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Drug treatment

Acta Ophthalmol. 2012 Nov 22. doi: 10.1111/j.1755-3768.2012.02493.x. [Epub ahead of print]

Treatment patterns, visual acuity and quality-of-life outcomes of the WAVE study - A noninterventional study of ranibizumab treatment for neovascular age-related macular degeneration in Germany.

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Department of Ophthalmology, University of Bonn, Bonn, Germany Department of Ophthalmology, University of Leipzig, Leipzig, Germany Novartis Ophthalmics, Novartis Pharma GmbH, Nuremberg, Germany.

Purpose: To evaluate effectiveness, tolerability and safety of repeated intravitreal injections of 0.5 mg ranibizumab for the treatment of neovascular age-related macular degeneration in routine medical practice in Germany.

Methods: A noninterventional study with 3470 patients treated in 274 medical centres according to German guidelines, with monthly intravitreal injections of 0.5 mg ranibizumab during upload (3 months) followed by a maintenance phase (9 months) with reinjections if medically indicated.

Results: Mean injection rate was 4.34 (SE = 0.05; median = 3.0). Best-corrected visual acuity (BCVA) remained stable (mean change 0.02 LogMAR, SE = 0.01, p = 0.0169) and central retinal thickness (CRT) decreased (by -78.9 µm, SE = 2.95 µm, p < 0.0001). The NEI-VFQ 25 summary score showed a positive stabilization with a mean change of 0.73 (SE = 0.37, p = 0.0501) compared with baseline. Adverse events were documented for 6.5% of the patients with 3.9% of these events being classified as serious.

Conclusions: The number of administered intravitreal injections of ranibizumab over the first year of treatment was very low but still achieved a stabilization of BCVA, a reduction in CRT and maintained vision-related quality of life. The management of patients with neovascular AMD in Germany needs to be improved to achieve better treatment results.

PMID: 23171290 [PubMed - as supplied by publisher]

Eye (Lond). 2012 Nov 23. doi: 10.1038/eye.2012.225. [Epub ahead of print]

Which visual acuity measurements define high-quality care for patients with neovascular age-related macular degeneration treated with ranibizumab?

Ross AH, Donachie PH, Sallam A, Stratton IM, Mohamed Q, Scanlon PH, Kirkpatrick JN, Johnston RL

Ophthalmology Department, Gloucestershire Hospitals, Cheltenham, UK.

Purpose: The purpose of this study is to define which visual acuity (VA) measurements are the best indicators of high-quality care for patients receiving intravitreal ranibizumab for neovascular age-related macular degeneration (nAMD).

Methods: Analysis of prospectively collected data recorded within an electronic medical record system on treatment-naive, first-eligible eyes with nAMD, treated with ranibizumab using an as-needed treatment regimen with a minimum follow-up of 1 year. Data collection included the following: age, gender, laterality, type of nAMD, VA, central 1 mm OCT retinal thickness, number of intravitreal injections, and number of follow-up assessments.

Results: Data were available on the first-treated eye from 406 patients with at least 1 year follow-up; of these, 198 had data at 2 years. The mean baseline VA of 54.4 Early Treatment Diabetic Retinopathy Study letters improved to 58.5 letters at 12 months and to 56.8 letters at 24 months. The mean VA changes from baseline to 1 year were +6.5, +7.5, +1.7, and -1.5 letters, respectively, for baseline VA categories of 23-35, 36-55, 56-70, and >70 letters. Change in mean VA from the end of the loading phase to year 1 ranged from -2.9 to +1.4 letters for the different baseline VA categories. The mean number of injections were similar across baseline VA categories ranging from 5.7 to 6.0 injections in year 1 and from 3.3 to 3.8 in year 2.

Conclusions: This large, real-world series demonstrates that mean change in VA is largely a function of selection criteria and baseline VA. The quality of a service is therefore better judged by actual VA outcomes and maintenance of vision after the loading phase.Eye advance online publication, 23 November 2012; doi:10.1038/eye.2012.225.

PMID: 23174752 [PubMed - as supplied by publisher

Eur J Ophthalmol. 2012 Nov 15:0. doi: 10.5301/ejo.5000159. [Epub ahead of print]

Effect of topical pressure-lowering medication on prevention of intraocular pressure spikes after intravitreal injection.

El Chehab H, Le Corre A, Agard E, Ract-Madoux G, Coste O, Dot C.

Desgenettes Hospital, Department of Ophthalmology, Lyon - France.

Purpose: The aim of this study was to evaluate pressure increases after intravitreal injections (IVI) and the interest in using prophylactic pressure-lowering medications.

Methods: This was a prospective study of 250 anti-vascular endothelial growth factor IVI (ranibizumab) divided into 5 groups of 50 IVI (group 1: no intraocular pressure [IOP]-lowering medication; group 2: apraclonidine 1%; group 3: acetazolamide; group 4: fixed association brimonidine + timolol; group 5: fixed association dorzolamide + timolol). The IOP was measured before, immediately after (T1), 15 minutes after (T15), and 45 minutes after (T45) the IVI using a tonometer. The data were analyzed by analysis of variance followed by a Bonferroni as post hoc test if necessary.

Results: The mean IOP peak in group 1 was 46.4±10 mmHg at T1, 21.7±10.2 mmHg at T15, and 15.4±8.6 mmHg at T45. It was not correlated with axial length (r=0.04, p=0.81) or lens status (phakic vs pseudophakic: p=0.88). A mild but significant correlation was found with age (r=0.36, p=0.006). Topical medications produced a significant reduction of IOP at every time point, of around 9 mmHg at T1. The reduction in IOP obtained with acetazolamide was not significant at T1 (-1.6 mmHg, p=0.12), but became significant at T15 and T45 (p=0.011 and p=0.015).

Conclusions: Intraocular pressure spike was high but transient. Topical medications, however, produced a significant reduction in IOP spike as well as in the duration of the increased pressure. It would be advisable to prevent this IOP spike, especially when procedures are repeated, notably in patients with glaucoma.

PMID: 23161177 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Semin Ophthalmol. 2012 Sep;27(5-6):214-7. doi: 10.3109/08820538.2012.708807.

Enhanced Depth Imaging Optical Coherence Tomography in Age-related Macular Degeneration.

Skondra D, Papakostas T, Vavvas DG.

Massachusetts Eye and Ear infirmary, Retina Service, Harvard Medical School , Boston, MA , USA.

Abstract: Imaging of the choroidal layer has been limited with the conventional commercial SD-OCTs. Enhanced depth imaging optical coherence tomography (EDI-OCT) is a modification of the standard spectral-domain OCT (SD-OCT) technique that enables better non-invasive imaging of the choroid. This review contains an introduction of EDI imaging technique and principles and summarizes the findings of EDI-OCT imaging in age-related macular degeneration.

PMID: 23163278 [PubMed - in process]

Graefes Arch Clin Exp Ophthalmol. 2012 Nov 17. [Epub ahead of print]

Enhanced depth imaging of the choroid in patients with neovascular age-related macular degeneration treated with anti-VEGF therapy versus untreated patients.

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PURPOSE: To compare the subfoveal choroidal thickness (SFCT) between patients with neovascular age-related macular degeneration (nAMD) who had multiple intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents and those with treatment-naïve nAMD.

METHODS: This retrospective case-control study included 15 patients in group 1 (nAMD in one eye which had received at least three anti-VEGF injections and early AMD in the fellow eye) and 15 patients in group 2 (newly diagnosed nAMD in one eye which had not received any treatment and early AMD in the fellow eye). They underwent enhanced depth imaging optical coherence tomography (OCT), and two OCT readers manually measured the SFCT. Inter-ocular difference in SFCT (nAMD eye minus fellow eye) was calculated for each patient.

RESULTS: The nAMD eyes in group 1 had received a median (range) of four (3-8) intravitreal injections of anti-VEGF agents, and the OCT scans were performed at a median (range) of 9 (4-17) months after the first injection. The median inter-ocular difference in SFCT in groups 1 and 2 were not significantly different (13.5 and 3.0 μm in groups 1 and 2 respectively, $p = 0.60$). There was also no statistically significant difference in SFCT between nAMD and fellow eyes ($p = 0.16$), although there was a trend for greater median SFCT in the nAMD eyes.

CONCLUSION: The data from this small cohort suggests that no gross reduction in SFCT appears in nAMD patients after a time interval of at least 4 months between initiating repeated treatment with anti-VEGF therapy and OCT imaging. However, a study with a much larger sample size or longitudinal design is required to detect possible small fluctuations in SFCT in nAMD eyes receiving anti-VEGF therapy.

PMID: 23160538 [PubMed - as supplied by publisher]

Semin Ophthalmol. 2012 Sep;27(5-6):207-13. doi: 10.3109/08820538.2012.708806.

Near infrared autofluorescence imaging of retinal diseases.

Skondra D, Papakostas TD, Hunter R, Vavvas DG.

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Abstract: Near infrared autofluorescence (excitation 787 nm, emission >800 nm) is a non-invasive imaging technology that provides information on the distribution of melanin within the retinal pigment epithelial cell/choroid complex. This review contains an introduction to near infrared autofluorescence imaging methods. Characteristics of near infrared imaging in a variety of retinal diseases, including age-related macular degeneration, choroidal nevus, retinal degenerations, retinal dystrophies, central serous chorioretinopathy, pseudoxanthoma elasticum and chloroquine retinopathy, are summarized.

PMID: 23163277 [PubMed - in process]

Semin Ophthalmol. 2012 Sep;27(5-6):202-6. doi: 10.3109/08820538.2012.711415.

Lipofuscin and the principles of fundus autofluorescence: a review.

Nandakumar N, Buzney S, Weiter JJ.

Massachusetts Eye and Ear Infirmary , Boston MA.

Abstract: Fundus autofluorescence is a non-invasive imaging modality that measures lipofuscin that has accumulated in the retinal pigment epithelium (RPE). Excessive lipofuscin in the RPE is a common pathway found in several diseases including Stargardt's disease and age-related macular degeneration. This review discusses the role of photooxidative damage in the development of lipofuscin and the principles of fundus autofluorescence.

PMID: 23163276 [PubMed - in process]

Ophthalmologica. 2012 Nov 20. [Epub ahead of print]

Assessment of a Spectral Domain OCT Segmentation Software in a Retrospective Cohort Study of Exudative AMD Patients.

Tilleul J, Querques G, Canoui-Poitrine F, Leveziel N, Souied EH.

Service d'ophtalmologie, Hôpital Intercommunal de Créteil, Créteil, France.

Background: To assess the ability of the Spectralis optical coherence tomography (OCT) segmentation software to identify the inner limiting membrane and Bruch's membrane in exudative age-related macular degeneration (AMD) patients.

Methods: Thirty-eight eyes of 38 naive exudative AMD patients were retrospectively included. They all had a complete ophthalmologic examination including Spectralis OCT at baseline, at month 1 and 2. Reliability of the segmentation software was assessed by 2 ophthalmologists. Reliability of the segmentation software was defined as good if both inner limiting membrane and Bruch's membrane were correctly drawn.

Results: A total of 38 patients charts were reviewed (114 scans). The inner limiting membrane was correctly drawn by the segmentation software in 114/114 spectral domain OCT scans (100%). Conversely, Bruch's membrane was correctly drawn in 59/114 scans (51.8%). The software was less reliable in locating Bruch's membrane in case of pigment epithelium detachment (PED) than without PED (42.5 vs. 73.5%, respectively; $p = 0.049$), but its reliability was not associated with SRF or CME ($p = 0.55$ and $p = 0.10$, respectively).

Conclusion: Segmentation of the inner limiting membrane was constantly trustworthy but Bruch's membrane segmentation was poorly reliable using the automatic Spectralis segmentation software. Based on

this software, evaluation of retinal thickness may be incorrect, particularly in case of PED. PED is effectively an important parameter which is not included when measuring retinal thickness.

PMID: 23171503 [PubMed - as supplied by publisher.]

Ophthalmology. 2012 Nov 19. pii: S0161-6420(12)00722-1. doi: 10.1016/j.ophtha.2012.07.068. [Epub ahead of print]

Epimacular Brachytherapy for Neovascular Age-Related Macular Degeneration: A Randomized, Controlled Trial (CABERNET).

Dugel PU, Bebchuk JD, Nau J, Reichel E, Singer M, Barak A, Binder S, Jackson TL; CABERNET Study Group.

Retinal Consultants of Arizona, Phoenix, Arizona.

PURPOSE: To evaluate the safety and efficacy of epimacular brachytherapy (EMBT) for the treatment of neovascular age-related macular degeneration (AMD).

DESIGN: Multicenter, randomized, active-controlled, phase III clinical trial.

PARTICIPANTS: Four hundred ninety-four participants with treatment-naïve neovascular AMD.

METHODS: Participants with classic, minimally classic, and occult lesions were randomized in a 2:1 ratio to EMBT or a ranibizumab monotherapy control arm. The EMBT arm received 2 mandated, monthly loading injections of 0.5 mg ranibizumab. The control arm received 3 mandated, monthly loading injections of ranibizumab then quarterly injections. Both arms also received monthly as needed (pro re nata) retreatment.

MAIN OUTCOME MEASURES: The proportion of participants losing fewer than 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters from baseline visual acuity (VA) and the proportion gaining more than 15 ETDRS letters from baseline VA.

RESULTS: At 24 months, 77% of the EMBT group and 90% of the control group lost fewer than 15 letters. This difference did not meet the prespecified 10% noninferiority margin. This end point was noninferior using a 20% margin and a 95% confidence interval for the group as a whole and for classic and minimally classic lesions, but not for occult lesions. The EMBT did not meet the superiority end point for the proportion of participants gaining more than 15 letters (16% for the EMBT group vs. 26% for the control group): this difference was statistically significant (favoring controls) for occult lesions, but not for predominantly classic and minimally classic lesions. Mean VA change was -2.5 letters in the EMBT arm and +4.4 letters in the control arm. Participants in the EMBT arm received a mean of 6.2 ranibizumab injections versus 10.4 in the control arm. At least 1 serious adverse event occurred in 54% of the EMBT arm, most commonly postvitrectomy cataract, versus 18% in the control arm. Mild, nonproliferative radiation retinopathy occurred in 3% of the EMBT participants, but no case was vision threatening.

CONCLUSIONS: The 2-year efficacy data do not support the routine use of EMBT for treatment-naïve wet AMD, despite an acceptable safety profile. Further safety review is required.

PMID: 23174399 [PubMed - as supplied by publisher]

Pathogenesis

Int J Ophthalmol. 2012;5(5):609-13. doi: 10.3980/j.issn.2222-3959.2012.05.13. Epub 2012 Oct 18.

Tissue factor with age-related macular degeneration.

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Abstract: Wet age-related macular degeneration which incidence increases year by year is a blinding eye disease, but current clinical methods of treatment on this disease are limited and the outcome is not ideal. Recent studies have found abnormally high expression of tissue factors which are targets for the treatment of wet age-related macular degeneration to achieve a certain effect in the choroidal neovascularization. Related literatures are reviewed as following.

PMID: 23166874 [PubMed - in process] PMCID: PMC3484712

Nutrition

Ophthalmologica. 2012 Nov 20. [Epub ahead of print]

Micronutrients in Age-Related Macular Degeneration.

Aslam T, Delcourt C, Silva R, Holz FG, Leys A, Garcià Layana A, Souied E.

Manchester Royal Eye Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre and Institute of Human Development, University of Manchester, Manchester, UK.

Abstract: Several lines of evidence from in vitro and in vivo studies suggest that specific micronutrients may have beneficial effects in age-related macular degeneration (AMD). Such effects appear to be complex and may include filtering short wavelength light and attenuating oxidative and inflammatory damage as well as other structural and physiological factors. There is clinical evidence for potential benefits from vitamin C, β-carotene, vitamin E and zinc, as well as emerging epidemiological and clinical data for the carotenoids lutein and zeaxanthin and for omega-3 fatty acids. A survey of the literature suggests that some specific micronutrients may be of value in treating or preventing AMD, but further prospective studies are needed to further identify and characterize their effects and place in therapy.

PMID: 23171595 [PubMed - as supplied by publisher]