Tom Sheidow^{2,11}, Geoff Williams^{3,8}, Mark Greve^{4,9}, Ivan John Galic¹⁰, Emmanouil Rampakakis⁵, Bernard Bourgault⁶, Anne-Sophie Courseau⁶. ¹Sunnybrook Health Sciences Center, Toronto, ON, Canada; ²Ivey Eye Institute, London, ON, Canada; ³Calgary Retina Consultants, Calgary, AB, Canada; ⁴Alberta Retina Consultants, Edmonton, AB, Canada; ⁵JSS Medical Research, Saint-Laurent, QC, Canada; ⁶Novartis Canada, Dorval, QC, Canada; ⁷University of Toronto, Toronto, ON, Canada; ⁸University of Calgary, Calgary, AB, Canada; ⁹University of Alberta, Edmonton, AB, Canada; ¹⁰Institut de la rétine de Montréal, Montreal, QC, Canada; ¹¹Western University, London, ON, Canada.

Purpose: The concept of individualized *pro re nata* regimens based on BCVA stability over 3 months has been demonstrated. Given that recurrence of disease instability leads to vision loss, the role of OCT in evaluating nAMD activity for decision making needs to be assessed. Furthermore, to date, only retrospective evidence exists. The aim of this 24-month prospective, randomized (1:1), open-label, multicenter, post-authorization study is to assess the non-inferiority of an OCT-based treat-and-extend (T&E) regimen with ranibizumab compared to monthly dosing (Monthly) in treatment-naïve patients with neovascular AMD.

Methods: A 12-month interim analysis assessing baseline characteristics, visual acuity, and injection frequency was performed. Summary statistics including the mean and standard deviation for continuous variables and counts and percentages for categorical variables were produced.

Results: As of November 4th, 2015, 441 patients ($N_{T\&E}=223$; $N_{Monthly}=218$) were recruited; 215 patients ($N_{T\&E}=109$; $N_{Monthly}=106$) had 12-month follow-up data. Mean (SD) age was 79.6 (7.6) and 59.9% were females, with no differences between groups. In these patients with at least 12 months of follow-up data, mean (SD) baseline BCVA was 57.3 (14.5) and 59.5 (13.5) [total study cohort: 57.7 (14.4) and 58.4 (13.5), respectively] for the T&E and Monthly groups, respectively. At month-12, after an average of 9.7 (T&E) and 11.8 (Monthly) injections, mean (SD) BCVA improvement was 8.5 (13.3) and 6.0 (11.8) letters, respectively.

Conclusions: The results of this interim analysis suggest that comparable or greater improvement in BCVA may be achieved in a real-world setting with fewer injections required with T&E using an OCT-based treatment algorithm compared to a monthly dosing regimen.

Commercial Relationships: Peter Kertes, Bayer (S), Alcon (S), Novartis (S); Tom Sheidow, Bayer (S), Alcon (S), Novartis (S); Geoff Williams, Bayer (S), Arctic Dx (I), Novartis (S), Abbvie (S); Mark Greve, Novartis (S), Alcon (S); Ivan John Galic, Novartis (R); Emmanouil Rampakakis, JSS Medical Research, Novartis (F); Bernard Bourgault, Novartis; Anne-Sophie Courseau, Novartis **Clinical Trial:** NCT02103738

Program Number: 539 **Poster Board Number:** A0176

Presentation Time: 1:30 PM–3:15 PM

Comparison of anti-VEGF ranibizumab^R and aflibercept^R : a 18 months, real-life study in naïve patients

Arnaud George, Valérie Reitzer, Jean Paul Bellamy. Ophthalmologie, GLOB, PLERIN, France.

Purpose: To compare the evolution in visual acuity, anatomy and number of intravitreal injections (IVT) in two cohorts of naïve wet age-related macular degeneration (wAMD) patients, treated either

by ranibizumab^R or aflibercept^R, in the real life, in a French private practice center, at baseline, 12 and 18 months.

Methods: We enrolled two cohorts of 14 naïve patients, one treated by ranibizumab^R, the other by aflibercept^R for wAMD. No selection was realized, the only criteria of exclusion was precedent treatment for wet AMD in the same eye. We retrospectively reviewed the charts of the patients treated by anti VEGF. Following data were collected at baseline, 12 and 18 months : age, sex, visual acuity, central retinal thickness (CRT, as measured by spectral-domain Optical Coherence Tomography), presence or not of pigment epithelial detachment (PED), number of IVT. We collected the data from all patients at 18 months.

Results: No statistical significant difference ($p>0.5$) was found for the following criteria :

- demographics
- number of IVT at 12 and 18 months; a trend for more IVT was found for aflibercept^R.
- visual acuity was slightly better at baseline in the ranibizumab^R group.
- CRT was more important in aflibercept^R group at baseline.
- at 12 months, decrease in ECR was higher in aflibercept^R group.
- at 18 months, decrease in ECR was higher in ranibizumab^R group
- same results for PED at 12 and 18 months.

Conclusions: In this real-life study, we confirmed the results of the pivotal studies, i.e no statistical differences between the two anti-VEGF molecules routinely in use, ranibizumab^R and aflibercept^R. We found trends for a slight better diminution of CRT at 12 months for aflibercept^R, but no confirmation at 18 months. Gain of visual acuity was mostly acquired at 12 months, with stabilization at 18 months. No statistical difference was found for number of IVT, for a pro renata protocol.

Commercial Relationships: Arnaud George, Valérie Reitzer, None; Jean Paul Bellamy, None

Program Number: 540 **Poster Board Number:** A0177

Presentation Time: 1:30 PM–3:15 PM

The Short-term Outcomes of Treat and Extend Regimens: Aflibercept versus Ranibizumab

Kwan Bok Lee, Jung-Il Han, Dong-Won Lee, Moon-Jung Choi, Young Ju Lew, Hyung-Suk Kim, Han-Joo Cho, Jae-Hui Kim.

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Purpose: To compare the short-term outcomes of “treat and extend” regimens with aflibercept versus with ranibizumab in wet age-related macular degeneration patients.

Methods: This prospective study enrolled 23 patients with wet age-related macular degeneration (ARMD) who divided into two groups, a treat and extend (TAE) regimen with ranibizumab group (Group 1, n=13) and a same regimen with aflibercept group (Group 2, n=10). The central macular thickness (CMT) measured with spectral domain (SD) optical coherence tomography (OCT). We compared the mean gains in best-corrected visual acuity (VA) as well as the mean decreases of CMT.

Results: Two groups had no significant differences in baseline characteristics including age, visual acuity, CMT, and presences of intraretinal or subretinal fluid at initial presentation. At 8 months, the VA (LogMAR) was significantly improved (Group 1: -0.17 ± 0.16 , and group 2: -0.16 ± 0.21) and the CMT was significantly decreased (Group 1: $-193.23 \pm 165.91 \mu\text{m}$, and group 2: $-152.10 \pm 144.19 \mu\text{m}$) in each groups, but there is no significant difference between the two groups. One patient of group 1 was worsened in VA, and two patients of group 1 showed recurrence, but those are not statistically significant. And at last follow up, Group 2 showed less intraretinal or subretinal fluid.

Conclusions: The treat and extend regimens with aflibercept and ranibizumab significantly improved VA and decreased CMT in patients with ARMD.

Commercial Relationships: Kwan Bok Lee, None; Jung-II Han, None; Dong-Won Lee, None; Moon-Jung Choi, None; Young Ju Lew, None; Hyung-Suk Kim, None; Han-Joo Cho, None; Jae-Hui Kim, None

Program Number: 541 **Poster Board Number:** A0178

Presentation Time: 1:30 PM–3:15 PM

Long-term outcomes of intravitreal anti-VEGF therapy in eyes with both neovascular age-related macular degeneration and diabetic retinopathy

Lea Querques¹, Francesco Bandello¹, Federico Corvi¹, Carlo La Spina¹, Lucia Benatti¹, David Sarraf², K Bailey Freund³, Maurizio Battaglia Parodi¹, Eric H. Souied⁴, Giuseppe Querques¹.

¹Ophthalmology, University Vita-Salute San Raffaele, IRCCS Ospedale San Raffaele, Milan, Italy; ²Stein Eye Institute, Los Angeles, CA; ³Vitreous Retina Macula Consultants of New York, New York, NY; ⁴University Paris Est Creteil, Creteil, France.

Purpose: To investigate the long-term outcomes of intravitreal anti-VEGF therapy in eyes with both neovascular age-related macular degeneration (AMD) and diabetic retinopathy (DR).

Methods: Patients from 4 high-volume referral centers who presented with concomitant neovascular AMD and DR, and received intravitreal anti-VEGF therapy, were retrospectively enrolled into this study. Data retrieved from medical records and multi-modal imaging were analyzed.

Results: Forty-one eyes of 38 patients (21 male, 17 female; mean age 78±8 years) were enrolled. Median follow up was 28±19 [12-72] months. During follow-up, a mean of 9.2±7.4 intravitreal anti-VEGF injections per eye were administered: 13 eyes (32%) received a mean of 5.7±3.7 injections of bevacizumab, 35 eyes (85%) received a mean of 6.6±4.3 injections of ranibizumab, 1 eye (2%) received 7 injections of pegaptanib, and 8 eyes (20%) received a mean of 6.1±5.5 injections of aflibercept. Best-corrected visual acuity was 0.5±0.3 LogMAR at baseline; it improved significantly at 1 year (0.3±0.3 LogMAR; p=0.02) and returned to baseline values at last follow up visit (0.6±0.4 LogMAR; p=0.26). Mean central macular thickness (CMT) significantly decreased from 408±150 µm at baseline to 328±104 µm at one year (p=0.021) and to 335±127 µm at last follow up visit (p=0.032). No adverse events were recorded. The baseline severity of DR (International Clinical Diabetic Retinopathy Disease Severity Scale) was graded as mild non proliferative diabetic retinopathy (NPDR) in 21 (51%) eyes, moderate NPDR in 15 (36%) eyes, severe NPDR in 3 (7%) eyes, and proliferative diabetic retinopathy (PDR), but inactive due to panretinal photocoagulation, in 2 (5%) eyes; at last follow-up visit, 1 eye graded as moderate NPDR at baseline improved to mild, 1 eye graded as severe NPDR at baseline improved to mild and one eye graded as severe NPDR was inactivated due to photocoagulation

Conclusions: Long-term analysis of intravitreal anti-VEGF therapy for eyes with both neovascular AMD and DR showed stabilization of BCVA and a reduction in CMT, along with stable or improved DR throughout follow-up.

Commercial Relationships: Lea Querques; Francesco Bandello, Novartis (C), Bayer (C), Allergan (C); Federico Corvi, None; Carlo La Spina, None; Lucia Benatti, None; David Sarraf, Regeneron (C), Genentech (C); K Bailey Freund, Regeneron (C), Genentech (C); Maurizio Battaglia Parodi, Novartis (C), Allergan (C), Bayer (C); Eric H. Souied, Novartis (C), Bayer (C), Allergan (C); Giuseppe Querques, Bayer (C), Allergan (C), Novartis (C)

Program Number: 542 **Poster Board Number:** A0179

Presentation Time: 1:30 PM–3:15 PM

AFLIBERCEPT IN TREATMENT-NAÏVE PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: PROSPECTIVE PILOT STUDY

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²Hospital de Manises, Valencia, Spain.

Purpose: To assess the 13-month effectiveness and safety of aflibercept in naïve patients with neovascular age-related macular degeneration (nvAMD) in a real-life clinical setting

Methods: Thirty-two treatment-naïve patients with nvAMD participated in a prospective two-center study. Patients received intravitreal injections of aflibercept (Eylea®), three loading doses of 2 mg (0.05 mL) every 4 weeks for the first 3 months, followed by intravitreal injections every 2 months.

Results: At 3 and 13 months, the mean best-corrected visual acuity (BCVA) improved significantly as compared with baseline (logMAR 0.53 ± 0.30 and 0.55 ± 0.32 vs. 0.30 ± 0.24, respectively, *P* < 0.001). At 3 and 13 months, 46.8% of patients (n = 15) gained ≥ 15 EDTRS letters. The mean decrease in central macular thickness was also significant at 3 months (252 ± 35 µm) and at 13 months (249 ± 38 µm) as compared with pre-treatment values (383 ± 76 µm) (*P* < 0.01). Also, 50% resolution of pigment epithelial detachment (PED) was observed in 8 of 9 eyes (88.9%) with PDE at baseline. Intravitreal injections were well tolerated and no adverse events were recorded.

Conclusions: Aflibercept was effective and safe for treating nvAMD in naïve patients in routine daily practice.

Commercial Relationships: Patricia Udaondo;

SALVADOR GARCIA-DELPECH, None; DAVID SALOM, None; Ana Hervas-Ontiveros, None; Ricardo Diaz-Cespedes, None

Program Number: 543 **Poster Board Number:** A0180

Presentation Time: 1:30 PM–3:15 PM

Effect of Intravitreal Aflibercept for Refractory Pigment Epithelial Detachment and/or Subretinal Fluid Secondary to Age-Related Macular Degeneration

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Ophthalmology, Kyung Hee University Hospital, Seoul, Korea (the Republic of).

Purpose: To evaluate the efficacy of bimonthly intravitreal aflibercept on refractory subretinal fluid (SRF) and/or pigment epithelial detachment (PED) in patients with neovascular age-related macular degeneration (AMD).

Methods: Prospective, nonrandomized, interventional case series of 40 patients with persistent SRF and/or PED previously treated with at least 3 injections of intravitreal bevacizumab or ranibizumab were included. A dose of 2.0mg intravitreal aflibercept was administered as 3 initial loading doses in every 4 weeks, followed by pro re nata retreatment in every 8 weeks over 12 months upon visual acuity and optical coherence tomographic findings. Mean changes in Early Treatment Diabetic Retinopathy Study best-corrected visual acuity (BCVA), central subfield thickness (CST) and volume of SRF and/or PED were analyzed. Fluorescein angiography (FA) and indocyanine green angiography (ICGA) were also performed at both baseline and final visit.

Results: Mean age of patients was 70.7±7.3 years old and received 7.2±5.3 times of previous intravitreal injections. Further injections following initial loading doses were made in 18 eyes (45.0%) at week 24 and 13 eyes (32.5%) at week 48. Baseline BCVA was 47.5±19.8

letters and showed no significant difference at week 48 (51.3 ± 16.4 letters, $p=0.188$). Baseline CST was $319.9 \pm 94.6 \mu\text{m}$ and significantly reduced to $278.3 \pm 76.6 \mu\text{m}$ at week 48 ($p=0.009$). SRF volume was $0.52 \pm 0.64 \text{mm}^3$ at baseline and significantly reduced to $0.25 \pm 0.36 \text{mm}^3$ at week 48 ($p=0.023$). PED volume was $0.42 \pm 0.55 \text{mm}^3$ at baseline and significantly reduced to $0.23 \pm 0.32 \text{mm}^3$ at week 8 ($p=0.003$), but increased to $0.33 \pm 0.43 \text{mm}^3$ at week 48 which showed no significant difference to baseline ($p=0.350$). Persistent leakage from choroidal neovascularization on FA and ICGA was observed in 23 eyes (57.5%) at final visit.

Conclusions: Bimonthly intravitreal aflibercept is effective for reducing CST and SRF, while preserving visual acuity in treatment-resistant neovascular AMD. Despite the significant reduction after monthly loading doses, maintaining the reduction in PED volume may require more frequent injection than the bimonthly treatment.

Commercial Relationships: Hyung-Woo Kwak, Bayer (F), Zeiss (F), Allergan (F), Novartis (F); Yonguk Kim, None; Ji Ho Yang, None; Seung-Young Yu, Zeiss (F), Bayer (F), Novartis (F), Allergan (F)

Program Number: 544 **Poster Board Number:** A0181

Presentation Time: 1:30 PM–3:15 PM

Efficacy and Safety of Aflibercept in Fibrovascular Retinal Pigment Epithelium Detachment refractory to prior ranibizumab therapy in neovascular Age-related macular degeneration (AMD)

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¹Ophthalmology & Visual Sciences, Groupement des Hôpitaux Catholique de Lille, Lille, France; ²Clinique de la Louvière, Lille, France; ³Centre Ophtalmologique d'Odéon, Paris, France.

Purpose: To report efficacy and safety of aflibercept in the treatment of neovascular AMD with associated retinal pigment epithelium detachment (PED) refractory to ranibizumab with at least 6 months of follow-up.

Methods: This is a retrospective multicentric study including eyes with PED secondary to type 1 choroidal neovascularization (CNV) that had received at least 10 intravitreal injections of ranibizumab during the last 12 months. Exclusion criteria were: history of surgery within the last 3 months, previous thermal laser or photodynamic therapy, previous triamcinolone intravitreal injection, and any other active retinal disease. These eyes were treated with 3 loading dose of aflibercept (2mg/0.05ml) then followed every 4 weeks during 6 months. ETDRS visual acuity, slit lamp examination and SD-OCT were performed monthly, and eyes were treated as needed at the same visit.

Results: Results of 46 eyes were analyzed. Mean age was 79.3 ± 9.2 years. Mean history duration of PED was 42 (1-59) months. Mean interval between the last intravitreal ranibizumab and the first aflibercept injection was 2 ± 1.2 months. Mean number of aflibercept injections was 5.7 ± 1.2 during a mean follow-up of 35.6 weeks. Significant visual acuity improvement was observed at 12 weeks ($+3.4$ letters, $p=0.001$) and at last visit ($+2.7$ letters, $p=0.006$). Height of PED decreased from baseline to 12 weeks ($-33.8 \mu\text{m}$, $p=0.004$) and at last visit ($-36 \mu\text{m}$, $p=0.005$). No change was observed in central retinal thickness, macular volume and subfoveal choroidal thickness. Adverse events were found in 2 patients during the study duration.

Conclusions: Visual acuity improved and PED height regressed significantly after switching to aflibercept in patients insufficiently responding to prior therapy with ranibizumab after 3 loading dose and retreatment as needed on a 4 weeks interval. Further study is required to elucidate maintain of visual and anatomic improvement in the long term.

Commercial Relationships: Thi Ha Chau Tran, Bayer (R); Stephane DUMAS, None; Florence Coscas, Bayer (F)

Program Number: 545 **Poster Board Number:** A0182

Presentation Time: 1:30 PM–3:15 PM

2nd Year Visual Acuity Outcomes of AMD patients treated with Aflibercept : Data Analysis from the UK Aflibercept users group

Hussein Almuhtaseb^{1, 4}, James S. Talks², Rob Johnston³, Andrew J. Lotery^{1, 4}. ¹Eye Unit, Southampton General Hospital NHS Foundation Trust, Southampton, United Kingdom; ²Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom; ³Cheltenham General Hospital, Cheltenham, United Kingdom; ⁴Clinical and Experimental Sciences, University of Southampton, Southampton, United Kingdom.

Purpose: The VIEW 1 and 2 trials year 1 protocol has been adopted by many NHS centres. Conversely the year 2, a capped PRN regimen with monthly visits has not been widely adopted in the NHS due to health resources needed. We audited the visual outcomes achieved at the end of year two of therapy with aflibercept in 16 UK centres to see what year 2 outcomes were achieved when different treatment approaches were adopted.

Methods: Retrospective data analysis from an electronic medical record (EMR) system (Medisoft Ophthalmology) extracted from 16 centres in the UK. A consecutive series of treatment-naïve nAMD patients who received aflibercept for 2 consecutive years. During year one treatment was given according to the VIEW 1 and 2 trials' protocol. In year two, aflibercept was given according to an individualised treatment tailored to every patient's needs.

Results: 655 eyes contributed to the data set. 537 eyes were 1st treated eyes, and 118 were 2nd treated eyes. A mean of 4.2 injections (range 1-9) at a mean of 5.4 visits during the second year of treatment were observed. The mean baseline visual acuity (VA) at month 0 was 56L improving to 58L (+2L gain) at end of year 2. In 1st treated eyes the respective figures were: 55L at baseline, and 57L at end of year 2, +2L gain.

In 2nd treated eyes the respective figures were: 58L at baseline, and 59L at year 2, +1L gain. The proportion achieving 70L or more was 31%. 71.29% avoided moderate visual loss. The mean number of intravitreal injections (IVI)s during year 2 in 1st and 2nd treated eyes was 4 IVIs. Patients were stratified by number of IVIs into 3 groups: group A-36% of patients (≤ 3 IVIs); group B-36% of patients (4-5 IVIs); group C-28% of patients (6-9 IVIs). The mean VA at month 24 of groups A, B and C was 56, 59 and 63 L respectively. Eyes that received 6-9 IVIs (group 3) showed significantly higher mean visual acuity at month 24 than those that received < 3 IVIs (group 1) [$P < 0.01$]. The higher the number of IVIs given during year 2 the higher the visual acuity score at month 24 [$P=0.002$].

Conclusions: Baseline VAs were maintained through the 2-year treatment plan. A proactive regimen involving a higher number of IVIs resulted in a better VA score at the end of year 2. These results demonstrate the need for aggressive treatment in year 2 to maintain the treatment gains achieved in year 1 of therapy with aflibercept.

Commercial Relationships: Hussein Almuhtaseb; James S. Talks, None; Rob Johnston, None; Andrew J. Lotery, Bayer (R)

Program Number: 546 **Poster Board Number:** A0183

Presentation Time: 1:30 PM–3:15 PM

Anti-VEGF injection patterns and five year functional outcomes in patients with choroidal neovascularization or macular edema

Thomas Wecker, Christoph Ehlken, Anima Buehler, Clemens Lange, Hansjürgen Agostini, Daniel Boehringer, Andreas Stahl. Eye Center, Albert-Ludwigs-University of Freiburg, Freiburg, Germany.

Purpose: The introduction of anti-VEGF (vascular endothelial growth factor) revolutionized the treatment of patients with exudative age-related macular degeneration (AMD), diabetic macular edema (DME), retinal vein occlusion (RVO) and myopic

choroidal neovascularisation (CNV). The need for repeated intravitreal injections, however, still poses a major challenge for patients, physicians and health-care providers. In this monocentric retrospective study we analyzed long-term injection patterns and associated best-corrected visual acuity (BCVA) changes for up to five years of treatment.

Methods: After Ethics Board approval we analyzed all patients with AMD, DME, RVO or myopic CNV who were treated at our hospital between 2009 and 2014 and had at least one year of follow-up data available. All patients were treated using pro-re-nata (PRN) regimens. In total, 2,536 eyes of 2,034 patients (863 male and 1,171 female, mean age: 73.9 ± 11.7 years) qualified for analysis. AMD accounted for 1,661 eyes, DME for 479, RVO for 351 and myopic CNV for 45 eyes. The total number of injections for all eyes was 33,187. BCVA (extracted from medical reports) was available for 2,069 eyes from 1,682 patients. Outcome measures were change of BCVA, injection frequencies and cumulative injections over time. Statistical assessment was performed using Spearman's correlation.

Results: In year one, AMD patients received a median of 6 injections per eye (4-9, quartiles), 6 (3-9) for DME, 5 (3-8) for myopic CNV and 6 (3-8) for RVO. During the following years, median injection frequencies declined for all indications resulting in 3 (0.3 – 5.0) for AMD, 1.75 (0-4) for DME, 1 (0-3) for myopic CNV and 2 (0-4.8) for RVO. Proportion of patients gaining more than 15 letters was highest in RVO (30.2%). AMD patients, in contrast, showed the highest proportion of patients with more than 15 letters loss (25.3%). In all groups, between 75 and 83 % of patients remained either stable or gained vision.

Conclusions: Our real world VA data differ from the one- and two-year data reported from clinical trials, emphasizing the fact that (especially in AMD) initial VA gain cannot always be maintained long-term. Furthermore, this study provides information on expected treatment duration, injection frequencies and cumulative injection numbers that may be useful for counseling patients.

Commercial Relationships: Thomas Wecker, None; Christoph Ehlken, Novartis (C); Anima Buehler, None; Clemens Lange, None; Hansjürgen Agostini, Roche (C), Novartis (C), Bayer (C), Allergan (C), Zeiss (C); Daniel Boehringer, None; Andreas Stahl, Zeiss (C), Novartis (C), Boehringer Ingelheim (C), Novartis (F)

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Program Number: 547 **Poster Board Number:** A0184

Presentation Time: 1:30 PM–3:15 PM

Intravitreal Ranibizumab Therapy for Neovascular Age-Related Macular Degeneration and the Risk of Stroke: A 5-Year Follow-up Cohort Study

Sung Soo Kim, Tyler H. Rim, Christopher S. Lee, SungChul Lee, Do Wook Kim, Hyun Ju Park. Department of Ophthalmology, Severance Hospital, Institute of Vision Research, Yonsei University College of Medicine, Seoul, Korea (the Republic of).

Purpose: To evaluate the risk of stroke following ranibizumab treatment for neovascular age-related macular degeneration (AMD).

Methods: National registry data were used, comprising 1,025,340 random subjects in 2002. The ranibizumab group was composed of patients diagnosed with neovascular AMD and treated with ranibizumab between 2009 and 2013 (n=467). The two types of comparison groups were defined as comorbidity-matched controls (n=2,330) comprised of randomly selected patients (five per AMD

patient), who were matched to the ranibizumab group according to sociodemographic factors, hypertension, atrial fibrillation, and the Charlson comorbidities index, and sociodemographic-matched controls (n=2,248) comprised according to sociodemographic factors only. Each sampled patient was tracked until 2013. The Cox proportional hazard regression was used

Results: Strokes occurred in 6.6% of the ranibizumab group versus 7.0% of the comorbidity-matched controls and 6.7% of the sociodemographic-matched controls; these differences were not statistically significant. The overall incidence of stroke was similar for the ranibizumab group versus the comorbidity-matched controls and sociodemographic-matched controls, based on the multivariable Cox regression (hazard ratio [HR] =0.88; 95% confidence interval [CI], 0.60–1.30; HR=0.95, 95% CI, 0.65–1.41, respectively).

Conclusions: Ranibizumab treatment for neovascular AMD did not increase the overall risk of stroke, compared with comorbidity-matched controls or sociodemographic-matched controls.

Commercial Relationships: Sung Soo Kim, None; Tyler H. Rim, None; Christopher S. Lee, None; SungChul Lee, None; Do Wook Kim, None; Hyun Ju Park, None

Program Number: 548 **Poster Board Number:** A0185

Presentation Time: 1:30 PM–3:15 PM

Two year visual outcomes in patients with neovascular age-related macular degeneration treated with ranibizumab stratified by patient age and baseline visual acuity

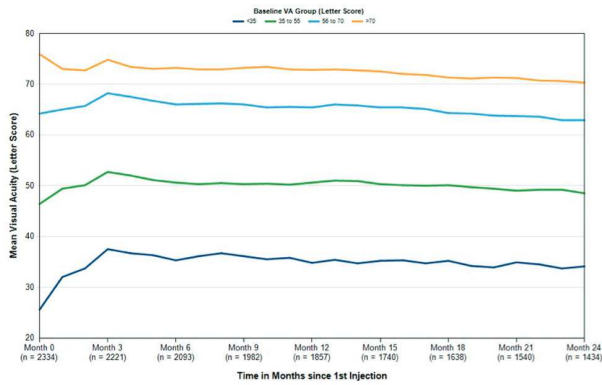
Elewys Hearne, Farid Afshar, Emily Fletcher, Quresh Mohamed, Rob Johnston. Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, United Kingdom.

Purpose: To report 2 year visual outcomes stratified by age and baseline visual acuity in patients with neovascular age-related macular degeneration (nAMD) treated with intravitreal ranibizumab in Gloucestershire NHS trust, UK.

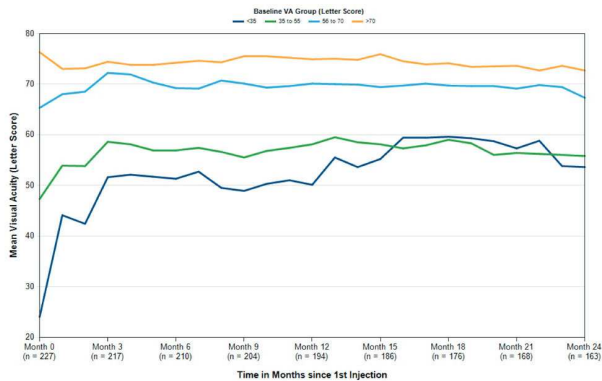
Methods: Data was collected prospectively using an electronic patient record system. Baseline visual acuity (VA) was categorised as under 35 letters, 35-55 letters, 56-70 letters and over 70 letters.

Results: In the groups with VA over 56 letters at baseline there was a slight deterioration in vision over 2 years. In the 56-70 letter group mean VA at baseline was 64.6 letters and 59.6 letters at 2 years. In the over 70 letters group mean VA was 74.7 letters and 70.3 letters respectively. In the 35-55 letters group mean VA remained stable from 45.2 to 43.9 letters. In the under 35 letters group mean VA improved from 24.4 to 27.5 letters (Figure 1). This pattern was reflected for baseline VA in the age groups 71-80, 81-90 and over 91. The largest improvement in mean VA was found in patients under 70 years old in the lower baseline VA groups. In patients aged under 70 years old mean VA in the under 35 letters group and 35-55 letters group improved from 25.5 to 59.4, and 47.1 to 59.8 letters respectively (Figure 2).

Conclusions: This large data set identifies that visual outcome in patients with nAMD treated with intravitreal ranibizumab is dependent on baseline visual acuity. The greatest improvement in visual outcome is found in younger patients with poor visual acuity at baseline.



Mean visual acuity of neovascular age-related macular degeneration patients of all ages, over time by baseline visual acuity groups, during the 2 year treatment with ranibizumab.



Mean visual acuity of neovascular age-related macular degeneration patients aged under 70 years old, over time by baseline visual acuity groups, during the 2 year treatment with ranibizumab.

Commercial Relationships: Elewys Hearne, None; Farid Afshar; Emily Fletcher, None; Quresh Mohamed, None; Rob Johnston, None

Program Number: 549 **Poster Board Number:** A0186

Presentation Time: 1:30 PM–3:15 PM

Non-responders to multiple ranibizumab injections in treatment of exudative age-related macular degeneration and the effect of the switch treatment to aflibercept

Katerina Manethova, Jan Ernest, Pavel Nemeč, Leos Rejmont, Fredy M. Folleco. Department of Ophthalmology of 1st Faculty of Medicine of the Charles University and the Military University Hospital Prague, Military University Hospital Prague, Prague, Czech Republic.

Purpose: Ocular anti-VEGF therapy has been in wide clinical use for many years. ANCHOR, MARINA and other follow-up trials proved high treatment efficiency, stabilization of visual functions after treatment and in significant amount of cases visual gain as well. However, anti-VEGF therapy is not successful in every patient with exudative AMD. Many eyes with regular dosing of ranibizumab injections manifest persistent fluid on time-domain optical coherence tomography (OCT) which limits further visual improvement. Now, 10 years after anti-VEGF treatment was introduced, it starts to show that approximately 12-17% of patients do not respond sufficiently to this treatment.

Methods: Retrospective cohort of 207 treatment naïve patients were treated with ranibizumab injections in pro re nata (PRN) regime. As

non-responders were assessed patients with visual loss ≥ 0.2 logMar and with evidence of persistent fluid on OCT.

Non-responders to ranibizumab treatment were switched to aflibercept treatment in fixed regime (2.0 mg aflibercept administered every 4 weeks for the first 3 months and then every other month).

Results: Results include the assessment of annual monitoring of 45 eyes after switch to aflibercept therapy. Following parameters were assessed: mean change in Early Treatment Diabetic Retinopathy Study best corrected visual acuity (ETDRS BCVA), central subfield retinal thickness (CRT), number of patients with no fluid on OCT and patients who lost > 15 letters.

Conclusions: The treatment switch from ranibizumab to aflibercept resulted in anatomical improvements. In the observed group, the central retinal thickness was reduced from the original 391,2 μm to 322,8 μm at the end of the observed period, but the change was not statistically significant.

Despite no improvements to the best-corrected visual acuity values, stabilisation of visual functions and OCT (optical coherence tomography) post therapy switch (due to non-response to the originally administered treatment connected with visual functions loss) represents both anatomical and functional success.

Non-responders percentage representation in the observed group (14,5 %) corresponds to the available published data.

In one case, tachyphylaxis developed gradually also to the Eylea treatment (aflibercept). After ranibizumab re-administration, anatomical and functional values stabilised

Commercial Relationships: katerina manethova; Jan Ernest, None; Pavel Nemeč, None; Leos Rejmont, None; Fredy M. Folleco, None

Program Number: 550 **Poster Board Number:** A0187

Presentation Time: 1:30 PM–3:15 PM

Eight Week Maintenance Dosing of Intravitreal Bevacizumab for Neovascular Age-Related Macular Degeneration

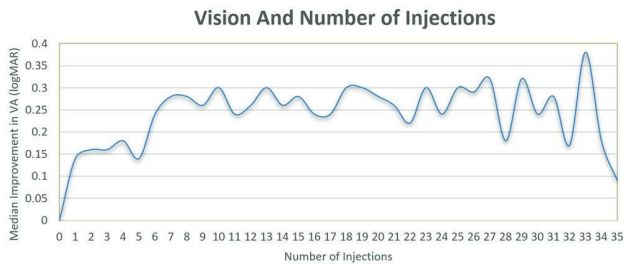
Tomas A. Moreno, Shriji Patel, Stephen J. Kim. Ophthalmology, Vanderbilt University, Nashville, TN.

Purpose: The purpose of the study is to analyze the long term visual acuity outcomes for the treatment of neovascular age-related macular degeneration (AMD) with every 8 week dosing of maintenance bevacizumab injection after an initial monthly series of injections.

Methods: This was a retrospective analysis of visual acuity data of 37 eyes of 33 patients treated with every 8 week maintenance bevacizumab injections for neovascular AMD with at least 16 months of follow up by a sole practitioner. Monthly injections were followed by every 8 week injections for the remainder of the time the patient was managed. Eyes were selected by obtaining the records of all patients in the year 2012 and 2011 with the ICD-9 code of wet age-related macular degeneration by a sole practitioner. Inclusion criteria included new diagnosis of neovascular AMD, no prior treatment for AMD, at least 1.5 year follow up, and maintenance bevacizumab injections of every 8 weeks without extension past 8 weeks. Injection number 11, 17, and 23 were used to estimate 12 month, 24 month, and 36 month time points.

Results: Visual acuity data of 37 eyes of 33 patients was analyzed. Mean follow up time was 3.4 years and mean number of injections per eye was 24.5. Improvement in visual acuity of 15 letters or more was seen in 43% of eyes at roughly 12 months (n=37) 41% of eyes at 24 months (n=32) and 44% of eyes at 36 months (n=25). Prevention of the loss of 15 letters or more was seen in 97% of eyes at 12 months, 94% of eyes at 24 months and 92% of eyes at 36 months. Average letters gained from baseline at 12 months, 24 months, and 36 months were 16, 13, and 12.5 respectively.

Conclusions: Every 8 week maintenance bevacizumab injections for neovascular AMD provides long-term, sustained gains in visual acuity over a three year period comparable to recent reports with ranibizumab.



Commercial Relationships: Tomas A. Moreno, None; Shriji Patel, None; Stephen J. Kim, None

Program Number: 551 **Poster Board Number:** A0188
Presentation Time: 1:30 PM–3:15 PM
Bevacizumab dosing every 2 weeks for neovascular age-related macular degeneration refractory to monthly dosing
Amit Meshi, Ori Segal. Ophthalmology, Meir Medical Center, Tel Aviv, Israel.

Purpose: To evaluate the efficacy of bevacizumab dosing every 2 weeks in patients with neovascular age-related macular degeneration (nvAMD) refractory to monthly dosing.
Methods: A retrospective chart review of nvAMD patients unresponsive to conventional monthly dosing of anti-vascular endothelial growth factor (VEGF) therapies which received one course of 3-4 intravitreal bevacizumab injections every 2 weeks.
Results: Twenty seven eyes of 24 patients (13 females) were identified. Mean (\pm SD) age was 82.08 ± 6.85 years. All patients failed monthly bevacizumab, 17 patients (70.8%) also failed monthly ranibizumab and 3 patients (12.5%) were unresponsive to all three anti-VEGF drugs. The mean (\pm SD) number of prior anti-VEGF injections was 21.33 ± 6.8 . Bevacizumab injections during the treatment course were administered at a mean (\pm SD) interval of 15.4 ± 1.37 days. Patients were examined 5.13 ± 1.67 weeks (\pm SD) after the last injection. The mean (\pm SD) logarithm of the minimum angle of resolution (logMAR) visual acuity did not change significantly between baseline (0.72 ± 0.59) and follow-up (0.76 ± 0.66 , $P = 0.56$). The objective spectral-domain optical coherence tomography (SD-OCT) parameters (mean central macular thickness and mean macular volume) did not change significantly between baseline and follow-up ($P > 0.05$). Six eyes (22.2%) showed anatomic improvement on SD-OCT scans, while 19 eyes (70.4%) remained stable.

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Conclusions: Biweekly bevacizumab dosing may cause anatomic benefit in some chronic cases of nvAMD refractory to anti-VEGF monthly dosing.

Commercial Relationships: Amit Meshi, None; Ori Segal, None

Program Number: 552 **Poster Board Number:** A0189
Presentation Time: 1:30 PM–3:15 PM
Randomized Clinical Trial Evaluating Reflux, IOP, and Pain, Following Intravitreal Anti Vascular Endothelial Growth Factors Injections Using 30g and 32g Needles

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Purpose: To assess the differences in reflux, IOP and pain scores, between intravitreal injections (IVI) performed with 30g and 32g needles.

Methods: A prospective, randomized interventional study of patients who required bilateral intravitreal anti-VEGF injection ($n=61$). One eye was randomized to receive a 30g needle and the contralateral eye to 32 g. Immediate postinjection reflux, our primary outcome, was noted at the time of injection and recorded as a binary outcome (yes or no); pain was quantified using a VAS pain scale and IOP pressure was measured before and 5 minutes after IVI. Our study was designed to detect a 10% difference in the proportion of patients with reflux, assuming an alpha of 0.05 and power of 80%.

Results: Postinjection reflux was present 40% in 30G and 24% in those who received injection with a 32G needle ($x^2=4.5$; p -value = 0.033). A trend was noted whereby eyes randomized to 32 g needle had less pain (31% reported no pain as compared to 23% in the 30 g Group). A trend was noted for a higher IOP with a 31% elevation in the 32 g Group, as compared to 25% in the 30 g Group. On average, patients preferred the 32 g needle.

Conclusions: In this study, 32 g Needles are associated with less postinjection reflux, a trend toward less pain, but a trend towards a transient increase in IOP. A patient preference for 32 g Needles was noted.

Commercial Relationships: Saeed Alshahrani, None; Vasudha Gupta, None; Uriel Rubin, None; Tom Gonder, None; Isabella Irrcher; Sanjay Sharma, None

Program Number: 553 **Poster Board Number:** A0190
Presentation Time: 1:30 PM–3:15 PM
The CNV Associated with PRPH2 C213W Missense Mutation Responds Favorably to Anti-VEGF Injections

Monique J. Leys, J Vernon Odom. Ophthalmology, WVU Eye Institute, Morgantown, WV.

Purpose: To describe a family with a new dominantly inherited Peripherin 2 missense mutation. There was a very favorable response to treatment for subretinal neovascularization in 4 affected eyes.

Methods: We describe a new PRPH2 mutation (C213W) in a 66 yr old female. She had undergone treatment for subretinal neovascularization for the last 10 years (PDT, intravitreal steroids and antiVEGF). Visual acuity at last exam was 20/25 in each eye.

Her 65 yr old sister had a 13 year history of subretinal neovascularization and had received antiVEGF treatment in both eyes with few injections and excellent response to treatment and best corrected visual acuity of 20/20 and 20/40. The 31 year old daughter presented with flavimaculatus like flecks and had a BCVA of 20/20.

Results: A pathogenic missense mutation [C213W] in the PRPH2 gene (c.639 C>G p.Cys213Trp) was found and confirmed (EyeGENE and GeneDx). This mutation has not previously been reported to our knowledge.

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In this family with low intrafamilial variability the subretinal neovascularization appears to occur in the sixth decade. The response to treatment is excellent and there is relatively slow growth of the CNV and limited subretinal atrophy.

Conclusions: This is the first report of PRPH2 (RDS) C213W missense mutation in a family with autosomal dominant pattern dystrophy. The associated subretinal CNV appears to respond well to anti-VEGF treatment.

Commercial Relationships: Monique J. Leys, None;
J Vernon Odom, None