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MD Research News

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Drug treatment

Retina. 2016 Jun 23. [Epub ahead of print]

INTRAVITREAL RANIBIZUMAB THERAPY FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION AND THE RISK OF STROKE: A National Sample Cohort Study.

Rim TH, Lee CS, Lee SC, Kim DW, Kim SS.

PURPOSE: To evaluate the risk of stroke after ranibizumab treatment for neovascular age-related macular degeneration.

METHODS: National registry data for 1,025,340 random subjects in the year 2002 were used. The ranibizumab group comprised patients diagnosed with neovascular age-related macular degeneration and treated with ranibizumab between 2009 and 2013 (n = 467). The two types of comparison groups were defined as comorbidity-matched controls (n = 2,330) comprised of randomly selected patients (5 per age-related macular degeneration patient), who were matched to the ranibizumab group according to sociodemographic factors, hypertension, atrial fibrillation, and the Charlson comorbidities index, and sociodemographic-matched controls (n = 2,331) matched according to sociodemographic factors only. Each sampled patient was tracked until 2013. The Cox proportional hazard regression was used.

RESULTS: Stroke occurred in 6.6% of the ranibizumab group versus 7.0% of the comorbidity-matched controls and 6.7% of the sociodemographic-matched controls; these differences were not statistically significant. The overall incidence of stroke was similar for the ranibizumab group versus the comorbidity-matched controls and sociodemographic-matched controls, based on the multivariable Cox regression (hazard ratio = 0.88; 95% confidence interval, 0.60-1.30; hazard ratio = 0.95, 95% confidence interval, 0.64-1.41, respectively).

CONCLUSION: Ranibizumab treatment for neovascular age-related macular degeneration did not increase the overall risk of stroke, compared with comorbidity-matched controls or sociodemographic-matched controls.

PMID: 27341664 [PubMed - as supplied by publisher]

Retina. 2016 Jun 22. [Epub ahead of print]

TREAT-AND-EXTEND REGIMEN WITH AFLIBERCEPT FOR RETINAL ANGIOMATOUS PROLIFERATION.

Matsumoto H, Sato T, Morimoto M, Mukai R, Takahashi M, Hiroe T, Ehara K, Takayama M, Mimura K, Kishi S.

PURPOSE: To evaluate the effects of aflibercept therapy using a treat-and-extend regimen on treatment-

naïve retinal angiomatous proliferation (RAP) and development of retinal pigment epithelium (RPE) atrophy.

METHODS: We retrospectively studied 17 treated eyes with RAP and 13 untreated fellow eyes. We assessed best-corrected visual acuity (BCVA) in logarithm of the minimal angle of resolution (logMAR) units and recorded the total number of injections for 12 months. Central macular thickness (CMT) and central choroidal thickness (CCT) were assessed by optical coherence tomography (OCT), and RPE atrophy extent in the macular area was assessed by fundus autofluorescence.

RESULTS: Average BCVA in eyes with RAP was 0.57 logMAR units (Snellen 20/74 or approximately 56.5 ETDRS letters) before treatment and significantly improved to 0.38 (Snellen 20/48 or approximately 66 ETDRS letters, $P < 0.01$) after 3 months and 0.32 (Snellen 20/42 or approximately 69 ETDRS letters, $P < 0.01$) after 12 months. Average CMT was 340 μm before treatment and significantly reduced to 133 μm ($P < 0.001$) after 3 months and 130 μm ($P < 0.001$) after 12 months. Average CCT was 147 μm before treatment, 123 μm ($P < 0.01$) after 3 months, and 131 μm ($P < 0.01$) after 12 months. Average total number of injections was 7.2. Average area of RPE atrophy enlarged by 1.00 mm in treated eyes compared with 0.34 mm in fellow eyes ($P < 0.01$). The enlarged area of RPE atrophy was inversely correlated with central choroidal thickness after 12 months ($rs = -0.49$, $P < 0.01$) and positively correlated with the number of injections ($rs = 0.58$, $P < 0.01$).

CONCLUSION: Treat-and-extend intravitreal therapy with aflibercept may be effective for improvement and stabilization of visual acuity and exudative change in eyes with RAP. However, choroidal thinning during the treatment regimen may accelerate enlargement of RPE atrophy.

PMID: 27336229 [PubMed - as supplied by publisher]

Drug Des Devel Ther. 2016 Jun 2;10:1857-67. eCollection 2016.

Resistance to anti-VEGF therapy in neovascular age-related macular degeneration: a comprehensive review.

Yang S, Zhao J, Sun X.

Abstract: As a progressive chronic disease, age-related macular degeneration (AMD) is the leading cause of irreversible vision impairment worldwide. Experimental and clinical evidence has demonstrated that vascular endothelial growth factor (VEGF) plays a vital role in the formation of choroidal neovascularization. Intravitreal injections of anti-VEGF agents have been recommended as a first-line treatment for neovascular AMD. However, persistent fluid or recurrent exudation still occurs despite standardized anti-VEGF therapy. Patients suffering from refractory or recurrent neovascular AMD may develop mechanisms of resistance to anti-VEGF therapy, which results in a diminished therapeutic effect. Until now, there has been no consensus on the definitions of refractory neovascular AMD and recurrent neovascular AMD. This article aims at clarifying these concepts to evaluate the efficacy of switching drugs, which contributes to making clinical decision more scientifically. Furthermore, insight into the causes of resistance to anti-VEGF therapy would be helpful for developing possible therapeutic approaches, such as combination therapy and multi-target treatment that can overcome this resistance.

PMID: 27330279 [PubMed - in process] PMCID: PMC4898027

Clin Ophthalmol. 2016 Jun 2;10:1023-9. eCollection 2016.

Grid laser with modified pro re nata injection of bevacizumab and ranibizumab in macular edema due to branch retinal vein occlusion: MARVEL report no 2.

Narayanan R, Panchal B, Stewart MW, Das T, Chhablani J, Jalali S, Hasnat Ali M.

PURPOSE: The purpose of this study was to prospectively study the efficacy of grid laser combined with

intravitreal bevacizumab or ranibizumab in eyes with macular edema due to branch retinal vein occlusion.

PATIENTS AND METHODS: Treatment-naïve eyes were enrolled to receive injections of ranibizumab or bevacizumab. During the first 6 months, patients were evaluated monthly and injected if the best-corrected visual acuity changed by five or more letters or fluid was noted on spectral domain optical coherence tomography (OCT); during the next 6 months, patients were evaluated bimonthly and injected only if the best-corrected visual acuity decreased by five or more letters with the associated fluid. Grid laser photocoagulation was performed if there was fluid on OCT and was repeated if patients were eligible after a minimum interval of 3 months.

RESULTS: The mean numbers of ranibizumab and bevacizumab injections were, respectively, 3.2±1.5 and 3.0±1.4 in the first 6 months and 0.3±0.6 and 0.3±0.6 in the last 6 months. Moreover, 55/75 (73.33%) participants did not receive any injections in the last 6 months. The mean reductions in central retinal thickness at 12 months were 165.67 μm (P<0.001; 95% confidence interval -221.50 to -135.0) in the ranibizumab group and 184.78 μm (P<0.001; 95% confidence interval -246.49 to -140.0) in the bevacizumab group (P=0.079). More patients in the bevacizumab group compared to those in the ranibizumab group required rescue laser at 12 months (20 vs eleven; P=0.06).

CONCLUSION: Bimonthly evaluations after month 6 with very few pro re nata injections were effective in maintaining visual gains achieved during the first 6 months. Grid laser photocoagulation is effective in maintaining the vision even in the presence of fluid on OCT, although it's required more often in patients treated with bevacizumab.

PMID: 27330272 [PubMed] PMCID: PMC4898411

Acta Ophthalmol. 2016 Jun 22. [Epub ahead of print]

Serum anti-endothelial cell antibodies in patients with age-related macular degeneration treated with intravitreal bevacizumab.

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

PURPOSE: To analyse the prevalence and changes in circulating anti-endothelial cell antibodies (AECA) during anti-vascular endothelial growth factor (anti-VEGF) therapy.

METHODS: Ninety-eight patients with exudative age-related macular degeneration (AMD) were treated with intravitreal bevacizumab. Fifty sex- and age-matched healthy subjects were used as controls. Serum AECA were detected using indirect immunofluorescence on primate skeletal muscle and cultivated human umbilical vein endothelial cells (HUVEC). These investigations were repeated at 4-week intervals within 8 months of follow-up.

RESULTS: At baseline examination, 30 of the 98 patients (30.6%) were positive for AECA. The titres of AECA ranged from 1:10 to 1:320. In the control group, AECA were present in only nine sera (18%) with titres ranging between 1:20 and 1:80 (p = 0.0000). The greatest rates of reduction of AECA titres were observed during the 'loading' phase of therapy. During the 'maintenance' phase, the rates of changes in serum AECA levels were less significant and remained constant. In follow-up period in 13 patients (13.3%), serum AECA were detected de novo in titres of 1:10 to 1:80. Statistical analysis did not show any significant correlation between the presence of AECA and activity of the disease.

CONCLUSIONS: There is growing evidence that AMD is an immune-mediated disease, and thus it cannot be excluded that AECA may be involved in its pathogenesis and progression. We also speculate that AECA develop in response to retinal damage and anti-VEGF therapy.

PMID: 27329255 [PubMed - as supplied by publisher]

Bioimpacts. 2016;6(1):49-67. Epub 2016 Mar 30.

Advanced drug delivery and targeting technologies for the ocular diseases.

Barar J, Aghanejad A, Fathi M, Omidi Y.

INTRODUCTION: Ocular targeted therapy has enormously been advanced by implementation of new methods of drug delivery and targeting using implantable drug delivery systems (DDSs) or devices (DDDs), stimuli-responsive advanced biomaterials, multimodal nanomedicines, cell therapy modalities and medical bioMEMs. These technologies tackle several ocular diseases such as inflammation-based diseases (e.g., scleritis, keratitis, uveitis, iritis, conjunctivitis, chorioretinitis, choroiditis, retinitis, retinochoroiditis), ocular hypertension and neuropathy, age-related macular degeneration and mucopolysaccharidosis (MPS) due to accumulation of glycosaminoglycans (GAGs). Such therapies appear to provide ultimate treatments, even though much more effective, yet biocompatible, noninvasive therapies are needed to control some disabling ocular diseases/disorders.

METHODS: In the current study, we have reviewed and discussed recent advancements on ocular targeted therapies.

RESULTS: On the ground that the pharmacokinetic and pharmacodynamic analyses of ophthalmic drugs need special techniques, most of ocular DDSs/devices developments have been designed to localized therapy within the eye. Application of advanced DDSs such as Subconjunctival insert/implants (e.g., latanoprost implant, Gamunex-C), episcleral implant (e.g., LX201), cationic emulsions (e.g., Cationorm™, Vekacia™, Cyclokat™), intac/punctal plug DDSs (latanoprost punctal plug delivery system, L-PPDS), and intravitreal implants (I-vitaion™, NT-501, NT- 503, MicroPump, Thethadur, IB-20089 Verisome™, Cortiject, DE-102, Retisert™, Iluvein™ and Ozurdex™) have significantly improved the treatment of ocular diseases. However, most of these DDSs/devices are applied invasively and even need surgical procedures. Of these, use of de novo technologies such as advanced stimuli-responsive nanomaterials, multimodal nanosystems (NSs)/nanoconjugates (NCs), biomacromolecualr scaffolds, and bioengineered cell therapies need to be further advanced to get better compliance and higher clinical impacts.

CONCLUSION: Despite mankind successful battle on ocular diseases, our challenge will continue to battle the ocular disease that happen with aging. Yet, we need to understand the molecular aspects of eye diseases in a holistic way and develop ultimate treatment protocols preferably as non-invasive systems.

PMID: 27340624 [PubMed]

Other treatment & diagnosis

Acta Clin Croat. 2016 Mar;55(1):87-92.

CORRELATION BETWEEN MACULAR CHANGES IN EXFOLIATION SYNDROME AND EXFOLIATIVE GLAUCOMA.

Prskalo MŠ, Tomić Ž, Novak-Lauš K, Prskalo Z.

Abstract: The aim of the study was to evaluate macular thickness and macular volume in unilateral and bilateral exfoliation syndrome and to compare them with exfoliative glaucoma and control eyes using optical coherence tomography. This prospective study included 114 subjects (228 eyes) divided into 4 groups according to the presence of exfoliation: 30 patients with unilateral syndrome, 24 patients with bilateral syndrome, 28 patients with bilateral glaucoma and control group without glaucoma or exfoliation syndrome (32 subjects). All subjects were older than 50 years. Patients with visual acuity under 0.6 according to Snellen were excluded, as well as those with refraction errors, i.e. hypermetropia over +3 spherical diopters, myopia over -5 spherical diopters, astigmatism over 2 cylindrical diopters, patients with affections that might affect the macula or the optic nerve, such as diabetic retinopathy, macular degeneration, macular edema, epiretinal membrane, vascular occlusions, neuropathies, and patients having undergone eye

surgery except for pseudophakic patients with visual acuity within the set limits. Study results confirmed the hypothesis on the existence of structural changes of macular parameters before the functional ones, thus representing an early sign of glaucomatous damage in risk groups such as unilateral and bilateral exfoliation syndrome. If the glaucoma had already manifested (exfoliative glaucoma in this study) with changes in optic disc and visual field, structural changes confirmed the clinical findings and warned of the disease severity.

PMID: 27333723 [PubMed - in process]

Saudi J Ophthalmol. 2016 Apr-Jun;30(2):88-91. Epub 2015 Nov 23.

Imaging drusens using Spectral Domain Optical Coherence Tomography.

Gella L, Raman R, Sharma T.

PURPOSE: The purpose was to evaluate pathological changes of photoreceptor layer and retinal pigment epithelium in eyes with drusens using Spectral Domain Optical Coherence Tomography (SD-OCT).

METHODS: Twenty-nine eyes of 29 patients with (drusens) dry age-related macular degeneration and 43 eyes of 43 controls were included in this study. All subjects underwent complete ophthalmic examination including SD-OCT. Central foveal thickness (CFT), photoreceptor layer (PRL) thickness and retinal pigment epithelial (RPE) thickness were measured and compared between the groups. P value < 0.05 was considered statistically significant.

RESULTS: Best corrected visual acuity (BCVA) ranged between 20/20 and 20/200. RPE (36.10 ± 5.48 μm Vs 39.27 ± 4.30) and PRL thickness (53.93 ± 7.36 μm Vs 61.20 ± 4.50 μm) were significantly reduced in patients with drusens compared to controls. Increase in age was a significant risk factor for drusens (OR: 1.22, p < 0.001) and increased PRL thickness was a protective factor (OR: 0.720, p = 0.002). PRL thickness was significantly associated with BCVA (p = 0.019).

CONCLUSION: With an increased resolution of SD-OCT, the involvement of the outer retinal layers was more clearly defined. SD-OCT may allow for the early detection of exudative changes.

PMID: 27330382 [PubMed] PMCID: PMC4908099

Pathogenesis

Curr Alzheimer Res. 2016 Jun 2. [Epub ahead of print]

Alzheimer`s disease and the early signs of age-related macular degeneration.

Frost S, Guymer R, Aung KZ, Macaulay SL, Sohrabi HR, Bourgeat P, Salvado O, Rowe CC, Ames D, Masters CL, Martins RN, Kanagasingam Y, Group AT.

Abstract: This study investigated signs of age related macular degeneration (AMD) in Alzheimer's disease (AD). These age-related diseases primarily affect different parts of the central nervous system but are substantially similar in terms of abnormal extracellular deposits, metabolic and oxidative stress, neuroinflammation and microvascular abnormalities. While AMD is a retinal disease, AD is reported to affect not only the brain but also the retina, with Aβ deposits, neurodegeneration and vascular changes. Large population based studies have provided conflicting results regarding the comorbidity of AD and AMD. This study investigated signs of AMD in a small but well characterized cohort from the Australian Imaging Biomarkers and Lifestyle study of aging (AIBL). The cohort consisted of 22 AD patients (age 70.2 ± 9.0 yrs, 13 male, 9 female) and 101 cognitively normal (CN) participants (age 71.3 ± 6.0 yrs, 40 male, 61 female). In comparison with the CN group, the AD group had a greater proportion of participants with early AMD (p < 0.0001, odds ratio 18.67, 95% CI 4.42 - 78.80). A logistic model for early AMD found a significant association with AD diagnosis (p < 0.0001), after adjusting for confounders (age, smoking, hypertension,

high and low density lipoproteins, cataract surgery and APOE ε4 carrier status). The results of this study are consistent with an increased risk of AMD in AD. While the pathophysiology of these diseases are unclear, understanding the shared features between them may provide further knowledge about their pathogenesis and could lead to accelerated development of therapies for both diseases.

PMID: 27335042 [PubMed - as supplied by publisher]

Sci Rep. 2016 Jun 24;6:28639.

HTRA1 promoter variant differentiates polypoidal choroidal vasculopathy from exudative age-related macular degeneration.

Ng TK, Liang XY, Lai TY, Ma L, Tam PO, Wang JX, Chen LJ, Chen H, Pang CP.

Abstract: Exudative age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV) share similar abnormal choroidal vasculature, but responses to treatments are different. In this study, we sequenced the whole HTRA1 gene and its promoter by direct sequencing in a Hong Kong Chinese PCV cohort. We identified rs11200638, c.34delCinsTCCT, c.59C>T, rs1049331 and rs2293870 significantly associated with PCV. Notably, rs2672598 was significantly associated with exudative AMD ($p = 1.31 \times 10(-4)$) than PCV ($p = 0.11$). Logistic regression indicated that rs2672598 ($p = 2.27 \times 10(-3)$) remained significant after adjusting for rs11200638 in exudative AMD. Moreover, the rs11200638-rs2672598 joint genotype AA-CC conferred higher risk to exudative AMD (43.11 folds) than PCV (3.68 folds). Promoter analysis showed that rs2672598 C-allele showed higher luciferase expression than wildtype T-allele ($p = 0.026$), independent of rs11200638 genotype ($p = 0.621$). Coherently, vitreous humor HTRA1 expression with rs2672598 CC genotype was significantly higher than that with TT genotype by 2.56 folds ($p = 0.02$). Furthermore, rs2672598 C-allele was predicted to alter the transcription factor binding sites, but not rs11200638 A-allele. Our results revealed that HTRA1 rs2672598 is more significantly associated with exudative AMD than PCV in ARMS2/HTRA1 region, and it is responsible for elevated HTRA1 transcriptional activity and HTRA1 protein expression.

PMID: 27338780 [PubMed - in process]

Cell Mol Life Sci. 2016 Jun 22. [Epub ahead of print]

One protein, multiple pathologies: multifaceted involvement of amyloid β in neurodegenerative disorders of the brain and retina.

Gupta V, Gupta VB, Chitranshi N, Gangoda S, Vander Wall R, Abbasi M, Golzan M, Dheer Y, Shah T, Avolio A, Chung R, Martins R, Graham S.

Abstract: Accumulation of amyloid β (Aβ) and its aggregates in the ageing central nervous system is regarded synonymous to Alzheimer's disease (AD) pathology. Despite unquestionable advances in mechanistic and diagnostic aspects of the disease understanding, the primary cause of Aβ accumulation as well as its in vivo roles remains elusive; nonetheless, the majority of the efforts to address pathological mechanisms for therapeutic development are focused towards moderating Aβ accumulation in the brain. More recently, Aβ deposition has been identified in the eye and is linked with distinct age-related diseases including age-related macular degeneration, glaucoma as well as AD. Awareness of the Aβ accumulation in these markedly different degenerative disorders has led to an increasing body of work exploring overlapping mechanisms, a prospective biomarker role for Aβ and the potential to use retina as a model for brain related neurodegenerative disorders. Here, we present an integrated view of current understanding of the retinal Aβ deposition discussing the accumulation mechanisms, anticipated impacts and outlining ameliorative approaches that can be extrapolated to the retina for potential therapeutic benefits. Further longitudinal investigations in humans and animal models will determine retinal Aβ association as a potential pathognomonic, diagnostic or prognostic biomarker.

PMID: 27333888 [PubMed - as supplied by publisher]

Int J Mol Sci. 2016 Jun 7;17(6).

miR-126 Regulation of Angiogenesis in Age-Related Macular Degeneration in CNV Mouse Model.

Wang L, Lee AY, Wigg JP, Peshavariya H, Liu P, Zhang H.

Abstract: miR-126 has recently been implicated in modulating angiogenic factors in vascular development. Understandings its biological significance might enable development of therapeutic interventions for diseases like age-related macular degeneration (AMD). We aimed to determine the role of miR-126 in AMD using a laser-induced choroidal neovascularization (CNV) mouse model. CNV was induced by laser photocoagulation in C57BL/6 mice. The CNV mice were transfected with scrambled miR or miR-126 mimic. The expression of miR-126, vascular endothelial growth factor-A (VEGF-A), Kinase insert domain receptor (KDR) and Sprouty-related EVH1 domain-containing protein 1 (SPRED-1) in ocular tissues were analyzed by qPCR and Western blot. The overexpression effects of miR-126 were also proven on human microvascular endothelial cells (HMECs). miR-126 showed a significant decrease in CNV mice ($p < 0.05$). Both mRNA and protein levels of VEGF-A, KDR and SPRED-1 were upregulated with CNV; these changes were ameliorated by restoration of miR-126 ($p < 0.05$). CNV was reduced after miR-126 transfection. Transfection of miR-126 reduced the HMECs 2D-capillary-like tube formation ($p < 0.01$) and migration ($p < 0.01$). miR-126 has been shown to be a negative modulator of angiogenesis in the eye. All together these results high lights the therapeutic potential of miR-126 suggests that it may contribute as a putative therapeutic target for AMD in humans.

PMID: 27338342 [PubMed - in process]

Am J Pathol. 2016 Jul;186(7):1890-9.

Targeting Platelet-Derived Growth Factor Receptor β(+) Scaffold Formation Inhibits Choroidal Neovascularization.

Strittmatter K, Pomeroy H, Marneros AG.

Abstract: Neovascular age-related macular degeneration is among the most common causes of irreversible blindness and manifests with choroidal neovascularization (CNV). Anti-vascular endothelial growth factor-A therapies are only partially effective and their chronic administration may impair functions of the choriocapillaris and retina. Thus, novel therapeutic targets are needed urgently. We have observed in a laser-induced model of CNV that a platelet-derived growth factor receptor β positive (PDGFRβ(+)) scaffold is formed before infiltration of neovessels into this scaffold to form CNV lesions, and that this scaffold limits the extent of neovascularization. Based on these observations we hypothesized that ablation of proliferating PDGFRβ(+) cells to prevent the formation of this scaffold might inhibit CNV growth and present a novel therapeutic approach for neovascular age-related macular degeneration. To test this hypothesis we targeted proliferating PDGFRβ(+) cells through independent distinct approaches after laser injury: i) by using an inducible genetic model to inhibit specifically proliferating PDGFRβ(+) cells, ii) by treating mice with a neutralizing anti-PDGFRβ antibody, iii) by administering an anti-PDGF-AB/BB aptamer, and iv) by using small chemical inhibitor approaches. The results show that therapeutic targeting of proliferating PDGFRβ(+) cells potently inhibits the formation of the pericyte-like scaffold, with concomitant attenuation of CNV. Moreover, we show that early inhibition of PDGFRβ(+) cell proliferation before neovessel formation is sufficient to inhibit scaffold formation and neovascularization.

PMID: 27338108 [PubMed - in process]

Epidemiology

Ophthalmic Epidemiol. 2016 Jun 24:1-6. [Epub ahead of print]

Burden of Wet Age-Related Macular Degeneration and Its Economic Implications in Singapore in

the Year 2030.

Saxena N, George PP, Hoon HB, Han LT, Onn YS.

PURPOSE: To estimate the prevalence of wet age-related macular degeneration (AMD) in Singapore in the year 2030. This projection will help in planning appropriate care provision and build health services capacity to cater to the increasing healthcare demand in 2030.

METHODS: The number of AMD patients aged 40-79 years from all Singaporeans was estimated using prevalence rates from a local study and using the United Nations population projections for Singapore to 2030. Age-specific mortality was accounted for. Additionally, two main scenarios were presented: (1) Projected number of wet AMD cases if patients were not taking preventive antioxidant vitamins; (2) projected number of wet AMD cases if patients were taking preventive antioxidant vitamins. Based on these scenarios, the economic burden was calculated. The number of quality-adjusted life years (QALYs) gained as a result of improvement in visual acuity (VA) due to anti-vascular endothelial growth factor (VEGF) treatment was also calculated.

RESULTS: An estimated growth of 42% in the number of wet AMD cases is expected by 2030. The estimated economic burden of wet AMD in 2030 for scenarios 1 and 2 is Singapore $203.1 million and $162.9 million, respectively. The QALYs gained as a result of improved VA from wet AMD treatment ranged from 10,114.4 to 14,058.8 over a 5-year period for the 2030 cohort.

CONCLUSION: The burden of wet AMD is set to increase over the next 15 years. Appropriate measures to build healthcare capacity and plan for this expected surge in patients should be a priority in Singapore.

PMID: 27340738 [PubMed - as supplied by publisher]

Genetics

Hum Genomics. 2016 Jun 21;10(1):23.

AMD and the alternative complement pathway: genetics and functional implications.

Tan PL, Bowes Rickman C, Katsanis N.

Abstract: Age-related macular degeneration (AMD) is an ocular neurodegenerative disorder and is the leading cause of legal blindness in Western societies, with a prevalence of up to 8 % over the age of 60, which continues to increase with age. AMD is characterized by the progressive breakdown of the macula (the central region of the retina), resulting in the loss of central vision including visual acuity. While its molecular etiology remains unclear, advances in genetics and genomics have illuminated the genetic architecture of the disease and have generated attractive pathomechanistic hypotheses. Here, we review the genetic architecture of AMD, considering the contribution of both common and rare alleles to susceptibility, and we explore the possible mechanistic links between photoreceptor degeneration and the alternative complement pathway, a cascade that has emerged as the most potent genetic driver of this disorder.

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Stem cells

Graefes Arch Clin Exp Ophthalmol. 2016 Jun 22. [Epub ahead of print]

Subretinal implantation of a monolayer of human embryonic stem cell-derived retinal pigment epithelium: a feasibility and safety study in Yucatán minipigs.

Koss MJ, Falabella P, Stefanini FR, Pfister M, Thomas BB, Kashani AH, Brant R, Zhu D, Clegg DO, Hinton DR, Humayun MS.

PURPOSE: A subretinal implant termed CPCB-RPE1 is currently being developed to surgically replace dystrophic RPE in patients with dry age-related macular degeneration (AMD) and severe vision loss. CPCB -RPE1 is composed of a terminally differentiated, polarized human embryonic stem cell-derived RPE (hESC-RPE) monolayer pre-grown on a biocompatible, mesh-supported submicron parylene C membrane. The objective of the present delivery study was to assess the feasibility and 1-month safety of CPCB-RPE1 implantation in Yucatán minipigs, whose eyes are similar to human eyes in size and gross retinal anatomy.

METHODS: This was a prospective, partially blinded, randomized study in 14 normal-sighted female Yucatán minipigs (aged 2 months, weighing 24-35 kg). Surgeons were blinded to the randomization codes and postoperative and post-mortem assessments were performed in a blinded manner. Eleven minipigs received CPCB-RPE1 while three control minipigs underwent sham surgery that generated subretinal blebs. All animals except two sham controls received combined local (Ozurdex™ dexamethasone intravitreal implant) and systemic (tacrolimus) immunosuppression or local immunosuppression alone. Correct placement of the CPCB-RPE1 implant was assessed by in vivo optical coherence tomography and post-mortem histology. hESC-RPE cells were identified using immunohistochemistry staining for TRA-1-85 (a human marker) and RPE65 (an RPE marker). As the study results of primary interest were nonnumerical no statistical analysis or tests were conducted.

RESULTS: CPCB-RPE1 implants were reliably placed, without implant breakage, in the subretinal space of the minipig eye using surgical techniques similar to those that would be used in humans. Histologically, hESC-RPE cells were found to survive as an intact monolayer for 1 month based on immunohistochemistry staining for TRA-1-85 and RPE65.

CONCLUSIONS: Although inconclusive regarding the necessity or benefit of systemic or local immunosuppression, our study demonstrates the feasibility and safety of CPCB-RPE1 subretinal implantation in a comparable animal model and provides an encouraging starting point for human studies.

PMID: 27335025 [PubMed - as supplied by publisher]