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A Review of Identification and Management of Retinal Disorders Among Diabetic Patients

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ABSTRACT: Diabetes mellitus is commonly known as diabetes, is a form of metabolic disorder characterized by increased blood sugar levels over a long period.Symptoms of high blood sugar includes polydypsia, polyphagia, polyuria. If left untreated, it can cause severe complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycaemic state, or it leads to death. Chronic complications include cardiovascular disease, stroke, chronic kidney disease,and cause damage to eyes.

Keywords: **Diabetic retinopathy, patients, treatment, blood sugar, complications.**

RETINAL DISORDERS AMONG DIABETIC PATIENTS:

1) Diabetic Retinopathy:

Ranibizumab 0.5 mg Combined with Panretinal Photocoagulation versus Panretinal Photocoagulation Monotherapy in High-Risk Proliferative Diabetic Retinopathy Patients with 12-Month PROTEUS Results.

Introduction:

The PROTEUS study compared the efficacy and safety of ranibizumab 0.5 mg (RBZ) + panretinal photocoagulation (PRP) versus PRP monotherapy in high-risk proliferative diabetic retinopathy (HR-PDR) patients over 12 months (M).

Methods:

A phase II/III, multicenter, prospective, open-label study that included patients (≥18 years) with Type I or II diabetes and HR-PDR. Patients (N = 87) were randomized (1:1) to receive RBZ+PRP (n = 41) or PRP monotherapy (n = 46). The RBZ + PRP group received 3 monthly RBZ injections along with standard PRP. The PRP monotherapy group received standard PRP between day 1 and M2; thereafter, treatments in both groups were at the investigators' discretion. Key objectives were to compare the efficacy of RBZ+PRP versus PRP monotherapy in neovascularization (NV) area regression (NV total [NVT], NV in disc [NVD], and NV elsewhere [NVE]) over 12M (primary); complete NVT remission at M12; mean best-corrected visual acuity (BCVA) at M12; treatment exposure; and safety (secondary). Results: Seventy-seven patients (88.5%) completed the study. Overall baseline demographics were similar for both groups. At M12, 92.7% of patients in the RBZ+PRP group presented NVT reduction versus only 70.5% of the PRP monotherapy patients (p = 0.009). The number of patients with NVD and NVE reductions were higher with RBZ+PRP (93.3% and 91.4%, respectively) versus PRP (68.8% and 73.7%, respectively); significant only for NVE (p = 0.048). Complete NVT remission was 43.9% in RBZ+PRP group versus 25.0% in PRP monotherapy group (p = 0.066). At M12, the mean BCVA was 75.2 letters in RBZ+PRP group versus 69.2 letters in PRP monotherapy group (p = 0.104). In the RBZ+PRP group, the mean number of treatments over 12M were 4.6 (RBZ) and 3.5 (PRP). No deaths were reported.

Conclusions:

Ranibizumab + PRP was more effective versus PRP monotherapy for NV regression, in HR-PDR patients over 12M. Overall, ranibizumab + PRP was well tolerated with no new safety findings.

Trans-Scleral Subthreshold Micropulse Diode Laser for Treatment of Diabetic Retinopathy.

Introduction:

Full thickness retinal damage may not be needed to obtain beneficial effect from laser. The retinal pigment epithelium (RPE) plays a significant role in repairing the outer and inner blood-retinal barrier regardless of the type and location of laser application. The absence of micropulse chorioretinal laser damage permits re-treatment of the same area. Our aim is to study the effect of diabetic retinopathy treatment by trans-scleral subthreshold micropulse diode laser.

Methods:

This study included 46 eyes of 34 patients who had diabetic macular edema and/or proliferative diabetic retinopathy. Patients were divided into 2 groups: Group 1 has macular edema thickness less than 400 µm. Group 2 has proliferative diabetic retinopathy with vitreous hemorrhage. Trans-scleral micropulse diode laser treatment was given to the periphery of the retina. Laser sitting ranged from 1 to 3 in the first group and up to 5 sittings in the second group. The same laser parameters were used for each patient. Only the number of laser shots varied between patients. Pre-laser treatment and in follow up, visual acuity, OCT, colored fundus photo and fluorescein angiography were done.

Results:

Patient follow-up ranged between one month to one year. Visual acuity was improved in 68% of treated eyes in group 1, and in 84% of eyes in group 2. Statistically significant reduction of macular edema was in 70% of eyes in group 1. Total disappearance of vitreous hemorrhage and reduction of diabetic retinopathy were observed in 80% of eyes in group 2. No adverse laser events occurred, no laser lesions were detectable clinically or angiographically after treatment.

Conclusions:

Trans-scleral subthreshold micro pulse diode laser treatment of diabetic macular edema and proliferative diabetic retinopathy is an easy new technique, effective and safe treatment way[1].

2) Choroid Thickness in Patients with Diabetes Mellitus:

Introduction:

To compare choroidal thickness (CT) in patients diagnosed with diabetes mellitus (DM), with and without diabetic retinopathy (DR). Then evaluate, in the subgroup with DR, the changes in CT according to the parameters: Proliferative DR (PDR) and the treatments performed (photocoagulation or anti-angiogenic injection).

Methods:

Cross-sectional analysis of the results obtained from a non-random sample of 62 eyes of DM patients, followed at the Ophthalmology appointment, from May to July 2015. Optical Coherence Tomography (OCT), using the enhanced depth imaging (EDI) program, was performed on all patients. CT values were measured manually. Comparison of CT between patients with (n = 42) and without RD (n = 20) was performed.

Results:

Subfoveal CT was not statistically significant higher in patients without DR (223.80 µm vs. 218.31 µm, p = 0.833). When only the subgroup with DR was analyzed, we observed that the CT is not significantly higher in the non-proliferative DR (Subfoveal CT with PDR = 206.67 µm vs. without PDR = 220.25 µm, p = 0.586). The same was observed in patients receiving anti-angiogenic treatment, lowest CT in patients who had this treatment. CT is statistically significantly higher in patients treated with photocoagulation (mean central CT, p = 0.006 and subfoveal CT, p = 0.029).

Conclusions:

CT seems to decrease when the eye begins to be one of the affected organs, in patients with DM. This study gives us an indication that the more severe DR, the more CT appears to decrease, as there is a lower CT in patients with proliferative DR and in those who required anti-angiogenic treatment. In contrast, in diabetic patients who underwent photocoagulation of the peripheral retina, there is a significant increase in CT at the macular level, appearing to be a response of the choroidal circulation to the decrease of the retinal tissue in ischemia[2].

3) Diabetic Macular Edema Switch from Bevacizumab to Ranibizumab Results:

Introduction:

Diabetic Retinopathy (DR) is the leading cause of blindness in the working age population of industrialized societies. Vascular Endothelial Growth Factor (VEGF) is a major driver of retinal changes in DR. Diabetic Macular Edema (DME) is an important cause of visual loss and requires different therapeutic combinations.

Methods:

Retrospective unicentric study, including patients with visual impairment secondary to DME submitted to at least three intravitreal injections (IVT) of Bevacizumab that had to be switched to Ranibizumab due to an institutional policy decision. Best

corrected visual acuity (BCVA) and anatomic outcomes with macular OCT at the baseline time, before anti-VEGF, after switch and in the last visit were obtained as well as other associations such as hypertension, insulin therapy, additional treatments or vitreoretinal interface pathology. Complete clinical information, macular OCT in the different periods and a minimum follow-up of 6 months were considered since last IVT.

Results:
A total of 35 eyes of 35 patients were included, 57.1% female. Mean age was 64.91 (SD 7.61) years old. Central Macular Thickness (CMT) averages were 577.69 (SD 157.53) µm; 562.23 (SD 189.51) µm after Bevacizumab and 361.09 (SD 133.62) µm after switch to Ranibizumab ($p < 0.05$). Mean BCVA at baseline was 0.89 (SD 0.35); after Bevacizumab 0.86 (SD 0.35) and in the final visit 0.70 (SD 0.32) ($p < 0.05$). Significant anatomical differences were identified in macular OCT after switch ($p < 0.05$). The mean number of Bevacizumab injections pre-switch was 4.09 (SD 1.03) and the mean number of Ranibizumab after switch was 3.11 (SD 1.51).

Conclusions:
Intravitreal anti-VEGF switch from Bevacizumab to Ranibizumab was demonstrated to be effective in this real life study, improving the functional and the anatomical results. The results are consistent with the well-known results for IVT switch in other bigger series[3].

4) Analysis and Comparison of Outer Retinal Layers Between Healthy Patients and in Type-2 Diabetes Mellitus Patients Without Diabetic Retinopathy:

Introduction:
The aim of this study is to measure and compare domelike appearance of inner outer segment junctions (IS/OS bulge) and external limiting membrane (ELM bulge) in healthy patients and in type 2 diabetes mellitus (DM) patients without diabetic retinopathy (DR) with the same age and gender distribution ($p > 0.05$; Mann-Whitney and Chi2, respectively), using optical coherence tomography (OCT).

Methods:
We analysed one hundred and seventy eyes of 82 males and 88 female, of which 97 were healthy patients while 76 had type 2 DM. OCT images were taken using a Cirrus HD-OCT 4000 (Carl Zeiss Meditec Inc., Dublin, CA; version 5.0.0). Outer foveal layers were classified as continuous (cat_2), discontinuous (cat_1), and no visible (cat_0). IS/OS thickness was defined as the distance between the IS/OS hyperreflective line and the inner border of the retinal pigment epithelium (RPE). ELM thickness represented the distance between this line and the inner border of RPE.

Results:
ELM, IS/OS and COST layers showed cat_2 in all healthy patients, whereas in type 2 DM patients EML displayed cat_2 = 96%, IS/OS = 98.7%. COST layer displayed cat_2 = 49.3% and cat_1 30.3% Mean IS/OS thickness was 44.08 µm (range: 50–38) with a standard deviation (SD) of 5.734 µm for healthy patients. DM patients showed IS/OS thickness = 34.61 µm (range: 40–28 µm) and SD = 6.263 µm. Mean ELM thickness was 72.32 µm (range: 84–60 µm), with SD = 12.52 µm for healthy patients. DM patients showed ELM thickness = 59.02 µm (range:67–50 µm) and SD = 8.04 um. In diabetics, both (IS/OS) and (ELM) showed a significant tendency to be shorter compared to the control group ($p = 0.0001$; Mann-Whitney test).

Conclusions:
Type 2 DM patients without clinical signs of DR tend to lose foveal bulges. This early alteration in central cone membranous discs might be related to the pathogenesis of DM[4].

5)Choroideremia: Findings in the Carrier State Plaza.

Introduction:
To further describe the findings in the unusual symptomatic CHM carrier state.

Methods:
Case report.

Results:
A 50-year-old woman presented with visual loss throughout the last year, as well as a molecular carrier state diagnosis of mutation c.161+1G>C in the CHM gene. Fundus examination showed atrophy of the RPE and choroid spreading to periphery and central retina, with large choroidal vessels on the naked sclera. Foveal structures were conserved in the right eye. A neovascular membrane was found in the left eye and treated with intravitreal ranibizumab. Fluorescein angiography demonstrated lack of filling of the choriocapillaris, with the right eye normal fovea showing hypofluorescence surrounded by the hyperfluorescence due to the window defect. Bilateral visual field defect with greater central impairment of the OS was detected. ERG showed markedly diminished amplitude of peripheral rings of both eyes. OCT angiography displayed areas of flow loss in the choriocapillaris and choroid.

Conclusions:
Choroideremia is a rare retinal dystrophy, in which female carriers often demonstrate slight patchy defects of the RPE or peripheral pigmentary granularity. However, severe retinal damage is possible, even in carriers, likely due to unbalanced X-chromosome inactivation. The ERG should be normal in female carriers even with characteristic fundus changes. However, abnormal responses may be in carriers with a dark-adapted white flash, a dim blue flash or a flickering stimulus, there are no specific test results in carrier status. It is important to consider that in such patients, the response of the abnormal retinal pigment epithelium can develop a CNV. Fibrosis due to neovascularization has been reported in few cases. New techniques of retinal imaging such as OCT angiography are allowing the best characterization of this kind of dystrophies and its progression[5].

6)Whipple's Disease and Ophthalmologic Complication:

Introduction:
Whipple's disease is a chronic bacterial infectious disease caused by Tropheryma whipplei, for which a genetic predisposition is suspected. Many structures can be affected including joints, the heart, the central nervous system, and the digestive system.

Methods:
We report the case of a 40-year-old patient referred by neurologists for a 1-month decline in bilateral visual acuity associated with hypoacousis, extrapyramidal syndrome, and vertigo. Initial examination found a visual acuity of 6.3P6/4P8 with a bilateral papillary pallor with neither retinal lesions nor hyalitis. Examination of the papilla on OCT confirmed bilateral optic atrophy and a diffuse atrophy of the ganglion cell layer. A concentric and bilateral narrowing of the visual field was found on Goldman, associated with a dyschromatopsia of blue-yellow axis. A cerebro-spinal MRI was normal. The ICG found a choroidal granulomatosis with multiple late hypocyanescent foci around the vascular arches. A sarcoidosis was initially suspected upon presence of mediastinal lymphadenopathy and upon biopsy of accessory salivary glands; the patient was placed under general corticosteroid therapy. After a quick improvement, the patient became worse when the treatment decreased. A PCR test for T. whipplei, as part of broader systematic investigations in internal medicine, returned as positive. The patient was treated with doxycycline, plaquenil and sulfamethoxazole trimethoprim for a probable Whipple disease with choroidal granulomatosis.

Results:
It is clear that the diagnosis of Whipple's disease is difficult to make, because of ocular involvement and complementary examination mimicking sarcoidosis. It was a systematic investigation into this atypical clinical picture that made it possible to eventually correct the diagnosis.

Conclusions:
Ophthalmologic involvement is rare in Whipple's disease: it appears late and must be considered upon presentation of bilateral choroidal granulomatosis in the context of general atypical pathology. Its rarity makes it a difficult diagnosis to make. Collaboration with internal medicine will help correct the diagnosis[6].

7) A Different Approach to Idiopathic Uveal Effusion Syndrome:

Introduction:
Idiopathic uveal effusion syndrome (IUES) is caused by a histochemical disorder in the sclera that produces a malfunction in the ocular venous drainage, this leads to disorders in nearly every ocular structure. The presumption diagnosis is clinical and the treatment options are limited with few described successful cases and a controverted management.

Methods:
Case report. Patient monitored with optical coherence tomography and ocular B-scan ultrasound imaging. Treated with scleral surgery.

Results:
A 50 year-old male, with chronic bronchitis, came to ophthalmology emergency room with red right eye (OD) and visual acuity (VA) 0.3 logMAR. In the biomicroscopy of OD there was dilated episcleral veins, narrow anterior chamber, intraocular pressure of 32 mm Hg, papilla edema and 360º serous peripheral retinal detachment (RD) that partially affected the macula with cystic macular edema. There was not any other remarkable finding. The left eye was normal. The B-scan ultrasonography showed a 360º ciliary body detachment. The axial length was normal. Orbital nuclear magnetic resonance and angio-computed tomography was performed and an arterio-venous fistula or any other compressive mass was ruled out; an OD little thickened sclera was described. The corticosteroid treatment worsened the serous RD and the VA diminished. We opted for surgical treatment (4 rectangular scleral flaps of 6 x 4 mm of 2/3 thickness, anterior to the equator) to improve the vortex vein drainage with little success.

Conclusions:
IUES results in a challenging diagnosis and treatment. In our case, corticosteroids worsened the symptoms and signs, and the surgery was insufficient. Other publications describe more aggressive treatments (4 scleral flap of 2/3 thickness 4x5 mm with scleral excision of 3x4 mm exposing the choroid, Ex-PRESS shunt inserted obliquely in the sclerotomy), some with better success. More publications and new therapeutic strategies addressed to increase the venous drainage would be necessary to reach an IUES management consensus[7].

8) Cystoid Macular Edema After Laser Retinopexy of a Retinal Break:

Introduction:
Acute symptomatic flap retinal tears are at greater risk of progressing to retinal detachment and these cases are generally treated prophylactically. In most cases laser retinopexy is the optimal technique as it is more precise, causing less collateral retinal damage, with a likely lower risk of epiretinal membrane formation than cryotherapy. Cystoid macular edema is rare after this treatment.

Methods:
The authors report the case of a 60 year-old woman, previously healthy, who was submitted to laser retinopexy of an acute symptomatic flap retinal tear of the left eye. Three weeks later, she complained of ipsilateral vision blurring. A complete ophthalmological evaluation and optical coherence tomography (OCT) were performed.

Results:
The best corrected visual acuity (BCVA) in the right eye was 20/20 and in the left eye was 20/50. Anterior segment observation was normal. Fundus examination revealed, in left eye, macular edema and adequate thermal barrier of the retinal break. No traction was found. Cystoid macular edema was confirmed by OCT. Topical treatment with nepafenac 1 mg/ml tid was prescribed. One month later BCVA in left eye was 20/200 and macular edema persisted. A different approach with combined intravitreal ranibizumab and subconjunctival triamcinolone acetonide injection was implemented. Two months after the injections, BCVA was 20/20 with resolution of the macular edema. Six months later, patient remained asymptomatic.

Conclusions:
Cystoid macular edema after laser retinopexy of a retinal break is rare, but can be adequately managed with a combined treatment of intravitreal ranibizumab and subconjunctival triamcinolone acetonide injection. This approach seems to be secure and effective in this condition[8].

9) Comparative Analysis of Treatment of Retrobulbar Neuritis:

Introduction:
The prevailing part of the inflammatory diseases of the optic nerve (ON) account for optic neuritis. In most cases, this pathology affects young people. Moreover, in 22%–25% of patients, the outcome of the disease, atrophy of the optic nerve, will grow with its serious violations of visual and visual fields.

Objective:
To compare the results of treatment of retrobulbar neuritis (RBN).

Methods:
The study included 28 patients (38 eyes) with RBN. All patients were divided into 2 groups. In the first (control) group (18 eyes) was applied the traditional treatment: antibiotics, decongestants, desensitizing and neuroprotective therapy, and besides those glucocorticosteroids (GCS) was administered dexamethasone in 0.5 ml parabulbarly during 7 days. In the second (main) group (20 eyes) was applied the same scheme of treatment, corticosteroids have applied as follows: 0.5 ml dexamethasone parabulbarly during 7 days, from the 8th day diprospan parabulbarly 0.5 ml single dose, and thereafter dexamethasone 0.1% in drops under the scheme.

Results:
Visual acuity increased at 1 month in group 2 from 0.4 to 0.6 in 7 cases, up to 0.7–1.0 observed in 8 cases, while in group 1, the visual acuity of 0.4 to 0, 6 notes only in 4 cases, from 0.7 to 1.0 were observed. According to the VEP in the study groups showed an increase in latency and decrease of amplitude, slowing of the pulse of 9 patients before treatment. After treatment, the amplitude of the VEP in the control group was not significantly increased in 7 patients. In the 2 group, it increased in 12 patients.

Conclusions:
Within 3–6 months after the treatment in the control group we observed recurrence of the disease in 6 patients, and in group 2 the recurrences were not observed[9].

10) Novel Homozygous Splicing Mutation in Mertk-Gene (RP38) Causing Recessive Retinal Dystrophy:

Introduction:
Describe genetic and ocular findings of a 12-year-old Italian girl showing cone-rod "pisciformlike" macular dystrophy to broaden the molecular spectrum of MERTK gene.

Methods:
Complete ophthalmological examination implemented with: OCT, autofluorescence, FA, ICGA, electrophysiology (flicker-ERG, pattern-ERG, PEV), contrast sensitivity, chromatic sense, computerized visual field (120p,30/2), orthoptic evaluation. The patient was followed from the age of 4 with final differential diagnosis between Stargardt disease and cone-rode dystrophy pointed out 8 years later, then investigated by geneticist. A panel of nearly 100 retinal dystrophy disease-causative genes was analyzed by next-generation sequencing techniques for diagnostic purpose. After a putative mutation was identified, Sanger sequencing confirmation of the distinct genomic fragment as well as segregation analysis in the family were performed. The pathogenic role of the mutation was predicted by in silico models.

Results:
The patient underwent craniotomy at age seven months for meningocele. Visual impairment was first noticed at 6 years of age and progressively increased until stabilization at 4/20 bilaterally. Severe dysfunction of both photoreceptor systems involved the macula at an early stage. Other findings include: nyctalopia, photoaversion, dyscromatopsia, visual field centrocecal mixed scotoma to the mid periphery, ERG b wave reduced in RE and absent in LE, reduced macular thickness (168 microns), RPE drusen-like changes, photoreceptors thinning with high reflectance bodies below the outer limiting membrane, without CME, discrete dot-like autofluorescent deposits hypocianescent on ICGA (hallmark of MERTK-specific retinal dystrophies). A nucleotide change affecting an obligatory splice site of intron 10 of the MERTK gene (c.1604+5G>A) was depicted in the proband in a homozygous state, while her parents were heterozygote carriers.

Conclusions:
We report a novel homozygous splicing mutation in the MERTK gene (OMIM*604705) emphasizing distinct ophthalmologic features of this rare cause of AR-retinal dystrophy (overall1%). In the personalized medicine era, a multidisciplinary approach allows precise diagnosis of retinal dystrophy and genebased pharmacological trials planni ng[10].

11) Argus II Retinal Prosthesis System Treatment:

Introduction:
The Argus II Retinal Prosthesis System (Second Sight Medical Products, Inc, Sylmar, CA) was developed to restore some vision to patients blind as a result of retinitis pigmentosa (RP) or outer retinal degeneration.

Methods:
10 Retinitis Pigmentosa patients have been implanted at the KKESH: 3 female and 7 male, average age 41.3 years, 6 OD and 4 OS implanted eyes. Mean duration was 2.1 years. The primary outcome measures were safety (the number, seriousness, and relatedness of adverse events) and visual function, as measured by 2 computer-based, objective tests.

Results:
All 10 patients remained implanted with functioning Argus II Systems at 4 years after implantation. Only 1 additional serious adverse event (suture exposure over the coil suture tab and over the inferior case suture tab) was experienced 2-years postimplant. Patients performed significantly better with the Argus II on than off on all visual function tests and functional vision tasks (Square Localization: mean error across the population of tested patients was 8.83 cm [SD 0.94 cm] while it was 16.11 cm [SD 1.56 cm] with the system "off"; Direction of Motion: mean error across the population of tested patients was 81.32 degrees [SD 6.22 degrees] while it was 90.60 degrees [SD 5.90 degrees] with the system "off."). This demonstrates the clinical benefit that Argus II patients implanted in our center receive, and it translates into real life improvements for the majority of patients.

Conclusions:
The 10 KKESH Argus II patients demonstrate a safety profile that is at up to 4 years post-implantation markedly better than that observed in the developmental phase of Argus II. The results confirm previous reports on the ability of the Argus II prosthesis to provide visual function and functional vision over several years of chronic device use[11].

12) Predictors for the Response to Antiangiogenic Therapy in Patients with Myopic Choroidal Neovascularization:

Introduction:
Factors influencing the efficacy of antiangiogenic therapy in patients with myopic choroidal neovascularization (mCNV) are limitedly studied. The purpose was to study ophthalmological and immunological parameters to find predictors of therapeutic response to anti-VEGFs in mCNV.

Methods:
19 patients (15 females, 4 males, mean age ± SD was 48.52 ± 15.49 years) (19 eyes) with active mCNV treated with ranibizumab were included to the study. Myopic refraction varied from –3.5 to –15.5 D (mean ± SD – 9.45 ± 4.73D). All patients underwent detailed ophthalmological examination during follow-up period (12 months). Immunological study of aqueous humor was performed before and 1 month after ranibizumab initial injection. Cytokines concentrations were measured using flow fluorometry with Bio-Plex Pro Human Cytokine Panel, 27-Plex («Bio-Rad Laboratories», USA).

Results:
CNV activity was suppressed in 17 patients (89.5%) with approximately 2.6 injections (from 2 to 4); these patients were considered as "good" responders. 2 patients (11.5%) received 7 ranibizumab injections during 12 months of follow-up, and the treatment was continued because of residual activity. The second group demonstrated "poor" response to the therapy characterized by myopic refraction –4.25 and –3.75 D, axial length not exceeding 26.0 mm (24.5 and 25.7 mm), higher baseline subretinal neovascular membrane length (more than 1230 μm) and macular volume (10.4 and 10.9 mm3 compared to 9.37 ± 1.2 mm3 in "good" responders). These two patients were also characterized by relatively high baseline VEGF level (159.58 and 368.03 pg/ml) and inflammatory cytokine IL-2 level (49.32 and 53.27 pg/ml compared to 25.11 ± 27.99 pg/ml in "good" responders); the level of PDGF – BB was below sensitivity threshold (<1.8 pg/ml compared to 21.70 ± 24.89 pg/ml in "good" responders).

Conclusions:
A number of ophthalmological and immunological characteristics that could be considered as possible predictors for the response to anti-VEGF therapy in mCNV were found, which requires further studies[12].

13) Ranibizumab versus Verteporfin Photodynamic Therapy in Asian Patients with Myopic Choroidal Neovascularisation: 12-Month Results from BRILLIANCE:

Introduction:
BRILLIANCE was a 12-month (M), phase III, randomised, double-masked, active-controlled study that evaluated the efficacy and safety of ranibizumab 0.5 mg versus verteporfin photodynamic therapy (vPDT) in Asian patients with myopic choroidal neovascularization (CNV).

Methods:
Eligible adult patients (N = 457) were randomised into Group 1 (G1, n = 182; ranibizumab on day 1, M1 and thereafter as needed guided by visual acuity [VA] stabilisation); G2 (n = 184; ranibizumab on day 1 and thereafter as needed guided by disease activity); or G3 (n = 91; vPDT on day 1 and treated with ranibizumab or vPDT or both as needed guided by disease activity from M3). The study objectives included superiority assessment of both ranibizumab treatments versus vPDT with respect to mean average best-corrected VA (BCVA) change from baseline to M1–3 (primary), non-inferiority of G2 versus G1 with respect to mean average BCVA change from baseline to M1–6 (secondary), mean BCVA change, treatment exposure and safety over 12M.

Results:
Overall, 431 (94.3%) patients completed the study. At baseline, mean age was 51.2 years, majority were female (68.1%) and mean VA was 53.5 letters. Ranibizumab treatment in G1 and G2 was superior to vPDT (G1: +9.5, G2: +9.8 vs. G3: +4.5 letters; $p < 0.001$) based on mean average change in BCVA from baseline to M1–3. Ranibizumab in G2 was non-inferior to G1 with respect to mean average change in BCVA from baseline to M1–6 (10.7 vs. 10.4 letters, $p < 0.001$). The mean BCVA change was 12.0 (G1), 13.1 (G2) and 10.3 (G3) letters with a mean of 4.6 (G1), 3.9 (G2) and 2.6 (G3) ranibizumab injections. No new safety findings were identified.

Conclusions:
Ranibizumab treatment, with re-treatment guided by VA or disease activity, demonstrated superior efficacy in BCVA gain compared to vPDT in Asian patients with myopic CNV up to M3. Overall, ranibizumab was well tolerated[13]

14) Antiproliferative Effect of Rapamycin on Human Retinal Pigment Epithelial Cells:

Introduction:
Proliferative vitreoretinopathy (PVR) represents an excess wound healing process in retinal surgery and refers to the migration and proliferation of cells into the subretinal space and vitreous cavity. Retinal pigment epithelial (RPE) cells are the main effector cells in this process. PVR is the common cause of postoperative complications following ocular injuries and primary retinal detachment. We evaluated the effect of rapamycin on RPE cells in an in vitro model of wound healing.

Methods:
RPE cells were obtained from human donors without any history of eye disease and cultured in Dulbecco modified Eagle medium. Rapamycin was added at a concentration ranging from 1 ng/ml to 100 ng/ml. After 24 and 72 hours of incubation, proliferative activity was assessed by 5'-bromo-2'-deoxyuridine (BrdU) incorporation into cellular DNA and the amount of cell proliferation was determined using the 3-(4,5-dimethylthiazol2yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Additionally, to determine cytotoxicity of rapamycin, RPE cells were grown to confluence and subsequently cultured in a serum-deficient medium and after 24 hours of incubation with deferent concentrations of rapamycin, the MTT test was performed.

Results:
The BrdU assay demonstrates a significant dose-related decrease of DNA synthesis activity for increasing concentrations of rapamycin starting with 10 ng/ml ($P < 0.05$). The MTT test shows decrease of the number of RPE cells after the exposition to the drug concentrations starting with 5 ng/ml ($P < 0.05$) after 24 and 72 hours of incubation. No toxic effect of rapamycin on RPE cells was observed until maximal examined concentration of 100 ng/ml.

Conclusions:
Rapamycin inhibits RPE cell proliferation without evidence of cytotoxic effect in vitro. These results show that rapamycin may be a promising tool in vitreoretinal surgery[14].

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