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MD Research News

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Drug treatment

Br J Ophthalmol. 2012 Sep 27. [Epub ahead of print]

Intravitreal injections: is there benefit for a theatre setting?

Abell RG, Kerr NM, Allen P, Vote BJ.

Launceston, Tasmania, Australia.

OBJECTIVE: To investigate and compare the rate of endophthalmitis after intravitreal injections performed in an in-office (dedicated procedure room) versus in-theatre setting.

METHODS: A retrospective comparative cohort study was performed of all patients consecutively treated by a single surgeon with intravitreal injection with either ranibizimab or bevacizumab for any recognised clinical indication. All cases received injections between March 2006 and March 2012, during which time all injections were prospectively recorded on an electronic medical record system. A search of the electronic database using a report building system was used to extract the total number of injections into location-specific grouping (ie, in office vs in theatre).

RESULTS: 12 249 injections were performed over a 6-year period. 3376 of these were performed in the in-office procedure room, compared with 8873 in the operating theatre. Of the 3376 injections performed in office, there were four cases of infective endophthalmitis compared with none of the 8873 injections performed in theatre (p=0.006). In-theatre intravitreal injections were associated with a 13-fold lower risk of endophthalmitis compared to in-office injections.

CONCLUSIONS: The theatre environment is a clinically appropriate location for any intravitreal injection procedures and was associated with a significantly lower risk of infective endophthalmitis in this single-surgeon comparative cohort study.

PMID: 23018424 [PubMed - as supplied by publisher]

Ophthalmology. 2012 Sep 19. pii: S0161-6420(12)00805-6. doi: 10.1016/j.ophtha.2012.08.022. [Epub ahead of print]

Intravitreal Ranibizumab for Diabetic Macular Edema with Prompt versus Deferred Laser Treatment: Three-Year Randomized Trial Results.

Diabetic Retinopathy Clinical Research Network, Elman MJ, Qin H, Aiello LP, Beck RW, Bressler NM,

Ferris FL 3rd, Glassman AR, Maturi RK, Melia M.

Elman Retina Group, Baltimore, Maryland.

OBJECTIVE: To report the 3-year follow-up results within a previously reported randomized trial evaluating prompt versus deferred (for ≥24 weeks) focal/grid laser treatment in eyes treated with intravitreal 0.5 mg ranibizumab for diabetic macular edema (DME).

DESIGN: Multicenter, randomized clinical trial.

PARTICIPANTS: Three hundred sixty-one participants with visual acuity of 20/32 to 20/320 (approximate Snellen equivalent) and DME involving the fovea.

METHODS: Ranibizumab every 4 weeks until no longer improving (with resumption if worsening) and random assignment to prompt or deferred (≥24 weeks) focal/grid laser treatment.

MAIN OUTCOME MEASURES: Best-corrected visual acuity and safety at the 156-week (3-year) visit.

RESULTS: The estimated mean change in visual acuity letter score from baseline through the 3-year visit was 2.9 letters more (9.7 vs. 6.8 letters; mean difference, 2.9 letters; 95% confidence interval, 0.4-5.4 letters; P = 0.02) in the deferral group compared with the prompt laser treatment group. In the prompt laser treatment group and deferral group, respectively, the percentage of eyes with a ≥10-letter gain/loss was 42% and 56% (P = 0.02), whereas the respective percentage of eyes with a ≥10-letter gain/loss was 10% and 5% (P = 0.12). Up to the 3-year visit, the median numbers of injections were 12 and 15 in the prompt and deferral groups, respectively (P = 0.007), including 1 and 2 injections, respectively, from the 2-year up to the 3-year visit. At the 3-year visit, the percentages of eyes with central subfield thickness of 250 μm or more on time-domain optical coherence tomography were 36% in both groups (P = 0.90). In the deferral group, 54% did not receive laser treatment during the trial. Systemic adverse events seemed to be similar in the 2 groups.

CONCLUSIONS: These 3-year results suggest that focal/grid laser treatment at the initiation of intravitreal ranibizumab is no better, and possibly worse, for vision outcomes than deferring laser treatment for 24 weeks or more in eyes with DME involving the fovea and with vision impairment. Some of the observed differences in visual acuity at 3 years may be related to fewer cumulative ranibizumab injections during follow-up in the prompt laser treatment group. Follow-up through 5 years continues.

PMID: 22999634 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2012 Sep 21. [Epub ahead of print]

Measuring the benefit of 4 years of intravitreal ranibizumab treatment for neovascular age-related macular degeneration.

Pushpoth S, Sykakis E, Merchant K, Browning AC, Gupta R, Talks SJ.

The Royal Victoria Infirmary, Newcastle upon Tyne, UK.

AIM: To analyse the benefit of intravitreal ranibizumab over 4 years for patients with neovascular age-related macular degeneration (AMD).

METHODS: A retrospective case note review of all patients who started treatment between August 2007 and September 2009 in our unit, minimum follow-up 2 years, maximum 4 years. The main outcome measures were: numbers of patients with different levels of vision, changes in visual acuity, number of treatments and numbers remaining under follow-up.

RESULTS: 1086 eyes of 1017 patients received treatment. Numbers of patients remaining under follow-up were 892/1017 (87.71%) at 12 months, 730/1017 (71.78%) at 24 months, 468/730 (64.11%) at 36 months

and 110/217 (50.69%) at48 months. The main reasons for patients no longer being under follow-up were the consequences of old age or transfer of care. 50% of patients had 6/18 or better over 4 years. Patients received on average 5.79±2.53, 9.15±3.79, 11.22±4.92 and 13.7±7.84 injections by 12, 24, 36 and 48 months, respectively.

CONCLUSIONS: We suggest that the numbers of patients with a particular level of vision may best reflect the actual benefit of AMD treatment provided by a service. Long-term follow-up is required as only 72/730 (10%) had been discharged at 36 months, half of whom had good vision of greater than 60 letters. 83% and 65% of patients needed treatment in the third and fourth year. Follow-up may be for the rest of the patients' life or at some point they may no longer be well enough to attend.

PMID: 23001255 [PubMed - as supplied by publisher]

Retina. 2012 Oct;32(9):1821-8.

Cerebrovascular accidents in patients treated for choroidal neovascularization with ranibizumab in randomized controlled trials.

Bressler NM, Boyer DS, Williams DF, Butler S, Francom SF, Brown B, Nucci FD, Cramm T, Tuomi LL, Ianchulev T, Rubio RG.

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PURPOSE: To analyze cerebrovascular accidents (CVAs) pooled from large, randomized, controlled clinical trials of ranibizumab treatment for neovascular age-related macular degeneration.

METHODS: Events in five trials (FOCUS, MARINA, ANCHOR, PIER, and SAILOR) were analyzed using a standard safety monitoring process. Exact methods, stratified by study, were used to test for treatment differences based on odds ratios. A stepwise logistic regression model was fit to classify subjects' risk for CVA based on medical history. Treatment differences in CVA rates at 1 year or 2 years were evaluated within risk groups using stratified exact methods.

RESULTS: Pooled 2-year CVA rates were <3%; odds ratios (95% confidence intervals) for CVA risk were 1.2 (0.4-4.4) for ranibizumab 0.3-mg versus control, 2.2 (0.8-7.1) for 0.5 mg versus control, and 1.5 (0.8-3.0) for 0.5-mg versus 0.3-mg ranibizumab. No substantial increased risk of CVA for 0.5 mg versus 0.3 mg was identified in pooled analyses or any of the individual trials. In pooled analyses, the difference between 0.5-mg ranibizumab and control was larger (7.7 [1.2-177]) among high-risk CVA patients.

CONCLUSION: This analysis provided some evidence, although not definitive, of a potential increased risk of CVA with ranibizumab versus control or with 0.5-mg versus 0.3-mg ranibizumab. Continued monitoring for CVA within clinical trials seems warrented.

PMID: 23011184 [PubMed - in process]

Ophthalmology. 2012 Sep 22. pii: S0161-6420(12)00661-6. doi: 10.1016/j.ophtha.2012.07.027. [Epub ahead of print]

Driving Ability Reported by Neovascular Age-Related Macular Degeneration Patients after Treatment with Ranibizumab.

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OBJECTIVES: To determine the impact of ranibizumab on driving status, driving ability perception, and having 20/40 vision or better in patients with choroidal neovascularization resulting from age-related macular degeneration (AMD).

DESIGN: Phase III, multicenter, randomized clinical trials (Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration [MARINA] and Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration [ANCHOR]).

PARTICIPANTS: One thousand one hundred twenty-six patients with choroidal neovascularization resulting from AMD.

METHODS: Participants were assigned randomly to sham (n = 238), 0.3-mg ranibizumab monthly injections (n = 238), or 0.5-mg ranibizumab monthly injections (n = 240) for 24 months (MARINA), or were randomized to verteporfin photodynamic therapy (PDT; n = 143), 0.3-mg ranibizumab monthly injections (n = 140), or 0.5-mg ranibizumab monthly injections (n = 140) for 24 months (ANCHOR).

MAIN OUTCOME MEASURES: Self-reported driving status and driving ability perception were assessed as exploratory outcomes at baseline through 24 months after baseline using the 25-item National Eye Institute Visual Function Questionnaire. Best-corrected visual acuity in each eye was assessed monthly through 24 months.

RESULTS: At baseline, 68.6% of patients in the MARINA trial and 62.7% of patients in the ANCHOR trial reported driving. Among patients driving at baseline in the MARINA trial 2 years after randomization, 67.2% (95% confidence interval [CI], 59.2-75.2) of sham patients and 78.4% (95% CI, 71.8-85.0) of 0.5-mg patients reported that they were still driving. Among patients driving at baseline in the ANCHOR trial at 2 years after randomization, 71.6% (95% CI, 60.8-82.4) of PDT patients and 91.4% (95% CI, 85.3-97.5) of 0.5-mg patients were still driving. Also in the ANCHOR trial, ranibizumab-treated patients who were not driving at baseline seemed more likely to drive by months 12 and 24 than PDT patients. Perception of driving ability was correlated with improvement in visual acuity (VA) in the better-seeing eye at 12 and 24 months ($R(2) = 0.17$ and $R(2) = 0.20$ at 12 and 24 months, respectively [$P<0.001$], in the MARINA trial; $R(2) = 0.13$ and $R(2) = 0.14$, respectively [$P<0.001$], in the ANCHOR trial). Visual acuity in one or both eyes 2 years after randomization was more likely to be 20/40 or better in the ranibizumab-treated groups.

CONCLUSIONS: These results suggest that patients with neovascular AMD treated with ranibizumab are more likely to report driving ability and have vision of at least 20/40 than patients given sham treatment or PDT.

PMID: 23009891 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2012 Aug 12. [Epub ahead of print]

Balancing risk in ophthalmic prescribing: assessing the safety of anti-VEGF therapies and the risks associated with unlicensed medicines.

Kaiser PK, Cruess AF, Bogaert P, Khunti K, Kelly SP.

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Abstract

Vascular endothelial growth factor (VEGF) inhibitor medications such as ranibizumab, pegaptanib and bevacizumab are in use for the treatment of neovascular age-related macular degeneration (AMD) and

other retinal conditions, although only ranibizumab and pegaptanib are approved for these conditions. In contrast, bevacizumab was developed for the intravenous systemic treatment of colorectal cancer and is not formulated for intravitreal use, but is commonly used off-label in ophthalmology. European Union legislation permits the use of drugs outside the terms of their licence ('off-label') only under certain circumstances, such as during clinical trials, compassionate/named patient use in the absence of a licensed alternative, emergency scenarios (e.g., pandemics) or at the discretion of a treating physician. In such cases, patients should be fully informed regarding their treatment and any potential risks involved. Off-label drug use can be an important tool to provide patients with treatment in cases of unmet medical need. However, the use of an unlicensed medicinal product, when a suitable licensed alternative is available, puts prescribing physicians at risk of liability if safety issues arise. Emerging clinical evidence suggests safety differences exist between ranibizumab and bevacizumab.

PMID: 23011000 [PubMed - as supplied by publisher]

Prescrire Int. 2012 Sep;21(130):207.

Ranibizumab and retinal vein occlusion. Too many outstanding questions.

[No authors listed]

A loss of visual acuity due to macular oedema is a complication of retinal vein occlusion. Vision improves spontaneously within 3 to 6 months in about 50% of cases. There are no drugs with proven benefits in this setting. In addition to its indications in the treatment of age-related macular degeneration (AMD) and diabetic macular oedema, ranibizumab, an anti-VEGF antibody, has now been approved in the European Union for the treatment of visual impairment associated with macular oedema due to retinal vein occlusion. In this setting, clinical evaluation of ranibizumab (Lucentis, Novartis) is based on two double-blind randomised trials comparing ranibizumab (0.3 mg or 0.5 mg) versus placebo in a total of 795 patients. Compared with placebo, about 30% more patients receiving ranibizumab (0.3 mg or 0.5 mg) experienced a tangible improvement in their visual acuity (gain of at least 15 letters on the ETDRS scale) after 6 months of treatment. Efficacy was similar in patients with central retinal vein occlusion and those with occlusion of a peripheral branch. All patients received ranibizumab after the initial 6-month period; the lack of a placebo group means that the long-term effects of ranibizumab cannot be distinguished from spontaneous improvement. There were too few cases of ischaemic occlusion to assess the efficacy of ranibizumab in this subgroup of patients, who are most in need of treatment. The adverse effects of ranibizumab were the same as those observed in other clinical situations. They mainly consisted of ocular adverse reactions, such as haemorrhage, pain, and elevated intraocular pressure. Uncertainties persist as to the long-term risk of recurrent occlusion or progression to retinal ischaemia. The frequency of systemic adverse events was similar in the ranibizumab and placebo groups. The incidence of heart failure and transient ischaemic attacks was higher during the second year of ranibizumab therapy than during the first year of treatment. The packaging (bottles) available in early 2012 creates a risk of handling errors, and improvements are needed to prevent these errors. Monthly ranibizumab administration is expensive. In practice, the decision to grant marketing authorisation for ranibizumab in macular oedema due to retinal vein occlusion was premature. Ranibizumab is one option that should be assessed in clinical trials. Patients should be informed of the potential adverse effects and uncertainties and be reminded that this condition improves spontaneously in about 50% of cases.

PMID: 23016250 [PubMed - in process]

Other treatment & diagnosis

Acta Ophthalmol. 2012 Sep 23. doi: 10.1111/j.1755-3768.2012.02556.x. [Epub ahead of print]

Correlation between components of newly diagnosed exudative age-related macular degeneration lesion and focal retinal sensitivity.

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Purpose: To analyse lesion components determining retinal sensitivity in microperimetry in eyes with newly diagnosed exudative age-related macular degeneration (AMD).

Methods: Visual acuity, contrast sensitivity, microperimetry, optical coherence tomography (OCT), and fluorescein (FA) and indocyanine green (ICGA) angiographies of 23 eyes of 23 patients were analysed. Central microperimetry grids with 28 test stimulus sites were automatically aligned with three-dimensional OCTs and manually aligned with angiographies. Thicknesses of the neuroretina, neuroepithelial detachment (NED), retinal pigment epithelial (RPE) elevation and subretinal tissue were measured under the 644 microperimetry stimulus sites. Areas of classic and occult choroidal neovascularizations (CNVs), subretinal and intraretinal haemorrhage, and late hyperfluorescence in ICGA were identified. The impact of the lesion components on retinal sensitivity was evaluated with correlation analysis and multivariate modelling.

Results: Decreased retinal sensitivity correlated significantly with the presence of CNV, haemorrhage, subretinal tissue and RPE elevation. Out of the OCT parameters, the most important determinant of sensitivity was the thickness of RPE elevation (Spearman's rho, $r = -0.202$, $p < 0.0001$). The thicknesses of subretinal tissue ($r = -0.168$, $p < 0.0001$) and NED had weaker effects ($r = -0.147$, $p < 0.0001$), and the neuroretinal thickness remained nonsignificant. In multivariate modelling, RPE elevation and subretinal tissue in OCT, CNV membranes in angiographies and haemorrhage had the strongest impacts on retinal sensitivity.

Conclusion: The most important lesion components affecting retinal function were RPE elevation and subretinal tissue in OCT as well as neovascular membranes and haemorrhage in angiographies. NED and neuroretinal thickening remained less significant.

PMID: 22998103 [PubMed - as supplied by publisher]

Int Ophthalmol. 2012 Sep 22. [Epub ahead of print]

Inter-observer agreement for spectral- and time-domain optical coherence tomography image grading: a prospective study.

Knecht PB, Kordic H, Kurz-Levin M, Sturm V, Menke MN.

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Abstract

The purpose of this study was to compare inter-observer agreement of Stratus™ OCT versus Spectralis™ OCT image grading in patients with neovascular age-related macular degeneration (AMD). Thirty eyes with neovascular AMD were examined with Stratus™ OCT and Spectralis™ OCT. Four different scan protocols were used for imaging. Three observers graded the images for the presence of various pathologies. Inter-observer agreement between OCT models was assessed by calculating intra-class correlation coefficients (ICC). In Stratus™ OCT highest interobserver agreement was found for subretinal fluid (ICC: 0.79), and in Spectralis™ OCT for intraretinal cysts (IRC) (ICC: 0.93). Spectralis™ OCT showed superior interobserver agreement for IRC and epiretinal membranes (ERM) (ICC(Stratus™): for IRC 0.61; for ERM 0.56; ICC (Spectralis™): for IRC 0.93; for ERM 0.84). Increased image resolution of Spectralis™ OCT did improve the inter-observer agreement for grading intraretinal cysts and epiretinal membranes but not for other retinal changes.

PMID: 23001716 [PubMed - as supplied by publisher]

Ophthalmologica. 2012 Sep 19. [Epub ahead of print]

Hyperreflective Dots: A New Spectral-Domain Optical Coherence Tomography Entity for Follow-Up and Prognosis in Exudative Age-Related Macular Degeneration.

Coscas G, De Benedetto U, Coscas F, Li Calzi CI, Vismara S, Roudot-Thoraval F, Bandello F, Souied E.

Centre d'Ophtalmologie, University Paris-Est Créteil, Paris XII, France.

Purpose: Spectral-domain optical coherence tomography (SD-OCT) enables high-resolution analysis of retinal layers and previously unseen hyperreflective dots (HRD). HRD morphological characteristics, evolution, possible origin and prognostic value are discussed.

Methods: We conducted a prospective study of 100 patients with exudative age-related macular degeneration (AMD), who were treated and followed up with monthly imaging examinations. Statistical correlations between visual acuity (VA) and pre-/post- treatment HRD characteristics were evaluated.

Results: HRD were present in all cases, mainly in the outer retinal layers but also elsewhere. After treatment, HRD regressed in a few days, 1 month ($p < 0.04$) and 3 months ($p < 0.01$). Regression was evident in all VA and morphological subsets. Resolution was associated with better final VA ($p < 0.001$).

Conclusions: Presence of initial/recurrent HRD, rapid treatment response and the growing role that early biological inflammatory reaction plays in AMD suggests HRD are activated microglia cells. The correlation between VA and HRD could make HRD a clinical marker for early decisions about treatment and retreatment.

PMID: 23006969 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2012 Sep 25. [Epub ahead of print]

Cost of epimacular brachytherapy for treatment-naive neovascular age-related macular degeneration. [Letter]

Jackson TL, Kirkpatrick L, Tang G, Prasad S.

King's College London, London, UK.

PMID: 23012308 [PubMed - as supplied by publisher]

Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. 2012 Aug;29(4):754-9.

[Research on and design of visual prosthesis based on visual information processing]. [Article in Chinese]

Li S, Hu J, Chai X, Ren Q, Peng Y.

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Abstract

Induced by a variety of retinopathy, visual loss has become the most serious form of disability, which influences the quality of human life. With the rapid development and crossing among the information science, microelectronics, material science and biomedical disciplines, the visual prosthesis makes reparation possible for the visual blindness caused by retinitis pigmentosa, age-related macular degeneration, and other eye, retina, optic nerve and visual cortex lesions. With technology innovation, the

prosthesis design, manufacturing and surgical technique are no longer the biggest obstacles to the future development of the visual prosthesis, but how to construct effective transmission of information between the brain and the prosthesis. However, due to the complex structure of the human visual system, the visual prosthesis manufacturing and visual information signal mapping are facing some difficulties. Thus, we can only study the representation strategy of image information and micro-electrode array stimulation basing on limited pixels of simulated prosthesis visual information. By studying the visual information processing of the visual prosthesis, we propose a visual prosthesis design which is based on biological, mechanical, and electronic integration.

PMID: 23016430 [PubMed - in process]

Pathogenesis & pre-clinical

Br J Pharmacol. 2012 Sep 25. doi: 10.1111/j.1476-5381.2012.02227.x. [Epub ahead of print]

Silibinin inhibits VEGF secretion and age-related macular degeneration in a hypoxia-dependent manner through the PI-3 kinase/Akt/mTOR pathway.

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BACKGROUND AND PURPOSE: Hypoxia-mediated neovascularization plays an important role in age-related macular degeneration (AMD). There are few animal models or effective treatments for AMD. Here, we investigated the effects of the flavonoid silibinin on hypoxia-induced angiogenesis in a rat AMD model.

EXPERIMENTAL APPROACH: Retinal pigmented epithelial (RPE) cells were subjected to hypoxia in vitro and the effects of silibinin on activation of key hypoxia-induced pathways were examined by elucidating the hypoxia-inducible factor-1 alpha (HIF-1α) protein level by western blot. A rat model of AMD was developed by intravitreal injection of vascular endothelial growth factor (VEGF) in Brown Norway rats, with or without concomitant exposure of animals to hypoxia. Animals were treated with oral silibinin starting at day 7 post-VEGF injection and AMD changes were followed by fluorescein angiography on days 14 and 28 post-injection.

KEY RESULTS: Silibinin pretreatment of RPE cells increased proline hydroxylase-2 expression, inhibited HIF-1α subunit accumulation, and inhibited VEGF secretion. Silibinin-induced HIF-1α and VEGF downregulation required suppression of hypoxia-induced phosphatidylinositol 3-kinase/Akt/mammalian target of rapamycin (mTOR) pathway. In the rat model of AMD, silibinin administration prevented VEGF- and VEGF plus hypoxia-induced retinal edema and neovascularization.

CONCLUSION AND IMPLICATIONS: The effects of silibinin, both in vitro and in vivo, support its potential as a therapeutic for the prevention of neovascular AMD.

PMID: 23004355 [PubMed - as supplied by publisher]

Curr Eye Res. 2012 Sep 27. [Epub ahead of print]

Antiangiogenic Effects of Axitinib, an Inhibitor of Vascular Endothelial Growth Factor Receptor Tyrosine Kinase, on Laser-Induced Choroidal Neovascularization in Mice.

Kang S, Roh CR, Cho WK, Park KC, Yang KJ, Choi HS, Kim SH, Roh YJ.

Department of Ophthalmology and Visual Science.

Purpose: To investigate the effects of axitinib, an inhibitor of vascular endothelial growth factor receptors,

on choroidal neovascularization (CNV) in an animal model of neovascular age-related macular degeneration (AMD).

Methods: Experimental CNV lesions were induced in C57BL/6 mice by laser photocoagulation. Beginning 1 day after CNV induction, mice were treated with axitinib (5 mg/kg/day) or vehicle for 2 weeks. In other groups of mice, axitinib or vehicle treatment was started 7 days after the laser application to determine the effect of the drug on established CNV. Untreated mice were used as a baseline group. Two weeks after laser injury, the extent of CNV was assessed from choroidal flat mounts perfused with fluorescein-labeled dextran. Immunofluorescence staining with isolectin IB4 was also used to quantify the CNV lesions.

Results: Orally administered axitinib inhibited CNV growth in the laser-induced CNV model. Axitinib caused a 70.1% inhibition of CNV lesions compared to vehicle-treatment ($p < 0.001$). Axitinib also caused a significant regression of established CNV, reducing the area by 71.1% compared to vehicle treatment ($p < 0.001$). Moreover, immunofluorescence staining showed that the area of isolectin IB4 labeled vessels was smaller in the axitinib-treated group compared to the vehicle-treated group ($p < 0.001$).

Conclusions: Axitinib effectively inhibits the progression of CNV in an experimental animal model. These results suggest that axitinib could constitute a therapeutic alternative for the treatment of neovascular AMD.

PMID: 23013553 [PubMed - as supplied by publisher]

Genetics

Ophthalmology. 2012 Sep 22. pii: S0161-6420(12)00602-1. doi: 10.1016/j.ophtha.2012.06.042. [Epub ahead of print]

Genetic Studies of Age-Related Macular Degeneration: Lessons, Challenges, and Opportunities for Disease Management.

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BACKGROUND: Age-related macular degeneration (AMD) is a common cause of visual impairment in individuals >55 years of age worldwide. The varying clinical phenotypes of AMD result from contributions of genetic, epigenetic, and nongenetic (environmental) factors. Genetic studies of AMD have come of age as a direct result of tremendous gains from the human genome project, genome-wide association studies, and identification of numerous susceptibility loci. These findings have implicated immune response, high-density lipoprotein cholesterol metabolism, extracellular matrix, and angiogenesis signaling pathways in disease pathophysiology.

MAIN OUTCOME MEASURES: Herein, we address how the wealth of genetic findings in AMD is expected to impact the practice of medicine, providing opportunities for improved risk assessment, molecular diagnosis, preventive, and therapeutic intervention.

CONCLUSIONS: We propose that the potential of using genetic variants for monitoring treatment response (pharmacogenetics) may usher in a new era of personalized medicine in the clinical management of AMD.

PMID: 23009893 [PubMed - as supplied by publisher]