Intravitreal faricimab for Neovascular Age-related Macular Degeneration: Consensus Pathway by an Expert Panel of UK Retina Specialists

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Key Clinical Question

What are the recommendations and guidelines for implementing faricimab into routine clinical practice in the UK to treat patients with neovascular Age-related Macular Degeneration (nAMD) ?

Introduction

- In September 2022 and January 2023, roundtable meetings with an expert panel of UK retina specialists were held to update the current consensus on the management of neovascular age-related macular degeneration (nAMD) and review pivotal clinical trial results evaluating faricimab for nAMD, the licensed posology for faricimab and National Institute for Health and Care Excellence (NICE) appraisal guidance.
- The expert panel developed a consensus statement that reflects evidence-based best practice as well as clinical experience in the treatment of nAMD and suggested pathway recommendations for integrating faricimab as a novel treatment option for nAMD into UK clinical practice, as part of evolving medical retina protocols. This poster summarises the expert panel's consensus and recommendations.
- The expert panel meetings, as well as this publication and its development, were commissioned and funded by Roche Products Ltd.

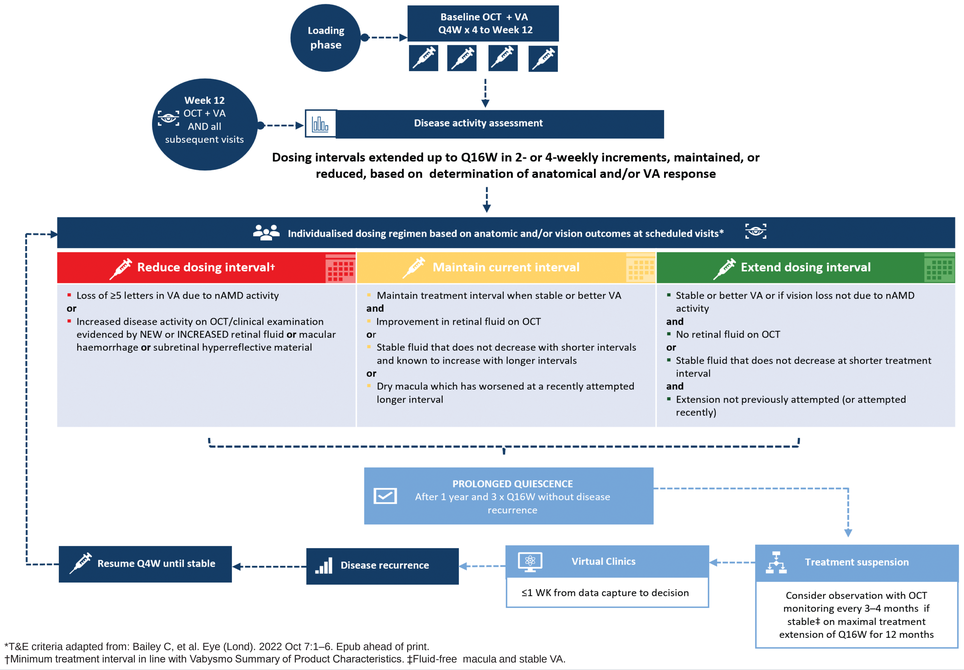
Methods

- The National nAMD Consensus Statement was published in Eye News February 2023.
- The expert panel of UK retina specialists created consensus recommendations for:
  - Integrating faricimab for nAMD into clinical practice including the preferred practice in the management of treatment naïve patients with nAMD
  - Integrating faricimab into existing nAMD treatment pathways
  - Switching of anti-VEGF agents for patients with persistent or refractory disease activity due to nAMD
  - Service organisation and implementation of faricimab in nAMD clinic services and treatment suspension in nAMD.
  - Review of pivotal clinical trial data, marketing authorisation and NICE guidance

Conclusions

- This is the first national consensus group, formed by an expert panel of UK retina specialists, to review recent clinical data, the recommended posology for faricimab in nAMD and to develop and propose a personalised T&E pathway for faricimab in nAMD to inform and guide implementation in clinical practice.
- Faricimab is a novel, bispecific antibody targeting both Ang-2 and VEGF-A pathways. The durability of faricimab treatment has been tested in Phase 3 clinical trials and shown to maintain disease control up to 16 weeks between injections making it ideal for a personalised T&E regimen.
- Faricimab is a useful addition to the clinicians armamentarium of nAMD therapies which is effective, durable and well tolerated. It should help to reduce the treatment burden for a large proportion of patients with nAMD and their carers and liberate capacity in our AMD services.

1. Management of nAMD with faricimab: recommended clinical pathway.



*T&E criteria adapted from: Bailey C, et al. Eye (Lond). 2022 Oct 7:1–6. Epub ahead of print.
†Minimum treatment interval in line with Vabysmo Summary of Product Characteristics. ‡Fluid-free macula and stable VA.

2. General considerations and implementation recommendations

Preferred practice in the management of treatment-naïve patients with nAMD

- Treatment initiation with a loading phase of Q4W IVT anti-VEGF injections is recommended, followed by a T&E regimen based on VA and OCT assessment. Treatment may be extended by 2- or 4-week increments up to a maximum of 16 weeks based on disease activity and in accordance with the recommended drug posology[2].
- There is no requirement for monthly monitoring between injections unless there is sudden vision loss or fluid recurrence secondary to nAMD. However, the expert panel recommend OCT assessment at 12 weeks and all subsequent visits to help guide extension.
- Disease activity assessment is based on anatomic and visual outcomes using OCT, VA assessment and clinical examination. Presence and location of fluid should be considered; persistent IRF is associated with worse visual outcomes compared with resolved IRF, while small amounts of residual SRF only may be tolerated after initially aiming for a dry macula[3].
- Clinicians should assess for other potential causes of vision loss in the treated eye if visual acuity declines and are encouraged to actively monitor/consider the patient's fellow eye with OCT.
- When decreasing the treatment interval under a T&E protocol, return to the dosing interval at the last stable visit, with a scheduled follow-up review at the clinician's discretion. For eyes achieving stable anatomic and vision outcomes, consider resumption of extended dosing with 2- or 4-week interval adjustments.
- Some patients with nAMD require frequent retreatment to maintain vision; also, reactivation of exudative disease activity may occur after interval extension and treatment more frequently than every 8 weeks may be needed.

Integrating faricimab into existing nAMD treatment pathways

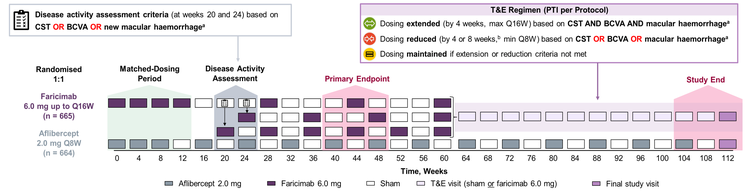
- Clinical trial evidence supports faricimab therapy for nAMD using a personalised, flexible T&E approach[4].
- When starting treatment with faricimab, adhere to the recommended posology of 4 initial monthly doses. Treatment may then be individualised using a T&E approach up to Q16W[3]. Most clinical centres are initially likely to extend dosing intervals progressively using the classic 2-week interval adjustment, although 4-week increments may be utilised.
- Interval reductions of up to 8 weeks may be implemented if deemed necessary. Treatment intervals shorter than 21 days between faricimab injections have not been studied[3].
- Following baseline assessment and after treatment initiation with a monthly loading phase, undertake OCT and visual acuity (refracted in some centres) assessment so treatment can be individualised; there is no need for additional slit-lamp examination or widefield imaging during the treatment loading phase.
- The expert panel were reassured that, in routine clinical practice, the recommended posology for faricimab in nAMD allows individualised Q4W–Q16W dosing intervals based on anatomic and visual acuity response. In cases of aggressive reactivation of disease after interval extension beyond Q4W dosing, clinicians may consider monthly treatment until stable.

Service organisation and implementation of faricimab in nAMD clinic services

- The standard of care for the treatment of nAMD is IVT anti-VEGF monotherapy however, discontinuation, under treatment and suboptimal visual outcomes with anti-VEGF monotherapy remain challenges in clinical practice[5].
- Clinician assessment to formulate an appropriate treatment plan should be completed no later than one week from acquisition/ transmission of patient data from virtual assessment clinics.
- Efficacy, durability, safety and overall costs are important considerations when choosing the most appropriate therapy.
- Faricimab is a novel treatment option for nAMD that may provide added flexibility by allowing rapid extension of dosing .after a loading phase, up to Q16W, in many patients without compromising visual acuity gains.
- The panel recommended that faricimab therapy should be integrated and delivered as part of existing medical retina treatment pathways, consistent with current clinical practice and professional guidance.

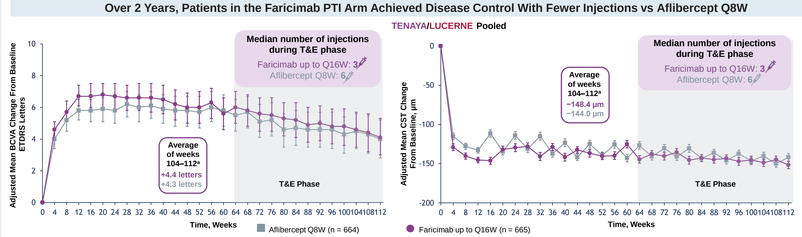
TENAYA/LUCERNE (NCT03823287/NCT03823300) were randomised, active comparator–controlled, 112-week trials that evaluated the efficacy, durability and safety of faricimab compared with aflibercept in patients with nAMD

TENAYA and LUCERNE Trial Design: Faricimab nAMD Trials Use Disease Criteria Reflective of Clinical Practice[6]



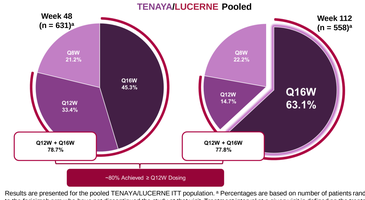
[a] Per the investigator. [b] If ≥ 2 of the reduction criteria were met or 1 criterion includes new macular haemorrhage, the interval was reduced to an 8-week interval.

Over 2 Years, Patients in the Faricimab PTI Arm Achieved Disease Control With Fewer Injections vs Aflibercept Q8W



Results are based on a mixed model for repeated measures analysis in the ITT population. The median number of injections is based on the safety-evaluable population. 95% CIs are shown. CST is measured as ILM-RPE, as graded by central reading centre.
[a]Adjusted mean change from baseline at 2 years, averaged over weeks 104, 108 and 112. PTI dosing regimen was delayed in some patients due to dose holds or missed visits.

~80% of Faricimab-Treated Patients Achieved ≥ Q12W Dosing at 2 Years



Results are presented for the pooled TENAYA/LUCERNE ITT population. [a] Percentages are based on number of patients randomised to the faricimab arm who have not discontinued the study at that visit. Treatment interval at a given visit is defined as the treatment interval decision followed at that visit. Interval at week 112 is calculated using data recorded at week 108. [b] Weeks 60–112.

Faricimab Was Well Tolerated Through Study End

	TENAYA/LUCERNE Pooled	
AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	Faricimab Up to Q16W n = 664	Aflibercept Q8W n = 662
Ocular AEs[b]	358 (53.9%)	345 (52.1%)
Serious ocular AEs[b]	29 (4.4%)	29 (4.4%)
Ocular AEs of special interest[c]	25 (3.8%)	27 (4.1%)
Intraocular inflammation events[d]	20 (3.0%)	15 (2.3%)
Uveitis	4 (0.6%)	3 (0.5%)
Iritis	8 (1.2%)	3 (0.5%)
Iridocyclitis	2 (0.3%)	1 (0.2%)
Vitritis	4 (0.6%)	1 (0.2%)
Post-procedural inflammation	0	5 (0.8%)
Chorioretinitis	1 (0.2%)	0
Keratic precipitates	2 (0.3%)	0
Non-infectious endophthalmitis	0	1 (0.2%)
Anterior chamber flare	0	1 (0.2%)
Endophthalmitis events	3 (0.5%)	2 (0.3%)
Retinal vasculitis events	0	0
Retinal occlusive events		
Retinal vein occlusion	0	0
Retinal artery occlusion	0	0
Retinal artery embolism	1 (0.2%)[e]	0
Serious non-ocular AEs	138 (20.8%)	162 (24.5%)
APTC events[f]	22 (3.3%)	20 (3.0%)

[a] Results are presented for the pooled TENAYA/LUCERNE safety-evaluable populations. Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. [b] Ocular AEs in the study eye only are presented. [c] Ocular AEs of special interest were defined as events associated with severe intraocular inflammation, events requiring surgical or medical intervention to prevent permanent loss of sight or events associated with BCVA loss of ≥ 30 letters for > 1 hour. [d] Excluding endophthalmitis. [e] Hollenhorst plaque that was reported at the end of year 1 and was not treatment related as per the investigator. [f] APTC events were adjudicated by an external independent committee; all other events were investigator reported.

Abbreviations: IVT, intravitreal; BCVA, best-corrected visual acuity; CST, central subfield thickness; max, maximum; min, minimum; nAMD, neovascular age-related macular degeneration; PTI, personalised treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat-and-extend. ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; ITT, intent-to-treat; RPE, retinal pigment epithelium; Q12W, every 12 weeks; AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; OCT, optical coherence tomography; VA, visual acuity; WK, week; Q4W, every 4 weeks

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Study and Product Disclosures

- Faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular edema in multiple countries worldwide and is not currently approved for use outside these indications
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