Characterising Anti-VEGF Treatment Patterns for Neovascular Age-Related Macular Degeneration (nAMD) in the United Kingdom

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Key Clinical Question

What are the anti–vascular endothelial growth factor (VEGF) treatment patterns and visual acuity (VA) outcomes in patients with neovascular age-related macular degeneration (nAMD) in routine clinical practice in the United Kingdom?

Introduction

- nAMD is the leading cause of blindness and visual impairment in the United Kingdom, despite the availability of effective intravitreal anti-VEGF treatments[1]
- Anti-VEGF agents for nAMD require frequent intravitreal injections and monitoring, which present a substantial burden to patients, caregivers and healthcare professionals[2]
- Real-world studies have found that patients treated with anti-VEGF injections for nAMD in routine clinical practice settings receive fewer injections and experience poorer visual outcomes versus patients receiving fixed, frequent injections in randomised controlled trials[3]

Methods

- This was a retrospective, multicentre, observational cohort study in the United Kingdom

Data Source: Medisoft EMR Database

- Medisoft is an electronic medical record (EMR) system developed by Medisoft Limited
- Structured data were anonymised at the source and then extracted from 9 National Health Service (NHS) ophthalmology sites in the United Kingdom, all using the Medisoft EMR in routine clinical practice:
  - Bristol Eye Hospital (University Hospitals Bristol and Weston NHS Foundation Trust)
  - Hull University Teaching Hospitals NHS Trust
  - Manchester University NHS Foundation Trust
  - Norfolk and Norwich University Hospitals NHS Foundation Trust
  - Peterborough City Hospital (North West Anglia NHS Foundation Trust)
  - Sheffield Teaching Hospitals NHS Foundation Trust
  - Torbay and South Devon NHS Foundation Trust
  - University Hospital Southampton NHS Foundation Trust
  - Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust

Inclusion Criteria

- Age ≥ 50 years
- Diagnosis of nAMD in ≥ 1 eye
- Initial diagnosis between 1 January 2014 and 31 December 2018[a]
- ≥ 2 practice visits in the 6 months following initial diagnosis
- ≥ 1 intravitreal injection of an authorised anti-VEGF drug (ranibizumab and aflibercept) or bevacizumab
- ≥ 12-month follow-up period following the first anti-VEGF treatment

Data Analysis

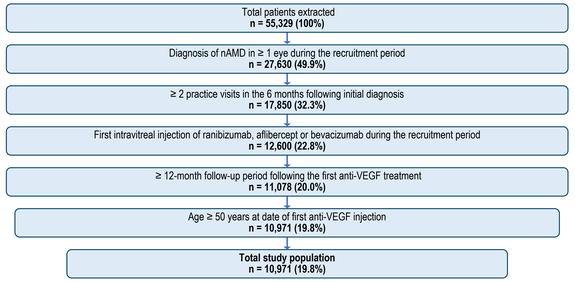
- For patients with bilateral disease (nAMD in both eyes), the eye with the earliest first anti-VEGF injection was selected. This allowed for the greatest potential length of patient follow-up
- For those with the same first anti-VEGF injection date, the eye with the worse VA at baseline was selected
- For those with the same first anti-VEGF injection date and VA in both eyes, the study eye was selected randomly
- The baseline VA period was defined as 120 to 0 days before the index date, where the index date is the date of the first anti-VEGF injection

[a] This period encompasses the availability of the medicinal products to be studied (ranibizumab and aflibercept, and to some extent bevacizumab) in the United Kingdom and allows a minimum of 12 months of patient follow-up before the potential impact of the COVID-19 pandemic on elective care.

Conclusions

- This routine clinical practice study provides data on key health resource utilisation measures and VA outcomes in the United Kingdom
- Overall, treatment patterns were consistent throughout the follow-up period, and data from years 2–5 suggest that the subset of patients initiating ranibizumab or aflibercept who returned during follow-up (and have not discontinued therapy due to the substantial burden of frequent injections and monitoring) maintained relatively stable treatment intervals, receiving anti-VEGF injections approximately every 8 weeks
- Over one-third of patients gained ≥ 10 letters from baseline to follow-up for each year, whereas the proportion of patients who lost ≥ 10 letters increased gradually over time
- Limitations of this study include the following:
  - VA measurements are often collected in clinics using usual correction, such as glasses or contacts, and patients are typically not refracted using the Early Treatment Diabetic Retinopathy Study VA measurement protocol. Consequently, a variety of corrections and notations may be used by each of the selected sites or within each patient's treatment pathway
  - VA results were manually recorded in the Medisoft EMR
  - The follow-up for this study was passive (ie, patients were not actively followed); thus, these results represent a subset of patients who returned to the NHS sites during follow-up and have not discontinued therapy due to the substantial burden of frequent injections and monitoring. VA changes among those who discontinue therapy are likely worse, based on results from randomised clinical studies[4-6]
  - These data may not be generalisable outside of the United Kingdom

1. Cohort Selection



One qualifying eye per patient was selected as the study eye. For patients with both eyes qualifying, the eye with the earliest first anti-VEGF injection was selected. For those with the same first anti-VEGF injection date, the eye with the worse baseline VA was selected. For those with the same first anti-VEGF injection date and VA in both eyes, the study eye was selected randomly.
nAMD, neovascular age-related macular degeneration; VA, visual acuity; VEGF, vascular endothelial growth factor.

2. Patient Demographic and Clinical Characteristics

Demographic Characteristics	Full Cohort (N = 10,971)
Age, years, mean (SD)	80.1 (8.3)
Age by category, n (%)	
< 65 years	506 (4.6)
65–74 years	2252 (20.5)
75–84 years	4931 (45.0)
≥ 85 years	3282 (29.9)
Female, n (%)[a]	6868 (62.6)

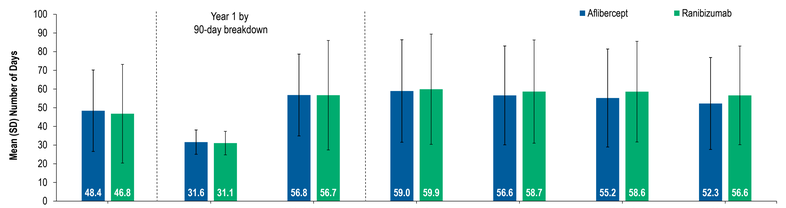
Clinical Characteristics	Full Cohort (N = 10,971)
Bilateral, n (%)	2912 (26.5)
Days from diagnosis to first anti-VEGF injection, mean (SD)	19.6 (102.2)

Clinical Characteristics (cont)	Full Cohort (N = 10,971)
Baseline VA, ETDRS letters, mean (SD)	53.9 (16.7)
Baseline VA by category, n (%)	
None	677 (6.2)
≤ 25 ETDRS letters	520 (4.7)
26–40 ETDRS letters	1656 (15.1)
41–55 ETDRS letters	3140 (28.6)
56–70 ETDRS letters	3678 (33.5)
71–85 ETDRS letters	1283 (11.7)
≥ 86 ETDRS letters	17 (0.2)
Ocular therapy before index date, n (%)	
Cataract surgery	2567 (23.4)

Baseline measurements were taken from a 120-day period immediately preceding (and including) the index date. Bilateral disease was defined as the patient receiving anti-VEGF injections in the fellow eye during the study period and while under active treatment/follow-up. Diagnosis date was assumed to be the date of first injection for patients with initial diagnosis recorded after the first injection. Where multiple VA measurements were recorded within the baseline window, the closest to the index date was used.
[a] 37.4% of patients were male; 0.03% not stated.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity; VEGF, vascular endothelial growth factor.

3. Mean Number of Days Between Consecutive Anti-VEGF Injections for the Study Eye for Year 1 and Years 2–5

- Patients initiating ranibizumab or aflibercept maintained relatively stable treatment intervals for years 2–5, receiving anti-VEGF injections approximately every 8 weeks

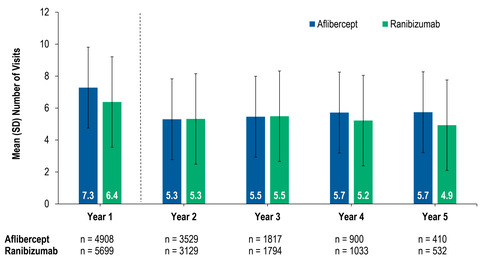


	Year 1	0–90 Days	91–365 Days	Year 2	Year 3	Year 4	Year 5
Aflibercept	n = 4908	n = 4908	n = 4447	n = 3523	n = 1812	n = 899	n = 409
Ranibizumab	n = 5699	n = 5699	n = 4413	n = 3128	n = 1791	n = 1032	n = 530

VEGF, vascular endothelial growth factor.

4. Mean Number of Treatment Visits and Injections for Year 1 and Years 2–5

- Number of treatment visits and number of injections were highest for year 1 and relatively stable for years 2–5 for patients initiating ranibizumab or aflibercept



	Year 1	Year 2	Year 3	Year 4	Year 5
Aflibercept	n = 4908	n = 3529	n = 1817	n = 900	n = 410
Ranibizumab	n = 5699	n = 3129	n = 1794	n = 1033	n = 532

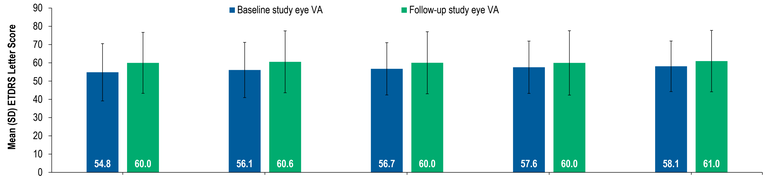
Mean (SD) Number of Injections in the Study Eye[a]

Treatment	Year 1	Year 2	Year 3	Year 4	Year 5
Aflibercept	6.9 (2.1)	4.9 (2.7)	4.9 (2.8)	5.0 (2.9)	5.0 (3.1)
Ranibizumab	6.1 (2.6)	5.0 (2.6)	5.1 (2.5)	4.9 (2.6)	4.6 (2.7)

Treatment visit defined as a date where the patient received an anti-VEGF injection in the study eye or fellow eye.
[a] n values for the number of injections in the study eye are the same as those listed in Panel 3.
VEGF, vascular endothelial growth factor.

5. Changes in VA From Baseline to Follow-up for Each Year

- In clinical practice, patients initiating ranibizumab or aflibercept gained ~1 line of vision in the first year

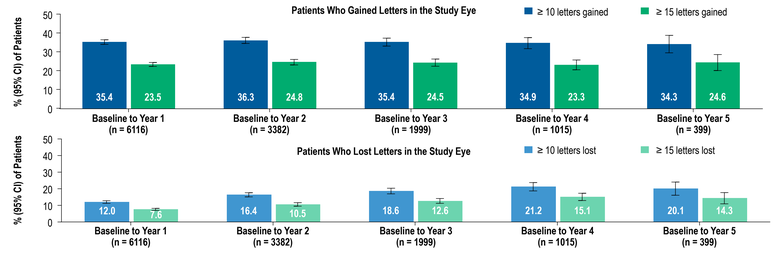


Follow-up period	Baseline to Year 1 (n = 6116)	Baseline to Year 2 (n = 3382)	Baseline to Year 3 (n = 1999)	Baseline to Year 4 (n = 1015)	Baseline to Year 5 (n = 399)
Mean (95% CI) change from baseline in VA, ETDRS letter score	5.2 (4.8, 5.5)	4.5 (3.9, 5.0)	3.3 (2.6, 4.1)	2.4 (1.3, 3.5)	2.9 (1.2, 4.5)

Where multiple VA measurements were recorded within the baseline window, closest to index date was used. Where multiple VA measurements were recorded within a follow-up window, closest to centre date was used. Best VA measurement of habitual correction and unaided on the date was used, or pinhole if neither were recorded. VA was only analysed for patients when a baseline and follow-up measurement both existed for that patient. Patients did not require a VA measurement in each follow-up interval to be analysed.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity.

6. Percentage of Patients With ≥ 10- or ≥ 15-Letter Change in VA in the Study Eye From Baseline to Follow-up for Each Year

- Over one-third of patients gained ≥ 10 letters from baseline to follow-up for each year, whereas the percentage of patients who lost ≥ 10 letters increased gradually over time



Letters indicate ETDRS letters. Where multiple VA measurements were recorded within the baseline window, closest to index date was used. Where multiple VA measurements were recorded within a follow-up window, closest to centre date was used. Best VA measurement of habitual correction and unaided on the date was used, or pinhole if neither were recorded. VA was only analysed for patients when a baseline and follow-up measurement both existed for that patient. Patients did not require a VA measurement in each follow-up interval to be analysed. Data for patients with change in VA of ± 5 letters not shown.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity.

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References

1. Pezzullo L et al. *BMC Health Serv Res*. 2018;18:63.
2. Monés J et al. *Ophthalmologica*. 2020;243(1):1-8.
3. Ciulla TA et al. *Ophthalmol Retina*. 2020;4(1):19-30.
4. Brown DM et al. *Ophthalmology*. 2009;116(1):57-65.e5.
5. Rosenfeld PJ et al. *N Engl J Med*. 2006;355(14):1419-1431.
6. Brown DM et al. *N Engl J Med*. 2006;355(14):1432-1444.

Financial Disclosures

- MJ: Clinical Fellow Ophthalmology at Roche during the time of this analysis; Consultant: Roche
- RAC: Employee: Genentech, Inc.; Stock Owner: Roche
- JDC, DJ: Employee: Roche
- MD, SMG: Employee: Medisoft Limited
- CB: Advisory Board: Alimera, Bayer, Boehringer Ingelheim, Janssen, Novartis, Roche

Study Disclosures

- This study includes research conducted on human subjects
- Study exempt from Institutional Review Board approval due to deidentified data
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