E.6.2 Anti-VEGF treatment in people presenting with visual acuity better than 6/12 or worse than 6/96

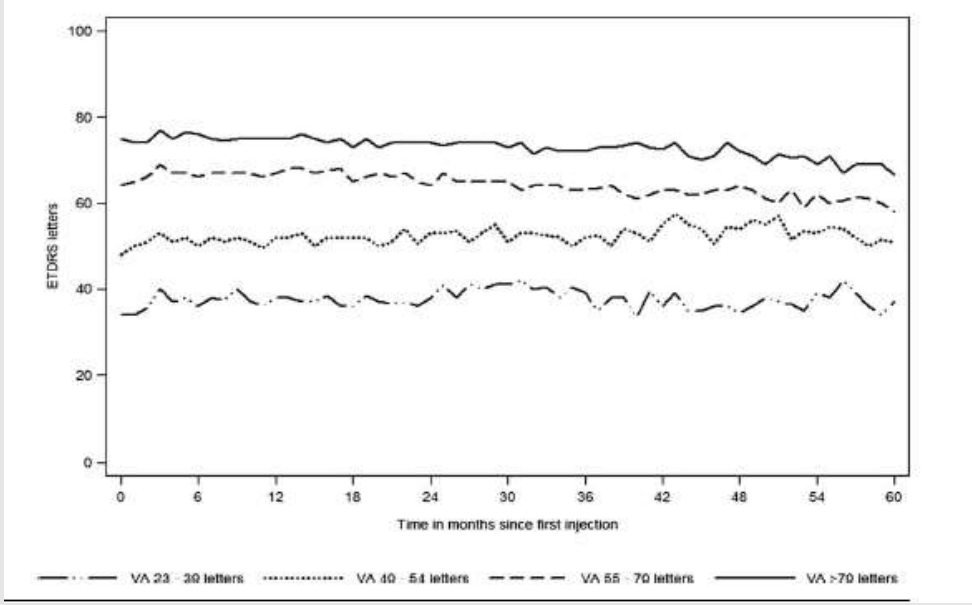
RQ10: What is the effectiveness of treatment of neovascular AMD in people presenting with visual acuity better than 6/12?

RQ25: What is the effectiveness of treatment of neovascular AMD in people presenting with visual acuity worse than 6/96?

Bibliographic reference	**Buckle M; Donachie P H; Johnston R L. Long-term outcomes of intravitreal ranibizumab for neovascular age-related macular degeneration in a well defined region of the UK. British Journal of Ophthalmology 100 (2): 240-5. 2014.**
Country/ies where the study was carried out	UK
Study type	Observational study
Aim of the study	To study long-term, whole population 'real world' clinical outcomes of ranibizumab therapy in treatment-navie eyes for neovascular age-related macular degeneration.
Study dates	Published 2014
Source of funding	Not reported
Sample size	1483 eyes eligible for analysis from 1278 patients.
Inclusion criteria	Treatment-navie eyes with a presenting visual acuity of 23 letters or more that were treated exclusively with ranibizumab
Exclusion criteria	Prior treatment with ranibizumab or bevacicumab privately Prior or concurrent photodynamic therapy Visual acuity <23 ETDRS letters at baseline and failure to complete the loading phrase of injections.
Patient characteristics	Age, median: 82.5 years, range: 50.2 to 100.8 years Gender, M, %: 35.1% (n=448) Visual acuity (ETDRS letters) 23-39 letters: 17.3% (n=257) 40-54 letters: 23.1% (n=343) 55-69 letters: 42.7% (n=633) >70 letters: 16.9% (n=250)

Bibliographic reference	**Buckle M; Donachie P H; Johnston R L. Long-term outcomes of intravitreal ranibizumab for neovascular age-related macular degeneration in a well defined region of the UK. British Journal of Ophthalmology 100 (2): 240-5. 2014.**
	Comorbidities affecting the eye (e.g. glaucoma and diabetic retinopathy) – at least one ocular co-pathology 7.3% (n=108)
Details	The study was performed at a single centre where a highly structured data set (defined before the introduction of the anti-VEGF service) is prospectively collected in an EMR system (Medisoft Ophthalmology, Leeds, UK) in the context of a paperless service. Data collected included: Demographics, Early Treatment Diabetic Retinopathy Study (ETDRS) VA at baseline and every visit, injection dates, Ocular copathology, central 1 mm retinal thickness (CRT) measurements using spectral domain ocular coherence tomography (SD OCT; Heidelberg Spectralis, Hemel Hempstead, UK), and Operative and postoperative complications.
Treatment	The department uses a pro re nata treatment posology after an initial loading phase of three injections at monthly intervals. All intravitreal injections are administered in dedicated treatment rooms with povidone iodine being used before and after injections. After each injection the patient is asked to confirm they can still count fingers as a surrogate measure of intraocular pressure (IOP) and if they cannot (or if the patient has glaucoma) then the IOP is checked and treated as appropriate. Patients are followed up at monthly intervals with SD OCT and fundal examination until no injections have been required to either eye for 6 months, after which follow-up intervals are gradually extended. If no injections have been required for 1 year patients are discharged and advised to return if they notice any new symptoms of blurring or distortion of vision in either eye.
Results	<table><tr><td>Baseline visual acuity</td><td>>70 letters</td><td>≤70 letters</td><td>Total (%)</td><td>Effect (95%CI) RR</td></tr><tr><td>No. of patients at baseline</td><td>250</td><td>1233</td><td></td><td></td></tr><tr><td>No. of people had a gain of 15 letters or more, n(%)</td><td></td><td></td><td></td><td></td></tr><tr><td>End of loading phase</td><td>Not reported</td><td>227 (18.2%)</td><td>Not reported</td><td></td></tr></table>

Bibliographic reference	Buckle M; Donachie P H; Johnston R L. Long-term outcomes of intravitreal ranibizumab for neovascular age-related macular degeneration in a well defined region of the UK. British Journal of Ophthalmology 100 (2): 240-5. 2014.				
	Year 1	Not reported	184 (16.8%)	Not reported	
	Year 2	Not reported	137 (18.8%)	Not reported	
	Year 3	Not reported	70 (15.9%)	Not reported	
	Year 4	Not reported	39 (15.5%)	Not reported	
	Year 5	Not reported	8 (8.2%)	Not reported	
	No. of people had a loss of 15 letters or more, n (%)				
	End of loading phase	19 (8.5%)	56 (4.5%)	75 (5.1%)	1.93 (1.17, 3.19)
	Year 1	18 (9.0%)	108 (9.8%)	126 (9.7%)	0.90 (0.56, 1.45)
	Year 2	13 (10.0%)	98 (13.4%)	111 (12.9%)	0.74 (0.43, 1.27)
	Year 3	12 (18.0%)	95 (21.6%)	107 (21.1%)	0.83 (0.48, 1.43)
	Year 4	6 (18.5%)	58 (23.0%)	64 (22.4%)	0.77 (0.36, 1.64)
	Year 5	3 (29.0%)	27 (27.4%)	30 (27.5%)	0.99 (0.36, 2.74)

<table>
<tr><th>Bibliographic reference</th><th>Buckle M; Donachie P H; Johnston R L. Long-term outcomes of intravitreal ranibizumab for neovascular age-related macular degeneration in a well defined region of the UK. British Journal of Ophthalmology 100 (2): 240-5. 2014.</th></tr>
<tr><td></td><td>Median visual acuity over time according to baseline visual acuity (n=1483 eyes at baseline)
 
</td></tr>
<tr><td>Others</td><td>A limitation of this study is that the sample sizes decrease with each year leading to higher SEs for the estimates in the latter years of the study period. Based on the study results, the number of eyes were as following from end of loading phase to year 5:
<table>
<tr><td></td><td>>70 letters</td><td>≤70 letters1</td><td>No. of eyes</td></tr>
<tr><td>Loading phase</td><td>224</td><td>1247</td><td>1471</td></tr>
<tr><td>Year 1</td><td>203</td><td>1095</td><td>1299</td></tr>
</table></td></tr>
</table>

Bibliographic reference	Buckle M; Donachie P H; Johnston R L. Long-term outcomes of intravitreal ranibizumab for neovascular age-related macular degeneration in a well defined region of the UK. British Journal of Ophthalmology 100 (2): 240-5. 2014.

Year 2	131	728	860
Year 3	67	440	507
Year 4	34	52	286
Year 5	11	98	109

1. Total number of people with visual acuity (≤70 letters) were calculated based on the percentage number of people with ≤70 letters gained 15 or more letters reported in the study.

Bibliographic reference	Fang Kai ; Tian Jun ; Qing Xueying ; Li Shuai ; Hou Jing ; Li Juan ; Yu Wenzhen ; Chen Dafang ; Hu Yonghua ; Li Xiaoxin. Predictors of visual response to intravitreal bevacizumab for treatment of neovascular age-related macular degeneration. Journal of Ophthalmology 2013.
Country/ies where the study was carried out	China
Study type	Observational study
Aim of the study	To identify the predictors of visual response to the bevacizumab treatment of neovascular age-related macular degeneration (AMD).
Study dates	Published 2013
Source of funding	Not reported
Sample size	144 patients
Inclusion criteria	People with neovascular AMD
Exclusion criteria	Not reported

Bibliographic reference	**Fang Kai ; Tian Jun ; Qing Xueying ; Li Shuai ; Hou Jing ; Li Juan ; Yu Wenzhen ; Chen Dafang ; Hu Yonghua ; Li Xiaoxin. Predictors of visual response to intravitreal bevacizumab for treatment of neovascular age-related macular degeneration. Journal of Ophthalmology 2013.**
Patient characteristics	Age, mean (+SD): 68.8 (8.6) years Gender, M, %: 66.0% (n=95) Mean VA score, letters (SD): 37.5 (18.4) Visual acuity (ETDRS letters) BCVA <20 letters (n=23) BCVA 20 and 39 letters (n=56) BCVA 40 and 59 letters (n=45) BCVA ≥ 60letters (n=20) Duration of neovascular AMD <1 month: no (%) 5 (3.8%) 1-6.9 months: 70 (53.0%) 7-12 months: 26 (19.7%) >12 months: 31 (23.5%)
Details	All patients received comprehensive ophthalmologic examinations before each intravitreal injection, including measurements of the best-corrected Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity at 2m, slit lamp biomicroscopy, fundus examination, fundus fluorescein angiography (FFA) (Topcon TRC-50EX, Tokyo, Japan), indocyanine green angiography (ICGA) (Heidelberg Spectralis HRA, Heidelberg, Germany), and optical coherence tomography (OCT) spectral domain type, Zeiss-Humphrey, CA, USA; program, retinal mapping program version 6.2). OCT was used to measure the 1mm central retinal thickness. A total of 185 patients (eyes) were enrolled from January 2008 to January 2010, of which baseline behaviour factors in 144 patients were available for analysis. Predictors of 3 visual response measures at the 6thmonth were evaluated, including change in VA score from baseline, Proportion of patients that gained ≥15 letters from baseline, and change in central retinal thickness (CRT) from baseline.

<table>
<tr><th>Bibliographic reference</th><td>Fang Kai ; Tian Jun ; Qing Xueying ; Li Shuai ; Hou Jing ; Li Juan ; Yu Wenzhen ; Chen Dafang ; Hu Yonghua ; Li Xiaoxin. Predictors of visual response to intravitreal bevacizumab for treatment of neovascular age-related macular degeneration. Journal of Ophthalmology 2013.</td></tr>
<tr><td></td><td>For the exploratory association analysis of the NATTB data, factors were considered including patients' baseline age, gender, cigarette smoking status, VA score, CNV lesion type, duration of neovascular AMD (defined as the interval from diagnosis of neovascular AMD to participation in the study), treatment regimen, and genotype.</td></tr>
<tr><td>Treatment</td><td>Patients were randomized into 2 treatment groups each with a different regimen of administration: bevacizumab was administered every 6 weeks for a total of 8 injections (regimen A), or bevacizumab was administered every 6 weeks (3 injections) and then every 12 weeks (2 injections) (regimen B). The dose of bevacizumab was 1.25 mg (in 0.05mL of solution). Follow up of the participants was conducted at 6- or 12-week intervals for more than 6 months after the initial treatment.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td>Predictors</td><td>Unstandardised coefficients B (SE)</td><td>Standardised coefficients B</td><td>t (p value)</td></tr>
<tr><td>Age</td><td>-2.998 (1.347)</td><td>-0.188</td><td>-2.227 (0.028)</td></tr>
<tr><td>Baseline VA score</td><td>-4.561 (1.217)</td><td>-0.303</td><td>-3.749 (<0.001)</td></tr>
<tr><td>Duration of nAMD</td><td>-3.040 (1.290)</td><td>-0.193</td><td>-2.357 (0.02)</td></tr>
</table>

Visual acuity change (letters), from baseline to 6 months follow-up
<table>
<tr><td></td><td>VA< 20 letters</td><td>60 ≥VA≥20</td><td>Effect (95%CI)</td></tr>
<tr><td>Number</td><td>23</td><td>121</td><td></td></tr>
<tr><td>Mean (SD) letter</td><td>13.8 (27.6)</td><td>8.3 (33.2)</td><td>5.50 (-7.24, 18.24)</td></tr>
</table>

Multivariate analysis of ≥15 letters gain from baseline to 6 months</td></tr>
</table>

Bibliographic reference	Fang Kai ; Tian Jun ; Qing Xueying ; Li Shuai ; Hou Jing ; Li Juan ; Yu Wenzhen ; Chen Dafang ; Hu Yonghua ; Li Xiaoxin. Predictors of visual response to intravitreal bevacizumab for treatment of neovascular age-related macular degeneration. Journal of Ophthalmology 2013.				
	Predicator	Total number of people	No. of events (%)	OR (95%CI)	Effect (95%CI) RR <20 letters vs ≥20 letters
	Baseline VA				
	<20 letters (G1)	23	10 (43.5)	1.000	1.46 (0.85, 2.15)
	20-39 letters	56	25 (44.6)	0.688 (0.227, 2.091)	
	40-59 letters	45	9 (20.0)	0.277 (0.081, 0.944)	
	≥60 letters	20	2 (10.0)	0.107(0.018, 0.638)	
	Duration of nAMD				Effect (95%CI) RR <1 month vs ≥1 month
	<1 month	5	4 (80.0)	1.000	2.75 (1.64, 4.60)
	1-6.9months	70	22 (31,4)	0.105 (0.010, 1.113)	
	7-12 months	26	10 (38.5)	0.134 (0.012, 1.542)	
	>12 months	31	5 (16.1)	0.047 (0.004, 0.571)	

Bibliographic reference	El-Mollayess G M; Mahfoud Z ; Schakal A R; Salti H I; Jaafar D ; Bashshur Z F. Intravitreal bevacizumab in the management of neovascular age-related macular degeneration: effect of baseline visual acuity. Retina 33(9): 1828-35. 2013.
Country/ies where the study was carried out	Lebanon
Study type	Observational study (prospective)
Aim of the study	To study prospectively the safety and efficacy of intravitreal bevacizumab for eyes with neovascular age-related macular degeneration with baseline visual acuity better than 70 letters (Snellen equivalent better than 20/40)
Study dates	Published 2013
Source of funding	Not reported
Sample size	90 patients, as 30 patients were enrolled to each of the 3 groups: BCVA >70 letters (n=30) BCVA 70 and 61 letters (n=30) BCVA 60 and 51 letters (n=30)
Inclusion criteria	Age 50 years and older Subfoveal CNV caused by AMD diagnosed by FA Presence of subretinal fluid, cystic maculopathy, or CRT>250µm on OCT Best-corrected vision, using ETDS charters, betters than 20/100 (Snellen equivalent) Ability to understand and sign consent form
Exclusion criteria	Previous treatment for CNV Submacular haemorrhage involving the fovea Submacular scarring involving the fovea Retinal angiomatour proliferation or polypoidal choroidopathy Corneal, lenticular, or vitreous opacification that prevents good quality angiograms or OCT History of uveitis History of vitrectomy Diabetic retinopathy Other ocular conditions that affect vision Cardiovascular, cerebrovascular, or peripheral vascular event < 6 months before enrollment

<table>
<tr><th>Bibliographic reference</th><th>El-Mollayess G M; Mahfoud Z ; Schakal A R; Salti H I; Jaafar D ; Bashshur Z F. Intravitreal bevacizumab in the management of neovascular age-related macular degeneration: effect of baseline visual acuity. Retina 33(9): 1828-35. 2013.</th></tr>
<tr><td>Patient characteristics</td><td>Age, mean (+SD): 72.9 (11.9) years

Gender, M, %: 27.0% (n=30)

Visual acuity (ETDRS letters)
51-60 letters: 33.3% (n=30)
61-70 letters: 33.3% (n=30)
>70 letters: 33.3% (n=30)</td></tr>
<tr><td>Details</td><td>The study was conducted in the Retina clinical. Patients with neovascular AMD were enrolled if they met the eligibility criteria. Eligible eyes were enrolled into 1 of 3 groups based on the baseline BCVA. If both eyes of the same patients were eligible to enter the study, then the eye with the worse visual acuity were enrolled.</td></tr>
<tr><td>Treatment</td><td>All patients received the first and subsequent intravitreal bevacizumab injections based on a standard protocol. After initial injection, follow-up visits were carried out every 6 weeks. At each follow-up, the Early Treatment Diabetic Retinopathy Study BCVA, slit-lamp examination, dilated fundus examination, and OCT were performed. FA was repeated at the discretion of the treating physician.
There was no compulsory loading phase at the initial treatment. However, intravitreal bevacizumab was administered every 6 weeks until there was no evidence of fluid on OCT. One the macular was dry on OCT, follow-up was continued every 6 weeks for all the 3 groups. However, this could be reduced to every 4 weeks if deemed necessary by the treating physician.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td>Baseline visual acuity</td><td>>70 letters (G1)</td><td>61-70 letters (G2)</td><td>51-60 letters (G3)</td><td>Effect (95%CI),
(≥70 letters/51-70 letters)</td></tr>
<tr><td>No. of patients at baseline</td><td>30</td><td>30</td><td>30</td><td></td></tr>
<tr><td>Mean VA at baseline letters</td><td>78</td><td>66.2</td><td>56.9</td><td></td></tr>
<tr><td>Mean VA at 12-month, letters</td><td>78.4</td><td>70.0</td><td>61.1</td><td></td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**El-Mollayess G M; Mahfoud Z ; Schakal A R; Salti H I; Jaafar D ; Bashshur Z F. Intravitreal bevacizumab in the management of neovascular age-related macular degeneration: effect of baseline visual acuity. Retina 33(9): 1828-35. 2013.**				
	No. of people had a gain of 15 letters or more in VA, n(%)	0	4 (13.3%)	13 (36.7)	0.06 (0.00, 0.90)
	No. of people had a loss of 15 letters in VA, n(%)	0	5	6	0.09 (0.01, 1.40)
	No. of people had visual acuity 70 and 85 letters at 12-month, n(%)	28 (93.3%)	21 (70%)	14 (46.7%	1.60 (1.27, 2.02)
	No. of people had visual acuity 80 and 85 letters at 12-month, n(%)	20 (66.7%)	6 (20.0%)	3 (30%)	4.44 (2.31, 8.54)
	No. of people had visual acuity <35 letters at 12-month, n(%)	0	6 (20%)	2 (6.7%)	0.12 (0.01, 1.94)
	Mean number of injections	4.4	4.6	3.2	
	No severe ocular and systemic adverse events were noted in all the 3 groups over 12 months.				
Others	The number of injections in the study was lower than trial results (CATT).				

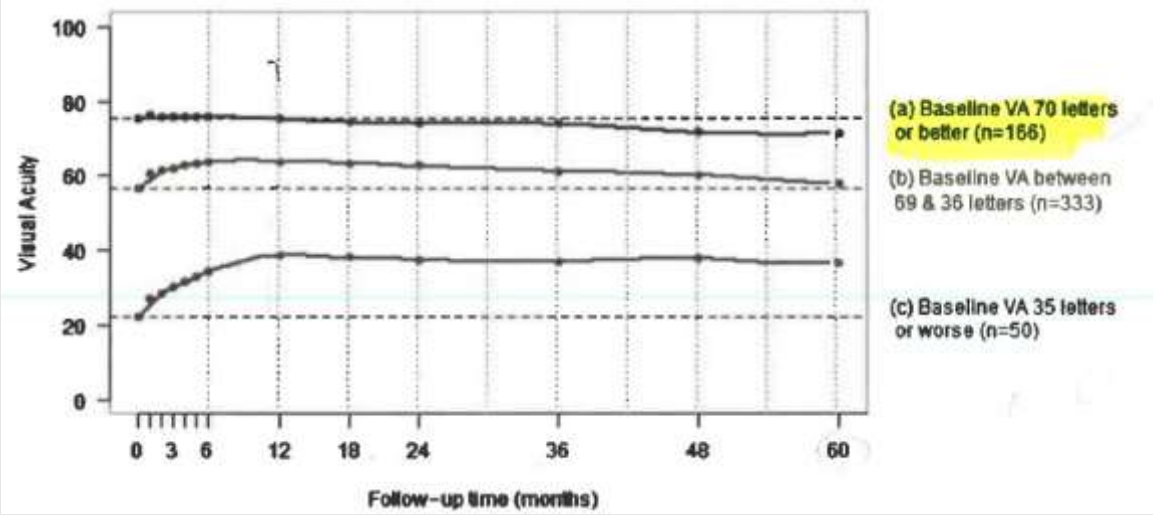
Bibliographic reference	**Gillies M C; Campain A ; Barthelmes D ; Simpson J M; Arnold J J; Guymer R H; McAllister I L; Essex R W; Morlet N ; Hunyor A P; Fight Retinal Blindness Study; Group . Long-Term Outcomes of Treatment of Neovascular Age-Related Macular Degeneration: Data from an Observational Study. Ophthalmology 122 (9): 1837-45.2015**
Country/ies where the study was carried out	The study included contributing practitioners located in Australia, New Zealand, and Switzerland.
Study type	Observational study

Bibliographic reference	**Gillies M C; Campain A ; Barthelmes D ; Simpson J M; Arnold J J; Guymer R H; McAllister I L; Essex R W; Morlet N ; Hunyor A P; Fight Retinal Blindness Study; Group . Long-Term Outcomes of Treatment of Neovascular Age-Related Macular Degeneration: Data from an Observational Study. Ophthalmology 122 (9): 1837-45.2015**
Aim of the study	To analyse the long-term outcomes of eyes with neovascular AMD starting treatment with anti-VEGF at least 5 years earlier.
Study dates	Published 2015
Source of funding	Supported by a grant from the Royal Australian New Zealand College of Ophthalmologist Eye Foundation and a grant from the National Health and Medical Research Council, Australia.
Sample size	1212 eyes (1043 people), and 549 eyes with data for at least 5 years
Inclusion criteria	Treatment-naive eyes, never having received any form of treatment for neovascular AMD, and were treated with intravitreal therapy at least 5 years of potential follow-up since stating treatment.
Exclusion criteria	Not reported
Patient characteristics	Age, mean: 79.1 years Gender, M, %: 39%% (n=407) Visual acuity, mean (+SD) (ETDRS letters): 55.1 (18.8) ≤ 35 letters: 17.0% (n=206) ≥70 letters: 23.0% (n=279)
Details	The study observed eye that commenced intravitreal therapy for neovascular AMD in routine practice at least 5 years and had been tracked in the Flight Retinal Blindness (FRB) database. This database collects data form each clinical visit, including the number of letters read on LogMAR VA chart, activity of choroidal neovascular membrane, treatment given, if any, ocular adverse, and whether the eye had received prior treatment for neovascular AMD.
Treatment	Most eyes were treated nonly 1 type of anti-VEGF treatment: 648 (53.5%) with ranibizumab, and 69 (5.7%) with bevacizumab Of the 495 eyes that were treated with multiple agent, 7.8% of injections were with ranibizumab, 10.5% were with bevacizumab, and 14.7% were with aflibercept.
Results	<table><tr><td>Baseline visual acuity</td><td>≥70 letters (G1)</td><td>36-69 letters (G2)</td><td>≤35 letters (G3)</td><td>Effect (G1 vs G2)</td></tr></table>

Bibliographic reference	Gillies M C; Campain A ; Barthelmes D ; Simpson J M; Arnold J J; Guymer R H; McAllister I L; Essex R W; Morlet N ; Hunyor A P; Fight Retinal Blindness Study; Group . Long-Term Outcomes of Treatment of Neovascular Age-Related Macular Degeneration: Data from an Observational Study. Ophthalmology 122 (9): 1837-45.2015

No. of eyes at baseline	166 eyes	333	50	
Mean VA at baseline, letters (SD)	75.2 (4.7)	56.6 (8.7)	22.6	18.60 (17.42, 19.78)
Mean VA at 5 years	70.7	58.6 (19.3)	35.2	

Regression curves over 5 years stratified by baseline visual acuity (VA)≥70 letters, between 36 and 69 letters, and ≤35 letters



All of visual improvement occurred in the first year of treatment.

Bibliographic reference	Gillies M C; Campain A ; Barthelmes D ; Simpson J M; Arnold J J; Guymer R H; McAllister I L; Essex R W; Morlet N ; Hunyor A P; Fight Retinal Blindness Study; Group . Long-Term Outcomes of Treatment of Neovascular Age-Related Macular Degeneration: Data from an Observational Study. Ophthalmology 122 (9): 1837-45.2015

	No. of injection (SD)	No. of visits (SD)
Year 1	6.1 (2.9)	9 (8.7)
Year 2	4.9 (3.1)	Median 7
Year 3	4.9 (3.5)	Median 7
Year 4	5.4 (3.3)	7.9 (3.7)
Year 5	4.9 (3.3)	7.4 (3.6)

Adverse event	No.	Risk rate per injection
Haemorrhage reducing BCVA by > 15 letters	28	0.11%
Infectious endophthalmitis	10	0.04%
Non-infectious endophthalmitis	3	0.01%
Intraocular surgery	82	0.33%

Bibliographic reference	**Gillies M C; Campain A ; Barthelmes D ; Simpson J M; Arnold J J; Guymer R H; McAllister I L; Essex R W; Morlet N ; Hunyor A P; Fight Retinal Blindness Study; Group . Long-Term Outcomes of Treatment of Neovascular Age-Related Macular Degeneration: Data from an Observational Study. Ophthalmology 122 (9): 1837-45.2015**
	Retinal detachment | 5 | 0.02% RPE tear | 9 | 0.04%
Others	Of 1212 eyes, 663 eyes from 631 people were lost to follow-up before 5 years.

Bibliographic reference	**Writing committee for the UK AMD EMR user group. The neovascular age-related macular degeneration database: Multicenter study of 92 976 ranibizumab injections: Report 1: Visual acuity manuscript no. 2013-568. Ophthalmology 121 (5): 1092-1101. 2014**
Country/ies where the study was carried out	UK
Study type	Observational study
Aim of the study	To study real-world ranibizumab therapy for treatment-naive eyes with neovascular age-related macular degeneration (nAMD) and to benchmark standards of care. Design Multicentre, national nAMD database study.
Study dates	Published 2014
Source of funding	Supported in part by an unrestricted grant from Novartis Pharmaceuticals UK Limited, Frimley, UK. No member or affiliate of Novartis had any input into data analysis, interpretation of the data, or writing the manuscript. This research received a proportion of its funding from the Department of Health's NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye Hospital and UCL Institute of Ophthalmology
Sample size	12,951 eyes of 11,135 patients who received a total of 92,976 ranibizumab injections at 14 UK hospital. 16.3% (n=1816) of these patients recruited treatment to both eyes during follow-up period.
Inclusion criteria	Treatment-naïve eyes undergoing ranibizumab therapy for nAMD.
Exclusion criteria	Eyes undergoing combined therapies or having bevacizumab in either eye during the study period were excluded.
Patient characteristics	Ethnic group – White, no. (%): 54.8% (n=6103) Mixed: 0.4% (n=41)

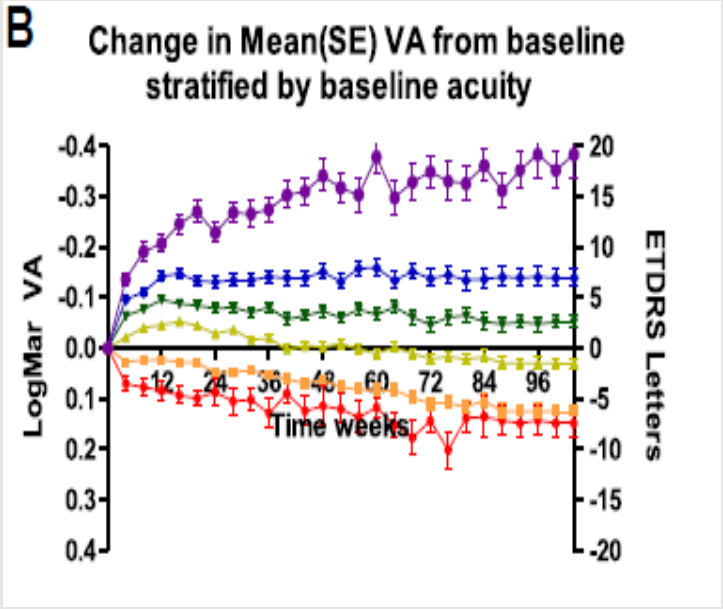
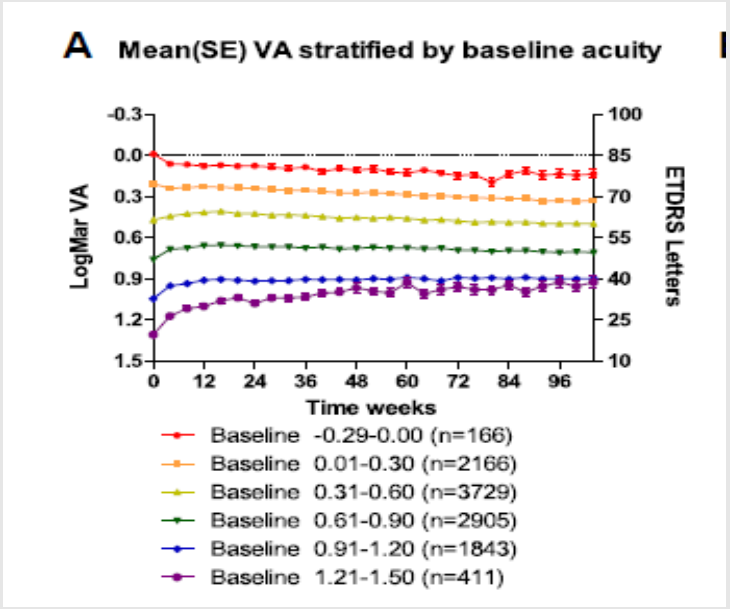
<table>
<tr><th>Bibliographic reference</th><td>Writing committee for the UK AMD EMR user group. The neovascular age-related macular degeneration database: Multicenter study of 92 976 ranibizumab injections: Report 1: Visual acuity manuscript no. 2013-568. Ophthalmology 121 (5): 1092-1101. 2014</td></tr>
<tr><td></td><td>Asian: 0.4% (n=40)

Age, mean: 79 years,

Gender, M, %: 36.6% (n=4071)</td></tr>
<tr><td>Details</td><td>The study was performed at 14 sites where a highly structured data set (defined before the introduction of the anti-VEGF service) is prospectively collected in an EMR system (Medisoft Ophthalmology, Leeds, UK) in the context of a paperless service.
Data collected included:
•Demographics,
•Early Treatment Diabetic Retinopathy Study (ETDRS) VA at baseline and every visit, injection dates,
•Ocular copathology, central 1 mm retinal thickness (CRT) measurements using spectral domain ocular coherence tomography (SD OCT; Heidelberg Spectralis, Hemel Hempstead, UK), and
•Operative and postoperative complications.

Data were extracted using Medisoft Ophthalmology (Medisoft Limited, Leeds, UK) for right and left eyes of patients who had had at least 1 intravitreal injection of ranibizumab.</td></tr>
<tr><td>Treatment</td><td>Ranibizumab</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td>Baseline visual acuity</td><td>-0.29-0.30 (≥6/12)</td><td><6/12 to 6/96</td><td>Effect (95%CI)</td><td>≤6/96 to 1/30</td><td><6/12 to 6/96</td><td>Effect (95%CI)</td></tr>
<tr><td>Number of people at baseline</td><td>2332</td><td>8477</td><td></td><td>411</td><td>8477</td><td></td></tr>
<tr><td>Visual acuity at year 1 (48 weeks) (SD)</td><td>71.83 (55.42)</td><td>53.53 (70.67)</td><td></td><td>36.5 (50.68)</td><td>53.53 (70.67)</td><td>-17.23 (-22.36, -12.10)</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	Writing committee for the UK AMD EMR user group. The neovascular age-related macular degeneration database: Multicenter study of 92 976 ranibizumab injections: Report 1: Visual acuity manuscript no. 2013-568. Ophthalmology 121 (5): 1092-1101. 2014						
	6 months, change in VA, letters	-2.64 (22.90)	3.54(35.74)	-6.18 (-7.38, -4.98)	11.4 (24.32)	3.54(35.74)	7.85 (5.39, 10.33)
	Year 1, change in VA, letters	-3.39 (36.27)	3.11 (33.33)	-6.50 (-8.13, -4.87)	17.1 (36.49)	3.11 (33.33)	13.99 (10.39, 17.59)
	Year 2, change in VA, letters	-6.27 (36.07)	1.68 (42.92)	-7.95 (-9.68, -6.22)	19.0 (42.57)	1.68 (42.92)	17.32 (13.10, 21.54)
	Change in mean(SE) visual acuity from baseline stratified by baseline acuity						

Bibliographic reference	Writing committee for the UK AMD EMR user group. The neovascular age-related macular degeneration database: Multicenter study of 92 976 ranibizumab injections: Report 1: Visual acuity manuscript no. 2013-568. Ophthalmology 121 (5): 1092-1101. 2014
	 
Others	Lee A Y; Lee C S; Butt T ; Xing W ; Johnston R L; Chakravarthy U ; Egan C ; Akerele T ; McKibbin M ; Downey L ; Natha S ; Bailey C ; Khan R ; Antcliff R ; Varma A ; Kumar V ; Tsaloumas M ; Mandal. UK AMD EMR USERS GROUP REPORT V: benefits of initiating ranibizumab therapy for neovascular AMD in eyes with vision better than 6/12. British Journal of Ophthalmology 99(8): 1045-50. 2015. To study the effectiveness and clinical relevance of eyes treated with good (better than 6/12 or 70 Early Treatment Diabetic retinopathy Study letters) visual acuity when initiating treatment with ranibizumab for neovascular AMD in the UK NHS.

	First eyes		Second eyes	
Baseline visual acuity	>6/12 (0.3logMAR)	6/12 to >6/24 (0.6 logMAR)	>6/12 (0.3logMAR)	6/12 to >6/24 (0.6 logMAR)

Bibliographic reference	Writing committee for the UK AMD EMR user group. The neovascular age-related macular degeneration database: Multicenter study of 92 976 ranibizumab injections: Report 1: Visual acuity manuscript no. 2013-568. Ophthalmology 121 (5): 1092-1101. 2014

Year 1	0.223 (6/10)	0.408 (6/15)	0.176 (6/9)	0.385 (6/15)
Year 2	0.306 (6/12)	0.464 (6/17)	0.197 (6/9)	0.401 (6/15)
Year 3	0.389 (6/15)	0.524 (6/20)	0.206 (6/10)	0.647 (6/27)

Bibliographic reference	Regillo C D; Busbee B G; Ho A C; Ding B ; Haskova Z. Baseline Predictors of 12-Month Treatment Response to Ranibizumab in Patients With Wet Age-Related Macular Degeneration. American Journal of Ophthalmology 160 (5): 1014-23. 2015.
Country/ies where the study was carried out	USA
Study type	Observational study (data from the HARBOR study) (retrospective)
Aim of the study	To identify baseline characteristics predictive of visual acuity (VA) outcomes at month 12 and treatment frequency in the first 12 months of the phase III HARBOUR study.
Study dates	Published 2015
Source of funding	GENENTECH, INC, South San Francisco, CA.
Sample size	500 people
Inclusion criteria	Treatment-naive patients aged 50 years and over with active subfoveal wet AMD.
Exclusion criteria	Not reported
Patient characteristics	Ethnic group - not reported Age, mean: 79 years Gender, M, %: not reported

Bibliographic reference	**Regillo C D; Busbee B G; Ho A C; Ding B ; Haskova Z. Baseline Predictors of 12-Month Treatment Response to Ranibizumab in Patients With Wet Age-Related Macular Degeneration. American Journal of Ophthalmology 160 (5): 1014-23. 2015.**
	Mean visual acuity (ETDRS letters): 20/80 (6/24)
Details	This retrospective, exploratory analysis of data from the HARBOR study investigated demographic and baseline characteristics predictive of VA outcomes at month 12 in the ranibizumab 0.5 mg monthly and 0.5 mg PRN groups, and treatment frequency in the first 12 months in the ranibizumab 0.5 mg PRN group. The main outcome measures that served as a basis for baseline predictors of VA outcomes at month 12 were BCVA change from baseline at month 12, the proportion of patients with a BCVA gain of >15 ETDRS letters from baseline at month 12, and the proportion of patients with a Snellen equivalent of 20/40 or better at month 12 in the ranibizumab 0.5 mg monthly and 0.5 mg PRN groups.
Treatment	HARBOR was a 24-month, phase III, randomized, multicenter, double-masked, active-treatment controlled study that evaluated the efficacy and safety of intravitreal ranibizumab 0.5 mg and 2.0 mg administered monthly or PRN after 3 monthly loading doses in treatment-naïve patients.
Results	<table><tr><td>Baseline visual acuity</td><td>>68 letters1 (Snellen 20/40)</td><td>≤68 letters (Snellen≤ 20/40)</td><td>Effect (95%CI)</td></tr><tr><td>No. of patients</td><td>62</td><td>438</td><td></td></tr><tr><td>No. of people had a gain of 15 letters or more at month 12, n(%)</td><td>7 (11%)</td><td>162 (37%)</td><td>0.31 (0.15, 0.62)</td></tr></table>

Bibliographic reference	**Vogel R N; Davis D B; Kimura B H; Rathinavelu S ; Graves G S; Szabo A ; Han D P. NEOVASCULAR AGE-RELATED MACULAR DEGENERATION WITH ADVANCED VISUAL LOSS TREATED WITH ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY: Clinical Outcome and Prognostic Indicators. Retina 2016**
Country/ies where the study was carried out	USA

[1] Study indicated 68 letters (Snellen >20/40)

Bibliographic reference	Vogel R N; Davis D B; Kimura B H; Rathinavelu S ; Graves G S; Szabo A ; Han D P. NEOVASCULAR AGE-RELATED MACULAR DEGENERATION WITH ADVANCED VISUAL LOSS TREATED WITH ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY: Clinical Outcome and Prognostic Indicators. Retina 2016
Study type	Observeational study
Aim of the study	To describe visual outcome and prognostic indicators in neovascular age-related macular degeneration with advanced visual loss at the initiation of anti-vascular endothelial growth factor therapy.
Study dates	Published 2016
Source of funding	Not reported
Sample size	A consecutive series of 1,410 patients with nAMD, 131 met study critieria
Inclusion criteria	Patients initiated on intravitreal antiVEGF therapy between January2006 and December2012 at the Medical College of Wisconsin with exudative senilemaculardegeneration. Patients' eyes were included if they received intravitreal injections with ranibizumab, bevacizumab or aflibercept within the study period with VA20/200 or worse at the initiation of therapy.
Exclusion criteria	Eyes were excluded from the study for visually limiting eye disease other than AMD, large submacular haemorrhage creating mass effect, follow-up period of less than six months, history of anti-VEGF therapy before the study period, and age less than 50 years.
Patient characteristics	Ethnic group - not reported Age, mean: 82.2 (7.2) years Gender, F, %: 78 (60.5%) Mean visual acuity logMAR (Snellen): 1.38 (20/480) (SD 0.38) Baseline VA≥20/400: 80 (61.5%)
Details	The change in VA at 6 months and 12 months of included patients was assessed compared with baseline. Visual improvement/worsening was defined as at least +/- 0.3 logMAR (equivalent to 15 ETDRS [Early Treatment Diabetic Retinopathy Study] letters) change. Other factors for analysis included number of injections received, drug type, and various clinical and imaging findings.
Treatment	Patients' eyes were included if they received intravitreal injections with ranibizumab, bevacizumab or aflibercept.

Bibliographic reference	Vogel R N; Davis D B; Kimura B H; Rathinavelu S ; Graves G S; Szabo A ; Han D P. NEOVASCULAR AGE-RELATED MACULAR DEGENERATION WITH ADVANCED VISUAL LOSS TREATED WITH ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY: Clinical Outcome and Prognostic Indicators. Retina 2016

Results

Baseline visual acuity	<20 letter (Snellen 20/400)	≥20 letters (Snellen≥ 20/400)	Effect (95%CI)
No. of patients at 12 months	30	65	
Change in ETDRS letters	15.0 (SD[2]=26.32)	5.5 (SD=18.88)	9.50 (-0.98, 19.98)
No. of people had a gain of 30 letters or more at month 12, n(%)	9 (30.0)	10 (15.4)	1.95 (0.89, 4.30)
No. of people had a gain of <30 and ≥15 letters or more at month 12, n(%)	8 (26.7)	16 (24.6)	1.08 (0.52, 2.25)
No change	7 (23.3)	26 (40.0)	0.58 (0.29, 1.19)
No. of people had a loss of <30 and ≥15 letters or more at month 12, n(%)	2 (6.7)	9 (13.8)	0.48 (0.11, 2.09)
No. of people had a loss of 30 letters or more at month 12, n(%)	4 (13.3)	4 (6.2)	2.17 (0.58, 8.08)

	<20 letter (Snellen 20/400)	≥20 letters (Snellen≥ 20/400)	Effect (95%CI)

[2] SD was calculated by p values reported in the study.

Bibliographic reference	Vogel R N; Davis D B; Kimura B H; Rathinavelu S ; Graves G S; Szabo A ; Han D P. NEOVASCULAR AGE-RELATED MACULAR DEGENERATION WITH ADVANCED VISUAL LOSS TREATED WITH ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY: Clinical Outcome and Prognostic Indicators. Retina 2016			
	≥55 (20/80)	3 (10.0)	12 (18.5)	0.54 (0.16, 1.78)
	≥35 and <55 (≥20/200 and <20/80)	6 (34.7)	27 (41.6)	0.48 (0.22, 1.04)
	≥20 and <35 (≥20/400 and <20/200)	8 (26.7)	13 (20.0)	1.33 (0.62, 2.87)
	<20 (<20/400)	13 (43.3)	13 (20.0)	2.17 (1.15, 4.09)

Bibliographic reference	Williams T A; Blyth C P. Outcome of ranibizumab treatment in neovascular age related macula degeneration in eyes with baseline visual acuity better than 6/12. Eye 25 (12): 1671-21. 2011
Country/ies where the study was carried out	UK
Study type	Observational study (prospectively)
Aim of the study	To assess the effect of baseline vision on outcome in ranibizumab-treated neovascular AMD.
Study dates	Published 2011
Source of funding	Not reported
Sample size	615 eyes
Inclusion criteria	Patients were managed at two centres in South East Wales (University Hospital of Wales (UHW), Cardiff and Royal Gwent Hospital (RGH), Newport) using the same management protocol. Eyes that had completed 52-week follow-up were included in the study
Exclusion criteria	CNV secondary to causes other than nAMD Previous treatment for nAMD in the affected eye (argon laser photocoagulation, photodynamic therapy or previous anti-VEGF
Patient characteristics	Ethnic group - not reported

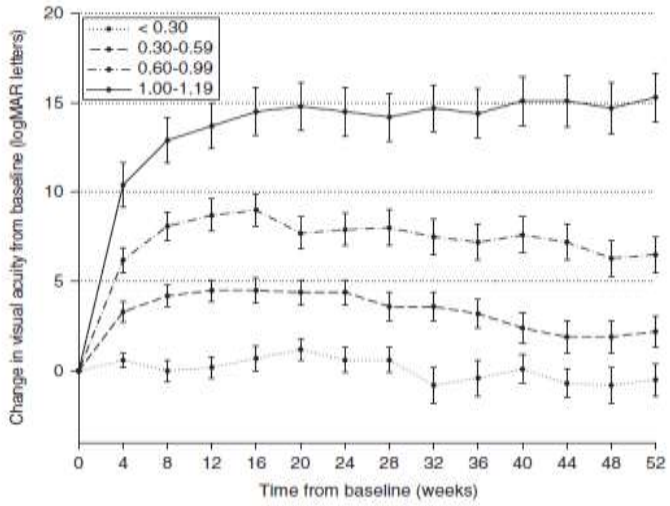
<table>
<tr><th>Bibliographic reference</th><th>Williams T A; Blyth C P. Outcome of ranibizumab treatment in neovascular age related macula degeneration in eyes with baseline visual acuity better than 6/12. Eye 25 (12): 1671-21. 2011</th></tr>
<tr><td></td><td>Age, mean: 79.3 years

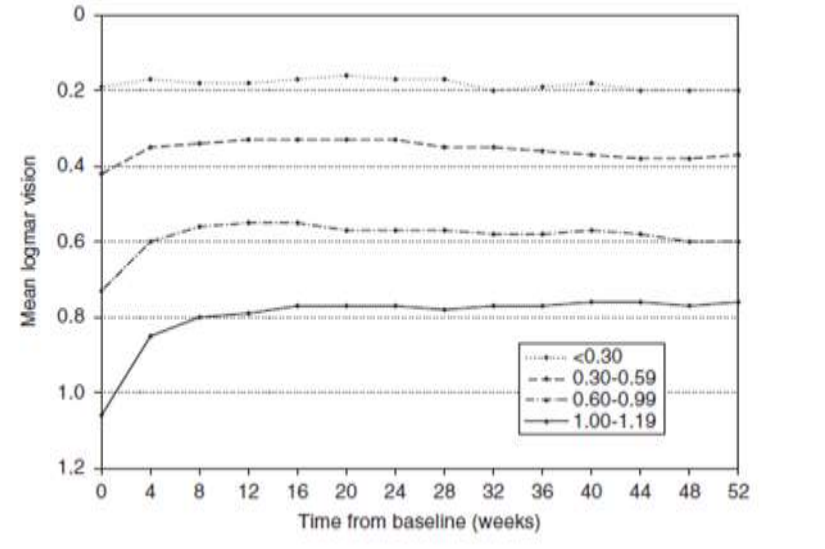
Gender, M, %: not reported

Visual acuity (ETDRS letters)
No. (%) (total=615)
<0.30 (6/12): 88 (14.3%)
0.30-0.59 (6/12-6/24): 210 (34.1%)
0.60-0.99 (6/24-6/60: 211 (34.3%)
1.00-1.20 (6/60-6/96): 106 (17.2%)</td></tr>
<tr><td>Details</td><td>A complete ophthalmological examination was completed for each patient including BCVA, intraocular pressure measurement, dilated fundus biomicroscopy, optical coherence tomography (OCT) and fluorescein angiography.</td></tr>
<tr><td>Treatment</td><td>Three loading doses of intravitreal ranibizumab (0.5mg in 0.05 ml) were administered at monthly intervals followed by PRN treatment 4–6 weekly based on OCT assessment (persistent or recurrent intraretinal and/or subretinal fluid) or slit lamp examination (new subretinal
or retinal haemorrhage). Time domain OCT was in use for the first 18 months of the study (Stratus OCT, Carl Zeiss, Welwyn Garden City, UK), but later it was replaced by spectral domain 3D OCT (Cirrus HD-OCT, Carl Zeiss; Topcon 3D OCT 1000 and 2000, Topcon, Newbury, UK).</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td>Baseline visual acuity</td><td><0.30 (6/12) (G1)</td><td>≥6/12 to <6/24 (G2)</td><td>≥6/24 to <6/60 (G3)</td><td>≥6/60 to ≤6/96 (G4)</td><td>Effect (95%CI) (>6/12 vs ≥6/12 to <696</td></tr>
<tr><td>No. of patients at baseline</td><td>88</td><td>210</td><td>211</td><td>106</td><td></td></tr>
<tr><td>Mean VA at week 52, logMAR</td><td>0.20</td><td>0.37</td><td>0.60</td><td>0.76</td><td></td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	Williams T A; Blyth C P. Outcome of ranibizumab treatment in neovascular age related macula degeneration in eyes with baseline visual acuity better than 6/12. Eye 25 (12): 1671-21. 2011					
	Mean change ETDRS letters at week 483	-0.5 (4.79)	2.0 (14.49)	6.5 (19.60)	15.1 (15.96)	MD -6.93 (-8.68, -5.18)
	No. of people had <15 letter loss (%)	82 (93%)	185 (88%)	194 (92%)	106 (100%)	RR 1.01 (0.95, 1.08)
	No. of people had >15 letter gain (%)	1 (1%)	34 (16%)	70 (33%)	49 (46%)	RR 0.04 (0.01, 0.26)

[3] Calculation of SD based on graph reported in the study.



Bibliographic reference	**Williams T A; Blyth C P. Outcome of ranibizumab treatment in neovascular age related macula degeneration in eyes with baseline visual acuity better than 6/12. Eye 25 (12): 1671-21. 2011**
	
Others	Owing to capacity and service constraints of our NHS setting, the mean interval between loading visits was 35 days and not 28 days as planned. Similarly during the PRN period, the mean interval was 45 days and not 4–6 weekly. These prolonged intervals between visits and therefore treatment are likely to have had a detrimental effect on visual outcome.

Bibliographic reference	**Ying G S; Huang J ; Maguire M G; Jaffe G J; Grunwald J E; Toth C ; Daniel E ; Klein M ; Pieramici D ; Wells J ; Martin D F; Comparison of Age-related Macular Degeneration Treatments Trials; Group . Baseline predictors for one-year visual outcomes with ranibizumab or bevacizumab for neovascular age-related macular degeneration. Ophthalmology 120 (1): 122-9. 2013**
Country/ies where the study was carried out	USA
Study type	Cohort study within the Comparison of AMR Treatment Trials

Bibliographic reference	**Ying G S; Huang J ; Maguire M G; Jaffe G J; Grunwald J E; Toth C ; Daniel E ; Klein M ; Pieramici D ; Wells J ; Martin D F; Comparison of Age-related Macular Degeneration Treatments Trials; Group . Baseline predictors for one-year visual outcomes with ranibizumab or bevacizumab for neovascular age-related macular degeneration. Ophthalmology 120 (1): 122-9. 2013**
Aim of the study	To determine baseline predictors of visual acuity (VA) outcomes at 1 year after treatment with ranibizumab or bevacizumab for neovascular age-related macular degeneration (AMD).
Study dates	Published 2014
Source of funding	Supported by cooperative agreements U10 EY017823, U10 EY017825, U10 EY017826, and U10 EY017828 from the National Eye Institute, National Institutes of Health, Department of Health and Human Services.
Sample size	1105 participants from CATT study and survived 1 year after study participation
Inclusion criteria	Treatment-naive eyes were treated exclusively with ranibizumab VA between 20/25 (6/7.5) and 20/320 (6/96)
Exclusion criteria	Not reported
Patient characteristics	Age, mean: 79 (SD=8) years Gender, M, %: 38% (n=420) Visual acuity (ETDRS letters): Study eye: 61 letters (Snellen=20/63) (SD=13) Fellow eye: 66 letter (Snellen=20/50) (SD=27)
Details	During the initial visit, participants provided information on demographic characteristics and medical history. Certified photographers followed a standard protocol for field definition and image sequencing to obtain stereoscopic, colour fundus photographs and fluoresce in angiograms. Photographs from all clinical centres were digital except photographs from one centre (film-based). Optical coherence tomography (OCT) was obtained with a Stratus (version 4.0 or higher) time domain OCT machine (Carl Zeiss Meditec, Dublin, California). At baseline and at follow-up weeks 4, 12, 24, 36 and 52, certified visual acuity examiners, masked to the treatment assignment, measured visual acuity after refraction in both eyes using the Electronic Visual Acuity Tester (EVA) following the protocol used in the Diabetic

Bibliographic reference	**Ying G S; Huang J ; Maguire M G; Jaffe G J; Grunwald J E; Toth C ; Daniel E ; Klein M ; Pieramici D ; Wells J ; Martin D F; Comparison of Age-related Macular Degeneration Treatments Trials; Group . Baseline predictors for one-year visual outcomes with ranibizumab or bevacizumab for neovascular age-related macular degeneration. Ophthalmology 120 (1): 122-9. 2013**
	Retinopathy Clinical Research Network.6 The VA scores (the number of letters read correctly on the ETDRS chart, measured with best-corrected visual acuity) from EVA can range from 0 to 100, corresponding to Snellen equivalents of worse than 20/800 to 20/10.
Treatment	Participants were enrolled from 43 clinical centers in the United States between 2008 through 2009, and randomized to one of the four treatment groups: (1) ranibizumab monthly; (2) bevacizumab monthly; (3) ranibizumab as needed (pro re nata, PRN); (4) bevacizumab PRN.

Results

Baseline visual acuity, study eye	68-82 letters (20-25-20/40 (G1)	53-67 letters, 20/50 to 20/80 (G2)	38-52 letters, 20/100 to 20/160 (G3)	23-37 letters, 20/200 to 20/320 (G4)	Effect (95%CI)		
					G1 vs G2	G1 vs G3	G1 vs G4
No. of people at year 1, (%)	397 (35.9%)	414 (37.5%)	223 (20.2%)	71 (6.4%)			
Mean VA at year 1, letter (SD)4	77.7 (13.9)	69.2 (14.2)	57.8 (14.9)	39.3 (14.3)	8.5 (6.6, 10.4)	19.9 (17.5, 22.3)	38.4 (34.8, 42.0)
Mean change in VA at year 1, letters (SD)	3.7 (13.9)	8.5 (14.2)	11.4 (14.9)	7.8(14.3)	-4.8 (-6.7, -2.8)	-7.7 (-10.1, -5.3)	-4.1 (-7.7. -0.5)
No. of people had ≥3-lines gain from baseline at year 1(%)	28 (7.1%)	150 (36.2%)	119 (53.4%)	30 (42.3%)	0.19 (0.13,0.28)	0.13 (0.09, 0.19)	0.17 (0.11, 0.26)

[4] The study reported SE, which was converted to SD (SD=SE *square root of number of people)

Bibliographic reference	Ying G S; Huang J ; Maguire M G; Jaffe G J; Grunwald J E; Toth C ; Daniel E ; Klein M ; Pieramici D ; Wells J ; Martin D F; Comparison of Age-related Macular Degeneration Treatments Trials; Group . Baseline predictors for one-year visual outcomes with ranibizumab or bevacizumab for neovascular age-related macular degeneration. Ophthalmology 120 (1): 122-9. 2013							
	Baseline visual acuity, fellow eye	83-100 letters(20/20 or betters)	68-82 letters, 20/25 to 20/40	0/67 letters , 20/50 or worse				
	No. of people at year 1, (%)	331 (30.0%)	433 (39.2%)	341 (30.9%)				
	Mean VA at year 1, letter (SD)	70.7 (18.2)	67.5 (18.7)	66.1 (18.5)	3.2 (0.56, 5.84)	4.6 (1.83 to 7.37)		
	Mean change in VA at year 1, letters (SD)	8.9 (14.6)	7.2 (14.2)	5.9 (14.8)	1.7 (-0.36, 3.76)	3.0 (0.78, 5.22)		
	No. of people had ≥3-lines gain from baseline at year 1(%)	110 (33.2%)	135 (31.2%)	82 (24.0%)				

Pooled results

Baseline visual acuity, study eye	68-82 letters (20-25-20/40)	53-67 letters, 20/50 to 20/320	Effect (95%CI)
No. of people at year 1, (%)	397 (35.9%)	708 (64.1%)	
Mean VA at year 1, letter (SD)5	77.7 (13.9)	62.6 (14.4)	MD 15.10 (13.37, 16.83)
Mean change in VA at year 1, letters (SD)	3.7 (13.9)	9.3 (14.4)	-5.60 (-7.33, -3.87)

[5] The study reported SE, which was converted to SD (SD=SE *square root of number of people)

Bibliographic reference	Ying G S; Huang J ; Maguire M G; Jaffe G J; Grunwald J E; Toth C ; Daniel E ; Klein M ; Pieramici D ; Wells J ; Martin D F; Comparison of Age-related Macular Degeneration Treatments Trials; Group . Baseline predictors for one-year visual outcomes with ranibizumab or bevacizumab for neovascular age-related macular degeneration. Ophthalmology 120 (1): 122-9. 2013			
	No. of people had ≥3-lines gain from baseline at year 1(%)	28 (7.1%)	299 (42.2%)	0.17 (0.12,0.24)
	Baseline visual acuity, fellow eye	>20/40	<20/40	
	No. of people at year 1, (%)	764	341 (30.9%)	
	Mean VA at year 1, letter (SD)	68.9 (18.5)	66.1 (18.5)	2.80 (0.44, 5.16)
	Mean change in VA at year 1, letters (SD)	7.9 (14.4)	5.9 (14.8)	2.00 (0.13, 3.87)
	No. of people had ≥3-lines gain from baseline at year 1(%)	245 (32.1%)	82 (24.0%)	1.33 (1.08, 1.65)

Bibliographic reference	Zhu M ; Chew J K; Broadhead G K; Luo K ; Joachim N ; Hong T ; Syed A ; Chang A A. Intravitreal Ranibizumab for neovascular Age-related macular degeneration in clinical practice: five-year treatment outcomes. Graefes Archive for Clinical & Experimental Ophthalmology 253 (8): 1217-25. 2015
Country/ies where the study was carried out	Australia
Study type	Observational study (retrospective)
Aim of the study	to assess the visual and anatomical outcomes and safety profile of intravitreal ranibizumab in treating nAMD over a period of five years

Bibliographic reference	Zhu M ; Chew J K; Broadhead G K; Luo K ; Joachim N ; Hong T ; Syed A ; Chang A A. Intravitreal Ranibizumab for neovascular Age-related macular degeneration in clinical practice: five-year treatment outcomes. Graefes Archive for Clinical & Experimental Ophthalmology 253 (8): 1217-25. 2015
Study dates	Published 2015
Source of funding	This research is supported in part by an unrestricted grant from Novartis Pharmaceuticals Australia Pty Limited. The sponsor had no role in the design or conduct of this research
Sample size	208 eyesof 208 people
Inclusion criteria	Patients treated with intravitreal ranibizumab for subfoveal nAMD
Exclusion criteria	The study eye underwent vitrectomy surgery at any time The study eye was treated with photodynamic therapy (PDT), given intravitreal bevacizumab or triamcinolone during the follow-up period, or received intravitreal ranibizumab prior to June 2007.
Patient characteristics	Ethnic group – Asian no=6 (2.9%) Age, mean: 78.4 (SD 7.2) years Gender, M, %: 31.3% (n=65) Visual acuity (ETDRS letters) 23-39 letters: 17.3% (n=257) 40-54 letters: 23.1% (n=343) 55-69 letters: 42.7% (n=633) >70 letters: 16.9% (n=250) Time history: no prior treatment (34.1%, n=71), one or more previous nAMD treatment (65.9%, n=137) Disease type: occult (72.9%, n=124), minimally classic (18.8%, n=32), predominantly (5.3%, n=9), classic (2.9%, n=5)
Details	At baseline, best corrected Snellen visual acuity (VA), intraocular pressure (IOP) measurement, and fundoscopy were conducted. Central macular thickness (CMT) was measured with Stratus time-domain optical coherence tomography (TDOCT, software version 5.0; Carl Zeiss Meditec, Dublin, CA, USA) using the fast macular thickness mapping protocol.

<table>
<tr><th>Bibliographic reference</th><th>Zhu M ; Chew J K; Broadhead G K; Luo K ; Joachim N ; Hong T ; Syed A ; Chang A A. Intravitreal Ranibizumab for neovascular Age-related macular degeneration in clinical practice: five-year treatment outcomes. Graefes Archive for Clinical & Experimental Ophthalmology 253 (8): 1217-25. 2015</th></tr>
<tr><td></td><td>The presence and type of choroidal neovascularisation (CNV) was determined by FFA. Patient medical history, concomitant medication, and previous treatment for nAMD were recorded.
Polypoidal choroidal vasculopathy (PCV) was not screened, as indocyanine green angiography (ICGA) was performed only in cases when the clinical presentation and demographic of the patient suggested PCV.

Patient follow-up intervals varied between one and six months, depending upon disease activity. At each visit, Snellen VA, OCT, ophthalmic examination, and fundoscopy were performed. OCT findings were used as a guide for treatment. At the five-year visit, OCT scans were performed using SD-OCT with either a Cirrus (OCT 3; Carl Zeiss Meditec, Dublin, CA, USA) or Spectralis device (Heidelberg
Engineering, Heidelberg, Germany). FFA and IOP measurement was performed at the discretion of the treating physician. The most common indication for repeat FFA was persistent fluid on OCT refractory to monthly treatment, and repeat IOP measurement was performed when patients showed signs of increased IOP after the treatment.</td></tr>
<tr><td>Treatment</td><td>The department uses a pro re nata treatment posology after an initial loading phase of three injections at monthly intervals. All intravitreal injections are administered in dedicated treatment rooms with povidone iodine being used before and after injections.
After each injection the patient is asked to confirm they can still count fingers as a surrogate measure of intraocular pressure (IOP) and if they cannot (or if the patient has glaucoma) then the IOP is checked and treated as appropriate.
Patients are followed up at monthly intervals with SD OCT and fundal examination until no injections have been required to either eye for 6 months, after which follow-up intervals are gradually extended. If no injections have been required for 1 year patients are discharged and advised to return if they notice any new symptoms of blurring or distortion of vision in either eye.

Criteria for retreatment included one or more of the following: reduction in Snellen vision of ≥1 line, persistent exudation or blood at the macula on clinical examination, presence of subretinal or intraretinal fluid on OCT, or development of new areas of CNV on FFA.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td>Baseline visual acuity</td><td>≥85 letters</td><td>≥70 and <85 letters</td><td>≥60 and <70 letters</td><td>≥35 and <60 letters</td><td><35 letters</td></tr>
<tr><td>No. of patients at baseline</td><td>6</td><td>34</td><td>46</td><td>100</td><td>22</td></tr>
</table>
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Bibliographic reference	Zhu M ; Chew J K; Broadhead G K; Luo K ; Joachim N ; Hong T ; Syed A ; Chang A A. Intravitreal Ranibizumab for neovascular Age-related macular degeneration in clinical practice: five-year treatment outcomes. Graefes Archive for Clinical & Experimental Ophthalmology 253 (8): 1217-25. 2015

Mean VA change 5 year, letters (95%CI)	-15.8 (-51.5, 19.9)	-12.9 (-19.2, -6.6)	-3.7 (-8.2 to 0.9)	-0.6 (-3.2 to 2.0)	11.5 (5.2 to 17.9)

Pooled results

Baseline visual acuity, study eye	≥70 letters	≥35 to <70 letters	Effect (95%CI)
No. of people at baseline	40	146	
Mean 5-year change in VA, letters (SD)	-13.33 (22.15)	-1.58 (14.04)	-11.75 (-18.98, -4.52)

Baseline visual acuity, study eye	<35 letters	≥35 to <70 letters	Effect (95%CI)
No. of people at baseline	22	146	
Mean 5-year change in VA, letters (SD)	11.5 (15.96)	-1.58 (14.04)	13.08 (6.04, 20.12)

Linear regression analysis of change in VA over 5 years

Baseline VA, letters	No.	Regression, coefficient* (95%CI)	P value
≥70	40	Reference	-

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	≥60 and <70	45	11.2 (4.9, 17.4)	<0.0005
	≥35 and <60	100	16.1 (10.5, 21.6)	<0.0005
	<35	12	30.7 (22.8, 38.6)	<0.005
	*Adjusted for baseline age and total number of ranibizumab injection			