Eligibility for faricimab in a real-world neovascular age-related macular degeneration population: a cross-sectional study

Irène Jern,1 Sara Forsell,2 Helena Norberg 1

ABSTRACT

Objectives To investigate the eligibility of a real-world neovascular age-related macular degeneration (nAMD) population for the TENAYA and LUCERNE trials (testing faricimab), and to compare the eligible real-world patients to trial participants.

Design, settings and participants In this retrospective cross-sectional study, we used data from the Swedish Macula Registry (SMR) between 1 January 2017 and 31 December 2020. Persons were eligible if they fulfilled the main inclusion criteria in TENAYA and LUCERNE: (1) nAMD diagnosis, (2) treatment naïve, (3) ≥50 years and (4) best-corrected visual acuity (BCVA) of 78–24 letters.

Main outcome measures Characteristics at the original visit of the eligible SMR population and baseline data from the clinical trials were compared.

Results In total, 27,962 individuals with nAMD were registered in SMR. A total of 15,399 (55%) individuals were treatment naïve; of these, 15,368 (55%) were ≥50 years and 13,265 (47%) also had BCVA of 78–24 letters and fulfilled eligibility. Among treatment-naïve individuals, 86% were eligible and the BCVA criterion was the most common reason for non-eligibility. The eligible SMR population was significantly older than either TENAYA or LUCERNE. SMR included more women and patients with worse visual acuity than TENAYA, while SMR patients were diagnosed more quickly than LUCERNE.

Conclusions Almost half of the real-world nAMD population in SMR fulfilled the main inclusion criteria of the TENAYA and LUCERNE trials. Among treatment-naïve individuals, 86% were eligible. Marginally differences were shown between the eligible SMR population and the trial populations. The SMR population were older and more similar to the population in LUCERNE than TENAYA.

INTRODUCTION

Age-related macular degeneration (AMD) is one of the leading causes of central vision loss among people aged 50 years and older worldwide.1 AMD affects quality of life because it reduces the ability of patients to manage their own lives. Loss of central vision causes difficulties in performing daily activities and managing leisure activities, such as reading, driving and recognising faces.2 3 Studies show that persons with AMD have a high risk for depression.1 Furthermore, individuals with AMD report comparably or worse quality of life than similar aged people without AMD.3

Treatment of neovascular AMD (nAMD) was revolutionised when anti-vascular endothelial growth factor (VEGF) intraocular injections were introduced, cutting the incidence of blindness due to nAMD by 50%.4 Previous research has demonstrated that the earlier nAMD is detected and anti-VEGF therapy initiated, the better prognosis.6 However, real-world studies show that undertreatment of nAMD is common in clinical practice and that treatment frequency declines over time.7–10 This is often owing to the high burden of frequent visits and injections on patients, caregivers and healthcare providers.11–14 Common barriers to anti-VEGF therapy reported by patients are fear of intraocular injection, anxiety for negative examination results, difficulties in travelling to and from the hospital, anxiety in the waiting room (anticipatory anxiety), fear of getting worse if the treatment did not work and possible injection-related side effects.15–17 Healthcare providers report injection frequency (as often as every 4–8 weeks with present anti-VEGF drugs) and the rate of patient visits as the major problems.11 In order to reduce the
burden of current anti-VEGF therapy, new treatments with longer durations of effects are desirable.\textsuperscript{18}

Faricimab is a bispecific antibody that inhibits both VEGF-A and angiopoietin-2 and has shown non-inferiority to aflibercept administered every 8 weeks in the two phase III trials: TENAYA and LUCERNE.\textsuperscript{19} An advantage that faricimab has over aflibercept is that treatment intervals can be extended to 16 weeks. The aim of this study is to investigate the proportion of patients possibly eligible for faricimab and the generalisability of the clinical trial results to the real-world nAMD population in the Swedish Macula Registry (SMR). The following questions will be addressed: (1) What proportion of the real-world nAMD population would have been eligible for faricimab according to the main inclusion criteria in the TENAYA and LUCERNE trials? (2) How comparable are the TENAYA and LUCERNE populations to eligible real-world patients?

METHODS

Population and register

Data for this register-based cross-sectional study were collected from the Swedish Macula Registry (SMR) between 1 January 2017 and 31 December 2020. SMR is a national database for treatments given to patients with nAMD, including both public and privately owned medical centres.\textsuperscript{20} Clinics and patients voluntarily join SMR and the register had a coverage of 85\% in 2020. The registry was started in 2003 and contains data on demographics, neovascular lesion type, vision outcomes (eg, Early Treatment Diabetic Retinopathy study (ETDRS) and Snellen), frequency of injections and clinical visits, administered intravitreal treatment and adverse events.

Selection process and eligibility criteria

This study was based on a systematic approach for local implementation of novel therapies in persons with chronic disease in Sweden.\textsuperscript{21} The model consists of seven steps and has previously been used to introduce novel heart failure medications into real-world practice and can be adjusted to any discipline.\textsuperscript{22, 23} Performing the first two steps of the model is recommended prior to getting marketing approval (at which point a more valid estimation of the proportion of eligible real-world patients is needed), and the first two steps were taken in this study. Step 1 is to decide a few specific criteria to apply for the specific treatment; step 2 is to perform a primary scan, that is, using a registry/database/medical record system to identify individuals eligible with those criteria.\textsuperscript{21}

In step 1, discussions were held with eye-care specialists to select relevant criteria from the phase III trials TENAYA and LUCERNE.\textsuperscript{19} The consensus of these specialists was to apply four out of six clinically relevant inclusion criteria: (1) nAMD diagnosis, (2) naïve to treatment, (3) 50 years or older, (4) best-corrected visual acuity (BCVA) in ETDRS 78–24 letters (20/32–20/320 approximate Snellen equivalent).

In step 2, eligible individuals were selected according to the above criteria based on their data in SMR. For patients with bilateral nAMD, the eye with the worst BCVA at diagnosis was included. Data were excluded for five counties with a coverage in SMR of <60\% per year.

Clinical parameters

Data from the original visit leading to inclusion in SMR (ie, the time when persons were diagnosed with nAMD) were compared with baseline characteristics of the study populations in TENAYA and LUCERNE. The following variables were available in both SMR and the phase III trials and included in the analyses: age, sex, time to AMD diagnosis, choroidal neovascularisation (CNV) location, CNV lesion type, and BCVA in ETDRS if measured (otherwise, according to an approximate ETDRS based on Snellen). If a time to AMD diagnosis was >365 days, this record was excluded due to incorrect registration. Subjects diagnosed with PCV were classified to occult CNV lesion type.

Statistics

Comparison between the real-world population in SMR and the study populations in TENAYA and LUCERNE was performed with Student’s t-test for continuous variables and $\chi^2$ test for categorical variables. Continuous variables are presented as mean and SD, and categorical variables as frequencies and proportions. Sensitivity analyses were performed by omitting the missing category for the variables time to AMD diagnosis, CNV location and CNV lesion type. P value <0.05 was chosen as the level of statistical significance. All analyses were performed with IBM SPSS Statistics V.26.

RESULTS

In total, 407752 clinical visits were recorded in SMR in 2017–2020 among 27962 patients with nAMD. Figure 1 shows the selection of patients when the main inclusion criteria from TENAYA and LUCERNE were applied. Out of the 27962 patients with nAMD, 15399 patients started anti-VEGF treatment during the study period, of which 15368 patients were 50 years or older. A total of 13265 patients had a BCVA of 78–24 letters at their original visit. Therefore, among all persons with nAMD, 47\% (13265 of 27962) were eligible based on all four inclusion criteria, which corresponds to 86\% (13265 of 15399) of treatment-naïve individuals.

Table 1 compares the TENAYA and LUCERNE trial populations to the eligible SMR population (n=13265). The SMR population was significantly older than both TENAYA (79.5±7.7 vs 75.9±8.6, p<0.001) and LUCERNE (79.5±7.7 vs 74.8±8.4, p<0.001). More women were included in SMR than in TENAYA (64\% vs 57\%, p<0.001), and SMR patients had worse visual acuity than TENAYA patients (mean BCVA 58.4±12.7 vs 61.3±12.5, p<0.001). There were no significant differences in these variables when SMR was compared with LUCERNE.
The proportion of individuals with time to AMD diagnosis <1 month was higher in SMR than in LUCERNE (74% vs 67%, p<0.001). There were also significant differences in CNV location and lesion type between SMR and TENAYA and LUCERNE. The three variables—time to AMD diagnosis, location and lesion type—had a high number of missing values in SMR compared with TENAYA and LUCERNE. Sensitivity analyses performed without the missing category in these three variables showed that these missing values had no effect on the results, except that differences in time to AMD diagnosis became non-significant when comparing SMR and TENAYA (p=0.010 increased to p=0.111) (online supplemental table 1).

DISCUSSION

This study showed that of all individuals with nAMD in SMR (2017–2020), 47% were eligible to the main inclusion criteria in the TENAYA and LUCERNE clinical trials. This result corresponds to 86% eligibility among treatment-naïve individuals in SMR. The comparison between characteristics at the original visit causing a patient to be in the SMR database and baseline data in the two clinical trials showed only marginal differences between these populations. The SMR population was slightly older, included a higher proportion of women and had worse visual acuity than TENAYA. The SMR population was slightly older and had been diagnosed more quickly than LUCERNE. To manage budget appropriations, these results indicate that further eligibility criteria might be necessary when faricimab is going to be implemented in clinical practice.

The strength of this study is that, by using SMR (which has high coverage in the majority of Swedish hospital regions), we were able to study a large, nationwide, real-world population over a time period of 4 years. Furthermore, SMR contains most of the variables studied in TENAYA/LUCERNE, which meant that we were able to compare the study populations to SMR’s real-world population. This study also has some limitations. First, like other national registries, SMR did have missing data for some of the included criteria. We accounted for the missing data by performing sensitivity analyses, which showed that the missing data did not affect the results except for time to AMD diagnosis in SMR versus TENAYA. Second, there were local differences in coverage in SMR, and we excluded regions with coverage under 60%, which makes the results less representative. There is also a risk for local discrepancies in how some of the variables in SMR were defined and interpreted between participating clinics/regions. For example, the variables ‘time to AMD diagnosis’ and ‘CNV lesion type’ can be defined and registered in different ways by different clinics. Previous validation studies based on data from SMR have estimated that the errors in the database are around 5% for ETDRS and 0%–13% for other variables. Continuous meetings are held among participating clinics to improve the consensus of variables in SMR and, in addition, some essential variables have been made obligatory in the registry to prevent data loss. Further, it is important to consider that even though the results from TENAYA/LUCERNE should be possible to generalise to the real world (as represented by SMR), those phase III trials only included a couple hundred participants. It is possible that rare adverse events were not found within the trial populations, but would or could show up when faricimab is implemented in clinical practice, which highlights the importance of doing follow-up studies of faricimab. Finally, previous studies have shown a negative association between lesion size and treatment outcome. Extremely large lesion size may also suggest chronicity of the disease. Excluding lesion size criteria is a limitation of this study.

Figure 1 Selection of patients in the Swedish Macula Registry (SMR) between 2017 and 2020 eligible according to the main inclusion criteria in the TENAYA and LUCERNE trials. BCVA, best-corrected visual acuity; nAMD, neovascular age-related macular degeneration.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SMR n=13265</th>
<th>TENAYA n=334</th>
<th>P value</th>
<th>LUCERNE n=331</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>79.5 (7.7)</td>
<td>75.9 (8.6)</td>
<td>&lt;0.001</td>
<td>74.8 (8.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>8462 (64%)</td>
<td>191 (57%)</td>
<td>0.013</td>
<td>203 (61%)</td>
<td>0.357</td>
</tr>
<tr>
<td>BCVA, ETDRS letters, mean (SD)</td>
<td>58.4 (12.7)</td>
<td>61.3 (12.5)</td>
<td>&lt;0.001</td>
<td>58.7 (14.0)</td>
<td>0.672</td>
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<td>BCVA categories, n (%)</td>
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<td>0.014</td>
<td></td>
<td>0.635</td>
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<tr>
<td>≥74</td>
<td>1616 (12%)</td>
<td>47 (14%)</td>
<td></td>
<td>45 (14%)</td>
<td></td>
</tr>
<tr>
<td>73–55</td>
<td>7183 (54%)</td>
<td>200 (60%)</td>
<td></td>
<td>181 (55%)</td>
<td></td>
</tr>
<tr>
<td>≤54</td>
<td>4466 (34%)</td>
<td>87 (26%)</td>
<td></td>
<td>105 (32%)</td>
<td></td>
</tr>
<tr>
<td>Time since AMD diagnosis*</td>
<td></td>
<td></td>
<td>0.010</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>≤1 month</td>
<td>9710 (74%)</td>
<td>248 (74%)</td>
<td></td>
<td>221 (67%)</td>
<td></td>
</tr>
<tr>
<td>&gt;1 month</td>
<td>2066 (16%)</td>
<td>66 (20%)</td>
<td></td>
<td>96 (29%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1354 (10%)</td>
<td>20 (6%)</td>
<td></td>
<td>14 (4%)</td>
<td></td>
</tr>
<tr>
<td>CNV location, n (%)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Subfoveal</td>
<td>7161 (54%)</td>
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<td>41 (12%)</td>
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<td>42 (13%)</td>
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<td>Missing</td>
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<td>7 (2%)</td>
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<td>CNV lesion type, n (%)</td>
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<td>&lt;0.001</td>
<td>&lt;0.001</td>
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</tr>
<tr>
<td>Occult†</td>
<td>4139 (31%)</td>
<td>177 (53%)</td>
<td></td>
<td>171 (52%)</td>
<td></td>
</tr>
<tr>
<td>Classic, including mixed membranes</td>
<td>2439 (18%)</td>
<td>133 (40%)</td>
<td></td>
<td>134 (41%)</td>
<td></td>
</tr>
<tr>
<td>RAP</td>
<td>1319 (10%)</td>
<td>14 (4%)</td>
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<tr>
<td>Missing</td>
<td>5368 (41%)</td>
<td>10 (3%)</td>
<td></td>
<td>12 (4%)</td>
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</tbody>
</table>

*One hundred thirty-five cases with a diagnosis time >365 days excluded from SMR.
†Four hundred eighteen PCV cases included.

AMD, age-related macular degeneration; BCVA, best-corrected visual acuity; CNV, choroidal neovascularisation; ETDRS, Early Treatment Diabetic Retinopathy Study; PCV, polypoidal choroidal vasculopathy; RAP, retinal angiomatous proliferation; SMR, Swedish Macula Register.
The proportion of treatment-naive individuals in SMR who were eligible (86%) is higher than had been found in a recent similar study investigating another population. Kim et al. performed a retrospective single-centre study to investigate eligibility for aflibercept (according to the entry criteria of the VIEW trial) among 512 eyes of 463 treatment-naïve individuals with nAMD, with the result that 55% would have been eligible according to all VIEW criteria. The most common criterion causing non-eligibility, in both VIEW and TENAYA/LUCERNE, was ETDRS (78–25 letters and 78–24 letters, respectively). The present study is based on a comparison to TENAYA/LUCERNE, which had different entry criteria from VIEW, thus the results are not completely comparable. However, the ETDRS criteria were wider in TENAYA/LUCERNE than VIEW, and Kim et al. used additional inclusion and exclusion criteria in the VIEW trial, indicating that the TENAYA/LUCERNE trial criteria were broader and that they studied a less strictly selected population than the VIEW trial.

Consultation with eye specialists resulted in consensus for applying four out of the six inclusion criteria in TENAYA/LUCERNE according to clinical relevance. The two omitted criteria were CNV location (subfoveal CNV or juxtafoveal/extrafoveal CNV with subfoveal component related to CNV activity) and lesion size (CNV lesion size of ≤9 disc areas and CNV component area of ≥50% of total lesion area). These criteria were considered less relevant because in clinical practice, all individuals with nAMD are treated with anti-VEGF regardless of location or lesion size based on the evidence that earlier treatment initiation results in a better prognosis.

Furthermore, we did not apply any of TENAYA/LUCERNE’s exclusion criteria because the majority of these criteria were met through (1) the selection of individuals with nAMD diagnosis and anti-VEGF treatment-naive individuals or (2) due to clinical practice routines of not treating individuals with anti-VEGF injections in the presence of, for example, active inflammation, uncontrolled glaucoma or current vitreous haemorrhage. Unfortunately, we did not have access to medical record data and could not exclude individuals who had cataract surgery within 3 months prior to nAMD diagnosis and initiation of anti-VEGF therapy. According to the seven-step model for implementation of novel therapies in persons with chronic disease, this exclusion criteria of cataract surgery would have been considered in step 3, in which medical records are scrutinised to apply remaining inclusion and exclusion criteria. Currently, there is inconsistent evidence about the risks of cataract surgery prior to or during nAMD treatment, and this topic remains a matter of debate. Hopefully, future studies will improve our understanding about cataract surgery and nAMD.

The most prominent difference between the eligible SMR population and trial participants found in the present study was that the real-world patients were about 4 years older. This may be a result from simplifying the inclusion criteria. However, location and lesion size do not necessarily have to do with peoples’ age. Lesion size does grow bigger with time but according to our clinical experience, this often happens over 6–12 months regardless of the individuals’ age. A more probable cause to the identified age difference may be the general problem that older people tend to be included in clinical trials to a lesser extent compared with younger people.

The large proportion of eligible treatment-naive individuals in SMR indicates that the inclusion criteria are relatively broad. Further, the four criteria applied in the present study were generally used in previous anti-VEGF clinical trials and are not specific TENAYA/LUCERNE criteria. Therefore, it needs to be pointed out that prioritisation will be necessary of which patients can be prescribed faricimab after marketing approval. As expected, the advantage of faricimab’s longer injection interval comes with a price, and faricimab is probably going to be more expensive than current anti-VEGF drugs. Healthcare providers will have to prioritise to what extent faricimab can be used in clinical practice in order to manage future budget allocations. Additional eligibility criteria can be added in the national or regional implementation process to reduce the number of eligible subjects. Exactly which criteria to add will need to be managed in forthcoming updates of treatment guidelines for nAMD.

When implementing novel medicines in clinical practice, both efficacy and safety are important to consider. At the time of this writing, the evidence in favour of faricimab primarily relies on the 1-year follow-up from the TENAYA and LUCERNE trials, which compared faricimab (given at up to 16-week intervals) with aflibercept (given at 8-week intervals). It should be mentioned that even though randomised controlled trials with aflibercept were made with 8 weeks dosing interval, in clinical practice many clinicians now choose the treat and extend routine with longer intervals also for aflibercept. The benefits of faricimab’s (up to) to 16-week interval might therefore to some degree have been overestimated by TENAYA and LUCERNE. The safety of faricimab needs to be further evaluated in the 2-year follow-up of TENAYA/LUCERNE, the ongoing long-term AVONELLE-X trial, and other post-marketing follow-up studies, in order to better understand the long-term safety and rare serious adverse events.

CONCLUSIONS

Almost half of the real-world nAMD population in SMR fulfilled the main inclusion criteria applied in the TENAYA and LUCERNE trials. Among treatment-naive individuals in SMR, 86% were eligible under those criteria. Marginal differences were shown between the eligible SMR population and the trial populations. The SMR population were older and generally more similar to the population in LUCERNE than in TENAYA. To manage future budget allocations, these results indicate that additional
eligibility criteria may be needed when faricimab is going to be implemented in clinical practice.

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Contributors UJ and HN reviewed and edited the manuscript and approved the final version of the manuscript. HN is responsible for the overall content as the guarantor.

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Competing interests HN has received research and lecturer grants from Roche, and lecturer grants from AbbVie, Bayer and Pfizer. UJ and SF declare no conflicts of interests.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the Swedish Ethical Review Authority (Dnr 2021-03004) and followed the Tenets of the Declaration of Helsinki. Data were obtained from the Swedish Macula Registry after approval from its steering committee. The patients are voluntarily registered in the Swedish Macula Registry after being informed that collected data will be used for quality assessments, statistics and research purposes after ethical approval, and that they have the right to deny registration.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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ORCID iD

Helena Norberg http://orcid.org/0000-0002-6785-2895

REFERENCES


4 Casten RU, Rovner BW. Update on depression and age-related macular degeneration. **Curr Opin Ophthalmol** 2013;24:239–43.


### Supplementary Table 1. Sensitivity analyses without the missing category for the eligible SMR population compared to the TENAYA and LUCERNE populations.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SMR n = 13,265</th>
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<th>p</th>
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<th>p</th>
</tr>
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<tbody>
<tr>
<td>Time since AMD-diagnosis*</td>
<td>0.111</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>≤ 1 month</td>
<td>9710 (82%)</td>
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<td>CNV location, n (%)</td>
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<tr>
<td>CNV lesion type, n (%)</td>
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</table>

AMD, age-related macular degeneration; CNV, choroidal neovascularization; PCV, polypoidal choroidal vasculopathy; SMR, The Swedish Macula Register; RAP, retinal angiomatous proliferation.
* 135 cases with a diagnosis time >365 days excluded from SMR.
** 418 PCV cases included.