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MD Research News

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Drug treatment

Retina. 2017 Apr 11. [Epub ahead of print]

VISUAL ACUITY IMPROVEMENT WHEN SWITCHING FROM RANIBIZUMAB TO AFLIBERCEPT IS NOT SUSTAINED.

Lee CS, Kim AJ, Baughman D, Egan C, Bailey C, Johnston RL, Natha S, Khan R, Brand C, Akerele T, McKibbin M, Downey L, Al-Husainy S, Lee AY, Tufail A.

PURPOSE: To assess whether visual benefits exist in switching to aflibercept in patients who have been chronically treated with ranibizumab for neovascular age-related macular degeneration.

METHODS: A multicenter, national, electronic medical record database study was performed. Patients undergoing six continuous monthly ranibizumab injections and then switched to continuous aflibercept were matched to those on continuous ranibizumab therapy. Matching was performed in a 2:1 ratio and based on visual acuity 6 months before and at the time of the switch, and the number of previous ranibizumab injections.

RESULTS: Patients who were switched to aflibercept demonstrated transiently significant improvement in visual acuity that peaked at an increase of 0.9 Early Treatment Diabetic Retinopathy Study letters 3 months after the switch, whereas control patients continued on ranibizumab treatment showed a steady decline in visual acuity. Visual acuity differences between the groups were significant ($P < 0.05$) at 2, 3, and 5 months after the switch. Beginning at 4 months after the switch, the switch group showed a visual acuity decline similar to the control group.

CONCLUSION: Transient, nonsustained improvement in visual acuity occurs when switching between anti-vascular endothelial growth factor agents, which may have implications in treating patients on chronic maintenance therapy on one anti-vascular endothelial growth factor medication.

PMID: 28406859

Ophthalmologica. 2017 Apr 11. [Epub ahead of print]

Bilateral Neovascular Age-Related Macular Degeneration: Comparisons between First and Second Eyes.

Chew JK, Zhu M, Broadhead GK, Luo K, Hong T, Chang AA.

PURPOSE: To compare 12-month outcomes and clinical presentations between first and second eyes of patients who developed neovascular age-related macular degeneration (nAMD) in both eyes and received ranibizumab intravitreal therapy (IVT).

METHODS: This is a retrospective case series of 45 patients undergoing IVT for unilateral nAMD who subsequently developed second-eye nAMD. At each visit, both eyes underwent visual acuity (VA) measurement and optical coherence tomography (OCT).

RESULTS: In second eyes, 53% were asymptomatic at baseline, with OCT retinal fluid as the only sign of nAMD among 33% of patients. In eyes with baseline VA >6/9, 82% of second treated eyes maintained this vision versus 12% of first eyes (p = 0.05). At 12 months, 70% of second eyes were fluid free versus 41% of first eyes (p = 0.02).

CONCLUSIONS: A large proportion of patients are asymptomatic at diagnosis of second-eye nAMD. Early intervention following earlier detection of nAMD in the second eye may lead to improved clinical outcomes.

PMID: 28395293

Ophthalmologica. 2017 Apr 13. [Epub ahead of print]

Comparison of pro re nata versus Bimonthly Injection of Intravitreal Aflibercept for Typical Neovascular Age-Related Macular Degeneration.

Mori R, Tanaka K, Haruyama M, Kawamura A, Furuya K, Yuzawa M.

PURPOSE: The aim of this study was to clarify the 1-year outcomes of pro re nata (PRN) and bimonthly intravitreal injections of aflibercept (IVA) for typical neovascular age-related macular degeneration (tAMD) after the initial 3 monthly IVA.

METHODS: We conducted a prospective, interventional study. Fifty-eight treatment-naïve patients with tAMD were randomly assigned to the PRN (30 patients) or the bimonthly (28 patients) treatment group. Both groups initially received 3 monthly IVA. Visual acuity, central macular retinal thickness (CRT), and central choroidal thickness (CCT) were evaluated at 12 months. Subanalysis was performed to identify factors associated with the best-corrected visual acuity (BCVA).

RESULTS: BCVA was significantly improved only in the bimonthly group at 12 months. CRT and CCT were significantly decreased in both groups. Subanalysis showed that the only factor associated with BCVA improvement at 12 months was the existence of pigment epithelial detachment at baseline.

CONCLUSIONS: BCVA showed significant improvement only in the bimonthly group but not in the PRN group at 12 months.

PMID: 28402983

PLoS One. 2017 Apr 13;12(4):e0175809. eCollection 2017.

Relation between macular morphology and treatment frequency during twelve months with ranibizumab for diabetic macular edema.

Mori Y, Murakami T, Suzuma K, Ishihara K, Yoshitake S, Fujimoto M, Dodo Y, Yoshitake T, Miwa Y, Tsujikawa A.

PURPOSE: To investigate whether baseline optical coherence tomography (OCT) parameters can predict the treatment frequency of intravitreal ranibizumab (IVR) injections during the first year in patients with diabetic macular edema (DME) treated with pro re nata (PRN) IVR injections.

METHODS: We retrospectively reviewed 68 eyes of 63 patients with center-involved DME who received IVR injections for 12 months or longer according to three monthly IVR injections followed by the PRN dosing. We measured the mean retinal thicknesses in the individual subfields of the Early Treatment

Diabetic Retinopathy Study grid and evaluated the qualitative and quantitative parameters on OCT sectional images. We investigated the relationship between these OCT parameters at baseline and the number of IVR injections during the 12-month follow-up.

RESULTS: Three loading doses were administered to 10 eyes; four to seven annualized IVR injections were administered to 34 eyes. The number of eyes that received IVR injections decreased gradually until month 6 and was almost constant from months 7 to 11. No relationships were seen between the treatment frequency and baseline systemic factors and the ophthalmic examination findings. Univariate analyses showed that the number of IVR injections during the first year was associated with the mean retinal thickness in the individual subfields and the transverse length of the disrupted external limiting membrane (ELM) and ellipsoid zone of the photoreceptors. Multivariate analysis showed a significant association with the thickness in the inferior subfield alone. The treatment frequency during the 12-month follow-up was not correlated with improved visual acuity but was associated with the decrease in the central subfield thickness and disrupted ELM.

CONCLUSION: The retinal thickness in the inferior subfield predicts the treatment frequency during the first year in eyes with DME treated with PRN IVR injections.

PMID: 28407012

Retina. 2017 Apr 11.[Epub ahead of print]

PREDICTIVE VALUE OF OPTICAL COHERENCE TOMOGRAPHIC FEATURES IN THE BEVACIZUMAB AND RANIBIZUMAB IN PATIENTS WITH DIABETIC MACULAR EDEMA (BRDME) STUDY.

Fickweiler W, Schauwvlieghe AM, Schlingemann RO, Maria Hooymans JM, Los LI, Verbraak FD; BRDME Research Group.

PURPOSE: To establish the predictive value of specific optical coherence tomography retinal features on visual outcomes and retinal thickness during anti-vascular endothelial growth factor treatment in patients with diabetic macular edema.

METHODS: Post hoc analysis of compound data of a prospective, 6-month, multicenter, randomized controlled trial of 119 patients with diabetic macular edema receiving either intravitreal bevacizumab or ranibizumab were analyzed to assess the associations between baseline retinal morphologic parameters and change in best-corrected visual acuity and central subfield thickness. Based on the study protocol of the core study, best-corrected visual acuity and central subfield thickness were obtained before each mandatory monthly injection during 6 months.

RESULTS: The presence of serous retinal detachment at baseline was associated with significant improvement in best-corrected visual acuity letter score at Month 3 and Month 6 ($P < 0.001$ and $P = 0.01$, respectively). In addition, the presence of disorganization of retinal inner layers was associated with lower best-corrected visual acuity letter score at Month 3 and Month 6 ($P < 0.05$ and $P = 0.01$, respectively).

CONCLUSION: This study found that serous retinal detachment and disorganization of retinal inner layers were associated with different treatment responses to anti-vascular endothelial growth factor therapy in patients with diabetic macular edema.

PMID: 28406860

Int Ophthalmol. 2017 Apr 12. [Epub ahead of print]

Outcomes of switching treatment to aflibercept in patients with macular oedema secondary to central retinal vein occlusion refractory to ranibizumab.

Konidaris V, Al-Hubeshy Z, Tsaousis KT, Gorgoli K, Banerjee S, Empeslidis T.

PURPOSE: To assess the treatment outcome of switching from ranibizumab to aflibercept intravitreal injections in patients with macular oedema secondary to central retinal vein occlusion (CRVO).

METHODS: A prospective interventional study was conducted in a tertiary retina service in Leicester Royal Infirmary, UK, where patients with CRVO and associated macular oedema were recruited. First-line treatment involved three monthly ranibizumab injections. Non-responders were defined as patients who despite a minimum of three consecutive injections had persistent intraretinal fluid one month after the last injection. In these cases, a treatment change to aflibercept injections on a per-needed basis was decided. Best-corrected visual acuity (BCVA) and central retinal thickness (CRT) were measured before and after switching of treatment. Follow-up period lasted for a minimum of 24 weeks after switching.

RESULTS: Twenty-nine eyes of 29 patients with refractory macular oedema secondary to CRVO were included. All eyes had an average of 4.5 ranibizumab intravitreal injections in a mean period of 6 months without reduction in intraretinal fluid and/or no visual acuity gain. A significant decrease in mean CRT from 633.67 ± 242.42 to 234.62 ± 78.28 μm and improvement in mean BCVA from 1.34 ± 0.66 log MAR to 0.91 ± 0.73 log MAR were noticed after switching treatment to aflibercept. The average number of aflibercept injections needed for oedema resolution was 2.19.

CONCLUSIONS: Aflibercept is an effective alternative treatment for macular oedema secondary to CRVO refractory to ranibizumab. Good anatomical and functional result can be achieved with few injections. The maintenance of these results after 6 months is yet to be investigated.

PMID: 28405787

Turk J Ophthalmol. 2017 Apr;47(2):115-118. Epub 2017 Apr 1.

Multiple Intravitreal Ranibizumab Injections for Persistant Choroidal Neovascularization Associated with Presumed Ocular Histoplasmosis Syndrome.

Yılmaz T, Dikci S, Genç O, Mutlu K.

Abstract: Presumed ocular histoplasmosis syndrome (POHS) is a clinical entity that is characterized by small, round, discrete, macular or mid peripheral atrophic (punched out) chorioretinal lesions (histo spots), peripapillary scarring, choroidal neovascularization (CNV), and the absence of anterior uveitis and vitritis. Diagnosis of this disorder is based upon characteristic clinical findings and a positive histoplasmin skin test or residence in an endemic region for Histoplasma capsulatum. There is no active systemic disease during diagnosis of POHS. Disciform scarring and macular CNV secondary to POHS is a well-known complication which leads to loss of visual acuity or visual disturbance. Without therapy, the visual prognosis in these patients is unfavorable. Submacular surgery, radiation, steroids, photodynamic therapy, and most recently anti-vascular endothelial growth factor therapy are current therapeutic options for this condition. We report a case with persistent CNV secondary to POHS in a middle-aged woman with moderate myopia and the clinical course of treatment with multiple intravitreal ranibizumab (Lucentis®, Novartis) injections.

PMID: 28405488 PMCID: PMC5384118

Nurs Stand. 2017 Apr 12;31(33):44-52.

Nurse-led ranibizumab intravitreal injections in wet age-related macular degeneration: a literature review.

Gregg E.

Abstract: Aim The aim of this literature review was to explore the development of the role of specialist

ophthalmic nurses in delivering ranibizumab intravitreal injections to patients with wet age-related macular degeneration (AMD), and to evaluate their contribution to reducing capacity pressures in medical retina services, while maintaining safe and effective standards of care. Method A systematic literature search was undertaken to identify relevant articles published between January 2000 and June 2015. A search of electronic databases was undertaken, and selected relevant journals were searched manually. A free text and subject heading search strategy was conducted, in which the abstracts of publications identified for review were assessed for relevance. Inclusion criteria were: nurses delivering ranibizumab intravitreal treatment; studies performed in the UK and other countries; and patients with AMD, diabetic macular oedema or central retinal vein occlusion receiving nurse-led ranibizumab (Lucentis) intravitreal treatment. Findings Five studies were identified from the literature search, which audited a total of 31,303 injections delivered by nurse practitioners between January 2007 and November 2013. The visual outcomes and the rate of complications from intravitreal injections delivered by trained ophthalmic nurse practitioners were comparable to intravitreal injections delivered by ophthalmologists. Four of the five studies reported increased patient satisfaction, patients consenting to nurse-delivered intravitreal injections, favourable pain experience, and absence of complaints. Conclusion Practice innovation is an example of a quality, innovation, productivity and prevention process. Role expansion, in which specialist ophthalmic nurses deliver intravitreal injections, has been shown to be economical, safe and effective. It enables timely delivery of the service, thereby preventing irreversible blindness for individuals with wet AMD.

PMID: 28399772

Ophthalmologe. 2017 Apr 12. [Epub ahead of print]

[Prognosis and treatment of macular bleeding in neovascular age-related macular degeneration]. [Article in German]

Agostini HT, Bopp S, Feltgen N.

Abstract: Macular bleeding is associated with an acute loss of visual function and is frequently a complication of neovascular age-related macular degeneration. Blood degradation products can lead to permanent retinal neuronal damage over time. The extent of the bleeding is correlated to the coagulation status of the patient. The treatment strategy depends on the age, size and exact location of the bleeding. The spectrum of therapeutic options ranges from watchful waiting to large scale vitrectomy with removal of subretinal mass bleeding.

PMID: 28405758

Ophthalmol Ther. 2017 Apr 8. [Epub ahead of print]

A Review of Current and Future Management of Geographic Atrophy.

Sacconi R, Corbelli E, Querques L, Bandello F, Querques G.

Abstract: Age-related macular degeneration (AMD) is a multifactorial disease and a leading cause of vision impairment in elderly people in Western society. Geographic atrophy (GA), the late stage of dry AMD, is typically defined as a round or oval area of atrophy of 175 µm or more. In GA patients, visual acuity (VA) can still be good if the macula is spared, but decreased if GA extends through the fovea causing a great impairment of quality of life. Because of a poor correlation between VA and GA lesions or progression, a multimodal imaging approach is necessary to better follow up GA patients. In the last years, the introduction in clinical practice of new non-invasive tools such as fundus autofluorescence, structural optical coherence tomography (OCT) and OCT angiography helped the ophthalmologists to better understand the natural course of GA patients. However, several pathways concerning the pathogenesis of the disease are not completely clarified yet and should be investigated further. Although no approved therapy exists for GA,

healthy lifestyle and nutritional intervention with some specific supplementations (e.g., vitamins C and E, beta-carotene, high dietary folate) may help to prevent the onset and to delay the progression of the disease. At the same time, several drugs are under evaluation in clinical trials with interesting results. These drugs try to stop several pathways implicated in the pathogenesis of GA, but probably only a few of these will prove truly effective, confirming the preliminary results, and will be available in clinical practice.

PMID: 28391446

Int J Ophthalmol. 2017 Mar 18;10(3):423-426. eCollection 2017.

Intravitreal aflibercept in neovascular age-related macular degeneration previously treated with ranibizumab.

Lim RH, Gupta B, Simcock P.

AIM: To report the change in visual acuity and central macular thickness (CMT) following treatment with intravitreal aflibercept injections in patients with neovascular age-related macular degeneration (nAMD) with suboptimum response to ranibizumab.

METHODS: This was a retrospective study. The inclusion criteria were patients with nAMD who responded poorly to ranibizumab. Patients then received either 3 consecutive aflibercept injections followed by pro re nata (PRN) treatment or PRN alone. Primary endpoints were mean change in best-corrected visual acuity (BCVA) and CMT at 12mo. Secondary endpoints were number of injections and adverse events.

RESULTS: Forty-nine eyes from 49 patients met the inclusion criteria and completed 12-month follow up on aflibercept. Thirty-eight eyes received 3 consecutive aflibercept injections followed by PRN treatment and 11 eyes received PRN injections alone. At 12mo, mean BCVA improved by one letters (logMAR 0.56±0.31 to 0.54±0.34) and mean CMT decreased from 303.9±82.1 to 259.2±108.3 μm. Four percent of eyes gained 15 letters or more, 6% lost more than 15 letters and the remaining 90% had stable BCVA. The mean number of aflibercept injections was 6. There was one case of infectious endophthalmitis.

CONCLUSION: Intravitreal aflibercept in patients with nAMD with a previous suboptimal response to ranibizumab resulted in an anatomical improvement in macular appearance at 12mo without a corresponding improvement in visual acuity.

PMID: 28393034 PMCID: PMC5360778

Graefes Arch Clin Exp Ophthalmol. 2017 Apr 8. [Epub ahead of print]

Re: Switching therapy from bevacizumab to aflibercept for the management of persistent diabetic macular edema.

Bahrami B, Hong T, Chang A.

PMID: 28391371

Other treatment & diagnosis

J Cataract Refract Surg. 2017 Mar;43(3):324-327.

Swept-source optical coherence tomography to screen for macular pathology in eyes having routine cataract surgery.

Zafar S, Siddiqui MAR, Shahzad R, Shahzad MH.

PURPOSE: To determine the incremental benefit of swept-source optical coherence tomography (SS-OCT) in identifying occult macular disease preoperatively in patients scheduled for routine cataract surgery.

DESIGN: Prospective case series.

METHODS: Preoperative SS-OCT scans were performed in all patients scheduled to have cataract surgery between January and March 2016. Scans were subsequently reviewed for the presence of macular abnormalities. Patients with clinically detectable retinal pathologies were excluded.

RESULTS: Of the 179 eligible patients, 155 were included in the study. Macular pathology was noted in 17 patients (10.9%). The most commonly identified conditions were age-related macular degeneration (n = 5), idiopathic epiretinal membrane (n = 4), and vitreomacular interface abnormalities (n = 4). Other abnormalities included cystoid macular edema (n = 2) and ellipsoid zone abnormalities (n = 2). Media opacities precluded interpretation of 9 scans (4.7%).

CONCLUSIONS: Swept-source OCT was an effective noninvasive modality for detecting macular structural abnormalities, especially in the presence media opacities. Optical coherence tomography imaging should be considered as an adjunct to routine dilated fundus examination for macular evaluation, particularly if premium intraocular lenses are being considered.

PMID: 28410712

J Clin Exp Ophthalmol. 2015 Oct 27;6:488.

Visual Function and Its Relationship with Severity of Early, and Activity of Neovascular, Age-Related Macular Degeneration.

Loughman J, Sabour-Pickett S, Nolan JM, Klein B, Klein R, Beatty S.

PURPOSE: To investigate the relationship between visual function and severity of early age-related macular degeneration (AMD) and activity of neovascular (nv-) AMD.

METHODS: The following data was collected from 66 eyes of 66 subjects with early AMD and 47 eyes of 47 subjects with active nv-AMD: corrected distance visual acuity (CDVA); contrast sensitivity (CS); glare disability (GD); and retinotopic ocular sensitivity (ROS) of the central 5° of the retina, by microperimetry. Fundus photographic grading of early AMD was performed in a masked fashion. Mean foveal thickness (MFT) was measured by spectral domain optical coherence tomography in patients with nv-AMD.

RESULTS: In subjects with early AMD, there was an inverse and statistically significant relationship between measures of ROS within the central 5° of retina (including fixation) and severity of early AMD (p=0.01). In eyes with active nv-AMD, an inverse and statistically significant relationship was observed between measures of MFT and measures of ROS at the central 5° of retina (r=-0.34; p=0.02). No other measures, including CDVA, were significantly related to severity of early AMD, or to MFT in nv-AMD.

CONCLUSION: Although ROS was cross-sectionally associated with disease severity, and inversely related to MFT, an important determinant of need-to-treat in cases of nv-AMD, further research is required to determine the appropriateness of ROS for monitoring early and active neovascular forms of this disease.

PMID: 28409060 PMCID: PMC5388184

Optom Vis Sci. 2017 Apr 12. [Epub ahead of print]

Characteristics of Submacular Hemorrhages in Age-Related Macular Degeneration.

Kim JH, Chang YS, Kim JW, Kim CG.

PURPOSE: The aims of this research are to report the incidence and characteristics of submacular hemorrhage secondary to neovascular age-related macular degeneration (AMD) and to compare the detailed morphologic features of hemorrhages between typical neovascular AMD and polypoidal choroidal vasculopathy (PCV).

METHODS: This retrospective observational study included 791 eyes of 791 patients who had newly diagnosed neovascular AMD at a single institution. The incidence and extent of submacular hemorrhage of one disc area or greater were estimated and compared between typical neovascular AMD and PCV. In addition, submacular hemorrhages were classified into groups according to location (location of fovea at the center of the hemorrhage versus at the periphery of the hemorrhage) and morphology (circular versus irregular margin). The proportion of each subtype of neovascular AMD was evaluated according to the aforementioned classification.

RESULTS: Among those included, 129 (16.3%) eyes exhibited submacular hemorrhage at initial presentation. Among the 627 eyes with available indocyanine green angiography findings, the incidence of submacular hemorrhage was greater in PCV (23.6%, 78 of 330 eyes) than in typical neovascular AMD (9.4%, 28 of 297 eyes; χ test, $P < .001$). When divided into four groups according to hemorrhage shape and location (central and circular, central and irregular, peripheral and circular, and peripheral irregular), the proportion of eyes in these groups was significantly different between the two disease groups (χ test, $P = .018$).

CONCLUSIONS: The incidence of submacular hemorrhage was greater in PCV than in typical neovascular AMD. The morphology and location of submacular hemorrhage may provide useful clues to differentiate PCV from typical neovascular AMD.

PMID: 28403037

Acta Ophthalmol. 2017 Apr 9. [Epub ahead of print]

Choroidal vascular changes in age-related macular degeneration.

Koh LH, Agrawal R, Khandelwal N, Sai Charan L, Chhablani J.

PURPOSE: To assess the choroidal vascular changes using choroidal vascularity index (CVI) in patients with age-related macular degeneration (AMD) compared to controls.

METHODS: Enhanced depth imaging (EDI) optical coherence tomography (OCT) scans of 64 patients with unilateral or bilateral AMD were obtained. Images with a poorly demarcated choroidal-scleral interface (CSI) were excluded from the analysis. Foveal scans of 63 AMD eyes and 35 'normal fellow' eyes were analysed. Images of 30 eyes from 18 age-matched healthy subjects were included as controls. Choroidal vascularity index (CVI) was derived from binarization of EDI OCT images, using fiji software.

RESULTS: The mean age was 56.50 ± 5.50 years for AMD patients and 52.25 ± 6.75 years for controls. All patients were treatment naïve. Subfoveal choroidal thickness (SFCT) in AMD, 'normal fellow' eyes and controls was 314.02 ± 78.80 μm, 300.88 ± 53.85 μm and 278.5 ± 65.31 μm, respectively. Choroidal vascularity index (CVI) in AMD, 'normal fellow' eyes and controls was 64.04 ± 2.43%, 64.66 ± 2.25% and 66.07 ± 1.72%, respectively. Choroidal vascularity index (CVI) of both AMD and 'normal fellow' eyes was significantly lower compared to controls ($p < 0.0001$ and $p = 0.007$). The SFCT of AMD eye was not found to be significantly different from 'normal fellow eyes' ($p = 0.45$).

CONCLUSION: There was no statistical difference in SFCT, but CVI was significantly lower in patients with AMD. Choroidal vascularity index (CVI) was also lower in 'normal fellow' AMD eyes as compared to controls. This suggests possible reduction in choroidal vascularity in eyes with AMD and also to a certain extent in the 'normal fellow' eyes without phenotypical manifestations and may suggest underlying choroidal morphological change leading to wet AMD.

PMID: 28391615

Open Ophthalmol J. 2017 Jan 31;11:17-23. eCollection 2017.

Macular Evaluation with Spectral Domain Type Optic Coherence Tomography in Eyes with Acute Nonarteritic Ischemic Optic Neuropathy at the Presentation Visit.

Donmez O, Kocaoglu G, Yaman A, Bajin MS, Saatci AO.

PURPOSE: To evaluate the macula with spectral domain type optic coherence tomography (OCT) in eyes with acute nonarteritic anterior ischemic optic neuropathy (NAION) at the presentation visit.

METHODS: Medical charts of the 133 patients who received the diagnosis of acute NAION between January 2008 and July 2014 at the Neuro-ophthalmology unit of Dokuz Eylul University were reviewed retrospectively. Sixtythree patients within 30 days of symptom onset with available baseline spectral domain type macular OCT were included in this study. Clinical and macular characteristics of the affected eye were assessed and compared to the fellow eyes.

RESULTS: Sixty-three eyes of 63 patients comprised the study group. Twenty one study eyes (33.3%) had normal posterior pole, 22 (34.9%) some evidence of subretinal fluid, 10 (15.8%) vitreomacular adhesion, five (7%) age-related macular degeneration related changes, four (6%) epiretinal membrane and one (1%) previous grid laser scars. On the other hand, 41 of 63 the fellow eyes (65%) had normal posterior pole, ten (15.8%), vitreomacular adhesion, seven (10.7%), age-related macular degeneration related changes, three (4%) epiretinal membrane and two (3%) other type of changes. OCT scan passing through the fovea exhibited 10 or more hyperreflective dots in 10 (15%) of the study eyes whereas two of the fellow eyes (3.2%) had 10 or more hyperreflective dots.

CONCLUSION: Macular OCT can be a part of the routine neuroophthalmologic examination in patients with acute NAION not only to show the NAION related changes such as the subretinal fluid accumulation but also to identify the other coexistent macular abnormalities.

PMID: 28400888 PMCID: PMC5362975

Invest Ophthalmol Vis Sci. 2017 Apr 1;58(4):2180-2186.

Vitreomacular Adhesion and Its Association With Age-Related Macular Degeneration in a Population-Based Setting: The Alienor Study.

Gattoussi S, Cougnard-Grégoire A, Delyfer MN, Rougier MB, Schweitzer C, Delcourt C, Korobelnik JF.

PURPOSE: The purpose of this study was to describe vitreomacular adhesion (VMA), diagnosed with spectral-domain optical coherence tomography (SD-OCT), its risk factors, and its association with AMD in a population-based study of French elderly subjects.

METHODS: Six hundred twenty-two of 624 (99.7%) participants of the Alienor study (Bordeaux, France), ≥75 years of age, had gradable SD-OCT scans of the macula in at least one eye. VMA was defined as visible perifoveal vitreous separation with remaining vitreomacular attachment and unperturbed foveal morphologic features. Late AMD was classified from retinal color photographs, SD-OCT, and ophthalmologic history. Early AMD was classified from retinal photographs and defined by the presence of large drusen and/or reticular drusen and/or pigmentary abnormalities.

RESULTS: The prevalence of VMA was 15.8%, decreased with age (18.1% in subjects 75 to 84 years of age versus 8.9% after 85 years of age), and was higher in men than women (20.6% vs. 12.8%). VMA also tended to be less frequent in eyes with a history of cataract surgery (odds ratio [OR] = 0.66, P = 0.05), after adjustment for age and sex. No associations of VMA with other risk factors (cardiovascular risk factors, dietary intake of omega-3 fatty acids, lifetime ultraviolet radiation exposure, major AMD genetic polymorphisms) were found. After multivariate adjustment, VMA was not significantly associated with early or late AMD (OR = 1.14, P = 0.70 and OR = 0.78, P = 0.51 for early and late AMD, respectively).

CONCLUSIONS: VMA was visible on SD-OCT in 16% in this sample of elderly French subjects but was not associated with AMD. Prospective studies of the associations of VMA with AMD are needed.

PMID: 28399268

Genetics

Br J Ophthalmol. 2016 Oct 21. [Epub ahead of print]

Association between VEGF-A and VEGFR-2 polymorphisms and response to treatment of neovascular AMD with anti-VEGF agents: a meta-analysis.

Wu M, Xiong H, Xu Y, Xiong X, Zou H, Zheng M, Wang X, Zhou X.

AIMS: The purpose of this study is to investigate whether gene polymorphisms of the vascular endothelial growth factor A (VEGF-A) and its receptor (VEGFR-2) have a pharmacogenetics effect on the anti-VEGF treatment for neovascular age-related macular degeneration (nAMD).

METHODS: We carried out a meta-analysis focusing on the relationship between VEGF-related gene polymorphisms and treatment response of nAMD.

RESULTS: For the single nucleotide polymorphisms (SNPs) within VEGF-A and VEGFR-2, anti-VEGF treatment was much more effective in patients with nAMD having rs833061 (CC vs TT:OR=2.222, 95% CI 1.252 to 3.944, p=0.006; CT vs TT: OR=2.537,95% CI 1.478 to 4.356, p=0.001 and CC vs CT+TT: OR=2.362, 95% CI 1.414 to 3.946, p=0.001), particularly for Asians (CC vs TT: OR=2.903, 95% CI 1.150 to 7.330, p=0.024; CT vs TT: OR=3.849, 95% CI 1.522 to 9.733, p=0.004 and CC vs CT+TT: OR=3.339, 95% CI 1.369 to 8.145, p=0.008, respectively). In subgroup analysis, rs833061 was more likely to be a predictor of response to anti-VEGF therapy specifically when ranibizumab (RBZ) only regime was adopted or visual acuity (VA) was taken as the standardised assessment of outcome. No association with response to anti-VEGF treatment was detected for the other eight polymorphisms.

CONCLUSIONS: Pharmacogenetics of VEGF-A polymorphism rs833061 may play a positive role in response to anti-VEGF therapy for nAMD.

PMID: 28400373

Crit Rev Biochem Mol Biol. 2017 Apr 12:1-26. [Epub ahead of print]

Going non-viral: the Sleeping Beauty transposon system breaks on through to the clinical side.

Hudecek M, Izsvák Z, Johnen S, Renner M, Thumann G, Ivics Z.

Abstract: Molecular medicine has entered a high-tech age that provides curative treatments of complex genetic diseases through genetically engineered cellular medicinal products. Their clinical implementation requires the ability to stably integrate genetic information through gene transfer vectors in a safe, effective and economically viable manner. The latest generation of Sleeping Beauty (SB) transposon vectors fulfills these requirements, and may overcome limitations associated with viral gene transfer vectors and transient non-viral gene delivery approaches that are prevalent in ongoing pre-clinical and translational research. The SB system enables high-level stable gene transfer and sustained transgene expression in multiple primary human somatic cell types, thereby representing a highly attractive gene transfer strategy for clinical use. Here we review several recent refinements of the system, including the development of optimized transposons and hyperactive SB variants, the vectorization of transposase and transposon as mRNA and

DNA minicircles (MCs) to enhance performance and facilitate vector production, as well as a detailed understanding of SB's genomic integration and biosafety features. This review also provides a perspective on the regulatory framework for clinical trials of gene delivery with SB, and illustrates the path to successful clinical implementation by using, as examples, gene therapy for age-related macular degeneration (AMD) and the engineering of chimeric antigen receptor (CAR)-modified T cells in cancer immunotherapy.

PMID: 28402189

Hum Mutat. 2017 Apr 10. [Epub ahead of print]

Genetic variants in microRNAs and their binding sites within gene 3'UTRs associate with susceptibility to age-related macular degeneration (AMD).

Ghanbari M, Erkeland SJ, Xu L, Colijn JM, Franco OH, Dehghan A, Klaver CC, Meester-Smoor MA.

Abstract: Age-related macular degeneration (AMD), the leading cause of blindness in the elderly, is a complex disease that results from multiple genetic and environmental factors. MicroRNAs (miRNAs) are small non-coding RNAs that post-transcriptionally regulate target mRNAs and are frequently implicated in human diseases. Here, we investigated the association of genetic variants in miRNAs and miRNA-binding sites within gene 3'UTRs with AMD using data from the largest AMD genome-wide association study. First, we identified three variants in miRNAs significantly associated with AMD. These include rs2168518:G>A in the miR-4513 seed sequence, rs41292412:C>T in pre-miR-122/miR-3591 and rs4351242:C>T in the terminal-loop of pre-miR-3135b. We demonstrated that these variants reduce expression levels of the mature miRNAs in vitro and pointed the target genes that may mediate downstream effects of these miRNAs in AMD. Second, we identified 54 variants (in 31 genes) in miRNA-binding sites associated with AMD. Based on stringent prioritization criteria, we highlighted the variants that are likely to have an impact on the miRNA-target interactions. Further, we selected rs4151672:C>T within the CFB 3'UTR and experimentally showed that, while miR-210-5p downregulates expression of CFB, the variant decreases miR-210-5p-mediated repression of CFB. Together, our findings support the notion that miRNAs may play a role in AMD. This article is protected by copyright. All rights reserved.

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Stem cells

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Stem cell therapies for retinal diseases: recapitulating development to replace degenerated cells.

Zhao C, Wang Q, Temple S.

Abstract: Retinal degenerative diseases are the leading causes of blindness worldwide. Replacing lost retinal cells via stem cell-based therapies is an exciting, rapidly advancing area of translational research that has already entered the clinic. Here, we review the status of these clinical efforts for several significant retinal diseases, describe the challenges involved and discuss how basic developmental studies have contributed to and are needed to advance clinical goals.

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Diet, lifestyle and low vision

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The Prevalence of Depression and Depressive Symptoms among Eye Disease Patients: A

Systematic Review and Meta-analysis.

Zheng Y, Wu X, Lin X, Lin H.

Abstract: The prevalence of depression among different eye disease patients varies across studies and has not been systematically reviewed. This study is to provide a summary of the prevalence of depression among eye disease patients. PubMed, Medline, Embase and Cochrane Library were searched from January, 1990 to December, 2015 to identify studies with information on the prevalence of depression among ophthalmic patients. A random/fixed-effects meta-analysis was used to estimate the pooled prevalence of depression among eye disease patients. Heterogeneity was assessed with the I2 test. 28 studies were selected from 3162 references. The overall pooled prevalence of depression or depressive symptoms with eye disease was 25% (1502/6589 individuals, 95% CI, 0.20-0.30) ranging from 5.4% to 57.0%. Regarding different disease categories, the highest prevalence was revealed for dry eye disease (DED) with 29%, followed by 25% for glaucoma patients, 24% for age-related macular degeneration (AMD) patients, 23% for cataract patients. The increased pooled prevalence of depression was identified in those with eye diseases compared with healthy controls (OR, 1.59; 95% CI, 1.40-1.81; I2 = 68.5%). Substantial heterogeneity was identified across most estimates (I2 > 75%). Further research is needed to identify effective strategies for preventing and treating depression among eye disease patients.

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Effects of Age-Related Macular Degeneration on Postural Sway.

Chatard H, Tepenier L, Jankowski O, Aussems A, Allieta A, Beydoun T, Salah S, Bucci MP.

Purpose: To compare the impact of unilateral vs. bilateral age-related macular degeneration (AMD) on postural sway, and the influence of different visual conditions. The hypothesis of our study was that the impact of AMD will be different between unilateral and bilateral AMD subjects compared to age-matched healthy elderly.

Methods: Postural stability was measured with a platform (TechnoConcept®) in 10 elderly unilateral AMD subjects (mean age: 71.1 ± 4.6 years), 10 elderly bilateral AMD subjects (mean age: 70.8 ± 6.1 years), and 10 healthy age-matched control subjects (mean age: 69.8 ± 6.3 years). Four visual conditions were tested: both eyes viewing condition (BEV), dominant eye viewing (DEV), non-dominant eye viewing (NDEV), and eyes closed (EC). We analyzed the surface area, the length, the mean speed, the anteroposterior (AP), and mediolateral (ML) displacement of the center of pressure (CoP).

Results: Bilateral AMD subjects had a surface area ($p < 0.05$) and AP displacement of the CoP ($p < 0.01$) higher than healthy elderly. Unilateral AMD subjects had more AP displacement of the CoP ($p < 0.05$) than healthy elderly.

Conclusions: We suggest that ADM subjects could have poor postural adaptive mechanisms leading to increase their postural instability. Further studies will aim to improve knowledge on such issue and to develop reeducation techniques in these patients.

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Analytical validation of an ultraviolet-visible procedure for determining lutein concentration and application to lutein-loaded nanoparticles.

Silva JT, Silva AC, Geiss JM, de Araújo PH, Becker D, Bracht L, Leimann FV, Bona E, Guerra GP,

Gonçalves OH.

Abstract: Lutein is a carotenoid presenting known anti-inflammatory and antioxidant properties. Lutein-rich diets have been associated with neurological improvement as well as reduction of the risk of vision loss due to Age-Related Macular Degeneration (AMD). Micro and nanoencapsulation have demonstrated to be effective techniques in protecting lutein against degradation and also in improving its bioavailability. However, actual lutein concentration inside the capsules and encapsulation efficiency are key parameters that must be precisely known when designing in vitro and in vivo tests. In this work an analytical procedure was validated for the determination of the actual lutein content in zein nanoparticles using ultraviolet-visible spectroscopy. Method validation followed the International Conference on Harmonisation (ICH) guidelines which evaluate linearity, detection limit, quantification limit, accuracy and precision. The validated methodology was applied to characterize lutein-loaded nanoparticles.

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