Health Technology Briefing
August 2022

Faricimab for macular oedema secondary to retinal vein occlusion

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33504	NICE ID: 11783	UKPS ID: 663105

Licensing and Market Availability Plans

In phase III clinical trials.

Summary

Faricimab is currently in clinical development for the treatment of macular oedema resulting from retinal vein occlusion (RVO). RVO is where a blockage happens in a vein in the back of the eye, stopping blood flow. Macular oedema is where fluid collects in the macula (area in the centre of the back of the eye important in detecting light to see things). This happens because the fluid cannot flow through the blocked veins. The build-up of fluid damages the eye and can result in irreversible vision problems. Faricimab is expected to reduce the treatment burden for patients as injections will be given less frequently than the treatments currently licensed.

Faricimab is a new type of antibody that exerts dual action by blocking the activity of two different proteins in the eye, vascular endothelial growth factor A (VEGF-A) and Ang-2, giving it a novel mechanism of action. Both proteins can lead to increased vision issues over time if not inhibited as they are released into the eye due to the blockage. The dual action of faricimab is expected to result in patients requiring less frequent dosages, compared to current treatment options that only target VEGF-A. Faricimab is administered via intravitreal injection into the eye. If licensed faricimab would offer a new treatment option for patients with macular oedema secondary to RVO.

Proposed Indication

Treatment of adult patients with macular oedema secondary to retinal vein occlusion (RVO).[1,2]

Technology

Description

Faricimab (vabysmo, RO6867461, RG7716) is a humanised bispecific IgG1 antibody that binds to and inhibits both vascular endothelial growth factor (VEGF)-A and angiopoietin-2 (Ang-2). VEGF-A inhibition by faricimab leads to the suppression of endothelial cell proliferation, neovascularization and vascular permeability. Ang-2 inhibition by faricimab is thought to promote vascular stability and desensitize blood vessels to the effects of VEGF-A.[3,4]

In the phase III studies COMINO and BALATON (NCT04740931, NCT04740905), faricimab will be administered to patients with macular oedema secondary to RVO, via intravitreal (IVT) injection (6mg, every four weeks for 24 weeks before being moved to a personalised treatment interval dosing regimen).[1,2]

Key Innovation

Faricimab is the first bispecific antibody designed for intraocular use. It has a novel mechanism of action by targeting and inhibiting both VEGF and Ang-2, different to already licensed drugs that only target VEGF. It is hypothesised that dual pathway inhibition of VEGF and Ang-2 could provide sustained efficacy (with enhanced durability relative to anti-VEGF therapy alone) in the treatment of retinal vascular diseases.[3]
The effectiveness of [VEGF therapies alone] in the real-world setting is frequently suboptimal, often attributed to poor adherence to treatment due to the burden of frequent monitoring and injections/treatment.[3] Visual benefits with faricimab given at up to 16-week intervals in the phase III trials TENAYA and LUCERNE demonstrates its potential to meaningfully extend the time between treatments with sustained efficacy, thereby reducing treatment burden in patients with nAMD, with results being non-inferior to aflibercept given every 8 weeks.[5] The advantages seen in other types of macular oedema for faricimab, may also be seen for RVO and would result in prolonged treatment intervals which would decrease treatment burden and improve patient compliance.[6] If licensed, faricimab will offer an additional treatment option for patients with macular oedema secondary to retinal vein occlusion.

Regulatory & Development Status

Faricimab has Marketing Authorisation in the UK for the treatment of adult patients with neovascular (wet) age-related macular degeneration, and visual impairment due to diabetic macular oedema.[4,7]

Faricimab is not in clinical trials for any other indications.[8]

Patient Group

Disease Area and Clinical Need

RVO occurs following a complete or partial obstruction (most commonly due to a blood clot) in the central retinal vein or one of its branches and results in a sudden or gradual, painless, reduction in vision.[9,10] Blockage of one of the veins draining blood out of the eye causes blood and other fluids to leak into the retina, causing bruising and swelling as well as lack of oxygen. This interferes with the light receptor cells

and reduces vision. Branch RVO is due to obstruction of one of the four retinal veins. Central RVO is due to obstruction of the main vein formed from the four branches which drain blood from the retina. In general, visual loss is more severe if the central retinal vein is occluded. Vision is reduced secondary to either damage to the retina caused by the obstruction of blood flow through the veins, or from a collection of fluid in the retina (macular oedema) which causes persistent bruising and swelling.[9] RVO is most common in people aged 60-80 and is rarely seen in those aged under 40 years. The most common risk factors include arterial hypertension, diabetes, hyperlipidaemia, glaucoma, smoking, and a history of certain conditions such as stroke or coagulation disorders.[9,10]

RVO is the second most common retinal vascular disorder and affected 16.4 million people worldwide in 2008, with the global prevalence of any type of RVO being 0.77% in those aged 30-89 in 2015.[11] No prevalence or incidence data has been identified for England and Wales.[12] In England (2020-21), there were 9,290 finished consultant episodes (FCE) for retinal vascular occlusions (ICD-10 code: H34), with 9,121 hospital admissions that resulted in 8,643 day cases and 994 FCE bed days.[13]

Recommended Treatment Options
NICE recommends the use of anti-VEGF IVT injections (aflibercept or ranibizumab), or a dexamethasone IVT implant for adults with macular oedema secondary to RVO in the branch or central veins.[14]

Clinical Trial Information

Trial	**COMINO;** NCT04740931, 2020-000441-13; A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of Faricimab in Patients With Macular Edema Secondary to Central Retinal or Hemiretinal Vein Occlusion **Phase III** – Active, not recruiting **Location(s):** 9 EU countries, UK, USA, and other countries **Primary completion date:** August 2022
Trial Design	Randomised, parallel assignment, double-masked, active comparator controlled
Population	N= 730; Subjects with macular oedema secondary to central retinal or hemiretinal vein occlusion; aged 18 years and older
Intervention(s)	Faricimab 6mg IVT injection, once every four weeks for 24 weeks before being moved to a personalised interval dosing regimen
Comparator(s)	Aflibercept 2mg IVT injection, once every four weeks for 20 weeks, then 6mg faricimab via IVT injection from week 24-72
Outcome(s)	Primary outcome: Change from baseline in best-corrected visual acuity (BCVA) at week 24 [Time Frame: Baseline and Week 24] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Trial	**BALATON;** NCT04740905, 2020-000440-63; A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of Faricimab in Patients With Macular Edema Secondary to Branch Retinal Vein Occlusion **Phase III** – Active, not recruiting **Location(s):** 9 EU countries, UK, USA, and other countries **Primary completion date:** July 2022
Trial Design	Randomised, parallel assignment, double-masked, active comparator controlled
Population	N= 553; Subjects with macular oedema secondary to branch retinal vein occlusion; aged 18 years and older
Intervention(s)	Faricimab 6mg IVT injection, once every four weeks for 24 weeks before being moved to a personalised interval dosing regimen
Comparator(s)	Aflibercept 2mg IVT injection, once every four weeks for 20 weeks, then 6mg faricimab via IVT injection from week 24-72
Outcome(s)	Primary outcome: Change from baseline in best-corrected visual acuity (BCVA) at week 24. [Time Frame: Baseline and Week 24] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The NHS list price of one 28.8mg/0.24ml vial of faricimab is £857.[4,15]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion (TA409). September 2016.
- NICE technology appraisal. Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion (TA305). February 2014.
- NICE technology appraisal. Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion (TA283). May 2013.
- NICE technology appraisal. Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion (TA229). July 2011.
- NICE interventional procedure guidance. Arteriovenous crossing shethotomy for branch retinal vein occlusion (IPG334). March 2010.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Ophthalmology (Adult). D12/S/a.

Other Guidance

- The College of Optometrists. Clinical management guidelines: Retinal vein occlusion. 2021.[10]
- The Royal College of Ophthalmologists. Clinical guidelines: Retinal vein occlusion (RVO) consultation document. 2021.[16]
- European Society of Retina Specialists. Guidelines for the management of retinal vein occlusion. 2019.[17]

Additional Information

References

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