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ORIGINAL RESEARCH

Cross-Sectional Survey of Real-World Physician Prescribing Practices for Anti-VEGF Agents in the Treatment of Neovascular Age-Related Macular Degeneration and Associated Patient Burden in the United States

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Purpose: This study aimed to address the lack of data on the real-world use of the anti-vascular endothelial growth factor (VEGF)/anti-angiopoietin 2 agent faricimab and purely anti-VEGF agents in neovascular age-related macular degeneration (nAMD) in the United States.

Patients and Methods: Data were derived from the Adelphi Real World nAMD Disease Specific Programme (DSP)™, a cross-sectional survey of patients with nAMD and their treating physicians, conducted in the US November 2023–May 2024. Ophthalmologists provided demographic and clinical data as well as reasons for agent and dosing strategy selection, for patients with nAMD, aged ≥55, prescribed anti-VEGF treatment at the time of survey.

Results: Sixty-four physicians (90.6% retinal specialists), reported on 497 patients (faricimab, n = 89 patients; anti-VEGF, n = 408 patients). Mean (± standard deviation) age was 76.0 ± 8.5, 52.1% were female and 88.5% White. Most common symptoms at survey were blurred vision (faricimab: 56.2%, anti-VEGF: 67.9%), distortion of central vision (faricimab: 44.9%, anti-VEGF: 50.7%) and loss of visual acuity (faricimab: 39.3%, anti-VEGF: 41.9%). Main reasons for agent selection were clinical factors/efficacy (faricimab 89.9%, anti-VEGF: 93.4%), and treatment administration/compliance (faricimab 71.9%, anti-VEGF: 41.4%), which included improved patient compliance and extended dosing intervals. Faricimab was commonly dosed as treat-and-extend (67.4%) and anti-VEGFs as fixed interval (38.5%). Reasons for dosing strategy selection included improvement in visual acuity, patient functionality, clinical evidence and fewer consultations for the patient. Most physicians agreed/strongly agreed that some insurers restrict (84.4%) or deny (85.9%), access to the most appropriate products for patients.

Conclusion: Despite receiving treatment, nAMD patients have substantial remaining symptom and treatment burden. Physicians may choose faricimab over purely anti-VEGF agents for its clinical efficacy and reduced treatment burden. Physicians take both clinical factors and patient burden into account when selecting agents and dosing regimens, while reimbursement concerns hinder prescribing in some patients.

Keywords: nAMD, anti-VEGF agents, prescribing practices, patient burden, United States

Introduction

Neovascular age-related macular degeneration (nAMD) is an eye disorder characterized by choroidal neovascularization of the macula, causing progressive loss of central vision.[1] The United States (US) prevalence of late-stage AMD, which includes nAMD, was estimated at almost 94/10,000 in 2019.[2] Patients with nAMD experience symptoms such as blurred and distorted vision, poor low-light vision and loss of contrast sensitivity, alongside clinical markers such as the presence of subretinal or intraretinal fluid.[1] These symptoms may also significantly impact patients' quality of life (QoL).[3]

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First-line treatment for nAMD is intravitreal injections of anti-vascular endothelial growth factor (VEGF) biologics, which inhibit neovascularization. Patients generally receive monthly loading doses, before switching to longer treatment intervals.[4] Treatment strategies include treat-and-extend, in which intervals between treatments are extended if disease activity is low, or treat-as-needed, in which clinic visits with evaluation occur at a fixed interval and treatment is administered only if disease activity is detected.[4] These treatment regimens have achieved good clinical efficacy with a reduction in injection burden.[5,6] One goal of current research is to develop newer treatments with longer durability, which may allow for longer dosing intervals.

The need for repeated intravitreal injections may represent a substantial burden on patients. Patients may consider repeated injections arduous,[7] report a high financial and/or travel burden,[7,8] and injections are frequently associated with anxiety and discomfort.[7–10] Post-injection discomfort, anxiety and travel logistics have also been cited as factors affecting patient treatment adherence.[8] These data illustrate a clear need for clinically efficacious treatment strategies for nAMD in order to reduce patient burden and achieve good treatment adherence, while optimizing clinical outcomes.

Faricimab, first approved for use in nAMD in the US in 2022,[11] is a bispecific monoclonal antibody targeting both VEGF and an additional pathway, angiopoietin 2. Clinical efficacy, with the possibility of longer dosing intervals, has been demonstrated in both clinical trials[12] and European real-world data.[13–19] Real-world data from two short-term, single-center studies have shown good clinical efficacy,[20,21] the larger FARETINA and TRUCKEE studies showed improvement in visual acuity and central subfield thickness,[22,23] and a number of ongoing studies have presented similar interim results.[24] However, to date, little information is available on the dosing regimens used in US real-world clinical practice or how treatment choices are made.

Therefore, this study aimed to use a real-world cohort of physicians and patients in the US to investigate treatments regimens used, reasons for medication selection, and the associated patient burden of anti-VEGF treatment in nAMD.

Methods

Study Design and Data Source

Data were derived from the Adelphi Real World nAMD Disease Specific Programme (DSP)™. The DSP methodology has been previously described,[25,26] validated,[27] and demonstrated to be representative and consistent over time.[28] Briefly, the DSP is a cross-sectional survey with retrospective data analysis of patients with nAMD and their treating physicians, conducted in the US between November 2023 and May 2024. Physicians were recruited by local fieldwork agencies based on publicly available information and included in the DSP following confirmation of eligibility through a screener survey. Physicians then completed patient record forms for their next 13 consecutively consulting patients with nAMD, containing demographics, clinical and prescribing details. Patients with nAMD were then invited to complete a voluntary patient survey containing questions on their experience of treatment and a number of standardized patient-reported outcome measures. A subset of responses entered by two analysts to ensure accuracy and physiologically implausible or logically impossible responses were removed.

Study Participants

Participating physicians were required to be an ophthalmologist with or without retinal specialty and were required to treat at least 20 patients with nAMD in a typical month. Patients were eligible for inclusion if they were at least 55 years of age, had a physician-confirmed diagnosis of nAMD, and were prescribed anti-VEGF treatment at the time of survey. Patients who were part of an nAMD clinical trial were excluded from the survey.

Study Measures

Physicians reported on patients' demographic characteristics, including age, biological sex, ethnicity, employment status, living circumstances, driving status, distance to appointments and care needs. Physician-reported clinical characteristics included eyes affected, symptoms at time of diagnosis and survey, central retinal thickness/central subfield thickness (CRT/CST) measurement at diagnosis and survey, and the presence of subretinal or intraretinal fluid at diagnosis and survey.

Disease severity at time of survey, and retrospectively at time of diagnosis, was calculated from physician-reported measures of visual acuity. Patients were considered to have mild disease with a Snellen score of 20/40 or better or an Early Treatment Diabetic Retinopathy Study (ETDRS) letter score of at least 70. Moderate disease was defined as a Snellen score of 20/40 to 20/80 or an ETDRS letter score of 55–69, while severe/profound disease was defined as a Snellen score of worse than 20/80 or an ETDRS letter score of 0–54. If both eyes were affected, the score of the worst seeing eye was reported. Physicians also provided a subjective clinical assessment of the prognosis of the patients' visual acuity, as "significantly improving", "somewhat improving", "stable", "somewhat deteriorating", "significantly deteriorating" or "too early to say".

Physicians also reported on treatment details, including agent prescribed at time of survey, duration of receiving this agent, prior agents used, number of agents given per treatment line, reasons for agent selection, reason for switch from prior agent, dosing regimen and reasons for selecting dosing regimen. A new treatment line was defined as the addition or cessation of an agent to the patients treatment regimen, or a switch to a different agent from the same or a different class, but not a change in dosing. Dosing regimen options included "treat and extend", defined as "treat and monitor at every visit and extend the dosing interval if the patient is stable", "treat at fixed interval", defined as "treat and monitor at every visit on a fixed interval", or "treat as needed", defined as "monitor at every visit and treat as needed", with "patient on loading dose regimen" or "undecided" being the other available options.

For each patient, physicians also reported insurance coverage and barriers to access to anti-VEGF agents. As measures of treatment compliance, physicians also reported on the number of missed/cancelled/delayed appointments and reasons thereof, and length of appointment delay.

Patients indicated their level of agreement with statements surrounding their treatment, as "strongly disagree", "disagree", "neither agree nor disagree", "agree" or "strongly agree", and completed patient-reported outcome measures.

Patient-Reported Outcomes Measures

The 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) investigates 11 domains of vision-related QoL, with domain scores and overall composite scored from 0 to 100, with 100 representing optimal functioning.[29]

The EQ-5D-5L and Visual Analog Scale (VAS) are measures of general QoL.[30] EQ-5D-5L utility values were calculated using the US tariff,[31] and ranged 1 (optimal QoL) to below 0 (equivalent to death). EQ-VAS scores ranged from 0 (worst possible health state) to 100 (best possible health state).

Statistical Analysis

Patients were stratified by treatment received, into those who received faricimab and those who received purely anti-VEGF treatments. Purely anti-VEGF agents included aflibercept, bevacizumab, ranibizumab (including ranibizumab, ranibizuman-eqrn, ranibizuman-nuna and Susvimo [prior to recall]) and brolucizumab. Patients who were receiving both faricimab and a purely anti-VEGF agent at time of survey were excluded from analysis. All analysis was descriptive, and data are presented as groups sizes with proportions for categorical variables, or mean with standard deviation (SD) or medians with interquartile range (IQR), as appropriate, for continuous variables. Missing data were not imputed, therefore the demonimator may vary between variables and is reported for each individual variable. Analyses were performed using Stata (version 18.0; StataCorp LP, College Station, TX, USA).

Ethical Approval

Exemption from ethical approval was granted by the Pearl Institutional Review Board (protocol number 2023–0387). The data collection was conducted in accordance with relevant market research and privacy regulations, including the US Health Insurance Portability and Accountability Act 1996[32] and Health Information Technology for Economic and Clinical Health Act legislation,[33] and followed the principles of the Helsinki declaration of 1964 and subsequent revisions.

Results

Cohort Description and Demographics

In total, 64 physicians were included in the DSP, of which 90.6% were retinal specialists. Physicians reported seeing a mean ± SD of 82.8 ± 27.0% of patients in their office, 29.4 ± 39.0% in an academic or teaching hospital and 15.2 ± 31.3% in a private hospital. Physicians reported data on 590 affected eyes in 497 patients (faricimab: 104 eyes in 89 patients, anti-VEGF: 486 eyes in 408 patients).

Physician-reported patient demographic characteristics of included patients are shown in Table 1. Mean ± SD patient age was 76.0 ± 8.5 years, 52.1% were female and 88.5% were White. Most patients were not working due to retirement (69.4%), and most lived with a partner (48.5%) or alone (26.0%). The majority of the overall patient cohort was able to drive at the time of survey (57.6%), this was the case for 68.4% of patients receiving faricimab and 55.3% of patients

Table 1 Physician-Reported Patient Demographics at Time of Survey, Stratified by Those Prescribed Faricimab or Purely Anti-VEGF Agents

	Overall	Faricimab	Anti-VEGF
Age (years)	n = 497	n = 89	n = 408
Mean ± SD	76.0 ± 8.5	76.1 ± 8.2	76.0 ± 8.6
Biological sex, n (%)	n = 497	n = 89	n = 408
Female	259 (52.1)	47 (52.8)	212 (52.0)
Male	238 (47.9)	42 (47.2)	196 (48.0)
Ethnicity, n (%)	n = 497	n = 89	n = 408
White	440 (88.5)	83 (93.3)	357 (87.5)
Black/African American/African or Caribbean	31 (6.2)	4 (4.5)	27 (6.6)
Other[a]	29 (5.8)	2 (2.2)	27 (6.6)
Employment status, n (%)	n = 497	n = 89	n = 408
Not working due to retirement	345 (69.4)	58 (65.2)	287 (70.3)
Working part-time	44 (8.9)	8 (9.0)	36 (8.8)
Working full-time	39 (7.8)	4 (4.5)	35 (8.6)
Homemaker	29 (5.8)	7 (7.9)	22 (5.4)
Other[b]	13 (2.6)	2 (2.2)	11 (2.7)
Unknown	27 (5.4)	10 (11.2)	17 (4.2)
Living circumstances, n (%)	n = 497	n = 89	n = 408
Lives with a partner	241 (48.5)	47 (52.8)	194 (47.5)
Lives alone	129 (26.0)	28 (31.5)	101 (24.8)
Lives with other family members	92 (18.5)	11 (12.4)	81 (19.9)
Lives in a nursing home	27 (5.4)	2 (2.2)	25 (6.1)
Other[c]	10 (2.0)	2 (2.2)	8 (2.0)
Patient driving status, n (%)	n = 441	n = 76	n = 365
Drives	254 (57.6)	52 (68.4)	202 (55.3)
Does not drive	187 (42.4)	24 (31.6)	163 (44.7)
Distance to appointments (miles)	n = 268	n = 43	n = 225
Mean ± SD	14.5 ± 16.3	21.5 ± 18.9	13.2 ± 15.4
Additional care/support needs, n (%)	n = 467	n = 82	n = 385
No additional care/support needed	234 (50.1)	45 (54.9)	189 (49.1)
Additional care/support needed	233 (49.9)	37 (45.1)	196 (50.9)

Notes: [a] Includes East or Southeast Asian, Middle Eastern or North African, South or Central American Native, South Asian (Indian subcontinent), Native Hawaiian or Pacific Islander or other. [b] Includes unemployed and long-term sick leave. [c] Includes living with friends and other (not specified).
Abbreviations: SD, standard deviation; VEGF, vascular endothelial growth factor.

receiving anti-VEGF agents. Mean ± SD distance travelled by patients to appointments was 14.5 ± 16.3 miles; this was 21.5 ± 18.9 miles for patients receiving faricimab, and 13.2 ± 15.4 miles for patients receiving anti-VEGF agents. Approximately half of patients had additional care/support needs; this was the case for 54.9% of the faricimab group, and 49.1% of patients receiving anti-VEGF agents.

Clinical Characteristics

Physician-reported disease severity is shown in Figure 1. Patients most commonly had severe or profound disease at time of diagnosis (44.7% of overall cohort), though notably, 31.1% of patients receiving faricimab and 19.4% of patients receiving other agents had mild disease at diagnosis. At time of survey, most patients receiving faricimab had mild disease (57.0%), while patients receiving anti-VEGF agents most commonly had moderate disease (39.1%).

The clinical signs and symptoms experienced by patients at time of diagnosis and survey are shown in Figure 2. At time of diagnosis (Figure 2a), the most common clinical signs and symptoms experienced by those receiving faricimab were the presence of subretinal fluid (88.1%), blurred vision (83.3%) and distortion of central vision (79.8%). For patients receiving anti-VEGF agents, these were blurred vision (85.5%), and presence of subretinal or intraretinal fluid (77.2% and 71.8%, respectively). At time of survey (Figure 2b), the most common signs and symptoms reported were similar for both groups; blurred vision (faricimab: 56.2%, anti-VEGF: 67.9%), distortion of central vision (faricimab: 44.9%, anti-VEGF: 50.7%) and loss of visual acuity (faricimab: 39.3%, anti-VEGF: 41.9%).

Additional physician-reported clinical characteristics of included patients are shown in Table 2. Most patients (81.3%) had unilateral nAMD. Most patients (78.3%) had subretinal fluid at diagnosis, while at time of survey 60.8% did not. However, while 27.0% of patients receiving faricimab continued to have subretinal fluid at time of survey, 38.2% of those on other agents did. Intraretinal fluid was present at time of diagnosis in most patients (70.6%), but not present in the majority of patients at time of survey (60.8%). Notably, 18.0% of those receiving faricimab continued to have intraretinal fluid at time of survey, while 37.5% of patients receiving anti-VEGF agents did. Physicians most commonly reported that their patients had a stable visual acuity prognosis (46.5% of all patients).

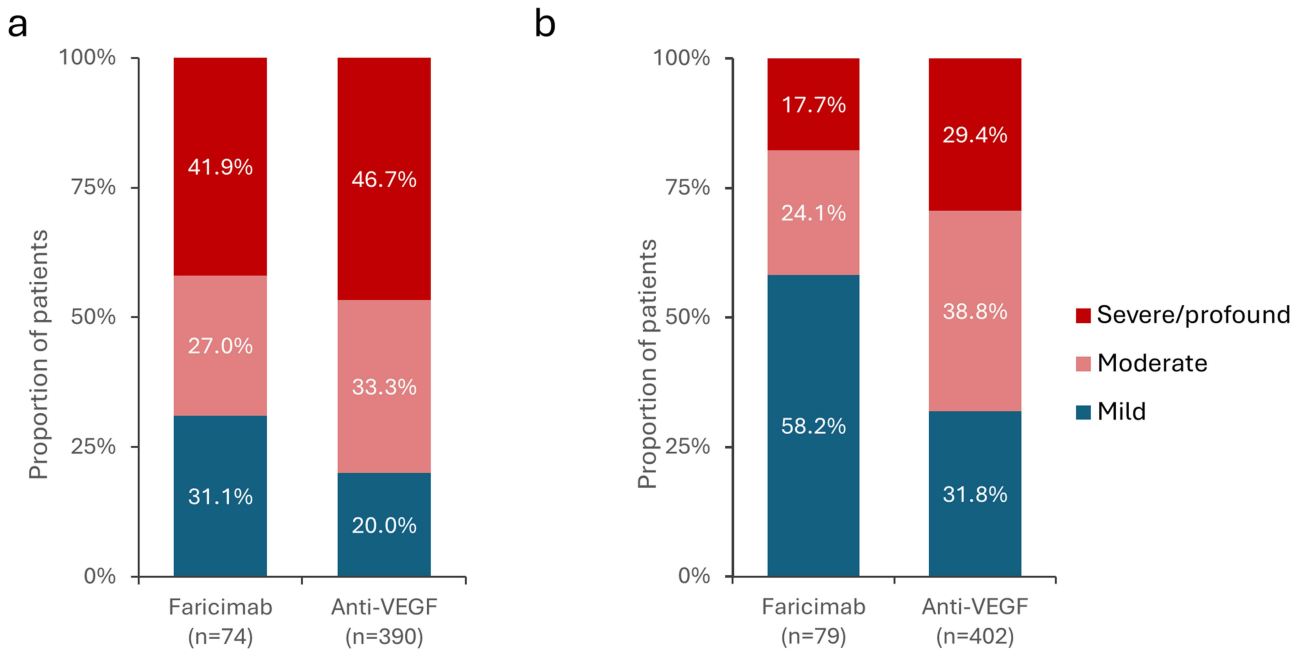

Figure 1 Proportion of patients with mild, moderate or severe/profound disease, stratified by those prescribed faricimab or purely anti-VEGF agents. (**a**) Disease severity at diagnosis. (**b**) Disease severity at survey. Patients were considered mild if they had a Snellen score of 20/40 or better, or an ETDRS letter score of at least 70; considered moderate if they had a Snellen score of 20/40 to 20/80, or an ETDRS letter score of 55–69; and considered severe/profound if they had a Snellen score of worse than 20/80, or an ETDRS letter score of 0–54.

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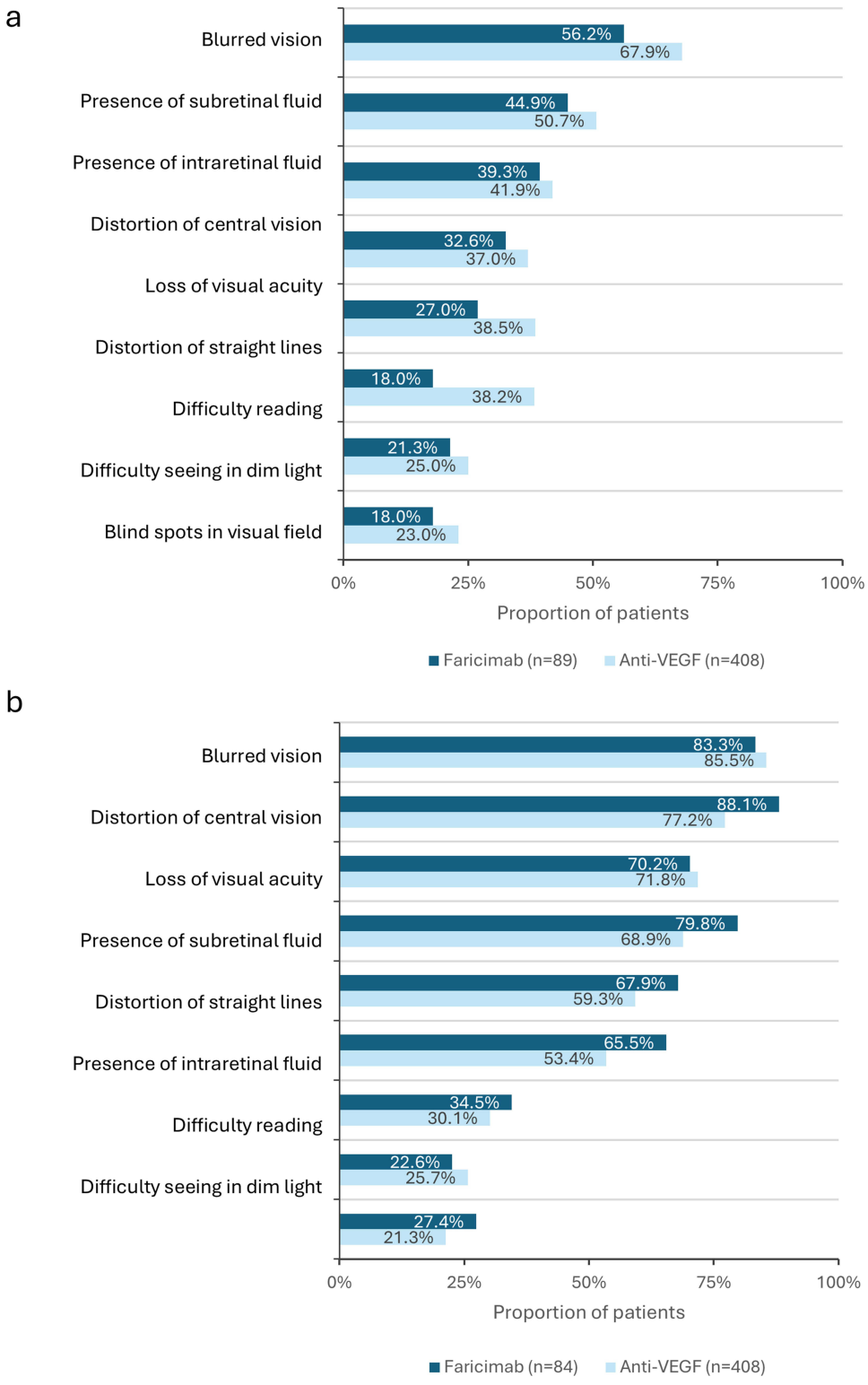

Figure 2 Proportion of patients for whom physician reported clinical signs and symptoms, stratified by those prescribed faricimab or purely anti-VEGF agents. (**a**) Symptoms at diagnosis. (**b**) Symptoms at survey. Signs and symptoms reported for ≥20% of the overall cohort are shown.

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Table 2 Physician-Reported Patient Clinical Characteristics, Stratified by Those Prescribed Faricimab or Purely Anti-VEGF Agents

	Overall	Faricimab	Anti-VEGF
Eyes affected by nAMD, n (%)	n = 497	n = 89	n = 408
Unilateral	404 (81.3)	74 (83.1)	330 (80.9)
Bilateral	93 (18.7)	15 (16.9)	78 (19.1)
Subretinal fluid at diagnosis, n (%)	n = 497	n = 89	n = 408
Present	389 (78.3)	74 (83.1)	315 (77.2)
Not present	69 (13.9)	8 (9.0)	61 (15.0)
Did not collect	39 (7.8)	7 (7.9)	32 (7.8)
Subretinal fluid at survey, n (%)	n = 497	n = 89	n = 408
Present	180 (36.2)	24 (27.0)	156 (38.2)
Not present	302 (60.8)	61 (68.5)	241 (59.1)
Did not collect	15 (3.0)	4 (4.5)	11 (2.7)
Intraretinal fluid at diagnosis, n (%)	n = 497	n = 89	n = 408
Present	351 (70.6)	59 (66.3)	292 (71.6)
Not present	98 (19.7)	20 (22.5)	78 (19.1)
Did not collect	48 (9.7)	10 (11.2)	38 (9.3)
Intraretinal fluid at survey, n (%)	n = 497	n = 89	n = 408
Present	169 (34.0)	16 (18.0)	153 (37.5)
Not present	307 (61.8)	68 (76.4)	239 (58.6)
Did not collect	21 (4.2)	5 (5.6)	16 (3.9)
Physician prognosis of visual acuity at survey, n (%)	n = 460	n = 81	n = 379
Significantly improving	59 (12.8)	10 (12.3)	49 (12.9)
Somewhat improving	130 (28.3)	23 (28.4)	107 (28.2)
Stable	214 (46.5)	39 (48.1)	175 (46.2)
Somewhat deteriorating	45 (9.8)	7 (8.6)	38 (10.0)
Significantly deteriorating	6 (1.3)	0 (0.0)	6 (1.6)
Too early to say	5 (1.1)	2 (2.5)	3 (0.8)
Unknown	1 (0.2)	0 (0.0)	1 (0.3)

Abbreviations: nAMD, neovascular age-related macular degeneration; SD, standard deviation; VEGF, vascular endothelial growth factor.

Treatment Received

Details of treatment received by patients are shown in Table 3. The anti-VEGF agents most commonly prescribed to those not receiving faricimab were aflibercept (55.6%) and bevacizumab (38.2%). Median (IQR) time since initiation of recent anti-VEGF agent in the overall cohort was 11.3 (4.7, 27.9) months. While this was 12.2 (4.1, 24.9) months for patients receiving faricimab, it was 11.1 (4.8, 30.8) months for those receiving anti-VEGF treatments. At time of survey, patients had received a mean ± SD of 1.6 ± 0.8 lines of treatment since diagnosis.

Appointments were missed or cancelled in 24.4% of patients in the overall cohort, and in 8.7% of cases, patients waited longer than the recommended time for an appointment, for a median (IQR) time of 14 (14, 21) days. In the majority of cases (68.4%), delays were caused by patient-related factors.

Reasons for Treatment Choice

Physician-reported reasons for agent choice and switch are shown in Figure 3, with individual reasons shown in Supplementary figures 1 and 2. Clinical factors and efficacy were the main type of motivation for agent selection in both groups (faricimab 89.9%, anti-VEGF: 93.4%, Figure 3a). Administration and compliance reasons for current agent choice were reported for 71.9% of patients receiving faricimab, and 41.4% of patients receiving anti-VEGF agents. The

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Table 3 Physician-Reported Treatment Details at Time of Survey and Patients' Appointment Attendance, Stratified by Those Prescribed Faricimab or Purely Anti-VEGF Agents

	Overall	Faricimab	Anti-VEGF
Anti-VEGF agent received at time of survey, n (%)	n = 497	n = 89	n = 408
Aflibercept	227 (45.7)	n/a	227 (55.6)
Bevacizumab	156 (31.4)	n/a	156 (38.2)
Ranibizumab[a]	25 (5.0)	n/a	25 (6.1)
Brolucizumab	5 (1.0)	n/a	5 (1.2)
Faricimab	89 (17.9)	89 (100.0)	n/a
Time on most recent agent(months)	n = 217	n = 37	n = 180
Median (IQR)	11.3 (4.7, 27.9)	12.2 (4.1, 24.9)	11.1 (4.8, 30.4)
Lines of treatment received[b]	n = 497	n = 89	n = 408
Mean ± SD	1.6 ± 0.8	1.9 ± 0.9	1.6 ± 0.8
Patient missed or cancelled appointment	n = 439	n = 76	n = 363
Yes	107 (24.4)	18 (23.7)	89 (24.5)
Patient waited longer than recommended time for appointment	n = 438	n = 74	n = 364
Yes	38 (8.7)	7 (9.5)	31 (8.5)
Days waited longer than recommended	n = 37	n = 7	n = 30
Median (IQR)	14.0 (14.0, 21.0)	14.0 (7.0, 21.0)	14.0 (14.0, 28.0)
Reasons for waiting longer than recommended	n = 38	n = 7	n = 31
Patient-related factors (including patient availability, caregiver availability)	26 (68.4)	6 (85.7)	20 (64.5)
Physician availability	10 (26.3)	4 (57.1)	6 (19.4)
Clinic/treatment room availability	4 (10.5)	1 (14.3)	3 (9.7)
Other	9 (23.7)	0 (0.0)	9 (29.0)

Notes: [a] Includes ranibizumab, ranibizuman-eqrn, ranibizuman-nuna and Susvimo (prior to recall). [b] A new line of treatment was defined as addition or cessation of any drug received, or switch to a different drug in the same treatment class, including repeat of a treatment after completion of original course eg, due to patient's non-response or relapse. Dosing changes or treatment holidays were not considered a new treatment line.
Abbreviations: SD, standard deviation; IQR, interquartile range; VEGF, vascular endothelial growth factor.

most common individual clinical reason (Supplementary figure 1) reported for both groups was improvement in visual acuity (faricimab 78.1%, anti-VEGF: 80.1%). Notably, extended dosing intervals, maximizing patient compliance and reducing the number of consultations were frequently mentioned reasons for selecting faricimab, in 47.2%, 31.5% and 29.2% of patients, and 14.5%, 15.0% and 9.1% of patients receiving other agents, respectively.

Physicians most commonly switched patients from their prior agent for clinical or efficacy reasons (Figure 3b). This was the case for both patients receiving faricimab and anti-VEGF agents (96.2% and 86.1% of patients, respectively). Switching related to treatment administration and compliance was reported for 60.4% of patients receiving faricimab, and 41.0% of patients receiving anti-VEGF agents. The most common individual reasons (Supplementary figure 2) for switching to faricimab were a desire for a longer dosing interval (60.4%), and availability of a new product or superior clinical trial data (43.4% each). Patients were most commonly switched to anti-VEGF agents due to lack of efficacy from the previous agent or the need for a longer dosing interval (41.0% each).

Dosing Regimens Used

Most patients receiving faricimab were on a treat-and-extend dosing regimen (67.4%), while treatment at fixed interval was most common (38.5%) in patients receiving anti-VEGF treatments, with 35.5% of patients being on treat-and-extend (Figure 4a).

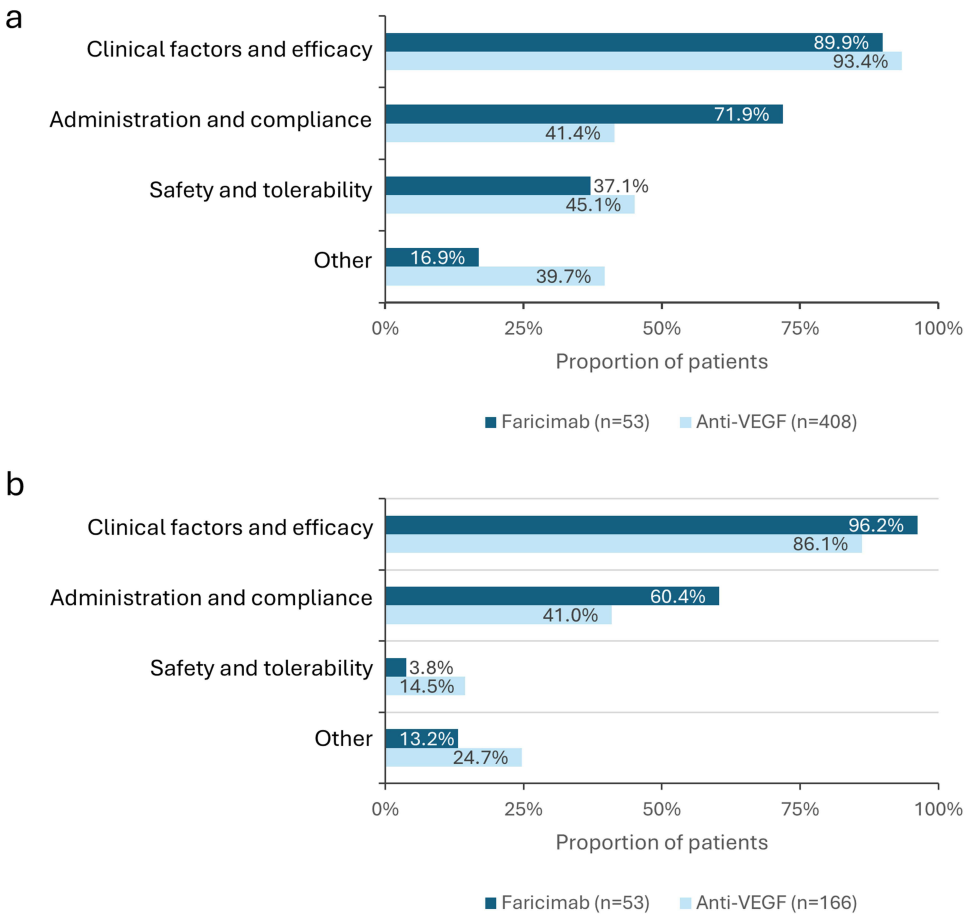

Figure 3 Physician-reported reasons for agent selection or switch, stratified by those prescribed faricimab or purely anti-VEGF agents. (**a**) Reasons for selection of agents received at time of survey. (**b**) Reasons for switching from prior agent to the agent received at time of survey.

Physician-reported reasons for selecting treatment regimens are shown in Figure 4b. The most common reasons for selecting treat-and-extend in patients receiving faricimab were improvements in visual acuity (76.6%), good clinical evidence (63.3%) and fewer patient consultations (58.3%). For those receiving anti-VEGF agents as treat-and-extend, these were visual acuity improvements (57.9%), fewer patient consultations (40.0%) and patient functionality (39.2%).

The most common reasons for selecting fixed-interval dosing for faricimab were improvement in visual acuity and fewer patient consultations (50.0% each), and patient functionality (44.4%). For anti-VEGF agents, these were patient functionality (53.2%), visual acuity improvement (41.0%) and anatomic improvement (26.3%).

Insurance Coverage and Barriers to Access

The majority of patients (67.8%) received Medicare, and most (65.8%) did not have secondary insurance coverage (Table 4). Physicians reported that coverage reimbursement was the driving factor in treatment choice in 22.3% of patients, however, this was the case for 9.0% of those receiving faricimab, and 25.2% of those receiving anti-VEGF agents. Faricimab was available without restrictions in 83.1% of patients, this was the case for anti-VEGF agents in 86.0% of patients. Most physicians agreed or strongly agreed that some insurers restrict or deny access to the most appropriate products for their patients (84.4% and 85.9% of physicians, respectively).

Patient Views on Treatment

Patient views on the treatment received are shown in Figure 5. In patients receiving faricimab, 54.2% disagreed or strongly disagreed with the statement that their medication did not improve their vision or kept it from worsening, while this was the case for 52.8% of patients receiving anti-VEGF agents. Although most patients did not think they had to

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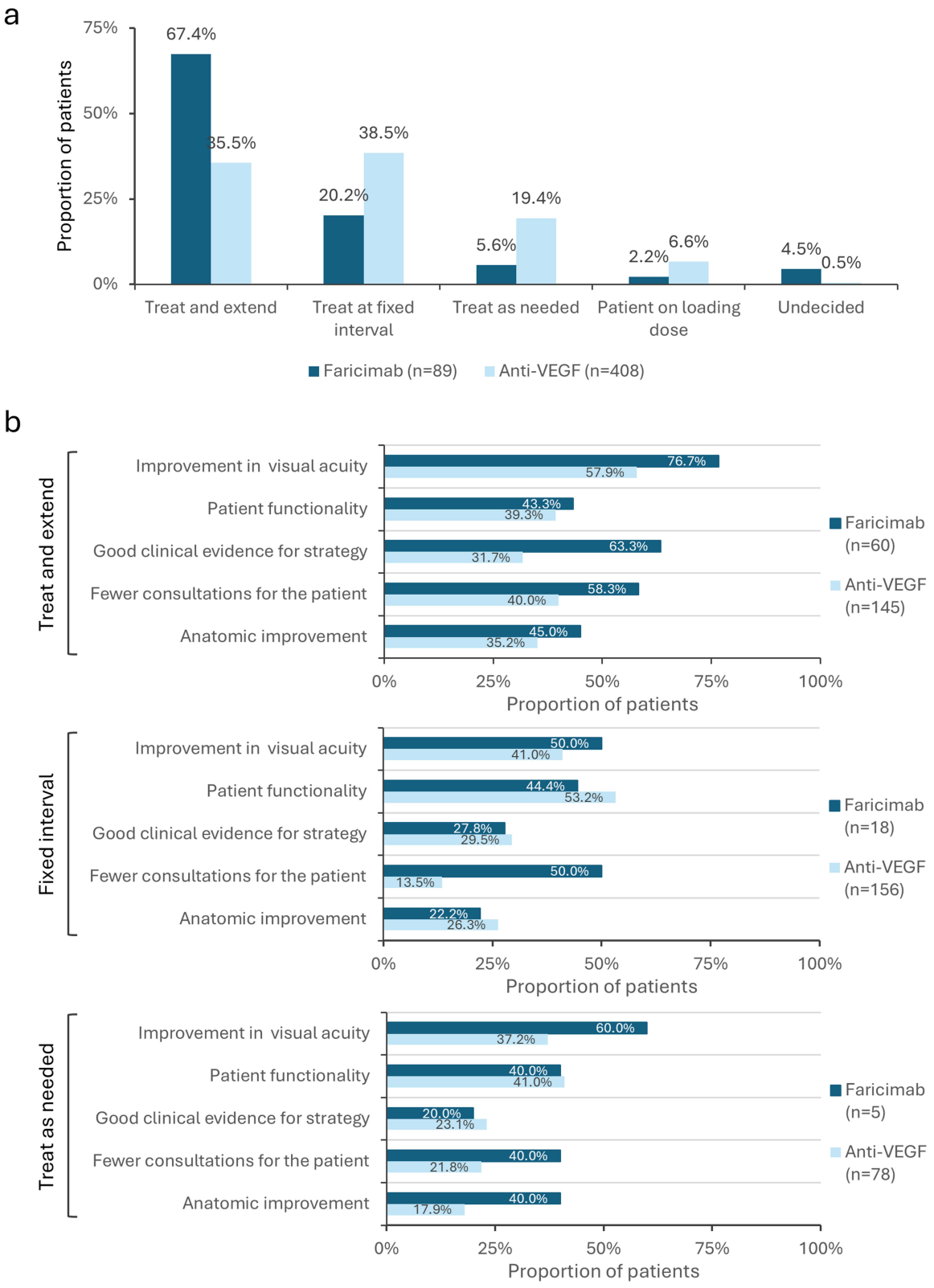

Figure 4 Dosing regimens used and physician reported reasons for selection, stratified by those prescribed faricimab or purely anti-VEGF agents. (**a**) Dosing regimens used at time of survey. (**b**) Most common reasons for selecting dosing regimens used.

Table 4 Physician-Reported Insurance Coverage and Barriers to Access, Stratified by Patients Prescribed Faricimab or Purely Anti-VEGF Agents, and General Physician Views on Insurance Coverage

	Overall	Faricimab	Anti-VEGF
Patient insurance coverage, n (%)	n = 485	n = 87	n = 398
Medicare[a]	329 (67.8)	64 (73.6)	265 (66.6)
Commercial insurance[b]	83 (17.1)	19 (21.8)	64 (16.1)
Medicaid (or equivalent)	34 (7.0)	2 (2.3)	32 (8.0)
Tricare/Veterans health care	24 (4.9)	2 (2.3)	22 (5.5)
Other[c]	15 (3.1)	0 (0.0)	15 (3.8)
Secondary insurance coverage, n (%)	n = 439	n = 80	n = 359
Yes	150 (34.2)	35 (43.8)	115 (32.0)
No	289 (65.8)	45 (56.3)	244 (68.0)
Was coverage reimbursement a driving reason for treatment choice in this patient? n (%)	n = 497	n = 89	n = 408
Yes	111 (22.3)	8 (9.0)	103 (25.2)
No	386 (77.7)	81 (91.0)	305 (74.8)
Level of availability of anti-VEGF agents, n (%)	n = 502	n = 89	n = 413
Available without restrictions[d]	429 (85.5)	74 (83.1)	355 (86.0)
Available with restrictions[d]	62 (12.4)	13 (14.6)	49 (11.9)
Not routinely available	11 (2.2)	2 (2.2)	9 (2.2)
Physician agreement with statement: "Some insurers restrict patients' access to most appropriate products"	n = 64[e]	n/a	n/a
Strongly disagree	0 (0.0)		
Disagree	0 (0.0)		
Neither agree nor disagree	10 (15.6)		
Agree	27 (42.2)		
Strongly agree	27 (42.2)		
Physician agreement with statement: "Some insurers deny patients' access to most appropriate products"	n = 64[e]	n/a	n/a
Strongly disagree	0 (0.0)		
Disagree	2 (3.1)		
Neither agree nor disagree	7 (10.9)		
Agree	31 (48.4)		
Strongly agree	24 (37.5)		

Notes: [a] Includes Medicare, Medicare Part D, Medicare medical savings account and Medicare Advantage. [b] Includes employer provided, partner's employer provided or privately arranged. [c] Includes health insurance exchange plan, Cobra (continuation coverage), non-Medicare retired benefit, no insurance coverage or unknown. [d] Other than approved labelling. [e] Number of physicians.

attend too many appointments, 13.0% of patients receiving faricimab and 18.0% of those receiving other agents agreed or strongly agreed they did. Similarly, 4.3% of those receiving faricimab and 15.6% of those on anti-VEGF agents felt they received too many tests at each appointment. Notably, 17.4% of those receiving faricimab were anxious prior to their appointment about receiving an injection, while 40.2% of patients receiving anti-VEGF agents agreed or strongly agreed they were anxious.

Patient-Reported Disease Burden

Outcomes of patient-completed PROMs are shown in Figure 6. Median (IQR) NEI VFQ-25 role difficulties score was 62.5 (50.0, 87.5), while median (IQR) mental health domain score was 68.8 (50.0, 87.5). Overall median (IQR) composite NEI VFQ-25 score was 56.5 (21.6, 71.1). Patients' median (IQR) EQ-5D-5L utility value was 0.80 (0.63, 0.94) while median (IQR) EQ-VAS score was 75.0 (60.0, 85.0).

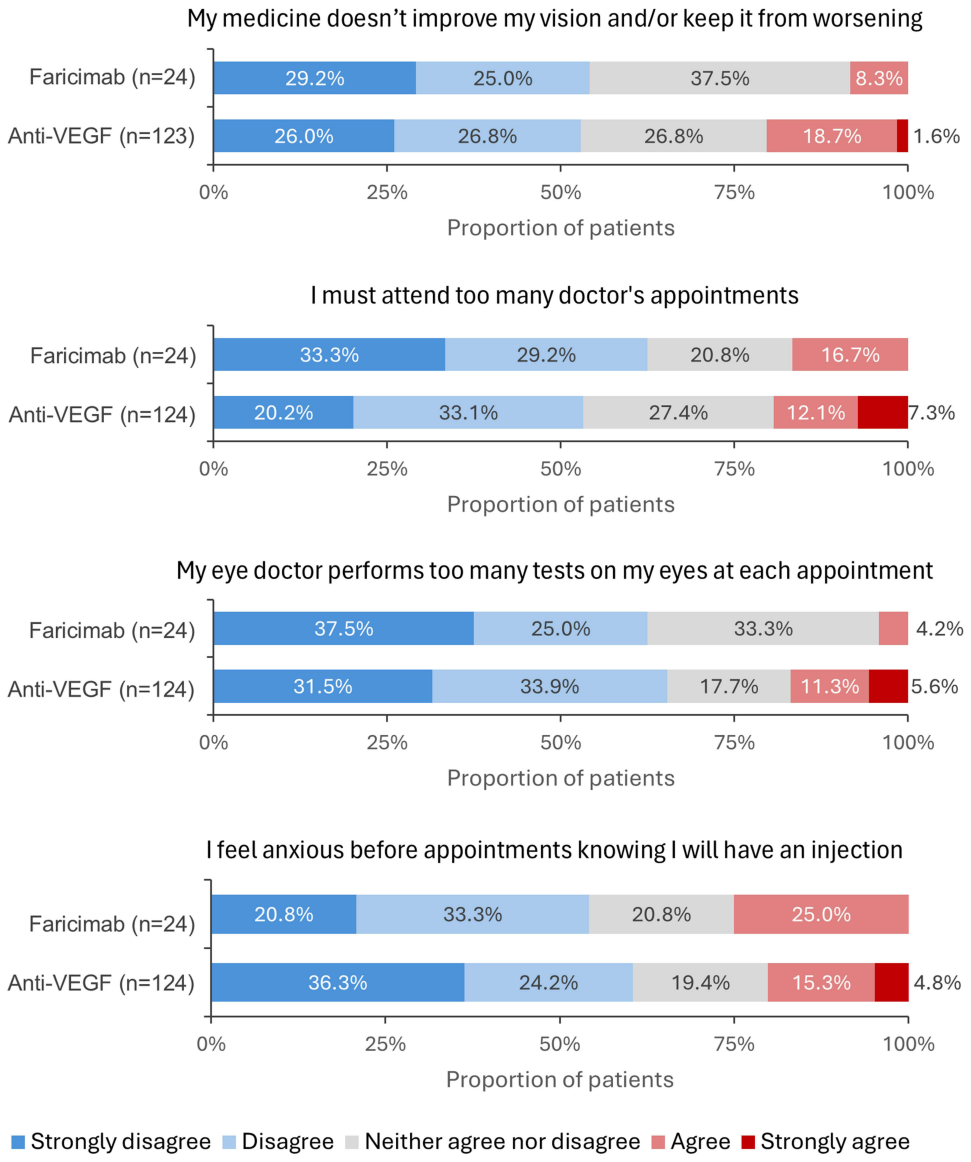

Figure 5 Patient-reported level of agreement with statements surrounding treatment received, stratified by those prescribed faricimab or purely anti-VEGF agents.

Discussion

Limited data exist on the real-world prescribing and dosing of faricimab and purely anti-VEGF agents for nAMD in the US, or how physicians select agents and dosing regimens. Here, using real-world data from patients and physicians, we show anti-VEGF treatment is prescribed in a variety of dosing regimens, with faricimab most commonly prescribed as treat-and-extend, while purely anti-VEGF agents were most commonly prescribed at fixed intervals. A range of clinical and non-clinical reasons, such as efficacy, dosing interval and reimbursement concerns, drove agent and dosing regimen selection. Despite receiving treatment, patients had a continuing symptom burden and impact on QoL.

Patients in our cohort most commonly received aflibercept, similar to data from prior to the introduction of faricimab.[34] Regardless of the agent received, patients were commonly on their second line of treatment, and were receiving a single agent at the time of survey. Despite receiving anti-VEGF treatment, patients continued to have a significant QoL burden. Symptoms such as blurred and distorted vision continued to be present in half of patients and over a third continued to have a loss of visual acuity. Almost half of patients had to stop driving due to their nAMD, further limiting patient independence.

Physicians indicated they selected agents for their patients based on both clinical and non-clinical factors. Clinical factors, such as improvements in visual acuity and quality of clinical evidence, were commonly cited. This is in line with

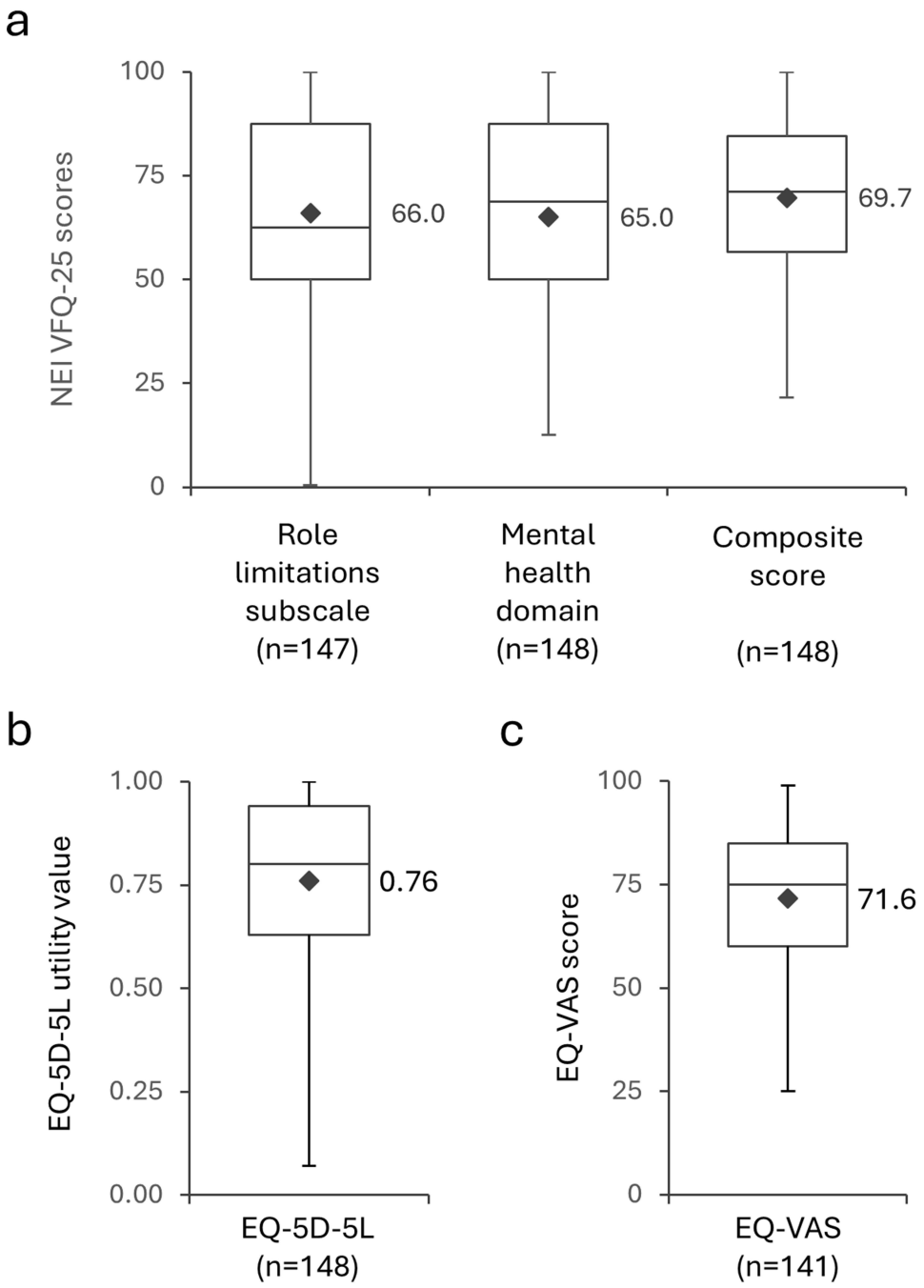

Figure 6 Patient-reported outcome measures, shown as mean with median, interquartile range and min-max range indicated. (**a**) Domain and composite scores of the NEI VFQ-25 measure. Higher scores indicate better levels of functioning. (**b**) Recorded EQ-5D-5L utility values, with 1.00 indicating perfect health. (**c**) Recorded EQ-VAS values, with 100 indicating optimal health state.

both clinical trial and real-world data, showing improvements of visual acuity following treatment with anti-VEGF agents.[22,23,35] Physicians also took factors such as patient functionality, consultation frequency and patient travel and out-of-pocket costs into account, with the need for a longer dosing interval also being a common reason for agent choice or switch. This aligns also with previous data showing such non-clinical factors were considered a burden by patients,[7–10] and shows physicians are likely to be actively trying to reduce patients' treatment burden. Up to a quarter of patients in our cohort had missed or delayed appointments, with appointments commonly being delayed two weeks or more, mostly due to patient-related factors. This also illustrates the difficulties patients may face attending frequent consultations and

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appointment frequency being recognized as a driver of poor adherence.[8] This may contribute to the poor adherence commonly observed in some patients with nAMD receiving anti-VEGF agents.[36]

In our cohort, faricimab was prescribed as treat-and-extend in the majority of patients, while purely anti-VEGF agents were most commonly prescribed at fixed intervals. The high proportion of patients receiving faricimab as treat-and-extend may be due to the fact many patients receiving faricimab were early on in their treatment journey, where physicians may be extending the treatment interval prior to setting on a suitable fixed interval. However, given that both groups had been receiving their treatment for a mean of year, this is unlikely. Physicians reported clinical improvements and the availability of clinical evidence as the main reasons for prescribing faricimab as treat-and-extend. Given the survey predated the publication of real-world evidence on faricimab dosing regimens, this is likely referring to clinical trial data available at the time.[12] This is also in line with previous work, showing a physician preference for treat-and-extend over fixed-interval dosing for anti-VEGF agents, even though this was not always achieved in clinical practice.[34]

Although physicians indicated that both faricimab and purely anti-VEGF agents were generally available without restrictions for the majority of their patients, they nonetheless agreed that insurers restricted or denied access to the most appropriate agents in some patients. This was further illustrated in our data by the fact that coverage reimbursement was the main driver for prescribing treatments in up to a quarter of patients receiving anti-VEGF agents, though this was the case for only 9% of patients receiving faricimab. Patient out-of-pocket costs and health plan coverage were also factors in physicians' treatment choice. Most patients in our cohort were covered by Medicare, which may not cover all costs of anti-VEGF agent,[37] and did not have secondary insurance coverage, highlighting the role payer restriction may play in treatment selection. Ensuring wider reimbursement and fewer restrictions on prescribing may allow for more optimal treatment selection. However, it must be noted that our study did not verify treatment authorizations, and that our data on barriers to prescribing are based on physicians' perceptions.

In our cohort, faricimab was associated with low levels of patient-reported dissatisfaction with efficacity and injection-related anxiety. Although only a minority of patients stated they had too many consultations or tests, this was particularly the case in patients receiving purely anti-VEGF agents. These data suggest that, although patients are largely satisfied with their treatment, faricimab may be viewed particularly favorably by patients.

Patients' vision-specific QoL, as assessed by the NEI VFQ-25 measure, was comparable to that previously recorded in nAMD clinical trial populations[38] but was likely substantially lower than that recorded in the general population.[39] Overall quality of life, as assessed by the EQ-5D-5L and EQ VAS measures also showed indications of being impaired in the study cohort, with mean values of 0.76 and 71.6 comparing to age-matched US population norms of 0.81 and 80.7, respectively.[40]

These data reinforce the continued burden experienced by patients with nAMD and highlight the need for more efficacious treatments. However, our data do suggest a possible lower disease burden in patients receiving faricimab, with high proportions of patients having mild disease and few presenting with sub/intraretinal fluid at time of survey. Future research is needed to confirm this is indeed the case.

Although our study has a number of strengths, including having both physician- and patient-reported data from a well-characterized cohort, we must also acknowledge a number of possible limitations. While minimal inclusion criteria governed the selection of participating physicians, participation was influenced by their willingness to complete the survey. Although patient selection bias was reduced by requiring physicians to provide data from a consecutive series of patients, participating patients may not reflect the general nAMD population since the DSP only includes consulting patients. Therefore, patients who consult infrequently were less likely to be included. Clustering by physicians and missing data may limit the accuracy and interpretability of our study. Recall bias may have affected physician responses. However, data were collected at the time of patient consultation and physicians had the ability to refer to patient records while returning data, minimizing recall bias, though medical records were not verified as part of the study. Overall disease severity may have been overestimated due to taking the worst affected eye as the overall patient disease severity in the case where patients had two affected eyes. Patient outcomes may have been influenced by previous treatments and disease history, which were not controlled for in our study.

Conclusion

Despite receiving treatment, nAMD patients experience a residual symptom burden and impacted QoL. Physicians may choose faricimab over purely anti-VEGF agents for its clinical efficacy and treatment burden. Physicians take both clinical factors and non-clinical burden for patients into account when selecting agents and dosing regimens, while reimbursement

concerns hinder prescribing in some patients. Optimizing treatment choices to help reduce patient treatment burden and ensuring increased access to established and newer, more innovative, treatments may help improve patients' outcomes.

Data Sharing Statement

All data, ie, methodology, materials, data and data analysis that support the findings of this survey are the intellectual property of Adelphi Real World and cannot be shared without appropriate access request. All requests for access should be addressed directly to Emily Coak at emily.coak@omc.com.

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Disclosure

SG consults for Eyepoint, Genentech and Regeneron. EC, DM and KL are employees of Adelphi Real World. NB and SK are employees of Genentech Inc. The authors report no other conflicts of interest in this work.

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