Japanese Journal of Ophthalmology (2024) 68:83–90
https://doi.org/10.1007/s10384-023-01040-4

THE OFFICIAL INTERNATIONAL JOURNAL OF THE JAPANESE OPHTHALMOLOGICAL SOCIETY

CLINICAL INVESTIGATION

One-year results of treat-and-extend regimen with intravitreal faricimab for treatment-naïve neovascular age-related macular degeneration

Hidetaka Matsumoto[1] · **Junki Hoshino**[1] · **Kosuke Nakamura**[1] · **Hideo Akiyama**[1]

Received: 28 October 2023 / Accepted: 8 December 2023 / Published online: 20 January 2024

Abstract

Purpose To evaluate 1-year outcomes of loading phase treatment followed by maintenance therapy using a treat-and-extend (TAE) regimen with intravitreal faricimab for neovascular age-related macular degeneration (nAMD).

Study design Retrospective, interventional case series.

Methods We retrospectively studied 40 eyes of 38 consecutive patients with treatment-naïve nAMD, assessing best-corrected visual acuity (BCVA), foveal thickness, central choroidal thickness (CCT), total number of injections over 1 year, and intended injection interval at the last visit.

Results Thirty eyes (75.0%) had completed the 1-year intravitreal faricimab treatment. Their BCVA showed significant improvement, with significant reductions in foveal thickness and CCT. The total number of injections during the 1-year treatment period was 6.6 ± 0.7. The intended injection interval at the last visit was 12.7 ± 3.3 weeks. Of the 10 eyes (25.0%) failing to complete the 1-year faricimab treatment, 1 eye developed intraocular inflammation after the loading phase treatment but showed no recurrence of exudative changes, and no further treatment was required. Moreover, 5 eyes switched to intravitreal brolucizumab injection due to persistent exudative changes with an 8-week interval of faricimab injections. The remaining 4 eyes either dropped out or the patient died.

Conclusions A loading phase treatment followed by a TAE regimen with intravitreal faricimab appears to be generally safe and effective for improving visual acuity and ameliorating exudative changes in eyes with nAMD. However, there might be cases in which exudative changes cannot be adequately controlled with injections of faricimab every 8 weeks in the maintenance phase.

Keywords Age-related macular degeneration · Anti-vascular endothelial growth factor · Faricimab · Treat-and-extend

Introduction

Currently, the first line treatment for neovascular age-related macular degeneration (nAMD) is the intravitreal injection of an anti-vascular endothelial growth factor (VEGF) agent, known to improve and maintain visual acuity in eyes with nAMD [1]. Lucentis® (ranibizumab 0.5 mg/0.05 ml), Eylea® (aflibercept 2 mg/0.05 ml), Beovu® (brolucizumab 6 mg/0.05 ml), and Vabysmo® (faricimab 6 mg/0.05 ml) are used as insurance-covered anti-VEGF agents in Japan. Ranibizumab, a recombinant humanized anti-VEGF monoclonal antibody Fab fragment, inhibits VEGF-A [2]. Aflibercept, a recombinant fusion protein consisting of portions of the VEGF receptor 1 and 2 extracellular domains fused to the Fc portion of human immunoglobulin (Ig) G, blocks not only VEGF-A but also VEGF-B and placental growth factor [3]. Brolucizumab, a recombinant humanized monoclonal single chain antibody fragment inhibiting VEGF-A, is characterized by high solubility attributable to its low molecular mass of 26 kD [4]. Faricimab is the first recombinant humanized bispecific IgG monoclonal antibody designed for intraocular use that can independently bind and neutralize both VEGF-A and angiopoietin-2 [5]. According to previous clinical studies, brolucizumab demonstrates the strongest

Corresponding Author: Hidetaka Matsumoto

✉ Hidetaka Matsumoto
hide-m@gunma-u.ac.jp

[1] Department of Ophthalmology, Gunma University Graduate School of Medicine, 3-39-15 Showa-machi, Maebashi, Gunma 371-8511, Japan

effect in terms of fluid control, polypoidal lesion regression, and choroidal thickness reduction, followed by aflibercept and then ranibizumab [6–16]. On the other hand, a meta-analysis demonstrated the risk of intraocular inflammation (IOI) as significantly higher with brolucizumab than with aflibercept [17]. Although faricimab was launched in 2022 following the TENAYA and LUCERN trials [18], its safety and efficacy have yet to be examined in sufficient detail.

We conducted loading phase treatment with intravitreal faricimab for 40 eyes with treatment-naïve nAMD and reported the results in 2023 [19]. All eyes completed 3 monthly injections of faricimab. Best-corrected visual acuity (BCVA) improved significantly. Furthermore, foveal thickness and central choroidal thickness (CCT) were both significantly reduced during the loading phase treatment. We found that 20.5% of patients had residual fluid at week 16, i.e., 8 weeks after completing 3 monthly injections. Compared to the results of loading phase treatment in prior studies, the fluid control effect of faricimab appeared to be superior to that of aflibercept but inferior to that of brolucizumab. The polypoidal lesion regression rate after 3 monthly faricimab injections was 61.1%. Moreover, the percentage of the baseline CCT value after the faricimab loading phase was 88.4%. The polypoidal lesion regression rate and choroidal thickness reduction might be comparable to those achieved by aflibercept while being more modest than those obtained with brolucizumab. As to adverse events, only 1 eye developed IOI without any visual loss at week 16. Similar findings in relation to the loading phase treatment with faricimab for treatment-naïve nAMD have also been reported by other research groups [20, 21].

In the current study, we evaluated the 1-year outcomes of loading phase treatment followed by maintenance therapy using a treat-and-extend (TAE) regimen with intravitreal faricimab in 40 eyes with treatment-naïve nAMD, as assessed in our previously reported results for the loading phase of faricimab treatment. To the best of our knowledge, this is the first study to demonstrate the 1-year outcomes of a TAE regimen employing intravitreal faricimab for treatment-naïve nAMD in a clinical setting.

Subjects and methods

We obtained approval for this study, which complied with the guidelines of the Declaration of Helsinki, from the Institutional Review Board of Gunma University Hospital. Informed consent was obtained from all individual study participants. We retrospectively studied 40 eyes of 38 patients with previously untreated nAMD. During the period from June 2022 through September 2022, the patients began the protocol of receiving 3 monthly intravitreal injections of faricimab as a loading phase followed by a TAE regimen with intravitreal faricimab as a maintenance phase at Gunma University Hospital.

All patients underwent complete ophthalmological examinations at baseline, including slit-lamp biomicroscopy with a noncontact fundus lens (SuperField lens; Volk Optical Inc), color fundus photography (Canon CX-1; Canon), ultra-widefield color fundus imaging (Optos 200Tx, Optos), fluorescein angiography (FA) and indocyanine green angiography (ICGA) (Spectralis HRA + OCT; Heidelberg Engineering), as well as swept-source optical coherence tomography (OCT) (DRI OCT-1 Triton; Topcon Corpand PLEX Elite 9000; Carl Zeiss Meditec). For the OCT examination, we obtained B-mode images of the horizontal and vertical line scans (12 mm) through the fovea as well as 12 radial scans (9 mm) centered on the fovea employing the DRI OCT-1 Triton. Then, we performed OCT angiography (OCTA) volume scanning, i.e., 300 × 300 pixels in the 3 × 3 mm area demonstrated by the PLEX Elite 9000. The OCTA was based on an optical microangiography algorithm. The diagnostic criteria for nAMD were based on a previous report detailing nAMD nomenclature [22]. The presence of polypoidal lesions was evaluated on ICGA and B-mode OCT images, i.e., polyp-like choroidal vessel dilation on ICGA and sharply peaked retinal pigment epithelium (RPE) detachment on B-mode OCT [23].

All eyes were treated with intravitreal faricimab injection (6 mg/0.05mL). Generally, 4 monthly injections of faricimab are administered as a loading phase treatment, whereas in the current study, 3 monthly injections were given to facilitate a comparison with previously reported treatment outcomes with other anti-VEGF agents. All patients again underwent FA and ICGA at week 12, i.e., 4 weeks after the third faricimab injection. No additional intravitreal injection of faricimab was administered even if there were exudative changes at week 12. During the maintenance phase, the injection interval was extended by 4 weeks whenever dry macula was achieved; otherwise, the interval was shortened by 4 weeks. Dry macula was defined as the macula showing no evidence of intraretinal, subretinal, or sub-RPE fluid accompanied by either no or diminishing hemorrhage. For this study, we set the treatment interval at a minimum of 8 weeks and a maximum of 16 weeks. In the event of non-infectious IOI developing, faricimab therapy was discontinued and 0.1% betamethasone eye drops (4 times/day) as well as posterior subtenon injection of triamcinolone acetonide (30 mg/0.75 mL) were administered. If dry macula was not achieved while administering the faricimab injections at an 8-week interval and the patients opted for a change in treatment, they were switched to another anti-VEGF agent, primarily brolucizumab.

BCVA, foveal thickness, and CCT were examined at every visit. BCVA was determined with manifest refraction and recorded as decimal values, then converted to the logarithm

of the minimal angle of resolution (logMAR) units. Foveal thickness and CCT were measured on B-scan OCT images employing the computer-based caliper measurement tool in the OCT system. Foveal thickness was, by definition, the distance between the internal limiting membrane and the RPE surface at the fovea. Foveal thickness included any intraretinal and subretinal fluid. CCT was defined as the distance between Bruch's membrane and the margin of the choroid and sclera under the fovea.

For statistical analyses, the Wilcoxon signed-rank test was applied for comparing the differences between BCVA, foveal thickness and CCT at baseline versus the other timepoints. Unpaired values of the number of injections and the injection interval were compared using the Mann–Whitney U test. The data analyses were performed employing Excel (Microsoft) with add-in software Statcel4 [24]. A $P<0.05$ was considered to indicate a statistically significant difference. All data are presented as the average ± standard deviation.

Results

The subjects were 40 eyes of 38 patients (24 eyes of 22 men; 16 eyes of 16 women, average age: 79.4 ± 8.9 years) with treatment-naïve nAMD. Macular neovascularization (MNV) subtypes were: type 1: 14 eyes, polypoidal choroidal vasculopathy (PCV): 17 eyes, mixed type 1 and type 2: 2 eyes, mixed PCV and type 2: 1 eye, type 2: 2 eyes, type 3: 4 eyes. Thirty eyes (75.0%) of 29 patients (16 eyes of 15 men; 14 eyes of 14 women, average age: 80.3 ± 7.4 years) completed 1 year of faricimab treatment. In those 30 eyes, the MNV subtypes were: type 1: 10 eyes, PCV: 13 eyes, mixed type 1 and type 2: 1 eye, mixed PCV and type 2: 1 eye, type 2: 1 eye, type 3: 4 eyes. The baseline demographic and clinical characteristics of patients with nAMD who completed the 1-year treatment with faricimab are presented in Table 1. Of the 10 eyes (25.0%) of 9 patients not completing the 1-year faricimab treatment, one developed IOI at week 16 and faricimab administration was stopped. Five patients, each with one eye being treated, elected to switch to intravitreal injections of brolucizumab due to persistent exudative changes after faricimab injections with an 8-week interval. Of those 5 eyes, 3 had type 1 MNV and 2 showed PCV. One patient, who had one eye treated, died after week 12 due to acute exacerbation of heart failure. The cause of death had no known association with the intravitreal faricimab regimen. Three eyes of 2 patients dropped out within 1 year after starting the faricimab treatment regimen.

In the 30 eyes that completed 1 year of faricimab treatment, BCVA at baseline, weeks 4, 8, and 16, either week 24 or 28, and finally week 44, 48, or 52 were 0.32 ± 0.40, 0.26 ± 0.38 ($P<0.05$), 0.22 ± 0.36 ($P<0.01$), 0.21 ± 0.37 ($P<0.01$), 0.21 ± 0.36 ($P<0.01$), and 0.17 ± 0.33 ($P<0.001$), respectively. BCVA showed significant improvement after the first faricimab injection (Fig. 1). Five eyes (16.7%) demonstrated a BCVA improvement of 0.3 or more over the 1-year study period, and there were no eyes that showed a BCVA deterioration of 0.3 or more. Foveal thicknesses at the time points were 289 ± 120, 199 ± 86 ($P<0.001$), 174 ± 57 ($P<0.001$), 167 ± 46 ($P<0.001$), 174 ± 51 ($P<0.001$), and 170 ± 47 ($P<0.001$) µm, respectively. Foveal thickness was significantly decreased after the first intravitreal faricimab administration (Fig. 2). CCT at the time points were 215 ± 97, 200 ± 92 ($P<0.001$), 195 ± 91 ($P<0.001$), 188 ± 89 ($P<0.001$), 187 ± 89 ($P<0.001$), and 184 ± 89 ($P<0.001$) µm. CCT was significantly decreased after the first faricimab injection (Fig. 3). The total number of injections over the 1-year study period was 6 in 17 eyes (56.7%), 7 in 9 eyes (30.0%), and 8 in 4 eyes (13.3%), with the average number of injections being 6.6 ± 0.7 (Fig. 4). The intended injection interval at the last visit was 8 weeks

Table 1 Baseline demographic and clinical characteristics of patients with nAMD who completed 1 year of faricimab treatment

Number of eyes	30	
Number of patients	29	
Age (years)	80.3 ± 7.4	
Male	15 (51.7%)	
Type of macular neovascularization	Type 1	10 (33.3%)
	PCV	13 (43.3%)
	Mixed type 1 and type 2	1 (3.3%)
	Mixed PCV and type 2	1 (3.3%)
	Type 2	1 (3.3%)
	Type 3	4 (13.3%)
Best-corrected visual acuity (logMAR)	0.32 ± 0.40	
Foveal thickness (µm)	289 ± 120	
Central choroidal thickness (µm)	215 ± 97	

nAMD neovascular age-related macular degeneration, *PCV* polypoidal choroidal vasculopathy

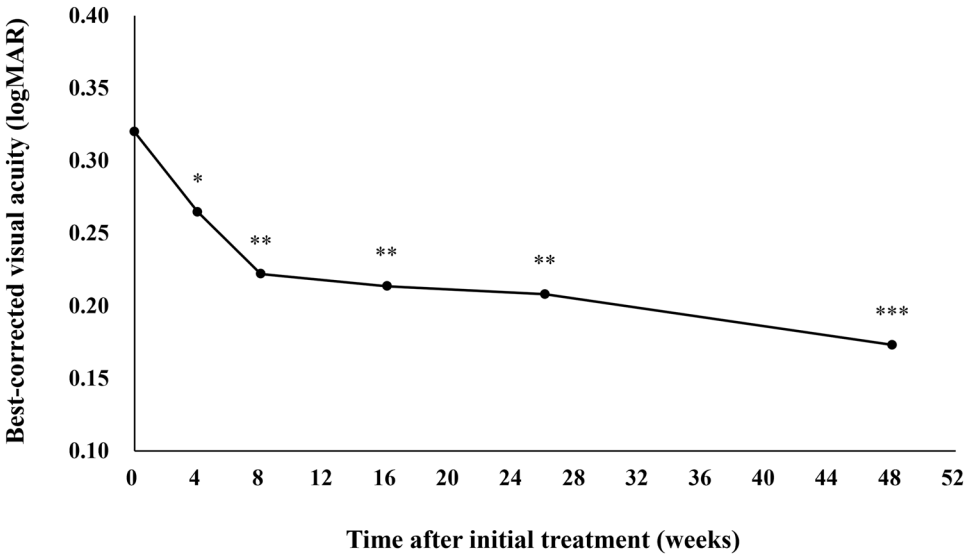

Fig. 1 Change of average best-corrected visual acuity (BCVA) in 30 eyes with neovascular age-related macular degeneration treated with 3 monthly intravitreal injections of faricimab followed by a treat-and-extend regimen with intravitreal faricimab. BCVA showed significant improvement after the first injection of faricimab (*P < 0.05, **P < 0.01, ***P < 0.001). Data are expressed as averages

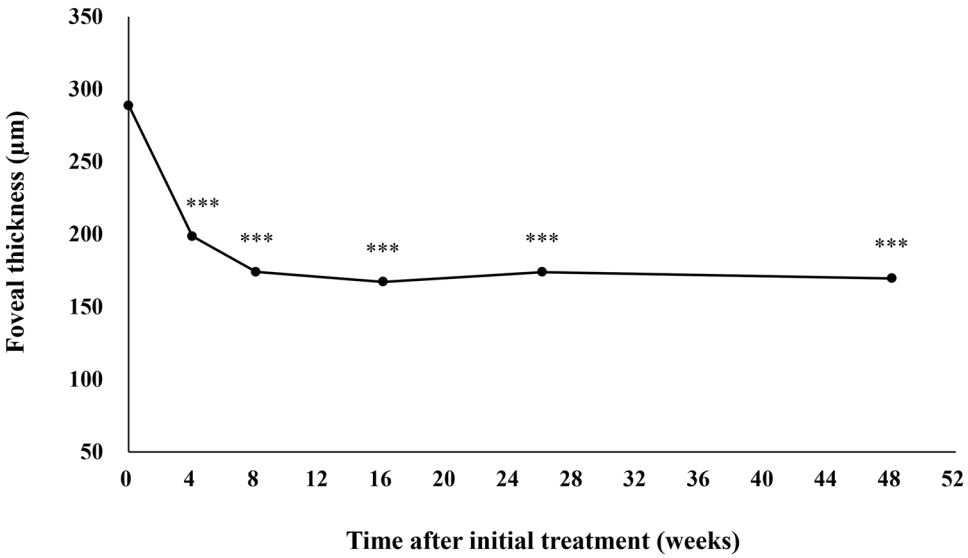

Fig. 2 Change of average foveal thickness in 30 eyes with neovascular age-related macular degeneration treated with 3 monthly intravitreal injections of faricimab followed by a treat-and-extend regimen with intravitreal faricimab. Foveal thickness showed significant improvement after the first faricimab injection (***P < 0.001). Data are expressed as averages

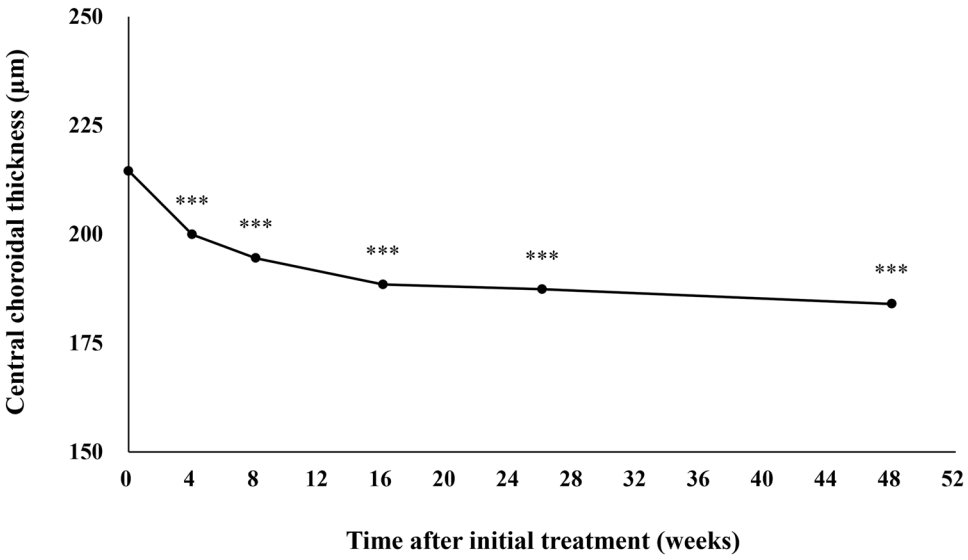

Fig. 3 Change of average central choroidal thickness (CCT) in 30 eyes with neovascular age-related macular degeneration treated with 3 monthly intravitreal injections of faricimab followed by a treat-and-extend regimen with intravitreal faricimab. CCT showed significant improvement after the first injection of faricimab (***P < 0.001). Data are expressed as averages

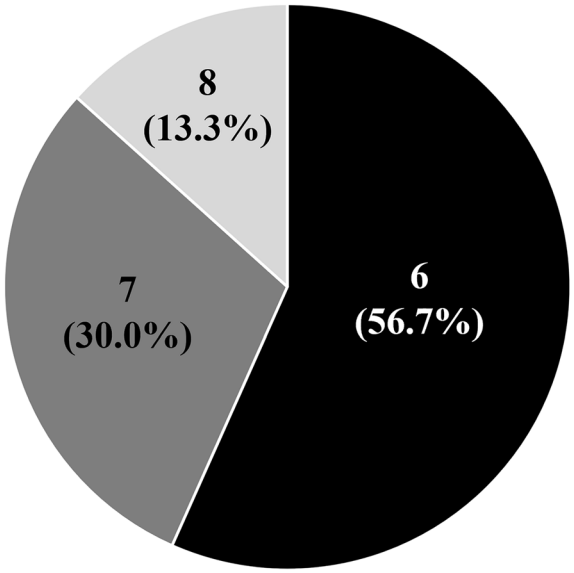

Fig. 4 Total number of injections over the 1-year study period in 30 eyes with neovascular age-related macular degeneration treated with 3 monthly intravitreal injections of faricimab followed by a treat-and-extend regimen with intravitreal faricimab

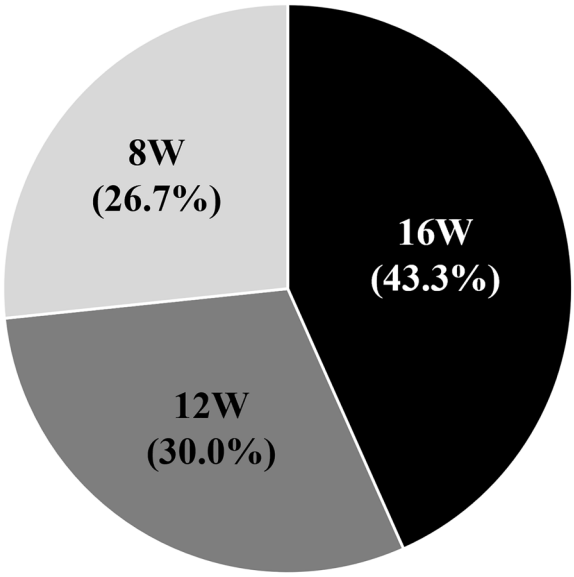

Fig. 5 Intended injection interval at the last visit up to week 52 in 30 eyes with neovascular age-related macular degeneration treated with 3 monthly intravitreal injections of faricimab followed by a treat-and-extend regimen with intravitreal faricimab

in 8 eyes (26.7%), 12 weeks in 9 eyes (30.0%), and 16 weeks in 13 eyes (43.3%), with an average injection interval of 12.7 ± 3.3 weeks (Fig. 5). During the maintenance phase, 13 eyes (43.3%) showed no recurrence of exudative changes and the injection interval was successfully extended. Dry macula was confirmed in 26 eyes (86.7%) at week 16. The total number of injections during the 1-year study period was significantly lower in the cases showing dry macula at week 16 than in the other cases (6.4 ± 0.6 vs. 7.5 ± 0.9, $P < 0.05$). Moreover, the intended injection interval at the last visit tended to be longer in those achieving dry macula at week 16, as compared to the others (13.1 ± 3.2 vs. 10.0 ± 2.0, $P = 0.08$). At the last visit, the achievement of dry macula was documented in 19 eyes (63.3%). A representative case is shown in Fig. 6.

Of the eyes failing to complete the 1-year treatment with faricimab, one developed vitritis at week 16 while exhibiting dry macula. The IOI was managed employing combination therapy with subtenon injections of triamcinolone acetonide (30 mg/0.75 ml) and 0.1% betamethasone eye drops. The vitritis showed amelioration without visual loss. The eye showed no recurrence of exudative changes related to MNV and required no further treatment throughout the 1-year study period. Five eyes were switched to intravitreal brolucizumab injection: 2 eyes at week 16, 1 eye at week 32, and 2 eyes at week 40. Among these 5 eyes, 4 (80.0%) did not show dry macula at week 16. One of the 5 eyes switched to intravitreal brolucizumab developed IOI after the second brolucizumab injection. As above, the IOI was treated with subtenon injection of triamcinolone acetonide (30 mg/0.75 ml) and 0.1% betamethasone eye drops. Subsequently, the MNV treatment was switched to intravitreal injection of aflibercept. In the 6 eyes that did not complete the 1-year treatment with faricimab, BCVA was unchanged while foveal thickness and CCT were significantly reduced at the end of the 1-year study period as compared to the baseline [BCVA: 0.22 ± 0.29 vs. 0.15 ± 0.16 ($P = 0.42$), foveal thickness: 247 ± 108 vs. 153 ± 52 μm ($P < 0.05$), CCT: 240 ± 111 vs. 198 ± 87 μm ($P < 0.05$)].

Discussion

We investigated the 1-year results of a TAE regimen with intravitreal faricimab for 40 eyes with treatment-naïve neovascular AMD. Thirty eyes (75.0%) completed the 1-year regimen with intravitreal faricimab. In those 30 cases, BCVA showed significant improvement. Furthermore, foveal thickness and CCT were significantly reduced after the initial faricimab injection and these reductions were maintained for up to 1 year. The total number of injections over the 1-year study period was 6.6 ± 0.7. The intended injection interval at the last visit was 12.7 ± 3.3 weeks.

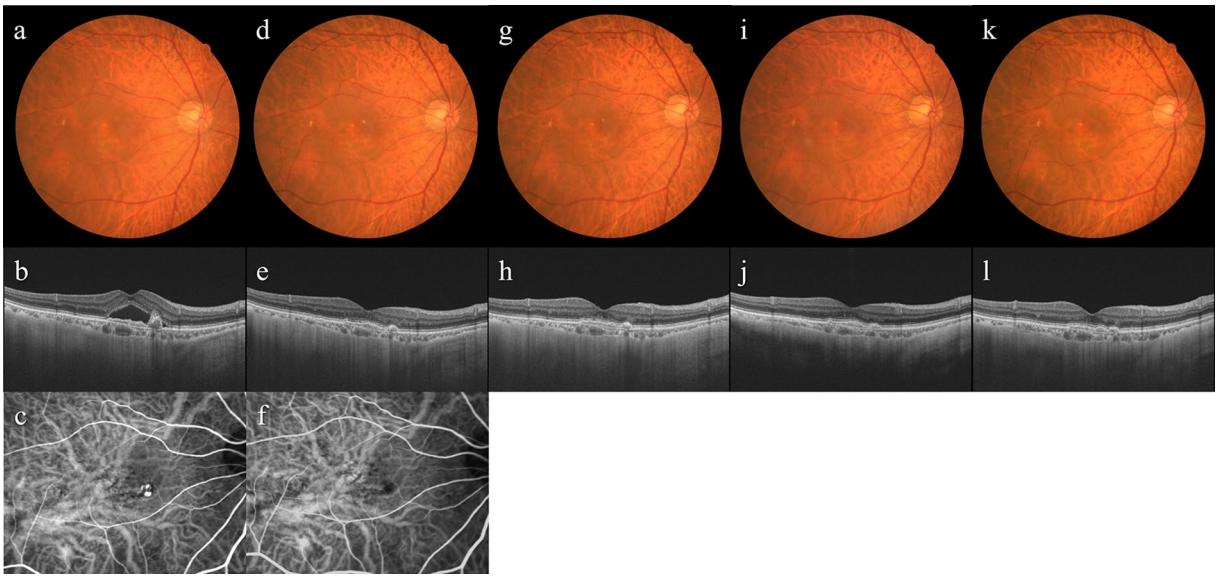

Fig. 6 Images of the right eye of a 77-year-old man with polypoidal choroidal vasculopathy. At baseline, best-corrected visual acuity (BCVA) was 0.30 logarithm of the minimum angle of resolution (logMAR) units. **a** Color fundus photograph shows retinal pigment epithelium (RPE) degeneration accompanied by subretinal fluid (SRF) at the macular area. **b** 9 mm B-mode optical coherence tomography (OCT) image, through the fovea and a polypoidal lesion, shows the double layer sign reflecting a branching neovascular network and sharply peaked RPE detachment due to the polypoidal lesion, which is accompanied by SRF. Moreover, focal choroidal thickening associated with dilatation of outer choroidal vessels can be seen under the double layer sign. The foveal thickness and central choroidal thickness (CCT) are 327 µm and 124 µm, respectively. **c** Indocyanine green angiography (ICGA) shows a branching neovascular network and polypoidal lesions at the macular area. At week 12, 4 weeks after the third injection of faricimab: BCVA of the right eye was 0.00 logMAR units. **d** Color fundus photograph shows RPE degeneration at the macular area. **e** 9 mm B-mode OCT image shows diminished RPE detachment without SRF. The foveal thickness and CCT are 162 µm and 98 µm, respectively. **f** ICGA shows no polypoidal lesions. At week 16: BCVA of the right eye was −0.08 logMAR units. **g**, **h** Color fundus photograph and 9 mm B-mode OCT image confirm that there is no recurrence of exudative changes. The foveal thickness and CCT are 160 µm and 97 µm, respectively. The fourth injection of faricimab was administered with an interval of 8 weeks. At week 28: BCVA of the right eye was 0.05 logMAR units. **i**, **j** Color fundus photograph and 9 mm B-mode OCT image confirm that there is no recurrence of exudative changes. The FT and CCT are 164 µm and 107 µm, respectively. The fifth injection of faricimab was administered with an interval of 12 weeks. At week 44: BCVA of the right eye was 0.05 logMAR units. **k**, **l** Color fundus photograph and 9 mm B-mode OCT image confirm that there is no recurrence of exudative changes. The foveal thickness and CCT are 157 µm and 119 µm, respectively. The sixth injection of faricimab was administered with an interval of 16 weeks. The intended interval for the next injection of brolucizumab was also 16 weeks. No adverse events, such as intraocular inflammation, were observed during the 1-year treatment period

During the maintenance phase, 43.3% of the eyes showed no recurrence of exudative changes. Of 10 eyes (25.0%) failing to complete the 1-year faricimab treatment regimen, 5 were switched to intravitreal injection of brolucizumab due to persistent exudative changes with the 8-week interval of faricimab injections.

ALTAIR was a randomized, open-label, phase 4 study focusing on the efficacy and safety of intravitreal aflibercept, employing two TAE regimens (2- and 4-week adjustments, which allowed a minimum interval of 8 weeks and a maximum interval of 16 weeks) in Japanese patients with treatment-naïve nAMD [25]. In the 4-week adjustment group, the intended injection interval at the last visit up to week 52 was an average of 11.8 ± 3.7 weeks, with 8 weeks for 39.8% and 16 weeks for 40.7% of patients. The total number of aflibercept injections over the 1-year period was 6.9 ± 1.0. In our present study, the intended injection interval at the last visit for 30 eyes completing 1 year of faricimab treatment was 12.7 ± 3.3 weeks on average, with 8 weeks for 26.7% and 16 weeks for 43.3% of the eyes. The total number of injections over the 1-year study period was 6.6 ± 0.7. Our results using faricimab appear to be slightly better than the results of the ALTAIL study utilizing aflibercept. However, it is important to note that in our current study, 5 eyes were switched to intravitreal brolucizumab due to persistent exudative changes with the 8-week interval of faricimab injections. These cases were not included either in the results of the intended injection interval at the last visit or the total number of injections over the 1-year period. Therefore, the fluid control effect of faricimab in the TAE regimen might be comparable to that of aflibercept, although our current results cannot be directly compared with the ALTAIR study. On the other hand, our previous study using brolucizumab for treatment-naïve nAMD with type 1 MNV, following the

same TAE regimen as that employed in the current study, revealed the intended injection interval at the last visit of 45 eyes completing 1 year of brolucizumab treatment to be an average of 14.0 ± 2.9 weeks, with 8 weeks for 13.3% and 16 weeks for 62.2% of the eyes [9]. The total number of injections over the 1-year study period was 6.4 ± 0.6 [9]. Intravitreal injection of an anti-VEGF agent is generally regarded as being somewhat less effective for sub-RPE MNV than for MNV above the RPE [20]. Hence, the fluid control effect of brolucizumab might be superior to that of aflibercept and faricimab.

Faricimab was designed to reduce systemic exposure and inflammation inducibility by modifying the Fc portion of IgG [5]. In the TENAYA trial, intravitreal injection of faricimab exerted no effects on blood VEGF-A levels at any time point up to week 48 [26], while blood VEGF levels after an intravitreal injection of either aflibercept or brolucizumab were reported to be significantly decreased [27]. The TENAYA and LUCERN trials revealed the incidence of IOI to be low and similar between faricimab and aflibercept [18]. In contrast, a meta-analysis, which included data from the HAWK and HARRIER trials, reported a significantly higher incidence of IOI with brolucizumab than with aflibercept [17]. In the present study, only 1 eye developed IOI. The IOI was detected at week 16 but was managed, without visual loss, employing subtenon injections of triamcinolone acetonide (30 mg/0.75 ml) and 0.1% betamethasone eye drops. One patient died due to acute worsening of heart failure. Whether there was any association with intravitreal faricimab could not be ascertained. Thus, intravitreal faricimab for patients with nAMD appears to be generally safe.

Based on the previously mentioned efficacy and safety, faricimab can be considered the primary choice of anti-VEGF agent for patients with nAMD. In the current study, 5 eyes with sub-RPE MNV had to switch their treatment to intravitreal brolucizumab due to persistent exudative changes with an 8-week interval of faricimab injections. Insufficient fluid control is known to carry the risk of long-term vision loss [28]. Therefore, switching to intravitreal brolucizumab or other anti-VEGF agents, as well as exploring photodynamic therapy for such cases, should be considered. In this study, in the cases that completed 1 year of faricimab treatment, the total number of injections was significantly lower and the intended injection interval at the last visit tended to be longer in those achieving dry macula at week 16 than in the other cases. It is noteworthy that similar results were obtained in previous studies [9, 10, 29], indicating that dry macula at week 16 might serve as a useful predicter of treatment outcomes with the TAE regimen. In fact, in the present study, 4 (80.0%) of 5 eyes that were switched to intravitreal brolucizumab injection regimen did not show dry macula at week 16.

Our study has limitations, including the retrospective single-center design and the small number of study subjects. All subjects were Japanese, so the results might not be generalizable to nAMD in Caucasians and other ethnic groups. Moreover, since we assessed only the 1-year results of intravitreal faricimab therapy for nAMD, long-term outcomes await evaluation.

In conclusion, loading phase treatment followed by a TAE regimen with intravitreal faricimab appears to be generally safe and effective for improving visual acuity and ameliorating exudative changes for 1 year in eyes with nAMD. However, there might be cases in which exudative changes cannot be adequately controlled with injections of faricimab every 8 weeks in the maintenance phase.

Declarations

Conflicts of interest H. Matsumoto, None; J. Hoshino, None; K. Nakamura, None; H. Akiyama, None.

References

1. Yamashiro K, Oishi A, Hata M, Takahashi A, Tsujikawa A. Visual acuity outcomes of anti-VEGF treatment for neovascular age-related macular degeneration in clinical trials. Jpn J Ophthalmol. 2021;65:741–60.
2. Ferrara N, Damico L, Shams N, Lowman H, Kim R. Development of ranibizumab, an anti-vascular endothelial growth factor antigen binding fragment, as therapy for neovascular age-related macular degeneration. Retina. 2006;26:859–70.
3. Papadopoulos N, Martin J, Ruan Q, Rafique A, Rosconi MP, Shi E, et al. Binding and neutralization of vascular endothelial growth factor (VEGF) and related ligands by VEGF trap, ranibizumab and bevacizumab. Angiogenesis. 2012;15:171–85.
4. Nguyen QD, Das A, Do DV, Dugel PU, Gomes A, Holz FG, et al. Brolucizumab: evolution through preclinical and clinical studies and the implications for the management of neovascular age-related macular degeneration. Ophthalmology. 2020;127:963–76.
5. Regula JT, von Lundh P, Foxton R, Barathi VA, Cheung CM, Bo Tun SB, et al. Targeting key angiogenic pathways with a bispecific CrossMAb optimized for neovascular eye diseases. EMBO Mol Med. 2016;8:1265–88.
6. Dugel PU, Koh A, Ogura Y, Jaffe GJ, Schmidt-Erfurth U, Brown DM, et al. HAWK and HARRIER: phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2020;127:72–84.
7. Dugel PU, Singh RP, Koh A, Ogura Y, Weissgerber G, Gedif K, et al. HAWK and HARRIER: ninety-six-week outcomes from the phase 3 trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2021;128:89–99.
8. Matsumoto H, Hoshino J, Mukai R, Nakamura K, Akiyama H. Short-term outcomes of intravitreal brolucizumab for treatment-naive neovascular age-related macular degeneration with type 1 choroidal neovascularization including polypoidal choroidal vasculopathy. Sci Rep. 2021;11:6759.
9. Matsumoto H, Hoshino J, Mukai R, Nakamura K, Akiyama H. One-year results of treat-and-extend regimen with intravitreal

brolucizumab for treatment-naive neovascular age-related macular degeneration with type 1 macular neovascularization. Sci Rep. 2022;12:8195.
10. Matsumoto H, Hoshino J, Nakamura K, Akiyama H. Two-year outcomes of treat-and-extend regimen with intravitreal brolucizumab for treatment-naive neovascular age-related macular degeneration with type 1 macular neovascularization. Sci Rep. 2023;13:3249.
11. Yamamoto A, Okada AA, Kano M, Koizumi H, Saito M, Maruko I, et al. One-year results of intravitreal aflibercept for polypoidal choroidal vasculopathy. Ophthalmology. 2015;122:1866–72.
12. Koizumi H, Kano M, Yamamoto A, Saito M, Maruko I, Kawasaki R, et al. Short-term changes in choroidal thickness after aflibercept therapy for neovascular age-related macular degeneration. Am J Ophthalmol. 2015;159:627–33.
13. Morimoto M, Matsumoto H, Mimura K, Akiyama H. Two-year results of a treat-and-extend regimen with aflibercept for polypoidal choroidal vasculopathy. Graefes Arch Clin Exp Ophthalmol. 2017;255:1891–7.
14. Hikichi T, Higuchi M, Matsushita T, Kosaka S, Matsushita R, Takami K, et al. One-year results of three monthly ranibizumab injections and as-needed reinjections for polypoidal choroidal vasculopathy in Japanese patients. Am J Ophthalmol. 2012;154:117–24 (**e1**).
15. Yamazaki T, Koizumi H, Yamagishi T, Kinoshita S. Subfoveal choroidal thickness after ranibizumab therapy for neovascular age-related macular degeneration: 12-month results. Ophthalmology. 2012;119:1621–7.
16. Koh A, Lai TYY, Takahashi K, Wong TY, Chen LJ, Ruamviboonsuk P, et al. Efficacy and safety of Ranibizumab with or without verteporfin photodynamic therapy for polypoidal choroidal vasculopathy: a randomized clinical trial. JAMA Ophthalmol. 2017;135:1206–13.
17. Patil NS, Dhoot AS, Popovic MM, Kertes PJ, Muni RH. Risk of intraocular inflammation after injection of antivascular endothelial growth factor agents: a meta-analysis. Retina. 2022;42:2134–42.
18. Heier JS, Khanani AM, Quezada Ruiz C, Basu K, Ferrone PJ, Brittain C, et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomised, double-masked, phase 3, non-inferiority trials. Lancet. 2022;399:729–40.
19. Matsumoto H, Hoshino J, Nakamura K, Nagashima T, Akiyama H. Short-term outcomes of intravitreal faricimab for treatment-naive neovascular age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 2023;261:2945–52.
20. Mukai R, Kataoka K, Tanaka K, Miyara Y, Maruko I, Nakayama M, et al. Three-month outcomes of faricimab loading therapy for wet age-related macular degeneration in Japan. Sci Rep. 2023;13:8747.
21. Maruyama-Inoue M, Yanagi Y, Inoue T, Kadonosono K. Comparison of functional and morphologic changes between brolucizumab and faricimab in neovascular age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 2023.
22. Spaide RF, Jaffe GJ, Sarraf D, Freund KB, Sadda SR, Staurenghi G, et al. Consensus nomenclature for reporting neovascular age-related macular degeneration data: consensus on neovascular age-related macular degeneration nomenclature study group. Ophthalmology. 2020;127:616–36.
23. Iijima H, Iida T, Imai M, Gohdo T, Tsukahara S. Optical coherence tomography of orange-red subretinal lesions in eyes with idiopathic polypoidal choroidal vasculopathy. Am J Ophthalmol. 2000;129:21–6.
24. Yanai H. Statcel—the useful add-in software forms on Excel. 4th ed. Tokyo: OMS; 2015.
25. Ohji M, Takahashi K, Okada AA, Kobayashi M, Matsuda Y, Terano Y, et al. Efficacy and safety of intravitreal aflibercept treat-and-extend regimens in exudative age-related macular degeneration: 52- and 96-week findings from ALTAIR: a randomized controlled trial. Adv Ther. 2020;37:1173–87.
26. Chugai Pharmaceutical Co., Ltd. Faricimab CTD: 2.7.2.2.4.3.3. Pharmacodynamics, 2022. Available at: https://www.pmda.go.jp/drugs/2022/P20220406001/index.html. Accessed 25th Oct 2023 (in Japanese).
27. Angermann R, Huber AL, Nowosielski Y, Salcher S, Gasser T, Seifarth C, et al. Changes in systemic levels of vascular endothelial growth factor after intravitreal injection of aflibercept or brolucizumab for neovascular age-related macular degeneration. Retina. 2022;42:503–10.
28. Schmidt-Erfurth U, Mulyukov Z, Gerendas BS, Reiter GS, Lorand D, Weissgerber G, et al. Therapeutic response in the HAWK and HARRIER trials using deep learning in retinal fluid volume and compartment analysis. Eye (Lond). 2023;37:1160–9.
29. Ohji M, Okada AA, Sasaki K, Moon SC, Machewitz T, Takahashi K, et al. Relationship between retinal fluid and visual acuity in patients with exudative age-related macular degeneration treated with intravitreal aflibercept using a treat-and-extend regimen: subgroup and post-hoc analyses from the ALTAIR study. Graefes Arch Clin Exp Ophthalmol. 2021;259:3637–47.