Drug treatment


Impact of baseline central retinal thickness on outcomes in the VIVID-DME and VISTA-DME studies.

Midena E, Gillies M, Katz TA, Metzig C, Lu C, Ogura Y.

Purpose: To report the impact of baseline central retinal thickness (CRT) on outcomes in patients with diabetic macular edema (DME) in VIVID-DME and VISTA-DME.

Methods: Post hoc analyses of two randomized controlled trials in which 862 DME patients were randomized 1 : 1 : 1 to treatment with intravitreal aflibercept 2.0 mg every 4 weeks (2q4), intravitreal aflibercept 2.0 mg every 8 weeks after five initial monthly doses (2q8), or macular laser photocoagulation at baseline and as needed. We compared visual and anatomical outcomes in subgroups of patients with baseline CRT < 400 μm and ≥400 μm.

Results: At weeks 52 and 100, outcomes with intravitreal aflibercept 2q4 and 2q8 were superior to those in laser control-treated patients regardless of baseline CRT. When looked at in a binary fashion, the treatment effect of intravitreal aflibercept versus laser was not significantly better in the ≥400 μm than the <400 μm group; when looked at as a continuous variable, baseline CRT seemed to have an impact on the treatment effect of intravitreal aflibercept versus laser.

Conclusions: Post hoc analyses of VIVID-DME and VISTA-DME demonstrated the benefits of intravitreal aflibercept treatment in DME patients with baseline CRT < 400 μm and ≥400 μm. This trial is registered with NCT01331681 and NCT01363440.

PMID: 29785301 PMCID: PMC5896224 DOI: 10.1155/2018/3640135


Vitreomacular interface abnormalities in patients with diabetic macular oedema and their implications on the response to anti-VEGF therapy.

Mikhail M, Stewart S, Seow F, Hogg R, Lois N.

Purpose: To determine whether the presence of vitreomacular interface abnormalities (VMIA) in patients with diabetic macular oedema (DMO) modifies the response to ranibizumab.

Methods: Medical records and spectral-domain optical coherence tomography (SD-OCT) scans of
consecutive patients with centre-involving DMO initiating therapy with ranibizumab between December 2013 and March 2014 at the Belfast Health and Social Care Trust were reviewed. Patients were identified through an electronic database. Demographics; systemic baseline characteristics; history of previous ocular surgery/laser; best-corrected visual acuity (BCVA), central retinal thickness (CRT) and stage of retinopathy at presentation; and BCVA, CRT and presence/absence of fluid at the last follow-up were recorded. OCT scans were reviewed by a masked investigator who graded them for the presence/absence of VMIA at baseline and during follow-up and for the change in the posterior hyaloid face during follow-up. The association between (1) VMIA at baseline and (2) the change in the posterior hyaloid face during the follow-up and functional/anatomical outcomes was evaluated.

Results: One hundred forty-six eyes of 100 patients (mean age 63.5 years) followed for a mean of 9 months (range 2-14 months; only 9/146 dropped to follow-up before month 6) were included. Statistically significant differences were observed at baseline in BCVA ($p = 0.007$), previous macular laser and panretinal photocoagulation (PRP) ($p = 0.006$) and previous cataract surgery ($p = 0.01$) between eyes with and without VMIA, with better levels of vision, higher frequency of macular laser and lower frequency of PRP in eyes where no VMIA was present. Multivariable regression analysis did not disclose any statistically significant associations between VMIA at baseline or change in the posterior hyaloid face during the follow-up and functional and anatomical outcomes following treatment.

Conclusion: VMIA are associated with worse presenting vision in patients with DMO; VMIA or change in the posterior hyaloid face during the follow-up did not modify the response to ranibizumab in this study.

PMID: 29779188 DOI: 10.1007/s00417-018-4009-6

Ophthalmologe. 2018 May 22. [Epub ahead of print]

Clinical parameters of patients with neovascular age-related macular degeneration: Longterm treatment results of an outpatient clinic.

[Article in German]

Wassel S, Tsompanidi E, Tahmaz E, Hörster B, Hoerster R.

Background: The clinical outcome of neovascular age-related macular degeneration (nAMD) depends on constant follow-up and consistent treatment. Data about the long-term course of intensive anti-vascular endothelial growth factor (VEGF) therapy from outpatient clinics are rare.

Objective: The aim of the study was to characterize a population of nAMD patients with long-term follow-up and intensive anti-VEGF therapy.

Patients and Methods: In a supra-regional outpatient clinic, we retrospectively identified patients who had received at least 30 intravitreal anti-VEGF injections and were followed for at least 4 years. All patients received an optical coherence tomography (OCT)-controlled Pro-Re-Nata (PRN) therapy regimen according to German guidelines.

Results: We identified 43 patients. Visual acuity at baseline was $0.44 \pm 0.24$ (1.0-0.1) logMAR. At the end of the follow-up period, visual acuity was $0.63 \pm 3.6$ (1.3-0.1) logMAR. Patients received a mean of $36.3 \pm 8.0$ (30-62) injections and were followed for a mean of $6.1 \pm 1.8$ (4-12) years. They received $6.12 \pm 1.5$ (3.1-9.9) injections per year. The number of injections in treatment-year one was with $3.67 \pm 1.9$ (1-8) significantly lower than the mean ($p < 0.0001$).

Conclusion: Despite intensive PRN therapy, visual acuity slowly decreased over time. The mean number of injections was comparable to that of prospective studies. The low number of injections in treatment-year 1 may have been due to a lack of experience with the new treatment agents. The slow decrease in visual acuity in clinical routine as opposed to clinical studies may be attributed to a delay between occurrence of disease activity and treatment.

Development of novel drugs for ocular diseases: possibilities for individualized therapy.
Lai TY, Chen LJ, Yam GH, Tham CC, Pang CP.

Abstract: In clinical ophthalmology, new and old drug regimens are available for the treatment of major eye diseases, including potentially blinding conditions, such as glaucoma, and various macular diseases. In glaucoma, therapeutic treatment mainly deals with control of intraocular pressure at low levels but the clinical courses of patients can be very variable. Very often, specific drug combinations and dosages have to be formulated for individual glaucoma patients. In neovascular age-related macular degeneration, choroidal neovascularization can lead to progressive and irreversible visual impairment if not treated early. In recent years, clinical trials using photodynamic therapy with verteporfin and various anti-VEGF antibodies, such as ranibizumab and bevacizumab, have enhanced the treatment outcomes of neovascular age-related macular degeneration. In diabetic macular edema, intravitreal triamcinolone acetonide and anti-VEGF therapy are effective in some patients. Again, responses to treatment are not uniform in all macular patients. Traditional herbal medicine has long been known to play a role in the practice of personalized formulations in Asia. Potential preventive and therapeutic effects have been claimed in individual eye patients. Meanwhile, advanced technologies in molecular biology have led to identification of genes associated with many eye diseases and development of the concept of individual medicine, in which the genotype of a person can be used as a basis for disease prediction or prophylactic treatments. Moreover, pharmacogenomic studies have demonstrated the association of various genotypes or haplotypes with responses to drug therapies, providing hope for tailormade personalized treatments. The combination of genotypic information with clinical features for the prescription of treatment modes in eye diseases is under vigorous research.


Assessing the role of ranibizumab in improving the outcome of glaucoma filtering surgery and neovascular glaucoma.
Katsanos A, Gorgoli K, Mikropoulos DG, Arranz-Marquez E, Athanasopoulos GP, Teus MA, Konstas AGP.

Abstract: Ranibizumab was the first anti-vascular endothelial growth factor (VEGF) agent approved for the treatment of neovascular age-related macular degeneration. The use of ranibizumab and other anti-VEGF medications in recent years has revolutionized the treatment of several sight-threatening retinal disorders. Emerging evidence has demonstrated that anti-VEGF treatment can offer advantages in the management of other ocular conditions where VEGFs play a key role: ocular scarring following glaucoma filtering surgery and neovascular glaucoma (NVG). Areas covered: We critically review available evidence on the use of ranibizumab as a wound healing modulator in glaucoma filtering surgery and as an adjunct in the management of NVG. Expert opinion: Based on the available evidence and the authors’ clinical experience, ranibizumab is a valuable adjunct in the management of NVG. In glaucoma filtering surgery, however, the role of ranibizumab is less clear and does not provide a significant advantage over mitomycin C. Drawbacks for its use in glaucoma include cost, its off-label use, uncertainty and limited evidence on the various routes of administration, the optimal dosing schemes and its toxicity profile. Future advances in ranibizumab delivery systems allowing less frequent dosing may change this treatment paradigm.
Real study: Re-treatment evaluated on visual acuity for Lucentis® in neovascular AMD.

Bellocq D, De Bats F, Rabilloud M, Kodjikian L.

Purpose: To assess the value of a monthly injection of Lucentis® until stable visual acuity (VA) is obtained for three consecutive months without exudation in patients with neovascular age macular degeneration (AMD).

Methods: Prospective, single-center, non-controlled trial including naïve AMD patients with neovascularization. An assessment of VA and a spectral domain optical coherence tomography (SD-OCT) were performed at baseline and every month. Monthly injections of Lucentis® were performed over three months. The monthly injections were then continued until three consecutive stable VA results were obtained with no signs of exudation.

Results: Fifteen out of the 21 patients included were anatomically good responders. A mean gain of +14Le (9) was obtained up to the point at which there was no exudation. There was no additional gain from this point until 3 consecutive stable VA results were obtained. During the PRN phase, an additional mean gain of +3.2Le (7.7) was obtained.

Conclusion: This initial VA-guided regimen with ranibizumab might prevent the slight decrease in VA observed during the first year of PRN studies.

PMID: 29779934 DOI: 10.1016/j.jfo.2017.10.014

Other treatment and diagnosis

Retina. 2018 May;38(5):962-969.

A randomized double-blind placebo-control pilot study of eplerenone for the treatment of central serous chorioretinopathy (ECSELSIOR).


Purpose: To evaluate the safety and effects of oral eplerenone in chronic central serous chorioretinopathy.

Methods: Prospective, randomized, double-blind, placebo-control study at a tertiary referral academic private practice. For a diagnosis of chronic central serous chorioretinopathy, patients must have had at least 3 months clinical follow-up demonstrating persistent symptoms, subfoveal fluid on spectral-domain optical coherence tomography, and <50% reduction in fluid thickness. Patients were randomized 2:1 (treatment:placebo) to receive eplerenone (25 mg daily for 1 week, then up to 50 mg daily for 8 weeks) or placebo once daily.

Results: Fifteen patients completed the study. Ten patients (15 eyes) were randomized into the eplerenone treatment arm, while the remaining 5 patients (6 eyes) received placebo. After 9 weeks of eplerenone therapy, mean logarithm of the minimal angle of resolution visual acuity improved from 0.394 (Snellen equivalent: 20/50) to 0.330 (20/43, P = 0.04). In the placebo group, the mean logarithm of the minimal angle of resolution visual acuity slightly decreased from 0.313 (20/41) to 0.342 (20/44) during the same period (P = 0.21). With respect to anatomic changes, mean maximal subretinal fluid height in the eplerenone group improved from 139.3 μm at baseline to 51.8 μm (P = 0.02), mean subfoveal fluid height improved from 121.4 μm to 29.4 μm (P = 0.01), and mean central subfield thickness improved from 366.2 μm to 283.7 μm (P = 0.02). In comparison with the placebo group, mean maximal subretinal fluid height worsened from 135.9 μm to 172.3 μm (P = 0.32), mean subfoveal fluid height worsened from 92.1 μm to 134.0 μm (P = 0.54), and mean central subfield thickness worsened from 345.0 μm to 380.0 μm (P = 0.37).
No patients in either group experienced serious adverse events to result in treatment discontinuation.

**Conclusion:** These findings suggest that oral eplerenone therapy is safe and potentially effective in the treatment of chronic central serous chorioretinopathy with persisting subretinal fluid.

PMID: 28426624 DOI: 10.1097/IAE.0000000000001649

**Eye (Lond). 2018 May 22. [Epub ahead of print]**

**Spectral analysis of fundus autofluorescence pattern as a tool to detect early stages of degeneration in the retina and retinal pigment epithelium.**

Feldman TB, Yakovleva MA, Larichev AV, Arbukhanova PM, Radchenko AS, Borzenok SA, Kuzmin VA, Ostrovsky MA.

**Purpose:** The aim of this work is the determination of quantitative diagnostic criteria based on the spectral characteristics of fundus autofluorescence to detect early stages of degeneration in the retina and retinal pigment epithelium (RPE).

**Methods:** RPE cell suspension samples were obtained from the cadaver eyes with and without signs of age-related macular degeneration (AMD). Fluorescence analysis at an excitation wavelength of 488 nm was performed. The fluorescence lifetimes of lipofuscin-granule fluorophores were measured by counting time-correlated photon method.

**Results:** Comparative analysis of fluorescence spectra of RPE cell suspensions from the cadaver eyes with and without signs of AMD showed a significant difference in fluorescence intensity at 530-580 nm in response to fluorescence excitation at 488 nm. It was notably higher in eyes with visual pathology than in normal eyes regardless of the age of the eye donor. Measurements of fluorescence lifetimes of lipofuscin fluorophores showed that the contribution of photooxidation and photodegradation products of bisretinoids to the total fluorescence at 530-580 nm of RPE cell suspensions was greater in eyes with visual pathology than in normal eyes.

**Conclusion:** Because photooxidation and photodegradation products of bisretinoids are markers of photodestructive processes, which can cause RPE cell death and initiate degenerative processes in the retina, quantitative determination of increases in these bisretinoid products in lipofuscin granules may be used to establish quantitative diagnostic criteria for degenerative processes in the retina and RPE.

PMID: 29786089 DOI: 10.1038/s41433-018-0109-0


**Preventing the growth of geographic atrophy: An important therapeutic target in age-related macular degeneration.**

Rosenfeld PJ.

**Abstract:** Loss of central vision from geographic atrophy (GA) is a late stage complication of age-related macular degeneration (AMD) as the central foveal region becomes consumed by the disease. Until recently, GA had not received the attention it deserved from the pharmaceutical industry. Over the years, most of the clinical trial community has been focused on the exudative or neovascular form of AMD due to the rapid and severe vision loss often associated with this form of the disease. With the success of vascular endothelial growth factor inhibitors in slowing and preventing the devastating vision loss from neovascularization in exudative AMD, the development of macular atrophy after anti-vascular endothelial growth factor therapy and growth of GA in nonexudative AMD have become the most common causes of vision loss from AMD.
Prognostic value of shape-descriptive factors for the progression of geographic atrophy secondary to age-related macular degeneration.


**Purpose:** To systematically compare the prognostic value of multiple shape-descriptive factors in the natural course of the disease.

**Methods:** A total of 296 eyes of 201 patients (female patients 130; mean age: 72.2 ± 13.08 years) with a median follow-up of 2.38 years from 2 prospective, noninterventional natural history studies (Fundus-Autofluorescence-in-Age-related-Macular-Degeneration [clinicaltrials.gov identifier NCT00393692], Directional-Spread-in-Geographic-Atrophy [NCT02051998]) were included in the analysis. Serial fundus autofluorescence images were annotated using semi-automated image analysis software to determine the lesion area, circularity, perimeter, and caliper diameters. These variables and the fundus autofluorescence phenotype were evaluated for prediction of the future square root progression rates using linear mixed-effects models.

**Results:** For the combined model, leave-one-out cross validation on patient level (Scenario 1: previously unknown patient) resulted in a goodness-to-fit (R value) of 0.244 and leave-one-out cross validation on visit level (Scenario 2: previous observation of the patient) in a R value of 0.391. This indicated that shape-descriptive factors could explain 24.4% of the variance in geographic atrophy progression in previously unknown patients and 39.1% in patients with previous observation.

**Conclusion:** These findings confirm the relevance of shape-descriptive factors and previous progression as prognostic variables for geographic atrophy progression. However, a substantial part of the remaining variation in geographic atrophy progression seems to depend on other variables, some of which are visible in optical coherence tomography.

PMID: 29781974 DOI: 10.1097/IAE.0000000000002206

**Pathogenesis**


Lashkari K, Teague G, Chen H, Lin YQ, Kumar S, McLaughlin MM, López FJ.

**Abstract:** Activation of the alternative complement cascade has been implicated in the pathogenesis of age related macular degeneration (AMD) and Alzheimer's disease (AD). Amyloid β (Aβ), a component of drusen, may promote complement activation by inhibiting CFI bioactivity. We determined whether Aβ reduced CFI bioactivity and whether antibodies against Aβ including a monoclonal antibody, GSK933776 could restore CFI bioactivity. We also measured CFI bioactivity in plasma of subjects with AMD and AD. In support of the GSK933776 development program in AMD (geographic atrophy), we developed a quantitative assay to measure CFI bioactivity based on its ability to cleave C3b to iC3b, and repeated it in presence or absence of Aβ and anti-Aβ antibodies. Using this assay, we measured CFI bioactivity in plasma of 194 subjects with AMD, and in samples from subjects with AD that had been treated with GSK933776 as part of the GSK933776 development program in AD. Aβ reduced the CFI bioactivity by 5-
fold and pre-incubation with GSK933776 restored CFI bioactivity. In subjects with AMD, plasma CFI levels and bioactivity were not significantly different from non-AMD controls. However, we detected a positive linear trend, suggesting increasing activity with disease severity. In subjects with AD, we observed a 10% and 27% increase in overall CFI bioactivity after treatment with GSK933776 during the second and third dose. Our studies indicate that CFI enzymatic activity can be inhibited by Aβ and be altered in proinflammatory diseases such as AMD and AD, in which deposition of Aβ and activation of the alternative complement cascade are believed to play a key role in the disease process.

PMID: 29782502 DOI: 10.1371/journal.pone.0195751

FASEB J. 2018 May 24:fj201800001RR. [Epub ahead of print]

APR3 modulates oxidative stress and mitochondrial function in ARPE-19 cells.


Abstract: Impairment of retinal pigment epithelial (RPE) cells is considered a key contributor to the development of age-related macular degeneration. Apoptosis-related protein 3 (APR3) was recently discovered after treatment with all-trans retinoic acid, a pivotal molecule in RPE cells. However, the function of APR3 remains poorly understood. In the present study, we found that APR3 could interact with nuclear factor (erythroid-derived 2)-like 2, which is a regulator of phase II enzymes, and that knockdown of APR3 promoted nuclear factor (erythroid-derived 2)-like 2 nuclear translocation and activated expression of phase II enzymes, which was accompanied by improved redox status and mitochondrial activity. Overexpression of APR3 revealed its mitochondrial localization and induced a robust production of reactive oxygen species that was accompanied by impaired mitochondrial oxygen consumption, complex activity, and lower ATP content, resulting in significant changes in mitochondrial structure, which may contribute to cell apoptosis. High doses of all-trans retinoic acid treatment were found to significantly induce APR3 expression, increase reactive oxygen species levels, and decrease ATP content, which were abolished by knockdown of APR3. These results indicate that APR3 plays a vital role in regulating redox status and mitochondrial activity and thus suggest APR3 might be a potential novel target for study of treatment of age-related macular degeneration.

PMID: 29792731 DOI: 10.1096/fj.201800001RR


Intra-vitreal αB crystallin fused to elastin-like polypeptide provides neuroprotection in a mouse model of age-related macular degeneration.


Abstract: Age-related macular degeneration (AMD) is the leading cause of severe and irreversible central vision loss, and the primary site of AMD pathology is the retinal pigment epithelium (RPE). Geographic atrophy (GA) is an advanced form of AMD characterized by extensive RPE cell loss, subsequent degeneration of photoreceptors, and thinning of retina. This report describes the protective potential of a peptide derived from the αB crystallin protein using a sodium iodate (NaIO3) induced mouse model of GA. Systemic NaIO3 challenge causes degeneration of the RPE and neighboring photoreceptors, which have similarities to retinas of GA patients. αB crystallin is an abundant ocular protein that maintains ocular clarity and retinal homeostasis, and a small peptide from this protein (mini cry) displays neuroprotective properties. To retain this peptide for longer in the vitreous, mini cry was fused to an elastin-like polypeptide (ELP). A single intra-vitreal treatment by this crySI fusion significantly inhibits retinal degeneration in comparison to free mini cry. While mini cry is cleared from the eye with a mean residence time of 0.4 days, crySI was retained with a mean residence time of 3.0 days; furthermore, fundus photography revealed evidence of retention at two weeks. Unlike the free mini cry, crySI protects the RPE against NaIO3
challenge for at least two weeks after administration. CrySI also inhibits RPE apoptosis and caspase-3 activation and protects the retina from cell death up to 1-month post NaIO3 challenge. These results show that intra-ocular ELP-linked peptides such as crySI hold promise as protective agents to prevent RPE atrophy and progressive retinal degeneration in AMD.

PMID: 29778783 DOI: 10.1016/j.jconrel.2018.05.014

**Epidemiology**

Ophthalmologe. 2018 May 22. [Epub ahead of print]


[Article in German]

Stahl A.

Background: The treatment of retinopathy of prematurity (ROP) has gained a new dynamic since the introduction of anti-vascular endothelial growth factor (VEGF) therapy. This review summarizes clinical trial data in order to aid informed decision-making.

Methods: In this article, pivotal clinical trials are summarized and discussed with regard to their implications for ROP therapy.

Results: The longest follow-up phase exists for children treated in the CRYO-ROP study, which used retinal cryocoagulation to treat ROP. Based on results of the ETROP study and others, retinal laser therapy has replaced cryotherapy as standard of care. For anti-VEGF treatment, three controlled clinical trials exist to date: BEAT-ROP, CARE-ROP, and the PEDIG study. Combined, these studies demonstrate efficacy of anti-VEGF in treating acute ROP. However, they also emphasize the risk of (late) recurrences and the largely unsolved questions regarding choice of drug and dose as well as long-term safety.

Conclusion: Treatment of ROP remains a highly individual decision in which many variables need to be considered. The data discussed in this article can help in decision-making and emphasize the unique characteristics of the available therapeutic approaches, in particular regarding postoperative follow-up.

PMID: 29789899 DOI: 10.1007/s00347-018-0720-2

**Cochrane Database Syst Rev. 2018 May 22;5:CD011977. [Epub ahead of print]**

Blue-light filtering intraocular lenses (IOLs) for protecting macular health.

Downie LE, Busija L, Keller PR.

Background: An intraocular lens (IOL) is a synthetic lens that is surgically implanted within the eye following removal of the crystalline lens, during cataract surgery. While all modern IOLs attenuate the transmission of ultra-violet (UV) light, some IOLs, called blue-blocking or blue-light filtering IOLs, also reduce short-wavelength visible light transmission. The rationale for blue-light filtering IOLs derives primarily from cell culture and animal studies, which suggest that short-wavelength visible light can induce retinal photoxicity. Blue-light filtering IOLs have been suggested to impart retinal protection and potentially prevent the development and progression of age-related macular degeneration (AMD). We sought to investigate the evidence relating to these suggested benefits of blue-light filtering IOLs, and to consider any potential adverse effects.

Objectives: To assess the effects of blue-light filtering IOLs compared with non-blue-light filtering IOLs, with respect to providing protection to macular health and function.
Search Methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (2017, Issue 9); Ovid MEDLINE; Ovid Embase; LILACS; the ISRCTN registry; ClinicalTrials.gov and the ICTRP. The date of the search was 25 October 2017.

Selection Criteria: We included randomised controlled trials (RCTs), involving adult participants undergoing cataract extraction, where a blue-light filtering IOL was compared with an equivalent non-blue-light filtering IOL.

Data Collection and Analysis: The prespecified primary outcome was the change in distance best-corrected visual acuity (BCVA), as a continuous outcome, between baseline and 12 months of follow-up. Prespecified secondary outcomes included postoperative contrast sensitivity, colour discrimination, macular pigment optical density (MPOD), proportion of eyes with a pathological finding at the macula (including, but not limited to the development or progression of AMD, or both), daytime alertness, reaction time and patient satisfaction. We evaluated findings related to ocular and systemic adverse effects. Two review authors independently screened abstracts and full-text articles, extracted data from eligible RCTs and judged the risk of bias using the Cochrane tool. We reached a consensus on any disagreements by discussion. Where appropriate, we pooled data relating to outcomes and used random-effects or fixed-effect models for the meta-analyses. We summarised the overall certainty of the evidence using GRADE.

Main Results: We included 51 RCTs from 17 different countries, although most studies either did not report relevant outcomes, or provided data in a format that could not be extracted. Together, the included studies considered the outcomes of IOL implantation in over 5000 eyes. The number of participants ranged from 13 to 300, and the follow-up period ranged from one month to five years. Only two of the studies had a trial registry record and no studies referred to a published protocol. We did not judge any of the studies to have a low risk of bias in all seven domains. We judged approximately two-thirds of the studies to have a high risk of bias in domains relating to ‘blinding of participants and personnel’ (performance bias) and ‘blinding of outcome assessment’ (detection bias). We found with moderate certainty, that distance BCVA with a blue-light filtering IOL, at six to 18 months postoperatively, and measured in logMAR, was not clearly different to distance BCVA with a non-blue-light filtering IOL (mean difference (MD) -0.01 logMAR, 95% confidence interval (CI) -0.03 to 0.02, P = 0.48; 2 studies, 131 eyes). There was very low-certainty evidence relating to any potential inter-intervention difference for the proportion of eyes that developed late-stage AMD at three years of follow-up, or any stage of AMD at one year of follow-up, as data derived from one trial and two trials respectively, and there were no events in either IOL intervention group, for either outcome. There was very low-certainty evidence for the outcome for the proportion of participants who lost 15 or more letters of distance BCVA at six months of follow-up; two trials that considered a total of 63 eyes reported no events, in either IOL intervention group. There were no relevant, combinable data available for outcomes relating to the effect on contrast sensitivity at six months, the proportion of eyes with a measurable loss of colour discrimination from baseline at six months, or the proportion of participants with adverse events with a probable causal link with the study interventions after six months. We were unable to draw reliable conclusions on the relative equivalence or superiority of blue-light filtering IOLs versus non-blue-light filtering IOLs in relation to longer-term effects on macular health. We were also not able to determine with any certainty whether blue-light filtering IOLs have any significant effects on MPOD, contrast sensitivity, colour discrimination, daytime alertness, reaction time or patient satisfaction, relative to non-blue-light filtering IOLs.

Authors' Conclusions: This systematic review shows with moderate certainty that there is no clinically meaningful difference in short-term BCVA with the two types of IOLs. Further, based upon available data, these findings suggest that there is no clinically meaningful difference in short-term contrast sensitivity with the two interventions, although there was a low level of certainty for this outcome due to a small number of included studies and their inherent risk of bias. Based upon current, best-available research evidence, it is unclear whether blue-light filtering IOLs preserve macular health or alter risks associated with the development and progression of AMD, or both. Further research is required to fully understand the effects of blue-light filtering IOLs for providing protection to macular health and function.

PMID: 29786830 DOI: 10.1002/14651858.CD011977.pub2
Predictive factors for proliferative vitreoretinopathy formation after uncomplicated primary retinal detachment repair.

Xu K, Chin EK, Bennett SR, Williams DF, Ryan EH, Dev S, Mittra RA, Quiram PA, Davies JB, Parke DW 3rd, Boldt HC, Almeida DRP.

**Purpose:** To determine predictive factors of proliferative vitreoretinopathy (PVR) formation after uncomplicated primary retinal detachment repair.

**Methods:** Retrospective, single-center, case-control study of 74 consecutive patients with (37 eyes) and without (37 eyes) PVR formation after undergoing uncomplicated primary surgery for retinal detachment repair. Logistic regression was used to assess factors associated with PVR formation.

**Results:** Retinal detachment involving the macula was 4.2 times (adjusted odds ratio; 95% confidence interval, 1.4-12.9; \( P = 0.0119 \)) more likely to have PVR formation compared with those without. Patients who were current or former smokers were 3.6 times (adjusted odds ratio; 95% confidence interval, 1.1-11.7; \( P = 0.0352 \)) more likely to have PVR formation compared with nonsmokers. Compared with 25-gauge (g) vitrectomy, larger gauge vitrectomy (20 g or 23 g) was 3.6 times (adjusted odds ratio; 95% confidence interval, 1.2-11.3; \( P = 0.0276 \)) more likely to have PVR formation. Duration of retinal detachment symptoms, high myopia, lens status, lattice degeneration, location of retinal break, number of retinal breaks, and surgical technique (e.g., scleral buckle with or without vitrectomy versus vitrectomy alone) were not found to be predictive of PVR formation.

**Conclusion:** Cigarette smoking and macular involvement are significant risk factors predictive of PVR formation after uncomplicated primary retinal detachment repair.

PMID: 29787465 DOI: 10.1097/IAE.0000000000002184
criteria.

Results: The median number of fulfilled items was 7 (95% CI 7 to 8). No abstract reported all 16 recommended items; the maximum total number was 14, the minimum 3 of 16 items. Multivariate analysis only demonstrated the abstracts’ word counts as being significantly associated with a better reporting of abstracts (Poisson regression-based IRR 1.002, 95% CI 1.001 to 1.003).

Conclusions: Reporting quality of RCT abstracts on AMD investigations showed a considerable potential for improvement to meet the CONSORT abstract reporting recommendations. Furthermore, word counts of abstracts were identified as significantly associated with the overall abstract reporting quality.

PMID: 29789352 DOI: 10.1136/bmjopen-2018-021912

Case Report


Longitudinal ophthalmic findings in a child with Helsmoortel-Van der Aa Syndrome.


Purpose: We present the first detailed ophthalmic description of a child with Helsmoortel-Van der Aa Syndrome (HVDAS), including longitudinal follow-up and analysis.

Observations: After extensive workup, a young child with poor visual behavior, hypotonic cerebral palsy, intellectual disability, and global developmental delay was found to have a heterozygous de novo mutation in the ADNP gene and diagnosed with HVDAS. Ophthalmic findings were remarkable for progressive nystagmus, macular pigment mottling, mild foveal hypoplasia with abnormal macular laminations, persistent rod dysfunction with electronegative waveform, and progressive cone degeneration.

Conclusions and importance: Patients with HVDAS are known to have abnormal visual behavior due to refractive or cortical impairment. However, we present the first description, to our knowledge, of an association with retinal mal-development and degeneration. Thus, patients with HVDAS should be referred for ophthalmic genetics evaluation, and HVDAS should be on the differential diagnosis for young children with global developmental delay who present with nystagmus, rod and cone dysfunction with electronegative waveform, and relative lack of severe structural degeneration on optical coherence tomography.

PMID: 29780943 PMCID: PMC5956711 DOI: 10.1016/j.ajoc.2018.03.015