Drug treatment


Replacing ranibizumab with bevacizumab on the Pharmaceutical Benefits Scheme: where does the current evidence leave us?

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Abstract

The battle between two anti-vascular endothelial growth factor (VEGF) treatment options (ranibizumab and bevacizumab) for neovascular macular degeneration is a topic of particular significance to eye health professionals with an interest in cost-effective treatment. Being the first of its kind directly comparing the two anti-VEGF, a recent large multicentre clinical trial has shown that bevacizumab is not inferior when compared with ranibizumab in regards to efficacy of visual acuity outcomes; the evidence at this stage is inconclusive for safety outcomes. Before bevacizumab can be considered a justifiable replacement for the much more expensive ranibizumab on the Pharmaceutical Benefits Scheme (PBS), its safety in treatment needs further supporting evidence.

PMID: 22621684 [PubMed - as supplied by publisher]


Focal macular electroretinograms after intravitreal injections of bevacizumab for age-related macular degeneration.


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Purpose: To evaluate the changes in the best-corrected visual acuity (BCVA), macular thickness, and focal macular electroretinograms (FMERGs) after three intravitreal injections of bevacizumab for a choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD).

Methods: The medical records of 18 eyes of 18 patients who had received three consecutive monthly intravitreal injections of bevacizumab were retrospectively studied. The BCVA, macular thickness determined by optical coherence tomography (OCT), and FMERGs were measured before the first
injection, and 10 days after each of the intravitreal bevacizumab injections.

Results: The number of eyes whose BCVA improved after the first injection was one (6%), after the second injection was four (22%), and after the third injection was five (28%). The number of eyes whose macular thickness was reduced was four (33%), eight (44%), and ten (56%) after each of the three injections. The number of eyes whose b-wave amplitude of the FMERGs was increased was seven (38%), six (33%), and ten (56%) after each of the three each injections. The mean macular thickness was significantly thinner after the first injection, and the mean BCVA was significantly better after the second injection. The mean amplitude and implicit time of the b-wave of the FMERGs were significantly improved only after the third injection (P <0.05).

Conclusion: All parameters improved but the best was after the third injection indicating that three monthly intravitreous injection with bevacizumab may be an effective treatment regimen for AMD.

PMID: 22618591 [PubMed - as supplied by publisher]
well as pharmacokinetic profiling following a single IVT injection of PF-04523655.

Results: Doses of PF-04523655 ≥400 μg were generally detectable in the plasma at 1, 4, and 24 h post-injection. And all doses were below the lowest level of quantification by day 14. A single IVT injection of 50 to 3000 μg of PF-045237655 was generally safe and well tolerated over 24 months. There were no dose-limiting toxicities.

Conclusion: A single IVT injection of PF-0523655 ≤3000 μg seems safe and well tolerated in eyes with neovascular AMD.

PMID: 22627477 [PubMed - as supplied by publisher]

Other treatment & diagnosis


Plasma polymer coatings to aid retinal pigment epithelial growth for transplantation in the treatment of age related macular degeneration.

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Abstract

Subretinal transplantation of functioning retinal pigment epithelial (RPE) cells grown on a synthetic substrate is a potential treatment for age-related macular degeneration (AMD), a common cause of irreversible vision loss in developed countries. Plasma polymers give the opportunity to tailor the surface chemistry of the artificial substrate whilst maintaining the bulk properties. In this study, plasma polymers with different functionalities were investigated in terms of their effect on RPE attachment and growth. Plasma polymers of acrylic acid (AC), allyl amine (AM) and allyl alcohol (AL) were fabricated and characterised using X-ray photoelectron spectroscopy (XPS) and water contact angle measurements. Octadiene (OD) hydrocarbon films and tissue culture polystyrene were used as controls. Wettability varied from hydrophobic OD to relatively hydrophilic AC. XPS demonstrated four very different surfaces with the expected functionalities. Attachment, proliferation and morphological examination of an RPE cell line and primary RPE cells were investigated. Both cell types grew on all surfaces, with the exception of OD, although the proliferation rate of primary cells was low. Good epithelial morphology was also demonstrated. Plasma polymerised films show potential as cell carrier surfaces for RPE cells in the treatment of AMD.

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Klin Monbl Augenheilkd. 2012 May 21. [Epub ahead of print]

[Adapted and Standardised Patient Management in the Treatment of Neovascular AMD in the Outpatient Setting of a University Eye Hospital.]

[Article in German]

Framme C, Wolf-Schnurrbusch UE, Lobsiger H, Bayer S, Wolf S.

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Abstract

Visual results in treating neovascular age-related macular degeneration (AMD) using intravitreal injected anti-VEGF (IVT) clearly depend on injection frequency. Regarding to the European approval Ranibizumab
has to be used only in cases of recurrent visual loss after the loading phase. In contrast monthly treatment - as also provided in the ANCHOR and MARINA studies - is generally allowed in Switzerland. However, it is commonly tried to reduce the injection frequency because of the particular cost situation in all health systems and of cause also due to the necessary strict monitoring and reinjection regimes, which raise management problems with increasing patient numbers. In this article the special treatment regimes of our University Eye Hospital is presented, in which a reduced injection frequency basically leads to the same increased and stable visual results as in ANCHOR and MARINA; however, needing significantly more injections as generally provided in other countries of Europe. The main focus for achieving this in a large number of patients is placed on re-structuring our outpatient flow for IVT patients with particular emphasis on patient separation and standardisation of treatment steps leading to significantly reduced time consumption per patient. Measurements of timing and patient satisfaction before and after restructuring underline its importance in order to be able to treat more patients at a high quality even in the future. The exceptional importance of spectral domain OCT measurements as the most important criterium for indicating re-treatment is illustrated.

PMID: 22615063 [PubMed - as supplied by publisher]

**Pathogenesis**

**Development. 2012 May 23. [Epub ahead of print]**

**Von Hippel-Lindau protein in the RPE is essential for normal ocular growth and vascular development.**


Abstract

Molecular oxygen is essential for the development, growth and survival of multicellular organisms. Hypoxic microenvironments and oxygen gradients are generated physiologically during embryogenesis and organogenesis. In the eye, oxygen plays a crucial role in both physiological vascular development and common blinding diseases. The retinal pigment epithelium (RPE) is a monolayer of cells essential for normal ocular development and in the mature retina provides support for overlying photoreceptors and their vascular supply. Hypoxia at the level of the RPE is closely implicated in pathogenesis of age-related macular degeneration. Adaptive tissue responses to hypoxia are orchestrated by sophisticated oxygen sensing mechanisms. In particular, the von Hippel-Lindau tumour suppressor protein (pVhl) controls hypoxia-inducible transcription factor (HIF)-mediated adaptation. However, the role of Vhl/Hif1a in the RPE in the development of the eye and its vasculature is unknown. In this study we explored the function of Vhl and Hif1a in the developing RPE using a tissue-specific conditional-knockout approach. We found that deletion of Vhl in the RPE results in RPE apoptosis, aniridia and microphthalmia. Increased levels of Hif1a, Hif2a, Epo and Vegf are associated with a highly disorganised retinal vasculature, chorioretinal anastomoses and the persistence of embryonic vascular structures into adulthood. Additional inactivation of Hif1a in the RPE rescues the RPE morphology, aniridia, microphthalmia and anterior vasoproliferation, but does not rescue retinal vasoproliferation. These data demonstrate that Vhl-dependent regulation of Hif1a in the RPE is essential for normal RPE and iris development, ocular growth and vascular development in the anterior chamber, whereas Vhl-dependent regulation of other downstream pathways is crucial for normal development and maintenance of the retinal vasculature.

PMID: 22627278 [PubMed - as supplied by publisher]
Spatial distribution of the pathways of cholesterol homeostasis in human retina.

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BACKGROUND: The retina is a light-sensitive tissue lining the inner surface of the eye and one of the few human organs whose cholesterol maintenance is still poorly understood. Challenges in studies of the retina include its complex multicellular and multilayered structure; unique cell types and functions; and specific physico-chemical environment.

METHODOLOGY/PRINCIPAL FINDINGS: We isolated specimens of the neural retina (NR) and underlying retinal pigment epithelium (RPE)/choroid from six deceased human donors and evaluated them for expression of genes and proteins representing the major pathways of cholesterol input, output and regulation. Eighty-four genes were studied by PCR array, 16 genes were assessed by quantitative real time PCR, and 13 proteins were characterized by immunohistochemistry. Cholesterol distribution among different retinal layers was analyzed as well by histochemical staining with filipin. Our major findings pertain to two adjacent retinal layers: the photoreceptor outer segments of NR and the RPE. We demonstrate that in the photoreceptor outer segments, cholesterol biosynthesis, catabolism and regulation via LXR and SREBP are weak or absent and cholesterol content is the lowest of all retinal layers. Cholesterol maintenance in the RPE is different, yet the gene expression also does not appear to be regulated by the SREBPs and varies significantly among different individuals.

CONCLUSIONS/SIGNIFICANCE: This comprehensive investigation provides important insights into the relationship and spatial distribution of different pathways of cholesterol input, output and regulation in the NR-RPE region. The data obtained are important for deciphering the putative link between cholesterol and age-related macular degeneration, a major cause of irreversible vision loss in the elderly.

PMID: 22629470 [PubMed - in process]

Epidemiology

Visual status and ocular morbidity in older adults living in residential care.

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BACKGROUND: The frequency of visual impairment and blindness increases with age and is more prevalent among older adults living in residential care centers. The main aim of this study was to assess the visual status and determine the prevalence and major causes of visual impairment and blindness among the older adults living in residential care centers of Kathmandu Valley, Nepal.

METHODS: A cross-sectional study was conducted on 385 residents of 60 years or older residing in seven residential care centers of Kathmandu Valley. Presenting distance visual acuity was assessed in each eye with a Snellen chart at 6-m distance in non-standardized outdoor illumination. Objective and subjective refractions were performed and the best-corrected distance visual acuity was considered in the better eye. Near acuity was assessed binocularly with The Lighthouse Near Acuity Card. Complete anterior and posterior segment examination was carried out.
RESULTS: The mean age of residents was 74.34 ± 8.19 years. The majority was female residents (78.2 %). The prevalence of visual impairment and blindness was 43.70 %. Adequate refractive correction could alone reduce the prevalence of visual impairment and blindness by 15.40 %. Cataract was the leading cause of visual impairment and blindness, which was followed by age-related macular degeneration, corneal opacity, glaucoma, and macular scar.

CONCLUSIONS: The prevalence of visual impairment and blindness is significant among the older adults living in residential care centers. The frequency of visual impairment and blindness can be prevented by adequate refractive correction, frequent eye examination, and appropriate high use of cataract surgery.

PMID: 22614911 [PubMed - as supplied by publisher]


Age-related macular degeneration in Nepal.

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Background: The Age related Macular Degeneration (AMD) is a common cause of visual impairment and blindness worldwide in elderly.

Objective: This study aimed to explore the demographic characteristics, pattern and risk factors for AMD at a tertiary referral eye centre in Nepal.

Methods: This is a hospital-based prospective study, conducted at Tilganga Institute of Ophthalmology, Nepal from September 2008 to May 2009. All the consecutive cases of AMD diagnosed at the institute were included.

Results: A total of 141 patients (266 eyes) with AMD recruited for the study. The mean age was 69.5 years (9.1SD) with three fifth males (58.9%). Housewives and occupations like agriculture comprised of 38.3% and 42.5% respectively. Three fourth (75.6%) of the patients were illiterate. The proportion of dry and wet AMD were found in 62.4% and 37.6% respectively. Bilateral involvement was seen in 88.7% of the subjects. Three fourth (71.4%) of the AMD eyes had presenting visual acuity less than 6/18. History of smoking was found in 69.9% of patients. Hypertension was the predominant systemic problem (45.4%) followed by diabetes mellitus (12.8%).

Conclusion: AMD is correlated with ageing in our study as well. Dry AMD is more in age groups 45-64 years and wet AMD at 65 years and older. Bilateral involvement with one eye dry and fellow eye wet AMD is more predominant (44%). Smoking and occupations like agriculture and housewife are significant risk factors for AMD. Likewise male sex, illiteracy and hypertension are other risk factors for AMD in hospital settings.

PMID: 22609500 [PubMed - in process]

Ophthalmology. 2012 May 16. [Epub ahead of print]

Prevalence of Age-Related Macular Degeneration in Elderly Caucasians: The Tromsø Eye Study.

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PURPOSE: To describe the sex- and age-specific prevalence of drusen, geographic atrophy, and
neovascular age-related macular degeneration (AMD).

DESIGN: Population-based, cross-sectional study.

PARTICIPANTS: Caucasian adults aged 65 to 87 years from the 6th Tromsø Study, a population-based study conducted in 2007-2008 in the municipality of Tromsø, Norway.

METHODS: Digital color fundus photographs were graded for predominant phenotype based on drusen size, geographic atrophy, and neovascular AMD.

MAIN OUTCOME MEASURES: Age-related macular degeneration.

RESULTS: A total of 3025 subjects participated; 89% of those were invited to the eye examinations. Gradable photographs were available for 2631 persons (mean age 72.3 years). Drusen 63-125 μm as the predominant phenotype were found in 34.9% of participants (95% confidence interval [CI], 33.1-36.8), drusen >125 μm were found in 24.1% (95% CI, 22.5-25.8), geographic atrophy was found in 1.0% of participants (95% CI, 0.6-1.4), and neovascular AMD was found in 2.5% of participants (95% CI, 1.9-3.1). Bilateral involvement of late AMD was present in 1.1% of the sample. Eyes with late AMD had a significantly lower refractive error (spherical equivalent 0.078 vs. 0.99 diopters, P<0.0001), and 42.5% of eyes had Snellen visual acuity ≤0.32.

CONCLUSIONS: The prevalence of AMD among the elderly persons in this study was similar to rates in other Caucasian populations. Late AMD was present in 10.9% of subjects aged 80 years or more. No sex differences in prevalence rates of large drusen or late AMD were observed. Lower refractive error was observed in eyes with late AMD than in eyes without late AMD.

PMID: 22608479 [PubMed - as supplied by publisher]


Five year incidence of visual field loss in adult chinese. The beijing eye study.

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PURPOSE: To describe the cumulative 5 year incidence of visual field loss in adult Chinese in Greater Beijing.

METHODS: The Beijing Eye Study 2006 included 3251 subjects (mean age 60.4±10.1 years) who had participated in the Beijing Eye Study 2001 and returned for re-examination. All participants underwent a comprehensive eye examination, including visual field test by frequency doubling threshold perimetry. An abnormal visual field was defined as reduced sensitivity in at least one test location. Incident visual field loss was defined as a change in visual field from normal at baseline to abnormal at follow-up.

RESULTS: An incident visual field loss was detected in 273 eyes (4.3±0.5%) /235 subjects (7.3±0.5%). It was significantly associated with higher age (P=0.001), higher intraocular pressure (P<0.001), and higher fasting blood glucose concentration (P=0.019). Considering only eyes (n=140) with a detected cause for visual field loss, the most frequent causes were cataract (68 (48.6%) eyes) followed by glaucoma (23 (16.4%) eyes), diabetic retinopathy (13 (9.3%) eyes), age-related macular degeneration (10 (7.1%) eyes), and myopic degenerative retinopathy (9 (6.4%) eyes). For 133 (48.7%) eyes with a visual field loss, the cause for the VFL remained unclear.

CONCLUSIONS: The 5-year incidence of visual field loss was 4.3±0.5% per eye or 7.3±0.5% per subject. It increased significantly with age, intraocular pressure, and fasting blood glucose level. Major causes for the incidence of visual field loss were cataract, glaucoma and diabetic retinopathy.

PMID: 22624000 [PubMed - in process]
Macular pigment optical density in wet age-related macular degeneration among Indians.

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Purpose: To estimate the value of macular pigment optical density (MPOD) in adult south Indian population with wet age-related macular degeneration (AMD).

Methods: A total of 33 patients with wet AMD and 29 age-matched controls >50 years of age underwent MPOD measurement with the macular densitometer. The patients were also tested for their dietary intake of carotenoids, smoking history, and lifetime UV exposure.

Results: The mean MPOD values in the Indian population with wet AMD was 0.23 (95% CI: 0.18-0.29) vs control was 0.43 (95% CI: 0.37-0.49), P<0.0001, at 0.5° eccentricity. Ex-smokers had a lower MPOD than non-smokers (0.16 (0.09-0.23) vs 0.28 (0.22-0.34), P=0.026) and the lowest level of carotenoids intake had 48% lower MPOD than the highest level (0.14 (0.08-0.21) vs 0.33 (0.24-0.43), P=0.012). There was no significant age-related decline or gender variation in MPOD.

Conclusion: This study establishes the MPOD in adult Indian population with wet AMD, with a lack of macular pigment in association with wet AMD.

PMID: 22627475 [PubMed - as supplied by publisher]

Genetics

Association of Genetic Polymorphisms and Age-related Macular Degeneration in Chinese population.

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PURPOSE: To explore associations between age-related macular degeneration (AMD) and genetic variants of 10 genes in a nationwide Chinese population.

METHODS: This was a multicenter case-control study. 535 AMD patients and 469 controls were recruited from 16 centers which spread from the north to the south of China. All participants underwent comprehensive eye examinations. 40 SNPs of 10 genes were selected. DNA samples were genotyped with MassArray system (Sequenom). The effect of the genotypes and haplotypes on AMD was assessed with logistic regression analysis, adjusted for age, gender, long-term residence and family origin.

RESULTS: 11 single nucleotide polymorphisms (SNPs) in complement H (CFH), 2 in age-related maculopathy susceptibility 2 (ARMS2) and 2 in high-temperature requirement factor A1 (HTRA1) were noted to be significantly associated with AMD. They were rs551397, rs800292, rs1329424, rs1061170, rs10801555, rs12124794, rs10733086, rs10737680, rs2274700, rs1410996 and rs380390 in CFH, rs10490924 and rs2736912 in ARMS2, rs11200638 and rs3793917 in HTRA1. Three haplotypes in CFH, significantly predisposed the patients to AMD (P < 0.001, P = 0.001, P < 0.001, respectively). With the sample size of this study, no relationship was found for AMD and the SNPs tested in complement 3 (C3), serpin peptidase inhibitor, clade G, member 1 (SERPING1), vascular endothelial growth factor (VEGF), cholesterol ester transfer protein ( CETP), lipoprotein lipase (LPL), hepatic lipase (LIPC) and metallopeptidase inhibitor 3 (TIMP3) genes.
CONCLUSIONS: Gene variants in CFH, ARMS2 and HTRA1 contribute to AMD in Chinese population.

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**Diet**


Obtaining lutein-rich extract from microalgal biomass at preparative scale.

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Abstract

Lutein extracts are in increasing demand due to their alleged role in the prevention of degenerative disorders such as age-related macular degeneration (AMD). Lutein extracts are currently obtained from plant sources, but microalgae have been demonstrated to be a competitive source likely to become an alternative. The extraction of lutein from microalgae possesses specific problems that arise from the different structure and composition of the source biomass. Here is presented a method for the recovery of lutein-rich carotenoid extracts from microalgal biomass in the kilogram scale.

PMID: 22623312 [PubMed - in process]


Novel zeaxanthin-producing bacteria isolated from a radioactive hot spring water.

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Abstract

Zeaxanthin is a powerful antioxidant that is widely found in vegetables and fruits. Epidemiological evidences suggest that increasing the consumption of zeaxanthin in the diet is associated with a lower risk of age-related macular degeneration, helps prevent glaucoma and cataracts, and supports normal eye health. Zeaxanthin is a promising nutraceutical with many applications in the feed, food, and pharmaceutical industries. Currently, the commercial production of zeaxanthin is still dependant on synthetic routes with limitation for the biological one. Nevertheless, the biotechnological production of zeaxanthin is emerging due to its safety, potential large-scale production, and consumers' demand and preference for natural additives. Using a rapid screening method based on 16S rRNA gene and effective high-performance liquid chromatography (HPLC)-Diodearray-MS methods for carotenoids' analysis, we isolated effective zeaxanthin-producing bacteria (strain TDMA-5(T) and -16(T)) that belong to the family Sphingobacteriaceae and Sphingomonadaceae, respectively. In this chapter, we provide a detailed description of the HPLC-Diodearray-MS methods used for rapid analysis and identification of the carotenoids produced by both strains. In addition, the polyphasic taxonomic analysis of both novel strains and the description of a novel species and genus are described.

PMID: 22623298 [PubMed - in process]