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MD Research News

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Drug treatment

Br J Ophthalmol. 2014 May 2. doi: 10.1136/bjophthalmol-2013-304474. [Epub ahead of print]

Early initial clinical experience with intravitreal aflibercept for wet age-related macular degeneration.

Ferrone PJ, Anwar F, Naysan J, Chaudhary K, Fastenberg D, Graham K, Deramo V.

BACKGROUND: Age-related macular degeneration (AMD) is a degenerative process that leads to severe vision loss. Wet AMD is defined by choroidal neovascularisation, leading to the accumulation of subretinal fluid (SRF), macular oedema (ME), and pigment epithelium detachments (PED). Purpose To evaluate the initial clinical experience of conversion from bevacizumab or ranibizumab to aflibercept in wet AMD patients.

METHODS: Records of 250 consecutive wet AMD patients were retrospectively reviewed. Of 250 patients, 29 were naive (with no previous treatment), and 221 were previously treated with bevacizumab (1/3) or ranibizumab (2/3). On average, converted patients received 14 injections every 6 weeks on a treat-and-extend regimen with Avastin or Lucentis before being converted to aflibercept every 7 weeks on average (no loading dose) for three doses. For the purposes of this study, we concentrated on the patients converted to aflibercept since the number of naive patients was too small to draw any conclusion from. Snellen (as logMar) visual acuities, and optical coherence tomography (OCT) were compared predrug and postdrug conversion.

RESULTS: Converted patients did not show a significant difference in visual acuity or average OCT thickness from preconversion values; however, small improvements in ME (p=0.0001), SRF (p=0.0001), and PED (p=0.008) grading were noted on average after conversion to aflibercept.

CONCLUSIONS: No significant difference in visual outcome or average OCT thickness was observed when switched from bevacizumab or ranibizumab q6 week to aflibercept 7-week dosing, on average. Mild anatomic improvements did occur in converted patients with regard to ME, SRF and PED improvement, on average, after conversion to aflibercept, and aflibercept was injected less frequently. No serious adverse reactions, including ocular infections or inflammation, as well as ocular and systemic effects were noted.

PMID: 24795335 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2014 May 2. doi: 10.1136/bjophthalmol-2013-304829. [Epub ahead of print]

Injection frequency and anatomic outcomes 1 year following conversion to aflibercept in patients with neovascular age-related macular degeneration.

Messenger WB, Campbell JP, Faridi A, Shippey L, Bailey ST, Lauer AK, Flaxel CJ, Hwang TS.

BACKGROUND/AIM: To evaluate the clinical, anatomic and functional effects of conversion to aflibercept following ranibizumab and/or bevacizumab in patients with neovascular age-related macular degeneration (AMD).

METHODS: A retrospective review of patients with neovascular AMD treated with intravitreal ranibizumab and/or bevacizumab who were switched to aflibercept was performed. The primary outcome was change in injection frequency in the year following the change. Secondary outcomes included change in central macular thickness (CMT) at 6 months and 1 year, presence of intraretinal and subretinal fluid at 6 months and visual acuity at 1 year.

RESULTS: A total of 109 eyes with neovascular AMD were switched to aflibercept and met inclusion criteria. Overall, aflibercept injection frequency was unchanged with patients receiving 7.4 antivascular endothelial growth factor (VEGF) injections the year prior to conversion compared with 7.2 aflibercept injections in the year following (p=0.47). However, the change to aflibercept was associated with improvement in CMT from 324 to 295 μm (p=0.0001) at 6 months and 299 μm (p=0.0047) at 1 year. There was no effect on visual acuity at 1 year. In a subgroup analysis, patients who had received ≥10 anti-VEGF injections in the year prior had fewer injections (11.1 to 8.4, p<0.0001) and clinic visits (13.9 to 9.6, p<0.0001) as well as a significant decrease in CMT (-35 μm, p=0.02).

CONCLUSIONS: In our population, switching to aflibercept therapy was not associated with a change in injection frequency nor improved visual acuity, but was associated with improved CMT at 6 months and 1 year. In patients who received at least 10 anti-VEGF injections in the year prior, transitioning to aflibercept was associated with a reduced injection frequency and CMT, suggesting potential cost savings in this population.

PMID: 24795334 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Apr 30. pii: S0161-6420(14)00250-4. doi: 10.1016/j.ophtha.2014.03.026. [Epub ahead of print]

Safety and Efficacy of Conbercept in Neovascular Age-Related Macular Degeneration: Results from a 12-Month Randomized Phase 2 Study: AURORA Study.

Li X, Xu G, Wang Y, Xu X, Liu X, Tang S, Zhang F, Zhang J, Tang L, Wu Q, Luo D, Ke X; AURORA Study Group.

PURPOSE: To assess the safety and efficacy of multiple injections of 0.5 and 2.0 mg conbercept using variable dosing regimens in patients with neovascular age-related macular degeneration (AMD).

DESIGN: Randomized, double-masked, multicenter, controlled-dose, and interval-ranging phase 2 clinical trial divided into a 3-month loading phase followed by a maintenance phase.

PARTICIPANTS: Patients with choroidal neovascularization secondary to AMD with lesion sizes of 12 disc areas or less and a best-corrected visual acuity (BCVA) letter score of between 73 and 24 were enrolled.

METHODS: Patients were randomized 1:1 to receive either 0.5 or 2.0 mg intravitreal conbercept for 3 consecutive monthly does. After the third dose, each group was reassigned randomly again to monthly (Q1M group) or as-needed (pro re nata [PRN] group) treatment without changing the drug assignment.

MAIN OUTCOME MEASURES: The primary end point was the mean change in BCVA from baseline to month 3, with secondary end points being the mean change in BCVA, mean change in central retinal thickness (CRT), and safety at month 12.

RESULTS: We enrolled 122 patients. At the primary end point at month 3, mean improvements in BCVA

from baseline in the 0.5- and 2.0-mg groups were 8.97 and 10.43 letters, respectively. At month 12, mean improvements in BCVA from baseline were 14.31, 9.31, 12.42, and 15.43 letters for the 0.5-mg PRN, 0.5-mg Q1M, 2.0-mg PRN, and 2.0-mg Q1M regimens, respectively. At month 12, mean reductions in CRT in the 4 regimens were 119.8, 129.7, 152.1, and 170.8 µm, respectively. There were no significant differences for the pairwise comparisons between all study groups. The difference in the number of injections between the 2 PRN groups was not statistically significant. Treatment with conbercept generally was safe and well tolerated.

CONCLUSIONS: The significant gains in BCVA at 3 months were the same or better at 12 months in all conbercept dosing groups of neovascular AMD patients. During the 12 months, repeated intravitreal injections of conbercept were well tolerated in these patients. Future clinical trials are required to confirm its long-term efficacy and safety.

PMID: 24793528 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2014 Apr 28;8:807-12. doi: 10.2147/OPTH.S56624. eCollection 2014.

Effect of initial retinal thickness on outcome of intravitreal bevacizumab therapy for diabetic macular edema.

Mushtaq B, Crosby NJ, Dimopoulos AT, Lip PL, Stavrou P, El-Sherbiny S, Yang Y.

PURPOSE: To investigate whether eyes with diabetic macular edema (DME) and central retinal thickness (CRT) >400 µm had better visual and anatomical outcomes compared to eyes with a CRT <400 µm when treated with intravitreal bevacizumab in a real-world setting.

PATIENTS AND METHODS: Patients undergoing intravitreal bevacizumab therapy for DME were identified from the departmental database of a tertiary referral unit. Following the initial injection, a retreatment was performed for any persistent macular edema, unless there had been no previous response to repeated doses. Recorded parameters included visual acuity, CRT on optical coherence tomography (spectral domain optical coherence tomography [SD-OCT]), and SD-OCT characteristics. Comparisons were made between data at baseline and 12 months after the first injection, and differences were tested for statistical significance using the Student's t-test.

RESULTS: In all, 175 eyes of 142 patients were analyzed. Patients in group 2 (CRT >400 µm) had significantly more injections than group 1 (CRT <400 µm) (4.0 versus 3.3; P=0.003). Both groups had similar numbers of eyes with preexisting epiretinal membrane and/or vitreomacular traction at baseline. The reduction in CRT was significantly greater in group 2 when compared to group 1 (P<0.0001). In terms of visual gain between baseline and month 12, each gained significantly by a mean of 0.12 logarithm of the minimum angle of resolution units (P=0.0001), but there was no difference between groups 1 and 2 (P=0.99).

CONCLUSION: These results do not support a 400 µm baseline CRT cut-off for treating DME with bevacizumab, in contrast to published data on ranibizumab. Our results also indicate that patients with a thicker CRT require more bevacizumab injections, making treatment less cost-effective for these patients. Our results could be used by practitioners to support the use of bevacizumab in DME without applying a CRT cut-off.

PMID: 24812486 [PubMed]

Eur J Ophthalmol. 2014 May 5:0. doi: 10.5301/ejo.5000478. [Epub ahead of print]

Retinal and choroidal thickness changes after single anti-VEGF injection in neovascular age-related macular degeneration: ranibizumab vs bevacizumab.

Sizmaz S, Kucukerdonmez C, Kal A, Pinarci EY, Canan H, Yilmaz G.

Purpose: To evaluate and compare the effects of single intravitreal injection of ranibizumab and bevacizumab on central retinal and choroidal thickness in patients with neovascular age-related macular degeneration (AMD).

Methods: Forty eyes of 40 patients with neovascular AMD that underwent intravitreal injection of vascular endothelial growth factor inhibitors (anti-VEGFs) were included. Patients were randomized into 2 groups: 20 eyes received ranibizumab and 20 eyes received bevacizumab injection. Central retinal and choroidal thicknesses of all eyes at baseline and 1 month postinjection scans were measured with Fourier-domain optical coherence tomography (OCT). Student t test and Mann-Whitney U test were used to compare the data.

Results: The mean central retinal thickness (CRT) showed significant decrease after single injection of ranibizumab (from 345.0 µm to 253.5 µm, $p<0.01$) and bevacizumab (from 329.5 µm to 251.0 µm, $p<0.01$) at the first month, respectively. There was no significant difference regarding the CRT change between groups ($p = 0.39$). The mean choroidal thickness decreased from 158.6 µm (115-317) to 155.5 µm (111-322) in the ranibizumab group and from 211.5 µm (143-284) to 201.5 µm (93-338) in bevacizumab group. The decrease was not significant between groups ($p = 0.35$).

Conclusions: Intravitreal injection of both ranibizumab and bevacizumab provided a significant decrease in CRT; however, the agents caused no significant change in choroidal thickness. Additionally, no difference between ranibizumab versus bevacizumab was observed related to macular edema inhibition.

PMID: 24803153 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2014 May 6. doi: 10.1111/aos.12435. [Epub ahead of print]

Circulating anti-retinal antibodies in response to anti-angiogenic therapy in exudative age-related macular degeneration.

Kubicka-Trząska A, Wilańska J, Romanowska-Dixon B, Sanak M.

PURPOSE: To determine changes in anti-retinal antibodies (ARAs) during anti-VEGF therapy in patients with exudative age-related macular degeneration (AMD) and to assess the correlations between ARAs and disease activity.

METHODS: The study comprised 98 patients treated with intravitreal bevacizumab. The ophthalmic examination included best corrected visual acuity (BCVA), slit lamp biomicroscopy, fundoscopy, fluorescein angiography (FA), and optical coherence tomography (OCT). Serum ARAs levels were assessed by indirect immunofluorescence (IIF) on normal monkey retina substrate. These studies were repeated at 4 week intervals within 8 months of a follow-up. The sera of 50 sex- and age-matched healthy subjects were used as controls.

RESULTS: At baseline examination, 94 (95.5%) of the 98 patients were positive for ARAs. The ARAs titres were significantly higher ($p = 0.0000$) than in controls. A positive correlation was found between titres of ARAs and the diameter of choroidal neovascularization (CNV) as measured by FA ($p = 0.0000$), and central retinal thickness (CRT) assessed by OCT ($p = 0.0000$). A positive correlation was also found between the diameter of CNV, CRT and the complexity of circulating ARAs. Following treatment all patients demonstrated significant decrease in ARAs levels as well as improvement of BCVA, reduction of subretinal fluid on OCT and decreased leakage on FA.

CONCLUSION: Changes in serum ARAs levels occurred in parallel with clinical outcomes of anti-VEGF therapy. Treatment reduced serum levels of ARAs, with the greatest reduction occurring during the 'loading' phase. This study demonstrated that ARAs may act as a serum biomarker of the efficacy of anti-VEGF therapy.

PMID: 24802549 [PubMed - as supplied by publisher]

Retina. 2014 May 5. [Epub ahead of print]

PROFILE OF INTRAOCULAR IMMUNE MEDIATORS IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION AND THE EFFECT OF INTRAVITREAL BEVACIZUMAB INJECTION.

Agawa T, Usui Y, Wakabayashi Y, Okunuki Y, Juan M, Umazume K, Kezuka T, Takeuchi M, Yamauchi Y, Goto H.

PURPOSE: To measure intraocular cytokine levels in patients with exudative age-related macular degeneration and analyze changes in the cytokine profile 2 days after intravitreal bevacizumab injection.

METHODS: This prospective case-control study enrolled 37 patients (37 eyes) with age-related macular degeneration including polypoidal choroidal vasculopathy. Twenty-eight age-matched patients (28 eyes) who underwent cataract surgery were used as controls. Undiluted aqueous humor samples were collected after intravitreal bevacizumab injection. Two days after intravitreal bevacizumab injection, cataract surgery was performed and undiluted aqueous humor samples were collected at the beginning of surgery (10 eyes). Twenty-three cytokines were measured using flow cytometry. P values were corrected in multiple comparisons using the conservative Bonferroni-Holm method. The level of significance was set at 0.0022 (0.05/23).

RESULTS: At baseline, aqueous humor levels of vascular endothelial growth factor, angiogenin, interferon gamma-inducible protein (IP)-10, macrophage inflammatory protein (MIP)-1β, monokine induced by interferon γ (Mig), and monocyte chemotactic protein (MCP)-1 were significantly higher in the age-related macular degeneration group than in the control group ($P < 0.0022$). The result of exploratory multivariate analysis showed that elevated angiogenin level was an important factor that discriminates the two groups ($P = 0.0004$). Two days after intravitreal bevacizumab injection, vascular endothelial growth factor levels tended to be reduced ($P = 0.049$), whereas interleukin (IL)-6 and IL-8 levels increased significantly ($P < 0.0022$).

CONCLUSION: Vascular endothelial growth factor and also angiogenin, IP-10, MCP-1, MIP-1β, and Mig may be related to the pathogenesis of age-related macular degeneration. Intravitreal bevacizumab injection increases inflammatory cytokine levels, suggesting the induction of an inflammatory process.

PMID: 24801651 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2014 May 1. pii: S0002-9394(14)00231-1. doi: 10.1016/j.ajo.2014.04.028. [Epub ahead of print]

Impact of vitreomacular adhesion on ranibizumab mono- and combination therapy for neovascular age-related macular degeneration.

Waldstein SM, Ritter M, Simader C, Mayr-Sponer U, Kundi M, Schmidt-Erfurth U.

PURPOSE: To investigate the influence of vitreomacular adhesion on the efficacy of pro-re-nata (PRN) ranibizumab mono- and verteporfin photodynamic therapy (PDT) combination therapy for neovascular age-related macular degeneration.

DESIGN: Post-hoc analysis of prospective randomized 12-month multicenter clinical trial data.

METHODS: Patient population: 255 treatment-naïve patients with subfoveal choroidal neovascularization. Observation procedure: Assessment of the vitreomacular interface on monthly optical coherence tomography with division of patients into the following categories according to continuous one-year grading: Posterior vitreous detachment (n=154), dynamic release of vitreomacular adhesion (n=32), stable vitreomacular adhesion (n=51). Main outcome measures: Mean best-corrected visual acuity (BCVA) letter and central retinal thickness changes at month 12 in the vitreomacular interface groups.

RESULTS: Mean BCVA changes at month 12 were +3.5 (posterior vitreous detachment), +4.3 (release of vitreomacular adhesion) and +6.3 (vitreomacular adhesion) in patients receiving monotherapy (p=0.767), and +0.1 (posterior vitreous detachment), +6.6 (release of vitreomacular adhesion) and +9.2 (vitreomacular adhesion) in patients receiving combination therapy (p=0.009). Mean central retinal thickness changes were -113µm (posterior vitreous detachment), -89µm (release of vitreomacular adhesion) and -122µm (vitreomacular adhesion) in monotherapy (p=0.725), and -121µm (posterior vitreous detachment), -113µm (release of vitreomacular adhesion) and -113µm (vitreomacular adhesion) in combination therapy (p=0.924). Mean ranibizumab retreatments during 12 months were 4.9 (posterior vitreous detachment), 6.6 (release of vitreomacular adhesion) and 5.3 (vitreomacular adhesion) in monotherapy (p=0.018), and 4.7 (posterior vitreous detachment), 5.2 (release of vitreomacular adhesion) and 5.8 (vitreomacular adhesion) in combination therapy (p=0.942).

CONCLUSION: This study adds evidence that the vitreomacular interface status impacts functional outcomes and retreatment requirements. Patients with posterior vitreous detachment achieve acceptable results with fewer injections in PRN monotherapy, but loose potential vision gain with PDT. Patients with other vitreomacular interface configurations may potentially achieve optimized vision outcomes by combination of antiangiogenic treatment and vasoocclusive PDT.

PMID: 24794282 [PubMed - as supplied by publisher]

Expert Opin Drug Saf. 2014 May 8. [Epub ahead of print]

Systemic thromboembolic adverse events in patients treated with intravitreal anti-VEGF drugs for neovascular age-related macular degeneration: an overview.

Semeraro F, Morescalchi F, Duse S, Gambicorti E, Romano MR, Costagliola C.

Introduction: Anti-VEGF therapy improved the quality of life for millions of patients suffering from wet age-related macular degeneration (wet-AMD); unfortunately, this therapy involves multiple injections over many years. The administration of anti-VEGF can overcome the blood-retinal barrier with agents entering the systemic circulation and causing a significant decrease in VEGF serum concentration. Although circulating VEGF protects the integrity and patency of vessels, prolonged anti-VEGF treatment has the potential to increase the risk of thromboembolic events.

Areas covered: In this review, we discuss the safety data from recent trials involving available anti-VEGF drugs.

Expert opinion: During the 2 years of follow-up in the relevant clinical trials, the rates of serious adverse events such as stroke, heart attack and death were similar for patients treated with different anti-VEGF drugs. Moreover the arterial thrombotic risk appears sufficiently low when compared with the natural incidence of arterial thrombotic events in this category of elderly patients and acceptably balanced against the advantage of improved vision. Since the use of these drugs is likely to become increasingly widespread and prolonged, it is desirable that the scientific community improves the pharmacovigilance program on all anti-VEGF drugs, expanding knowledge with studies that compares head to head all four compounds belonging to anti-VEGF armamentarium.

PMID: 24809388 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2014 May;231(5):527-34. doi: 10.1055/s-0033-1360360. Epub 2014 May 5.

[Treatment of Diabetic Macular Oedema with the VEGF Inhibitors Ranibizumab and Bevacizumab: Conclusions from Basic in vitro Studies]. [Article in German]

Lang GE, Lang GK, Deissler HL.

Abstract: Diabetic macular oedema (DMO) which may occur at all stages of diabetic retinopathy (DR) is a severe vision-threatening complication. In most cases, laser treatment does not improve visual acuity. Therefore research in ophthalmology focuses on the improvement of the prognosis of DMO patients with a drug-based DMO therapy. Vascular endothelial growth factor (VEGF) is considered the most important therapeutic target because this growth factor also is the most potent permeability factor affecting the inner retinal barrier formed by endothelial cells (ECs). Compared to its angiogenic stimulation of proliferation and migration of ECs, effects of VEGF on permeability have not been studied in all details. In vitro investigations on the behaviour of primary or immortalised retinal endothelial cells confirmed the key role of VEGF in the regulation of the permeability of the inner retinal barrier. Despite the presence of a variety of other factors found to be elevated in DR, a VEGF-disrupted barrier can be completely restored with the VEGF-inhibiting ranibizumab (Lucentis®) and bevacizumab (Avastin®) when applied at clinically achievable concentrations. The antibody bevacizumab, but not the antibody fragment ranibizumab, accumulates in both retinal EC and pigment epithelial cells during prolonged treatment. This observation might be relevant because patients are often treated for several years and additional long-term side effects may be recognised in the future.

PMID: 24799173 [PubMed - in process]

EMBO Mol Med. 2014 May 1;6(5):577-9. doi: 10.1002/emmm.201404026.

VEGF sticky-trap: the first report of a non-systemically acting angiogenesis inhibitor.

Favara DM, Harris AL.

Abstract: Current therapeutic anti-angiogenic biologics used for the treatment of pathological ocular angiogenesis such as in diabetic retinopathy and wet macular degeneration often lead to detrimental side effects due to their interference with normal blood vessel physiology. In this issue of EMBO Molecular Medicine, Michael et al report on a novel angiogenesis inhibitor with unique properties that allow for local inhibition of angiogenesis without detectable systemic side effects.

PMID: 24803395 [PubMed - in process]

Other treatment & diagnosis

Lab Chip. 2014 May 8. [Epub ahead of print]

A centrifugal fluidic immunoassay for ocular diagnostics with an enzymatically hydrolyzed fluorogenic substrate.

Walsh Iii DI, Sommer GJ, Schaff UY, Hahn PS, Jaffe GJ, Murthy SK.

Abstract: We present a novel "Lab-on-a-Disk" platform and demonstrate its capability for rapid and sensitive measurement of vascular endothelial growth factor (VEGF) intended for patients suffering from diabetic retinopathy (DR) and age-related macular degeneration (AMD). This approach combines sedimentation principles applied to microspheres under centrifugal force with signal amplification using an enzyme and a fluorogenic substrate for readout. The simple single channel per assay platform separates, washes and concentrates antibody-coated microspheres from excess label to produce a sensitive fluorogenic response proportional to the amount of VEGF in the sample. This platform has comparable sensitivity to conventional ELISA and can generate a readout within 16-18 min with no sample preparation beyond mixing assay reagents and loading on the disk. In the context of ocular diagnostics, this device has the potential to facilitate accurate dosing of anti-VEGF medications utilized to treat DR and AMD, as well as identify patients whose ocular VEGF levels are not elevated and who would therefore not benefit from standard anti -VEGF medications.

PMID: 24806296 [PubMed - as supplied by publisher]

PLoS One. 2014 May 5;9(5):e96742. doi: 10.1371/journal.pone.0096742. eCollection 2014.

Detection of early age-related macular degeneration using novel functional parameters of the focal cone electroretinogram.

Wood A, Margrain T, Binns AM.

Abstract: The focal cone electroretinogram is a sensitive marker for macular disease, but have we unlocked its full potential? Typically assessment of waveform parameters is subjective and focuses on a small number of locations (e.g. the a-wave). This study evaluated the discriminatory and diagnostic potential of 4 conventional and 15 novel, objectively determined, parameters in patients with early Age-related Macular Degeneration. Focal cone electroretinograms were recorded in 54 participants with early Age-related Macular Degeneration (72.9±8.2 years) and 54 healthy controls (69±7.7 years). Conventional a and b wave amplitudes and implicit times were measured and compared to novel parameters derived from both the 1st and 2nd derivatives and the frequency-domain power spectrum of the electroretinogram.Statistically significant differences between groups were shown for all conventional parameters, the majority of 1st and 2nd derivative parameters and the power spectrum at 25 and 30 Hz. Receiver operating characteristics showed that both conventional and 1st and 2nd derivative implicit times had provided the best diagnostic potential. A regression model showed a small improvement over any individual parameter investigated. The non-conventional parameters enhanced the objective evaluation of the focal electroretinogram, especially when the amplitude was low. Furthermore, the novel parameters described here allow the implicit time of the electroretinogram to be probed at points other than the peaks of the a and b waves. Consequently these novel analysis techniques could prove valuable in future electrophysiological investigation, detection and monitoring of Age-related Macular Degeneration.

PMID: 24796326 [PubMed - in process]

Am J Ophthalmol. 2014 May 1. pii: S0002-9394(14)00228-1. doi: 10.1016/j.ajo.2014.04.025. [Epub ahead of print]

Grey hyper-reflective subretinal exudative lesions in exudative age-related macular degeneration.

Ores R, Puche N, Querques G, Blanco-Garavito R, Merle B, Coscas G, Oubraham H, Semoun O, Souied EH.

PURPOSE: To investigate the effects of ranibizumab 0.5 mg on grey hyper-reflective subretinal lesions diagnosed by spectral-domain optical coherence tomography (SD-OCT) in patients with exudative age-related macular degeneration (AMD).

DESIGN: Retrospective interventional study.

METHODS: Data from 28 consecutive patients affected with neovascular AMD that presented subretinal hyper-reflective lesions as visualized by SD-OCT were collected. Grey hyper-reflective subretinal lesion characteristics were analyzed, before and after intravitreal ranibizumab 0.5 mg injection.

RESULTS: Thirty eyes of 28 patients (5 male, 23 female, aged 57-91 years) were included. At study entry, grey lesion was associated with exudative features in 24/30 eyes (80%), including subretinal fluid (SRF) in 20/30 of eyes (67%), and retinal cystoid spaces in 11/30 of eyes (37%). Twenty-four eyes with exudative features at study entry received prompt treatment; 6 eyes without exudative features at study entry received deferred treatment (after one-month observation), when exudative signs emerged (SRF in 3/6 eyes and retinal cystoid spaces in 5/6 eyes). Ninety-three percent of the grey lesions responded to ranibizumab treatment at two months and 77% at six months. Grey hyper-reflective subretinal lesion thickness was significantly reduced after treatment at both two months (from 482±116μm to 367±102μm, P<0.0001) and six months (from 482±116μm to 369 ±71μm, P<0.0001).

CONCLUSION: Our findings suggest that grey hyper-reflective subretinal lesions might be considered as a

qualitative criterion for retreatment of exudative AMD. It may represent an early sign of active choroidal neovascularization, and should prompt to early treatment.

PMID: 24794284 [PubMed - as supplied by publisher]

JAMA Ophthalmol. 2014 May 6. doi: 10.1001/jamaophthalmol.2014.1871. [Epub ahead of print]

Outer Retinal Corrugations in Age-Related Macular Degeneration.

Ooto S, Vongkulsiri S, Sato T, Suzuki M, Curcio CA, Spaide RF.

IMPORTANCE: Optical coherence tomography (OCT) abnormalities of age-related macular degeneration (AMD) have not been fully characterized because of the complex morphology and a lack of correlative histologic studies. Expansion of our ability to interpret increasing attributes brings us closer to the goal of in vivo histologic analysis of the eye by OCT.

OBJECTIVE: To describe a new outer retinal finding of AMD using spectral-domain (SD) OCT and suggest histopathologic correlates.

DESIGN, SETTING, AND PARTICIPANTS: Twenty-five eyes of 16 patients with AMD with severe atrophy due to either choroidal neovascularization (CNV) or geographic atrophy (GA) and 53 donor eyes of 53 patients with late AMD were included. Imaging studies were conducted at a referral retinal practice and histopathology was done at a university research laboratory.

EXPOSURES: Findings in the outer retina were evaluated in SD-OCT images in eyes with atrophy of the retinal pigment epithelium (RPE) and compared with histopathologic findings in eyes with GA or CNV that also showed loss of the RPE.

MAIN OUTCOMES AND MEASURES: Spectral-domain OCT and histologic characteristics of the outer retina. RESULTS The mean (SD) age of the 16 patients was 82.7 (7.9) years. Twenty eyes had CNV and 5 eyes had GA. The mean best-corrected visual acuity was 0.800 logMAR (interquartile range, 0.350-1.000 logMAR), a Snellen equivalent of 20/126. A curvilinear hyperreflective density was identified above the Bruch membrane line within the atrophic area in the SD-OCT images. At the internal border, the material was contiguous with the outer portion of the RPE band. Below the material was a relatively hyporeflective space. The material was thrown into folds in cases with atrophy following CNV or was seen as a sheet with numerous bumps in eyes with GA. Review of histopathologic findings of eyes with advanced GA and CNV revealed a rippled layer of basal laminar deposits in an area of RPE atrophy that was located in the same level as the curvilinear line seen in the OCT images.

CONCLUSIONS AND RELEVANCE: We have described a new entity, termed outer retinal corrugations, which may correspond to histological findings of basal laminar deposits, extracellular deposits that persist in eyes with late AMD. Observation of this undulating band does not necessarily mean there is exudation or leakage; as a consequence, these patients do not need treatment based on this solitary finding.

PMID: 24801396 [PubMed - as supplied by publisher]

Exp Eye Res. 2014 May 3. pii: S0014-4835(14)00110-9. doi: 10.1016/j.exer.2014.04.014. [Epub ahead of print]

Protective effect of a laser-induced sub-lethal temperature rise on RPE cells from oxidative stress.

Iwami H, Pruessner J, Shiraki K, Brinkmann R, Miura Y.

Abstract: Recently introduced new technologies that enable temperature-controlled laser irradiation on the RPE allowed us to investigate temperature-resolved RPE cell responses. In this study we aimed primarily

to establish an experimental setup that can realize laser irradiation on RPE cell culture with the similar temperature distribution as in the clinical application, with a precise time/temperature history. With this setup, we conducted investigations to elucidate the temperature-dependent RPE cell biochemical responses and the effect of transient hyperthermia on the responses of RPE cells to the secondary-exposed oxidative stress. Porcine RPE cells cultivated in a culture dish (inner diameter= 30 mm) with culture medium were used, on which laser radiation (λ=1940 nm, spot diameter= 30 mm) over 10 seconds was applied as a heat source. The irradiation provides a radially decreasing temperature profile which is close to a Gaussian shape with the highest temperature in the center. Power setting for irradiation was determined such that the peak temperature (Tmax) in the center of the laser spot at the cells reaches from 40°C to 58°C (40, 43, 46, 50, 58 °C). Cell viability was investigated with ethidium homodimer III staining at the time points of 3 and 24 hours following laser irradiation. Twenty four hours after laser irradiation the cells were exposed to hydrogen peroxide (H2O2) for 5 hours, followed by the measurement of intracellular glutathione, intracellular 4-hydroxynonenal (HNE)-protein adducts, and secreted vascular endothelial growth factor (VEGF). The mean temperature threshold for RPE cell death after 3 hours was found to be around 52°C, and for 24 hours around 50°C with the current irradiation setting. A sub-lethal preconditioning on Tmax=43 °C significantly induced the reduced glutathione (GSH)/ oxidized glutathione (GSSG) ratio, and decreased H2O2-induced increase of intracellular 4-HNE adducts. Although sub-lethal hyperthermia (Tmax=40 °C, 43 °C, and 46 °C) caused a slight increase of VEGF secretion in 6 hours directly following irradiation, secondary exposed H2O2-induced VEGF secretion was significantly reduced in the sub-lethally preheated groups, where the largest effect was seen following the irradiation with Tmax=43 °C. In summary, the current results suggest that sub-lethal thermal laser irradiation on the RPE at Tmax=43 °C for 10 seconds enhances cell defense system against oxidative stress, with increasing the GSH/GSSG ratio. Together with the results that the decreased amount of H2O2-induced 4-HNE in sub-lethally preheated RPE cells was accompanied by the lower secretion of VEGF, it is also strongly suggested that the sub-lethal hyperthermia may modify RPE cell functionality to protect RPE cells from oxidative stress and associated functional decrease, which are considered to play a significant role in the pathogenesis of age-related macular degeneration and other chorioretinal degenerative diseases.

PMID: 24800654 [PubMed - as supplied by publisher]

Clin Experiment Ophthalmol. 2014 May 7. doi: 10.1111/ceo.12353. [Epub ahead of print]

Reticular macular lesions: a review of the phenotypic hallmarks and their clinical significance.

Saade C, Smith RT.

Abstract: Reticular macular lesions, also known as "reticular macular disease," "reticular drusen," "reticular pseudodrusen," or "subretinal drusenoid deposits," are a pattern of lesions commonly found in age-related macular degeneration and best visualised using at least 2 imaging techniques in combination. Reticular lesions have 4 stages of progression observable on spectral domain optical coherence tomography, but they do not show the usual signs of regression of soft drusen (calcification and pigment changes). Furthermore, reticular lesions correlate histologically with subretinal drusenoid deposits localised between the retinal pigment epithelium and the inner segment ellipsoid band. Reticular lesions are most commonly seen in older age groups of female patients with age-related macular degeneration and are usually bilateral. They are not clearly associated with known age-related macular degeneration genes and are highly associated with late-stage age-related macular degeneration and an increased mortality rate. They are also associated with alterations in the neural retina and choroid.

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Pathogenesis

FASEB J. 2014 May 8. [Epub ahead of print]

DICER1 is essential for survival of postmitotic rod photoreceptor cells in mice.

Sundermeier TR, Zhang N, Vinberg F, Mustafi D, Kohno H, Golczak M, Bai X, Maeda A, Kefalov VJ, Palczewski K.

Abstract: Photoreceptor cell death is the proximal cause of blindness in many retinal degenerative disorders; hence, understanding the gene regulatory networks that promote photoreceptor survival is at the forefront of efforts to combat blindness. Down-regulation of the microRNA (miRNA)-processing enzyme DICER1 in the retinal pigmented epithelium has been implicated in geographic atrophy, an advanced form of age-related macular degeneration (AMD). However, little is known about the function of DICER1 in mature rod photoreceptor cells, another retinal cell type that is severely affected in AMD. Using a conditional-knockout (cKO) mouse model, we report that loss of DICER1 in mature postmitotic rods leads to robust retinal degeneration accompanied by loss of visual function. At 14 wk of age, cKO mice exhibit a 90% reduction in photoreceptor nuclei and a 97% reduction in visual chromophore compared with those in control littermates. Before degeneration, cKO mice do not exhibit significant defects in either phototransduction or the visual cycle, suggesting that miRNAs play a primary role in rod photoreceptor survival. Using comparative small RNA sequencing analysis, we identified rod photoreceptor miRNAs of the miR-22, miR-26, miR-30, miR-92, miR-124, and let-7 families as potential factors involved in regulating the survival of rods.

PMID: 24812086 [PubMed - as supplied by publisher]

Cold Spring Harb Perspect Med. 2014 May 5. pii: cshperspect.a017194v1. doi: 10.1101/cshperspect.a017194. [Epub ahead of print]

The Proteomics of Drusen.

Crabb JW.

Abstract: The formation of extracellular deposits known as drusen below the macular region of the retina correlates with increased risk of severe visual loss from age-related macular degeneration (AMD). Inflammation and complement dysregulation contribute to AMD progression; however, disease mechanisms remain incompletely defined. Multiple genetic and environmental factors influence AMD pathology, and although immune system processes play a central role, multiple molecular mechanisms appear to be involved. Drusen proteomics, including the analyses of constituent proteins, oxidative protein modifications, and pattern recognition receptors, provide a foundation for deciphering mechanisms of drusen biogenesis and AMD pathology.

PMID: 24799364 [PubMed - as supplied by publisher]

PLoS One. 2014 May 5;9(5):e96371. doi: 10.1371/journal.pone.0096371. eCollection 2014.

A Novel Antibody against Human Properdin Inhibits the Alternative Complement System and Specifically Detects Properdin from Blood Samples.

Pauly D, Nagel BM, Reinders J, Killian T, Wulf M, Ackermann S, Ehrenstein B, Zipfel PF, Skerka C, Weber BH.

Abstract: The complement system is an essential part of the innate immune system by acting as a first line of defense which is stabilized by properdin, the sole known positive regulator of the alternative complement

pathway. Dysregulation of complement can promote a diversity of human inflammatory diseases which are treated by complement inhibitors. Here, we generated a novel blocking monoclonal antibody (mAb) against properdin and devised a new diagnostic assay for this important complement regulator. Mouse mAb 1340 specifically detected native properdin from human samples with high avidity. MAb 1340 inhibited specifically the alternative complement mediated cell lysis within a concentration range of 1-10 µg/mL. Thus, in vitro anti-properdin mAb 1340 was up to fifteen times more efficient in blocking the complement system as compared to anti-C5 or anti-Ba antibodies. Computer-assisted modelling suggested a three-dimensional binding epitope in a properdin-C3(H2O)-clusterin complex to be responsible for the inhibition. Recovery of properdin in a newly established sandwich ELISA using mAb 1340 was determined at 80-125% for blood sample dilutions above 1:50. Reproducibility assays showed a variation below 25% at dilutions less than 1:1,000. Systemic properdin concentrations of healthy controls and patients with age-related macular degeneration or rheumatic diseases were all in the range of 13-30 µg/mL and did not reveal significant differences. These initial results encourage further investigation into the functional role of properdin in the development, progression and treatment of diseases related to the alternative complement pathway. Thus, mAb 1340 represents a potent properdin inhibitor suitable for further research to understand the exact mechanisms how properdin activates the complement C3-convertase and to determine quantitative levels of properdin in biological samples.

PMID: 24797388 [PubMed - in process]

Exp Eye Res. 2014 May 2. pii: S0014-4835(14)00113-4. doi: 10.1016/j.exer.2014.04.017. [Epub ahead of print]

Age-related macular degeneration and cognitive impairment show similarities in changes of neutral lipids in peripheral blood mononuclear cells.

Peiretti E, Mandas A, Abete C, Vinci M, Piludu S, Casu M, Caminiti G, Dessì S, Fossarello M.

Abstract: Starting from previous studies showing that patients with cognitive deficit present neutral lipids (NLs) accumulation in cytoplasm of their peripheral blood mononuclear cells (PBMCs) and considering that there is epidemiological evidence linking age-related macular degeneration (AMD) to cognitive deficit, the first purpose of this study was to test whether neutral lipids also accumulated in PBMCs from AMD subjects. Moreover, the impact of statin use on AMD was explored and whether such use in AMD subjects was associated with NLs accumulation in PBMCs. The study was conducted on 222 subjects: 136 AMD (36 of which - 26.5% - using statins], 48 cognitive deficit (20 of which - 41.7% - using statins) and 38 healthy controls (4 of which -10.1% - using statins), AMD lesions were assessed from color fundus photographs. Mini-mental state examination (MMSE), demographics, lifestyle factors and medical history were collected at interview. MMSE score was categorized as normal (24-30), and impaired (<24), NLs content was evaluated by oil red 0 (ORO) staining method. ORO determination showed that neutral lipids were generally absent or very low (score between 0 and 1) in healthy controls while most of PBMCs from cognitive deficit and AMD had ORO staining levels scoring 2-4. Post hoc analysis (Bonferroni) in a one-way ANOVA revealed that ORO score was significantly higher in cognitive deficit and AMD subjects compared to healthy controls and in cognitive deficit compared to AMD. Bonferroni-test also showed that AMD subjects had significantly lower total cholesterol (TC) levels compared to healthy controls while high density lipoprotein-cholesterol (HDL-C) did not reach statistical significance. The results also revealed a significant higher number of statin-users in AMD compared to healthy controls. Likewise when cognitive deficit vs healthy controls was analyzed, the number of statin users were found to be significant higher in cognitive deficit than in healthy controls. There were no significant differences in statin use between AMD and cognitive deficit. Compared to healthy controls, statin use in cognitive deficit and AMD groups was significantly associated with ORO scores of 2-4. This data supports the hypothesis that AMD and cognitive deficit share similar complex pathophysiology and risk factors including NLs accumulation in their PBMCs, although this does not necessarily imply that one disease causes the other. In addition, they provide further evidence that statin use may increase the risk of AMD.

PMID: 24792172 [PubMed - as supplied by publisher]

Transl Res. 2014 Apr 15. pii: S1931-5244(14)00129-7. doi: 10.1016/j.trsl.2014.04.005. [Epub ahead of print]

The role of proteases and inflammatory molecules in triggering neovascular age-related macular degeneration: basic science to clinical relevance.

Balasubramanian SA, Kumar KK, Baird PN.

Abstract: Age-related macular degeneration (AMD) causes severe vision impairment in aged individuals. The health impact and cost of the disease will dramatically increase over the years, with the increase in the aging population. Currently, antivascular endothelial growth factor agents are routinely used for managing late-stage AMD, and recent data have shown that up to 15%-33% of patients do not respond to this treatment. Henceforth, there is a need to develop better treatment options. One avenue is to investigate the role proteases and inflammatory molecules might have in regulating and being regulated by vascular endothelial growth factor. Moreover, emerging data indicate that proteases and inflammatory molecules might be critical in the development and progression of AMD. This article reviews recent literature that investigates proteases and inflammatory molecules involved in the development of AMD. Gaining insights into the proteolytic and inflammatory pathways associated with the pathophysiology of AMD could enable the development of additional or alternative drug strategies for the treatment of AMD.).

PMID: 24794954 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 May 8. pii: iovs.14-14107v1. doi: 10.1167/iovs.14-14107. [Epub ahead of print]

Dysregulation of CXCR3 expression on peripheral blood leukocytes in patients with neovascular AMD.

Falk MK, Singh A, Faber C, Nissen MH, Hviid T, Sørensen TL.

Purpose: The chemokine receptor CXCR3 has been strongly related to inhibition of angiogenesis. The purpose of this study was to investigate the association between expression of CXCR3 on peripheral blood leukocytes and Age-related Wet Macular Degeneration (AMD). Furthermore, we measured the plasma concentration of the chemokines CXCL9-11.

Methods: The study group consisted of patients with AMD attending our department. Patients referred for other reasons than AMD were enrolled as control persons. The expression of CXCR3 on T-cells and the plasma concentration of CXCL9-11 were measured using flow cytometry.

Results: We looked at all CD8+ T-cells expressing CXCR3 and found a significant lower percentage of these cells in the neovascular AMD group compared to the age-matched control group (p=0.05). When dividing the CD8+ cells in functional groups according to their expression of CXCR3, we found a significant lower percentage of CD8+ CXCR3high cells in the group with neovascular AMD compared to the control group (p=0.038). We found a lower percentage of CD4+CD69+CXCR3+ T-cells in the group of patients with neovascular AMD, when compared to the age-matched control group. (p=0.052).

Conclusions: Our results points towards a systemic dysregulation of CXCR3 in patients with neovascular AMD. Since there is evidence to suggest that CXCR3 is able to alter the response of VEGF the primary driver of CNV formation, low levels of CXCR3 could potentially drive some patients towards a more angiogenic profile leading to choroidal neovascularisation (CNV) formation and growth. CXCR3-enhancing molecules could therefore be a possible target for treatment of AMD.

PMID: 24812555 [PubMed - as supplied by publisher]

Epidemiology

Ophthalmology. 2014 Apr 11. pii: S0161-6420(14)00203-6. doi: 10.1016/j.ophtha.2014.03.005. [Epub ahead of print]

Vasodilators, Blood Pressure-Lowering Medications, and Age-related Macular Degeneration: The Beaver Dam Eye Study.

Klein R, Myers CE, Klein BE.

OBJECTIVE: To examine the association of vasodilator and antihypertensive medication use with the incidence of age-related macular degeneration (AMD).

DESIGN: Longitudinal population-based study.

PARTICIPANTS: Persons 43 to 86 years of age living in Beaver Dam, Wisconsin, from 1988 through 1990.

METHODS: Examinations were performed every 5 years over a 20-year period. There were 9676 total person-visits over the course of the study. Status of AMD was determined from grading retinal photographs.

MAIN OUTCOME MEASURES: Incidence of AMD.

RESULTS: The 5-year incidence of early AMD over the 20-year period was 8.4%; for late AMD, it was 1.4%; for pure geographic atrophy (GA), it was 0.6%; for exudative AMD, it was 0.9%; and for progression of AMD, it was 24.9%. While adjusting for age, gender, and other factors, using a vasodilator (hazard ratio [HR], 1.72; 95% confidence interval [CI], 1.25-2.38), particularly oral nitroglycerin (HR, 1.81; 95% CI, 1.14-2.90), was associated with an increased risk of early AMD. Using an oral β-blocker was associated with an increased hazard of incident exudative AMD (HR, 1.71; 95% CI, 1.04-2.82), but not pure GA (HR, 0.51; 95% CI, 0.20-1.29) or progression of AMD (HR, 0.92; 95% CI, 0.67-1.28) over the 20-year period.

CONCLUSIONS: Use of vasodilators is associated with a 72% increase in the hazard of incidence of early AMD, and use of oral β-blockers is associated with a 71% increase in the hazard of incident exudative AMD. If these findings are replicated, it may have implications for care of older adults because vasodilators and oral β-blockers are drugs that are used commonly by older persons.

PMID: 24793737 [PubMed - as supplied by publisher]

Genetics

Ophthalmology. 2014 May 6. pii: S0161-6420(14)00190-0. doi: 10.1016/j.ophtha.2013.12.044. [Epub ahead of print]

Re: Hagstrom et al.: Pharmacogenetics for Genes Associated with Age-related Macular Degeneration in the Comparison of AMD Treatments Trials (CATT). (Ophthalmology 2013;120:593-9).

Piermarocchi S, Miotto S.

PMID: 24811964 [PubMed - as supplied by publisher]

Ophthalmology. 2014 May 1. pii: S0161-6420(14)00195-X. doi: 10.1016/j.ophtha.2013.12.046. [Epub ahead of print]

Re: Awh et al.: CFH and ARMS2 Genetic Polymorphisms Predict Response to Antioxidants and Zinc in Patients with Age-Related Macular Degeneration. (Ophthalmology 2013;120:2317-23).

Schwartz SG.

PMID: 24793508 [PubMed - as supplied by publisher]

Diet & lifestyle

Am J Ophthalmol. 2014 Apr 29. pii: S0002-9394(14)00219-0. doi: 10.1016/j.ajo.2014.04.016. [Epub ahead of print]

The Relationship of Major American Dietary Patterns to Age-related Macular Degeneration.

Chiu CJ, Chang ML, Zhang FF, Li T, Gensler G, Schleicher M, Taylor A.

PURPOSE:We hypothesized that major American dietary patterns are associated with age-related macular degeneration (AMD) risk.

DESIGN:Cross-sectional study METHODS: 8,103 eyes from 4,088 eligible participants in the baseline Age-Related Eye Disease Study (AREDS) were classified into control (n=2,739), early AMD (n=4,599), and advanced AMD (n=765) by AREDS AMD Classification System. Food consumption data were collected by a 90-item food frequency questionnaire.

RESULTS: Two major dietary patterns were identified by factor (principle component) analysis based on 37 food groups and named Oriental and Western patterns. The Oriental pattern was characterized by higher intake of vegetables, legumes, fruit, whole grains, tomatoes, and seafood. The Western pattern was characterized by higher intake of red meat, processed meat, high-fat dairy products, French fries, refined grains, and eggs. We ranked our participants according to how closely their diets line up with the two patterns by calculating the two factor scores for each participant. For early AMD, multivariate-adjusted odds ratio (OR) from generalized estimating equation logistic analysis comparing the highest to lowest quintile of the Oriental pattern score was ORE5O=0.74 (95% confidence interval (CI): 0.59-0.91; Ptrend=0.01), and the OR comparing the highest to lowest quintile of the Western pattern score was ORE5W=1.56 (1.18-2.06; Ptrend=0.01). For advanced AMD, the ORA5O was 0.38 (0.27-0.54; Ptrend<0.0001), and the ORA5W was 3.70 (2.31-5.92; Ptrend<0.0001).

CONCLUSIONS: Our data indicate that overall diet is significantly associated with the odds of AMD and that dietary management as an AMD prevention strategy warrants further study.

PMID: 24792100 [PubMed - as supplied by publisher]

Cell Death Dis. 2014 May 8;5:e1218. doi: 10.1038/cddis.2014.190.

Zeaxanthin induces Nrf2-mediated phase II enzymes in protection of cell death.

Zou X, Gao J, Zheng Y, Wang X, Chen C, Cao K, Xu J, Li Y, Lu W, Liu J, Feng Z.

Abstract: Zeaxanthin (Zea) is a major carotenoid pigment contained in human retina, and its daily supplementation associated with lower risk of age-related macular degeneration. Despite known property of Zea as an antioxidant, its underlying molecular mechanisms of action remain poorly understood. In this study, we aim to study the regulation mechanism of Zea on phase II detoxification enzymes. In normal human retinal pigment epithelium cells, Zea promoted the nuclear translocation of NF-E2-related factor 2 (Nrf2) and induced mRNA and protein expression of phase II enzymes, the induction was suppressed by specific knockdown of Nrf2. Zea also effectively protected against tert-butyl hydroperoxide-induced mitochondrial dysfunction and apoptosis. Glutathione (GSH) as the most important antioxidant was also induced by Zea through Nrf2 activation in a time- and dose-dependent manner, whereas the protective effects of Zea were decimated by inhibition of GSH synthesis. Finally, Zea activated the PI3K/Akt and

MAPK/ERK pathway, whereas only PI3K/Akt activation correlated with phase II enzymes induction and Zea protection. In further in vivo analyses, Zea showed effects of inducing phase II enzymes and increased GSH content, which contributed to the reduced lipid and protein peroxidation in the retina as well as the liver, heart, and serum of the Sprague-Dawley rats. For the first time, Zea is presented as a phase II enzymes inducer instead of being an antioxidant. By activating Nrf2-mediated phase II enzymes, Zea could enhance anti-oxidative capacity and prevent cell death both in vivo and in vitro.

PMID: 24810054 [PubMed - in process]

Patient Prefer Adherence. 2014 Apr 25;8:565-74. doi: 10.2147/PPA.S61505. eCollection 2014.

Patient education preferences in ophthalmic care.

Rosdahl JA, Swamy L, Stinnett S, Muir KW.

BACKGROUND: The learning preferences of ophthalmology patients were examined.

METHODS: Results from a voluntary survey of ophthalmology patients were analyzed for education preferences and for correlation with race, age, and ophthalmic topic.

RESULTS: To learn about eye disease, patients preferred one-on-one sessions with providers as well as printed materials and websites recommended by providers. Patients currently learning from the provider were older (average age 59 years), and patients learning from the Internet (average age 49 years) and family and friends (average age 51 years) were younger. Patients interested in cataracts, glaucoma, macular degeneration, and dry eye were older; patients interested in double vision and glasses were younger. There were racial differences regarding topic preferences, with Black patients most interested in glaucoma (46%), diabetic retinopathy (31%), and cataracts (28%) and White patients most interested in cataracts (22%), glaucoma (22%), and macular degeneration (19%).

CONCLUSION: MOST OPHTHALMOLOGY PATIENTS PREFERRED PERSONALIZED EDUCATION: one-on-one with their provider or a health educator and materials (printed and electronic) recommended by their provider. Age-related topics were more popular with older patients, and diseases with racial risk factors were more popular with high risk racial groups.

PMID: 24812493 [PubMed]