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HEALTH TECHNOLOGY BRIEFING NOVEMBER 2020

Faricimab for neovascular age-related macular degeneration

NIHRIO ID	26674	**NICE ID**	10421
Developer/Company	Roche Products Limited	**UKPS ID**	657154

Licensing and market availability plans	Currently in phase III clinical trials.

SUMMARY

Faricimab is in clinical development for the treatment of neovascular (wet) age-related macular degeneration (nAMD). AMD is an eye condition that blurs the centre of a person's vision and is the most common cause of sight loss in the developed world. There are two types of AMD – wet and dry. Wet AMD develops when a protein called vascular endothelial growth factor-A (VEGF-A) causes abnormal blood vessels to grow in the back of the eye which leak blood or fluid that results in a rapid loss of central vision. Current treatment for wet AMD involves monthly injections of anti-VEGF agents to maintain vision. There is a need for treatments that have greater durability in order to reduce the treatment burden on patients, caregivers, healthcare professionals and healthcare systems.

Faricimab is an antibody given by intravitreal injection that binds to both VEGF-A and angiopoietin-2 which results in blood vessels becoming more stable, leaking less blood and fluid and reduced inflammation. Faricimab has been shown in clinical trials to have an extended durability compared to other anti-VEGF agents so fewer injections will be required. If licensed, faricimab will offer an additional treatment option for patients with neovascular AMD.

PROPOSED INDICATION

Treatment of adults aged 50 years and older with neovascular age-related macular degeneration (AMD).[1-3]

TECHNOLOGY

DESCRIPTION

Faricimab (RO6867461, RG7716) is the first bispecific antibody designed for intraocular use. Faricimab simultaneously and independently binds and neutralises vascular endothelial growth factor (VEGF)-A and angiopoietin-2 (Ang-2), leading to vascular stabilisation and decreased permeability and inflammation.[4,5] Modifications to the Fc region suppress effector function to reduce potential for inflammation and to facilitate systemic clearance for improved safety.[5]

Faricimab is currently in clinical development for the treatment of neovascular AMD. In the phase III clinical trials TENAYA (NCT03823287, EudraCT 2018-002152-32) and LUCERNE (NCT03823300, EudraCT 2018-004042-42) participants receive 120mg/ml of faricimab by intravitreal injection.[6,7]

INNOVATION AND/OR ADVANTAGES

Current standard of care for neovascular AMD involves frequent intravitreal anti-VEGF injections to maintain visual outcomes. However, frequent office visits and injections required to maintain vision gains place a significant treatment burden on patients, caregivers, healthcare professionals and health care systems.[4]

Simultaneous neutralisation of Ang-2 and VEGF-A with faricimab has demonstrated its potential to provide sustained efficacy through extended durability. This may allow for fewer injections, addressing the high unmet need for more sustained treatments in the real world.[4]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Faricimab does not currently have Marketing Authorisation in the EU/UK for any indication.

Faricimab is also currently in phase II/III development for diabetic macular edema.[8]

PATIENT GROUP

DISEASE BACKGROUND

AMD is an eye disease that can blur the centre of a person's vision, it is the most common cause of age-related sight loss in the developed world.[9,10] There are two forms of AMD – dry and wet.[11] Wet or advanced neovascular AMD, is a serious type of AMD that happens when a protein called vascular endothelial growth factor (VEGF) makes too many blood vessels grow in the back of the eye.[10] These abnormal vessels leak blood or fluid which leads to scarring of

the macula and rapid loss of central vision.[12] The disease has a profound effect on quality of life of affected individuals and can make everyday activities like reading and recognising faces difficult.[13,14] Symptoms of wet AMD include: gaps or dark spots in a person's vision, objects appearing to change shape, size or colour, colours fading, finding bright light glaring and uncomfortable, difficulty adapting when moving from dark to light environments, words disappearing when a person is reading, and straight lines such as door frames and lampposts appearing distorted or bent.[12]

The causes of AMD are still not fully understood but some factors may increase a person's risk of developing the disease. Risk factors include advancing age, smoking, family history of AMD, being female, caucasian ethnicity, prolonged sun exposure and being obese.[15]

CLINICAL NEED AND BURDEN OF DISEASE

AMD is thought to affect half of the 370,000 people registered as blind or partially sighted in the UK.[9]

The prevalence of late AMD in the UK among people aged 50 years or over is 2.4% (from a meta-analysis applied to the UK 2007-09 population data). This increases to 4.8% in people aged 65 years or over, and 12.2% in people aged 80 years or over. The same study found the prevalence of neovascular AMD to be 1.2 to 6.3%.[16] Estimates indicate that around 39,800 people develop neovascular AMD in the UK each year; given the mid-year 2019 UK population estimate of 66,796,800 million, this equates to 596 cases per million per year.[16,17]

According to hospital episode statistics for England in 2018-19 there were 55,681 finished consultant episodes (FCE) for degeneration of macula and posterior pole (ICD-10 code H35.3) resulting in 55,163 admissions, 54,155 day cases and 1,084 FCE bed days.[18]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Neovascular AMD can be treated if caught early. At present the most effective treatment is in the form of injections of anti-VEGF agents into the eye.[11] Some patients have a particular pattern of blood vessels growing beneath the retina, which may remain stable without treatment. Current NICE guidance is that patients with very good vision should be monitored initially and only treated if their vision starts to deteriorate because the small risk involved in the treatment may outweigh the benefits.[11,16]

CURRENT TREATMENT OPTIONS

NICE guidelines currently recommend the following anti-VEGF treatments for neovascular AMD:[19]

- aflibercept
- ranibizumab

PLACE OF TECHNOLOGY

If licensed, faricimab will offer an additional treatment option for patients with neovascular AMD.[1-3]

CLINICAL TRIAL INFORMATION

Trial	**LUCERNE**, NCT03823300, EudraCT 2018-004042-42; A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of Faricimab in Patients With Neovascular Age-Related Macular Degeneration **Phase III** – Active, not recruiting.[a] **Locations:** EU countries (not incl UK), USA and other countries **Estimated primary completion date:** August 2021
Trial design	Randomised, parallel assignment, triple-masked, active comparator-controlled study
Population	N=640; adults aged 50 years and older; treatment-naïve choroidal neovascularization (CNV) secondary to AMD in the study eye
Intervention(s)	120mg/ml faricimab by intravitreal injection
Comparator(s)	Active comparator • 40mg/ml aflibercept by intravitreal injection Sham procedure • procedure to mimic an intravitreal injection
Outcome(s)	Primary outcome measure: Average change from baseline in best-corrected visual acuity (BCVA) at week 48 [Time frame: from baseline up to 48 weeks] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

Trial	**TENEYA**, NCT03823287, EudraCT 2018-002152-32; A Phase III, Multicenter, Randomised, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of Faricimab in Patients With Neovascular Age-Related Macular Degeneration **Phase III** – Active, not recruiting **Locations:** EU countries (incl UK), USA, Canada and other countries **Estimated primary completion date:** August 2021
Trial design	Randomised, parallel assignment, triple masked, active comparator-controlled study
Population	N=640; adults aged 50 years and older; treatment-naïve CNV secondary to AMD in the study eye

Intervention(s)	120mg/ml faricimab by intravitreal injection
Comparator(s)	Active comparator • 40mg/ml aflibercept by intravitreal injection Sham procedure • procedure to mimic an intravitreal injection
Outcome(s)	Primary outcome measure: Average change from baseline in BVCA at Week 48 [Time Frame: from baseline up to 48 weeks] See trial record for full list of outcome measures
Results (efficacy)	-
Results (safety)	-

Trial	**AVENUE**, NCT02484690; A Proof-of-Concept Study of Faricimab (RO6867461) in Participants With Choroidal Neovascularization (CNV) Secondary to Age-Related Macular Degeneration (AMD) **Phase II** – Completed **Location:** United States **Primary completion date:** 26 September 2017
Trial design	Parallel assignment, double-masked, randomised, active comparator controlled
Population	N=273; adults aged 50 years and older; treatment-naïve with CNV secondary to AMD
Intervention(s)	4 experimental arms with different doses of faricimab (intravitreal injection) • 1.5mg every 4 weeks (Arm B) • 6mg every 4 weeks (Arm C) • 6mg every 4-8 weeks (Arm D) • 6mg + 0.5mg ranibizumab every 4 weeks (Arm E)
Comparator(s)	0.5mg ranibizumab every 4 weeks by intravitreal injection (Arm A)
Outcome(s)	Primary outcome measures: • Mean change from baseline in best corrected visual acuity (BCVA) letter score at week 36, in treatment-naïve participants [Time frame: baseline, week 36] • Mean change from week 12 in BVCA letter score at week 36, in anti-VEGF incomplete responders [Time frame: weeks 12 and 36]
Results (efficacy)	At week 36, adjusted mean change in BCVA vs ranibizumab was 1.6 letters for arm B (P=0.52), -1.6 letters for arm C (P=0.53) and -1.5 letters for arm D (P=0.53). For arm E, adjusted mean change from week 12 was -1.7 letters (P=0.30). This trial did not meet its primary end point of superiority of faricimab over ranibizumab in BVCA at week 36. Although not superior to monthly ranibizumab as given in this trial, overall visual and anatomical gains noted with faricimab support pursuing phase 3 trials for a potential alternative to monthly anti-VEGF therapy.[20]

Results (safety)	214/262 participants (81.7%) experienced ≥1 adverse event (AE) during the study with incidence and type of AE similar across treatment arms. Ocular and systemic safety findings for faricimab observed in this trial were comparable with the safety profile of intravitreal anti-VEGF monotherapy with ranibizumab.[20]

Trial	**STAIRWAY**, NCT03038880; Simultaneous Blockade of Angiopoietin-2 and VEGF-A With the Bispecific Antibody RO6867461 (RG7716) for Extended Durability in the Treatment of Neovascular Age-Related Macular Degeneration **Phase II** – Completed **Location**: USA **Primary Completion date:** 11 January 2018
Trial design	Randomised, parallel assignment, double masked
Population	N=76; adults aged 50 years and older; treatment-naïve CNV secondary to AMD
Intervention(s)	120mg/ml faricimab by intravitreal injection
Comparator(s)	Active comparator • ranibizumab by intravitreal injection Sham procedure procedure to mimic an intravitreal injection
Outcome(s)	Primary outcome measure: • Change from baseline at BCVA at Week 40 using the early treatment diabetic retinopathy study (ETDRS)- like charts [Time Frame: baseline to week 40] See trial record for full list of outcome measures
Results (efficacy)	Faricimab-treated patients had rapid initial BCVA gains that were maintained throughout the study in patients dosed every 12 weeks (q12w) and every 16 weeks (q16w). At week 52, mean BVCA gains from baseline were 11.4, 10.1 and 9.6 letters for patients randomised to the faricimab q16w, faricimab q12w and ranibizumab q4w arms respectively with 46.4%, 33.3% and 37.5% of patients, respectively gaining ≥15 letters from baseline.[21]
Results (safety)	No new or unexpected safety signals were identified.[21]

ESTIMATED COST

The estimated cost of faricimab is not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Brolucizumab for treating wet age-related macular degeneration (GID-TA10455). Expected date of issue to be confirmed.
- NICE technology appraisal. Aflibercept solution for injection for treating wet age-related macular degeneration (TA294). July 2013.
- NICE technology appraisal. Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (TA155). May 2012.
- NICE guideline. Age-related macular degeneration (NG82). January 2018.
- NICE quality standard. Serious eye disorders (QS180). February 2019.
- NICE interventional procedure guidance. Epiretinal brachytherapy for wet age-related macular degeneration (IPG415). December 2011.
- NICE interventional procedure guidance. Limited macular translocation for wet age-related macular degeneration. (IPG339). May 2010.
- NICE interventional procedure guidance. Macular translocation with 360˚ retinotomy for wet-age related macular degeneration (IPG340). May 2010.
- NICE interventional procedure guidance. Transpupillary thermotherapy for age-related macular degeneration (IPG58). May 2004.
- NICE interventional procedure guidance. Radiotherapy for age-related macular degeneration (IPG49). March 2004.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

No relevant guidance identified.

OTHER GUIDANCE

- NICE Clinical Knowledge Summary. Macular degeneration – age related. March 2016.[22]
- European Society of retina Specialists (EURETINA). Guidelines for the management of neovascular age-related macular degeneration. 2014.[13]
- The Royal College of Ophthalmologists. Age-Related Macular Degeneration: Guidelines for Management. 2013.[23]

ADDITIONAL INFORMATION

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