Innovation Observatory

NHS National Institute for Health Research

EVIDENCE BRIEFING AUGUST 2018

Abicipar pegol for wet age related macular degeneration

NIHRIO ID	7084	**NICE ID**	9724
Developer/Company	Allergan Ltd and Molecular Partners	**UKPS ID**	646978

Licensing and market availability plans	Currently in phase III trials

SUMMARY

Abicipar pegol is an anti-VEGF-A therapy in clinical development for the treatment of wet age-related macular degeneration. Wet age-related macular degeneration is a chronic eye disease characterised by the formation and proliferation of blood vessels in the centre of the retina (a layer of tissue in the back of the eye that senses light and sends images to the brain). Wet age-related macular degeneration is a leading cause of central sight loss and blindness. Current treatment options include anti-VEGF-A therapies which are the current standard of care.

Abicipar pegol is a novel therapeutic approach that uses a new generation of genetically engineered proteins that exhibit highly specific and high-affinity target protein binding. As an anti-VEGF-A, it works by inhibiting the growth of immature blood vessels that grow in the retina, reducing the haemorrhaging and scarring that leads to vision impairment. Abicipar pegol has the potential to require less frequent injections into the eye than the current standard of care, while providing equal improvements in vision. If licensed this could be an effective treatment option with greater compliance for patients with wet age-related macular degeneration.

PROPOSED INDICATION

Neovascular age-related macular degeneration[a]

TECHNOLOGY

DESCRIPTION

Abicipar pegol (AGN-150998; Anti-VEGF DARPin®) is a long-acting mono-designed ankyrin repeat protein (DARPin).[1] DARPins are genetically engineered antibody mimetic proteins typically exhibiting highly specific and high-affinity target protein binding.[2] DARPins constitute a new class of potent, specific and versatile small-protein therapies. Abicipar pegol uses the DARPin platform to inhibit vascular endothelial growth factor A (VEGF-A).[1] VEGF-A encodes a heparin-binding protein, which exists as a disulfide-linked homodimer. This growth factor induces proliferation and migration of vascular endothelial cells, and is essential for both physiological and pathological angiogenesis.[3]

Abicipar pegol is currently in development for the treatment of wet age related macular degeneration (wet AMD). In the two phase III clinical trials (NCT02462928 and NCT02462486) abicipar pegol is administered to the eye by intravitreal injection, at a dose of 2mg, on day 1, week 4, and week 12, followed by injections every 12 weeks through week 96 or on day 1, week 4, and week 8, followed by injections every 8 weeks through week 96.[4, 5]

INNOVATION AND/OR ADVANTAGES

Abicipar pegol combines its small molecule size, high potency and long intra-vitreal half-life to offer the potential for less frequent injections into the eye than the current anti-VEGF standard of care, while providing equal improvements in vision.[6, 7] This may lead to greater patient treatment adherence and better treatment outcomes.

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Abicipar pegol does not currently have Marketing Authorisation in the EU for any indication.

Abicipar pegol is in phase II development for diabetic macular edema.[8]

Abicipar pegol is at phase II of development in the US (Maple Study, 1771-201-008, NCT03539549) to evaluate the safety and efficacy of abicipar pegol in 100 patients.

[a] Information from UK Pharma Scan

PATIENT GROUP

DISEASE BACKGROUND

Age-related macular degeneration (AMD) is one of the leading causes of irreversible sight loss in people over the age of 50 years. AMD is associated with loss of central vision with opaque or dark patches and distortion of vision. There are two main types of AMD, wet (neovascular) and dry (non-neovascular) AMD.[9, 10]

Wet AMD is characterised by the formation of immature blood vessels that grow between the retinal pigment epithelial cells and the photoreceptor cells in the centre of the retina. This is known as choroidal neovascularisation (CNV). These blood vessels easily haemorrhage and cause scarring in the macula leading to vision impairment. Wet AMD usually progresses much more quickly than dry AMD.[9] Older age is the major risk factor for AMD, with more than 10% of people older than 80 years having late AMD.[10]

The majority of people are affected by dry (atrophic) AMD which has a gradual and chronic presentation. Wet AMD, accounts for 10% of all cases of AMD, but about 60% of those are considered advanced at presentation. Progression of wet AMD varies from a few months to three years. If left untreated, the diagnosis is poor with a significant visual loss (6/60 or worse) occurring within two to three years.[11]

People with macular degeneration retain their peripheral vision but lose central vision. Loss of central vision, particularly when affecting both eyes, is associated with a loss of quality of life, affecting the ability to read, recognise faces and drive, and with an increased risk of falls and potentially significant loss of independence. Rapidly deteriorating vision has a major impact on emotional wellbeing and individuals are likely to suffer depression and anxiety.[9]

CLINICAL NEED AND BURDEN OF DISEASE

The prevalence of late AMD in the UK among people aged 50 years or over is 2.4% (from a meta-analysis applied to 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. Estimates indicate that around 39,800 people develop wet AMD in the UK each year; given a total UK population of 60 million (at the time this study was published), this equates to 663 new cases per million per year.[12, 13]

The same study, using UK population data, found the prevalence of wet AMD to be 1.2−6.3%. Estimates from 2015 data indicate there may be 26,000 people with wet AMD eligible for treatment in the UK each year.[14]

Due to the aging population, the number of people with AMD will increase during the next decades.[13]

PATIENT TREATMENT PATHWAY

PATIENT PATHWAY

For most patients with AMD, management consists of 'best supportive care', this is mainly the case for those with the dry type of AMD. Visual rehabilitation, with teaching of skills and the provision of equipment to facilitate reading and other activities of daily living, may help people make the most of their remaining vision. However, the aim of therapy for people with wet AMD is to alter the progression of vision loss.[9, 14] In wet AMD, to stop vision loss from progressing regular eye injections and, very occasionally, photodynamic therapy is recommended.[15]

CURRENT TREATMENT OPTIONS

According to NICE guidelines for age-related macular degeneration (NG82) the following pharmacological and nonpharmacological treatments are considered for patients with AMD:[12]

Pharmacological management of wet AMD include:

- Antiangiogenic therapies such as ranibizumab and aflibercept

Non-pharmacological management of wet AMD include:

- Thermal laser therapy (for example, argon, diode) for treating drusen in people with early AMD (not to be offered alone or as adjunct to anti-VEGF as first-line treatment for wet AMD)

PLACE OF TECHNOLOGY

If approved, abicipar pegol has the potential to offer additional first line treatment with greater patient convenience offered through the less frequent eye injections needed than in current treatment options (ranibizumab and aflibercept).

CLINICAL TRIAL INFORMATION

Trial	**CEDAR, NCT02462928, EudraCT2014-004579-22 ; adults 50 years and older; abicipar pegol in combination with sham procedure to the study eye (experimental group A) vs abicipar pegol in combination with sham procedure to the study eye (experimental group B) vs ranibizumab; phase III**
Sponsor	Allergan
Status	Ongoing
Source of Information	Trial registry,[5] Press release[7]
Location	6 EU countries (not incl UK), USA and other countries.
Design	Randomised, active-controlled trial

Participants	n=939; aged over 50 years old; diagnosis of age-related macular degeneration in at least 1 eye; best corrected visual acuity of 20/40 to 20/320 in the study eye; best corrected visual acuity of 20/200 or better in the non-study eye
Schedule	Randomised to either: • Arm A: abicipar pegol 2 mg (group A). Abicipar pegol 2 mg administered to the study eye by intravitreal injection on day 1, week 4, and week 8, followed by injections every 8 weeks through week 96. A sham procedure to the study eye will be performed every 4th week that an injection of abicipar pegol is not performed; • Arm B: abicipar pegol 2 mg administered to the study eye by intravitreal injection on day 1, week 4, and week 12, followed by injections every 12 weeks through week 96. A sham procedure to the study eye will be performed every 4th week that an injection of abicipar pegol is not performed; • Arm C: ranibizumab (Lucentis®) administered to the study eye by intravitreal injection every 4 weeks from day 1 through week 96.
Follow-up	Not reported
Primary Outcomes	• Percentage of Patients with stable vision (i.e. patients who lose fewer than 15 letters in Best Corrected Visual Acuity (BCVA) from Baseline) at week 52[Time Frame: Baseline, Week 52]
Secondary Outcomes	• Mean change from Baseline in BCVA in the Study Eye [Time Frame: Baseline, Week 52] • Mean change from Baseline in Central Retinal Thickness (CRT) in the Study Eye [Time Frame: Baseline, Week 52] • Percentage of Patients with a BCVA Gain of ≥15 Letters in the Study Eye on the Early Treatment Diabetic Retinopathy Study (ETDRS) Scale [Time Frame: Baseline, Week 52] • Mean change from Baseline in the National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25) Composite Score [Time Frame: Baseline, Week 52] • EQ-5D collected at baseline and NEI-VFQ-25 – a disease specific PRO questionnaire that can be mapped to EQ-5D will be collected every 12 weeks throughout the study period[b]
Key Results	Preliminary results reported as: "The proportion of patients with stable vision in the abicipar dosed Q8 was 91.7 percent, in Q12 was 91.2 percent compared to ranibizumbab dosed Q4 95.5 percent"[7]
Adverse effects (AEs)	Preliminary AEs reported as: "Incidence of intraocular inflammation events was similar among the two abicipar treatment groups but higher than the ranibizumab arm and reported at 15.7 percent and 15.3 percent of patients in the abicipar Q8 and Q12 arms compared to 0.6 percent in the ranibizumab Q4 arm"[7]
Expected reporting date	Study completion date reported as May 2019

Trial	**SEQUOIA, NCT02462486, EudraCT2014-004580-20; abicipar pegol in combination with sham procedure to the study eye (experimental group A) vs abicipar pegol in combination with sham procedure to the study eye (experimental group B) vs ranibizumab; phase III**

[b] Information on quality of life measures provided by company

Sponsor	Allergan
Status	Ongoing
Source of Information	Trial registry,[4] Press release[7]
Location	6 EU countries (incl UK), Australia, Brazil, Canada, Japan, Peru, Russian Federation, South Africa, Taiwan, Turkey, United States
Design	Randomised, active-controlled trial
Participants	n=946; aged over 50 years old; diagnosis of age-related macular degeneration in at least 1 eye; best corrected visual acuity of 20/40 to 20/320 in the study eye; best corrected visual acuity of 20/200 or better in the non-study eye
Schedule	Randomised to either: • Arm A: abicipar pegol 2 mg (group A). Abicipar pegol 2 mg administered to the study eye by intravitreal injection on day 1, week 4, and week 8, followed by injections every 8 weeks through week 96. A sham procedure to the study eye will be performed every 4th week that an injection of abicipar pegol is not performed; • Arm B: abicipar pegol 2 mg administered to the study eye by intravitreal injection on day 1, week 4, and week 12, followed by injections every 12 weeks through week 96. A sham procedure to the study eye will be performed every 4th week that an injection of abicipar pegol is not performed; • Arm C: ranibizumab (Lucentis®) administered to the study eye by intravitreal injection every 4 weeks from day 1 through week 96.
Follow-up	Not reported
Primary Outcomes	• Percentage of Patients with stable vision (i.e. patients who lose fewer than 15 letters in Best Corrected Visual Acuity (BCVA) from Baseline) at week 52[Time Frame: Baseline, Week 52]
Secondary Outcomes	• Mean change from Baseline in BCVA in the Study Eye [Time Frame: Baseline, Week 52] • Mean change from Baseline in Central Retinal Thickness (CRT) in the Study Eye [Time Frame: Baseline, Week 52] • Percentage of Patients with a BCVA Gain of ≥15 Letters in the Study Eye on the Early Treatment Diabetic Retinopathy Study (ETDRS) Scale [Time Frame: Baseline, Week 52] • Mean change from Baseline in the National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25) Composite Score [Time Frame: Baseline, Week 52] • EQ-5D collected at baseline and NEI-VFQ-25 – a disease specific PRO questionnaire that can be mapped to EQ-5D will be collected every 12 weeks throughout the study period[c]
Key Results	Preliminary results reported as: "the proportion of patients with stable vision in abicipar dosed Q8 was 94.8 percent, in Q12 was 91.3 percent compared to ranibizumab dosed Q4 96.0 percent"[7]
Adverse effects (AEs)	Preliminary AEs reported as: "Overall treatment-emergent adverse events were similar among the 3 treatment arms, reported in 78.3 percent, 78.0 percent and 74.0 percent of patients receiving abicipar Q8, abicipar Q12 and ranibizumab Q4, respectively"[7]
Expected reporting date	Study completion date reported as May 2019

[c] Information on quality of life measures provided by company

ESTIMATED COST

The cost of abicipar pegol is not yet known.

The NHS indicative price of current treatment options is as follows:

- ranibizumab (Lucentis) 1.65mg/0.165ml solution for injection pre-filled syringes £551.00[16]
- aflibercept (Eylea) 2mg/50microlitres solution for injection vials £816.00[17]

ADDITIONAL INFORMATION

RELEVANT GUIDANCE

NICE GUIDANCE

- 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). August 2008. Last updated May 2012
- NICE guideline. Age-related macular degeneration (NG82). January 2018
- NICE interventional procedures guidance. Limited macular translocation for wet age-related macular degeneration (IPG339). May 2010
- NICE interventional procedures guidance. Macular translocation with 360° retinotomy for wet age-related macular degeneration (IPG340). May 2010

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- No relevant guidance identified

OTHER GUIDANCE

- NHS Coventry and Rugby. Clinical Commissioning policy for the Treatment of Wet Age-Related Macular Degeneration and Other Neovascularising Eye Conditions. January 2017.[18]
- The Royal College of Ophthalmologists. Age-Related Macular Degeneration: Guidelines for Management. September 2013.[19]

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NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.