Intravitreal therapy in bilateral neovascular age-related macular degeneration

Published in:
Ophthalmology

DOI:
10.1016/j.ophtha.2014.05.007

Document Version
Peer reviewed version

Link to publication in the UWA Research Repository

Rights statement
© 2014, Elsevier. Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International http://creativecommons.org/licenses/by-nc-nd/4.0/

General rights
Copyright owners retain the copyright for their material stored in the UWA Research Repository. The University grants no end-user rights beyond those which are provided by the Australian Copyright Act 1968. Users may make use of the material in the Repository providing due attribution is given and the use is in accordance with the Copyright Act 1968.

Take down policy
If you believe this document infringes copyright, raise a complaint by contacting repository-lib@uwa.edu.au. The document will be immediately withdrawn from public access while the complaint is being investigated.
Intravitreal Therapy in Bilateral Neovascular Age-Related Macular Degeneration

Daniel Barthelmes MD PhD\textsuperscript{1,2}, Richard J Walton MSc\textsuperscript{1}, Jennifer J Arnold MBBS\textsuperscript{3}, Ian L McAllister MBBS\textsuperscript{4}, Judy M Simpson BSc PhD\textsuperscript{5}, Anna Campain PhD\textsuperscript{1}, Alex P Hunyor MBBS\textsuperscript{1,6}, Robyn Guymer MBBS PhD\textsuperscript{7}, Rohan W Essex MBBS\textsuperscript{8}, Nigel Morlet MBBS\textsuperscript{9}, Mark C Gillies MBBS PhD\textsuperscript{1*} for the Fight Retinal Blindness! Project Investigators

Running head: Bilateral treatment for neovascular AMD

Supported by a grant from the Royal Australian NZ College of Ophthalmologists Eye Foundation (2007-2009) and a grant from the National Health and Medical Research Council, Australia (NHRMC 2010-1012). The authors state they have no conflicts of interest to declare. Mark Gillies is a Sydney Medical Foundation Fellow and is supported by an NHMRC practitioner fellowship. Robyn Guymer is also supported by an NHMRC practitioner fellowship (#529905), Daniel Barthelmes was supported by the Walter and Gertrud Siegenthaler Foundation Zurich, Switzerland, the Holcim Foundation and the Swiss National Foundation.

Conflict of interest: No conflicting relationship exists for any author.

\textsuperscript{1} The Save Sight Institute, Sydney Medical School, The University of Sydney, Sydney NSW, Australia
\textsuperscript{2} Department of Ophthalmology, University Hospital Zurich, University of Zurich, Zurich, Switzerland
\textsuperscript{3} Marsden Eye Specialists, Parramatta, Australia
\textsuperscript{4} The Lions Eye Institute, Center for Ophthalmology and Vision Science, University of Western Australia, Perth WA, Australia
\textsuperscript{5} Sydney School of Public Health, University of Sydney, Sydney NSW, Australia
\textsuperscript{6} Retina Associates, Chatswood NSW, Australia
\textsuperscript{7} Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, Melbourne VIC, Australia
\textsuperscript{8} Department of Ophthalmology, Canberra Hospital, Garran ACT, Australia
\textsuperscript{9} Department of Population Health, University of Western Australia, Perth WA, Australia

*Reprints requests: Professor Mark Gillies, Save Sight Institute, South Block, 8 Macquarie St. Sydney 2000 NSW, Australia. Email: mark.gillies@sydney.edu.au

Key words
AMD, intravitreal therapy, bilateral, outcomes, age-related macular degeneration, ranibizumab
Intravitreal anti vascular endothelial growth Factor (antiVEGF) agents such as ranibizumab are established as standard treatment for neovascular age-related macular degeneration (nAMD). For statistical reasons, most clinical trials include 1 study eye per patient. Although up to 50% of patients with nAMD in one eye may develop fellow eye involvement within 5 years, few data are available on treatment outcomes in these second-affected eyes. Here we report such outcomes in patients with bilateral disease from the collaborative Fight Retinal Blindness! (FRB!) Project, which has designed and established an efficient web-based system to track outcomes of patients receiving treatment for nAMD in clinical practice.

We studied all patients from the FRB! database with bilateral nAMD in whom the second eye was diagnosed at least 2 months after the first eye and in whom both eyes had at least 12 months of follow-up data. The delay between diagnoses was chosen to ensure diagnoses were made independently, thereby excluding patients who may have presented initially with bilateral disease. Ethics approval was obtained from the respective Human Research Ethics Committees of participating doctors. Data collected included age and angiographic lesion criteria (lesion type and greatest linear dimension [GLD] in µm) at commencement of treatment (index visit); best visual acuity (VA) score (with and without spectacles or pin hole) was recorded in LogMAR letters at each visit as well as treatment given. Data are presented as mean and interquartile range (Q1 and Q3).

Of the total cohort of 1992 patients in the FRB! database, 28% had bilateral disease, which is similar to previous studies. First and second eyes had been diagnosed with nAMD at least 2 months apart with at least 12 month follow-up data in 176 participants which formed the analysis set. Sixty-two percent of participants were female. Mean age at diagnosis of the first-affected eye was 78.6 (74 and 83) years and mean VA in first eyes was 49.7 (40 and 64) logMAR letters. Mean GLD in first eyes was 2840µm (1500 and 3500). Median time to diagnosis of the second eye was 427 days after the first eye. At their index visit, second eyes
had a mean VA of 61.2 (54 and 75) logMAR letters and a mean GLD of 2250µm (1000 and 2880). Twelve months after commencing intravitreal anti VEGF treatment with ranibizumab, first eyes had a mean VA of 56.9 (54 and 60) logMAR letters (mean 7.2 letter improvement compared to index visit, P<0.001, paired t-test), while second eyes had a mean VA of 65 (63 and 67) logMAR letters (mean 3.8 letters improvement compared to index visit, P<0.001, paired t-test). Although a greater mean change was observed in first eyes, their 12 month mean VA was still less than that of the second eye group at their index visit (Figure 1). In the first eye group a mean of 6.3 (4 and 8) injections were administered within the first 12 months, while second eyes received a mean of 7.3 (5 and 9) injections (difference of 0.9 injections, p< 0.001).

Choroidal neovascular (CNV) lesions were diagnosed by the treating physician as either occult, minimally classic, predominantly classic, retinal angiomatous proliferation; all other lesion types were combined into a single category. Overall, 64% of patients had the same lesion type in each eye (Cohen kappa=0.48) indicating fair to good concordance of lesion type between first and second affected eyes.

The present study evaluated characteristics and outcomes in a large cohort of patients in whom both eyes were diagnosed and treated for nAMD with intravitreal ranibizumab. The within-patient, paired data allows a close examination of characteristics at diagnosis and 12 month outcomes without extraneous variation as both eyes belonged to the same patient and were treated in the same practice. Second-affected eyes had smaller lesions and better vision when they started treatment. They had slightly more injections than first affected eyes over the first 12 months of their treatment (mean 7.3 vs. 6.3) and had better VA after 12 months of treatment than first-affected eyes, even though first-affected eyes had a greater mean VA improvement. This provides strong evidence that earlier diagnosis and treatment of nAMD leads to better outcomes.4
The fact that the mean VA of the first-affected eye group was 11 logMAR letters lower than the second-affected group at the index visit was expected. A recent analysis of approximately 1200 eyes with nAMD from patients treated in the United Kingdom found a 10 letter difference at presentation between first and second-affected eyes\textsuperscript{5}. A slow decline in VA in one eye may go unnoticed if the other eye still has good vision and that patients are likely to seek help more quickly when the better (second) eye is affected. It is also likely that second eye involvement would be detected earlier during the regular visits required for treatment of the first-affected eye. This is reflected by the better vision and smaller lesion size of second-affected eyes that we observed. The better VA at the index visit seems to be the main reason for better outcomes after 12 months of treatment since mean VA improvement of the first-affected eye group was significantly greater than that of the second-affected group. The relatively greater improvement in first eyes is most likely due to ceiling effects in the second affected eye which had higher starting VA.

We also observed concordance of CNV lesion types developing in the first- and second-affected eyes. This may be attributed to various factors, most likely genetic, although some discordance observed suggests that environmental factors may also contribute to lesion type.

Although not addressed in RCTs, second eye involvement is common. Hence, patient education that second eye involvement may occur and regular checks of the second eye during busy clinics in which the first-affected eye is being treated are strongly recommended in order to pick up changes early and institute treatments promptly.
Figure 1: Fitted LOESS lines to 12 month longitudinal visual acuity outcomes for 176 eyes diagnosed first and their fellow ‘second’ eyes. Individual visual acuity readings are shown as dots. Panel A shows data for first eyes, Panel B for second eyes.

References


