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HEALTH TECHNOLOGY BRIEFING
JANUARY 2021

Ranibizumab Biosimilar for Age-related Macular Degeneration

NIHRIO ID	29709	**NICE ID**	10531
Developer/Company	Biogen Inc	**UKPS ID**	Not available

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

SUMMARY

Neovascular age-related macular degeneration (nAMD), also known as wet age-related macular degeneration (wet AMD), is a chronic eye disease characterised by the formation and proliferation of blood vessels underneath the retina (a layer of tissue in the back of the eye that senses light and sends images to the brain). nAMD is a leading cause of central sight loss and blindness.

Ranibizumab biosimilar is a type of antibody that is targeted against a particular protein and administered via injection into the eye (intravitreal injection). Ranibizumab biosimilar has been designed to attach to and block a substance called vascular endothelial growth factor A (VEGF-A). VEGF-A is a protein that makes blood vessels grow and leak fluid and blood, damaging the macula (the central part of the retina). By blocking VEGF-A, ranibizumab biosimilar would reduce the growth of the blood vessels and control leakage and swelling.

PROPOSED INDICATION

Adult patients aged 50 years and older with age-related macular degeneration (AMD) with active subfoveal choroid neovascularization (CNV).[1]

TECHNOLOGY

DESCRIPTION

Biosimilars are molecules that show similarities to existing medicines. They should be comparable in pharmacokinetics, pharmacodynamics, immunogenicity, safety, and efficacy to the existing medicine to be classed as biosimilar, but do not necessarily need to be identical.[2]

Ranibizumab biosimilar (SB11) is a humanised recombinant monoclonal antibody fragment targeted against human vascular endothelial growth factor A (VEGF-A).[3] It binds with high affinity to the VEGFA isoforms (e.g. $VEGF_{110}$, $VEGF_{121}$ and $VEGF_{165}$), thereby preventing binding of VEGF-A to its receptors VEGFR-1 and VEGFR-2. Binding of VEGF-A to its receptors leads to endothelial cell proliferation and neovascularisation, as well as vascular leakage, all of which are thought to contribute to the progression of the neovascular form of age-related macular degeneration, pathologic myopia and choroidal neovascularisation (CNV), or to visual impairment caused by either diabetic macular oedema or macular oedema secondary to retinal vein occlusion (RVO) in adults.[3] Ranibizumab biosimilar shows similar efficacy and safety to ranibizumab (Lucentis).[4,5]

In phase III clinical trials (NCT03150589) patients received 0.5mg of ranibizumab biosimilar via intravitreal injection (ITV) every four weeks for 48 weeks.[1]

INNOVATION AND/OR ADVANTAGES

If licenced ranibizumab biosimilar will offer an additional treatment option for patients with AMD and active subfoveal CNV, showing similar efficacy and safety to ranibizumab.[4]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

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

PATIENT GROUP

DISEASE BACKGROUND

AMD is one of the most common causes of visual impairment[6,7], and the Royal National Institute of Blind People (RNIB) reports that AMD is the most common cause of certification

for vision impairment.[8] There are two main types of AMD, neovascular (wet; nAMD) and non-neovascular (dry) AMD.[7]

nAMD 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. A protein known as vascular endothelial growth factor (VEGF), which induces new blood vessel formation (angiogenesis), vascular permeability and inflammation, has been implicated in the development and progression of CNV. CNV can be subdivided into classic and occult forms according to its appearance on investigation by fluorescein angiography.[7] Classic lesions appear early, are well-defined and leak intensely, whereas occult lesions appear early to mid-phase, leak less intensely and are ill-defined.[9] A mixture of classic and occult CNV can occur in the same lesion. CNV can also be described in terms of its location: the fovea is the central part of the macula, and CNV that develops below the foveal area is termed "subfoveal CNV".[7]

The condition usually affects people who are over 50 years old and the risk increases significantly with age. The most cited risk factor for AMD is cigarette smoking; the risk of developing AMD is 3.6 times greater for current and former smokers than for people who have never smoked.[7] Hypertension, obesity, lack of exercise, a diet high in fat, a diet low in omega 3 and 6 and a family history of nAMD are also common risk factors.[8]

nAMD accounts for 10% of all cases of AMD, but about 60% of those are considered advanced at presentation. Progression of nAMD 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.[10]

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.[7]

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.[11] The prevalence of nAMD in the UK among people aged 50 years and over is between 1.2 and 6.3%. Estimates indicate that around 39,800 people develop nAMD in the UK each year.[8]

There has been a significant increase in hospital activity in England for episodes with a primary diagnosis of AMD, from less than 10,000 episodes in the years 2005/06 to over 75,000 episodes in the years 2013/14.[8] Due to the aging population, the number of people with nAMD will increase during the next decades.[12]

In England, between 2019-20, there were 55,681 finished consultant episodes (FCE) of degeneration of macular and posterior pole (ICD-10 code H35.3), which includes those with

nAMD and active subfoveal CNV.[13-15] Of those FCE there were 54,155 day cases and 1,084 FCE bed days.[13]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

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 in those with dry AMD. However, the aim of therapy for people with wet AMD is to alter the progression of vision loss.[16] In wet AMD, to stop vision loss from progressing regular eye injections and, very occasionally, photodynamic therapy are recommended.[17]

CURRENT TREATMENT OPTIONS

According to NICE guidelines for age-related macular degeneration the following pharmacological treatments are considered for patients with nAMD:[8]

- Ranibizumab
- Aflibercept

PLACE OF TECHNOLOGY

If licenced, ranibizumab biosimilar will offer an additional treatment option for patients with AMD and active subfoveal CNV.

CLINICAL TRIAL INFORMATION

Trial	NCT03150589; **A Phase III Randomised, Double-masked, Parallel Group, Multicentre Study to Compare the Efficacy, Safety, Pharmacokinetics and Immunogenicity Between SB11 and Lucentis® in Subjects With Neovascular Age-related Macular Degeneration** **Phase III –** Completed **Location(s):** Europe (inc UK), US, India, Russian Federation, and Republic of Korea **Study completion date:** Dec 2019
Trial design	Randomised, quadruple-masked (Participant, Care Provider, Investigator, Outcomes Assessor) parallel assignment.
Population	N= 705; aged 50 years and older; newly diagnosed active subfoveal choroid neovascularisation (CNV) lesion secondary to age-related macular degeneration (AMD) of the study eye
Intervention(s)	SB11 (proposed ranibizumab biosimilar) 0.5mg via ITV injection every four weeks.

Comparator(s)	Active comparator: Lucentis® (ranibizumab).
Outcome(s)	• Change from baseline in Best Corrected Visual Acuity (BCVA) [Time Frame: Baseline and Week 8] • Change from baseline in Central Subfield Thickness (CST) [Time Frame: Baseline and Week 4]
Results (efficacy)	Least-squares mean (SE) changes in BCVA from baseline at week 8 were 6.2 (0.5) letters in the SB11 group vs 7.0 (0.5) letters in the ranibizumab group, with an adjusted treatment difference of -0.8 letter (90% CI, -1.8 to 0.2 letters). Least-squares mean (SE) changes in CST from baseline at week 4 were -108 (5) µm in the SB11 group vs -100 (5) µm in the ranibizumab group, with an adjusted treatment difference of -8 µm (95% CI, -19 to 3 µm).[4]
Results (safety)	Incidences of treatment-emergent adverse events (231 of 350 [66.0%] in SB11 vs 237 of 354 [66.9%] in ranibizumab), including serious treatment-emergent adverse events (44 of 350 [12.6%] in vs 44 of 354 [12.4%]) and treatment-emergent adverse events leading to study drug discontinuation (8 of 350 [2.3%] vs 5 of 354 [1.4%]), were similar in the SB11 and ranibizumab groups respectively. Immunogenicity was low, with a cumulative incidence of antidrug antibodies up to week 24 of 3.0% (10 of 330) in the SB11 group and 3.1% (10 of 327) in the ranibizumab group.[4]

ESTIMATED COST

The cost of ranibizumab biosimilar is not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Brolucizumab for treating wet age-related macular degeneration. (ID1254). Expected date of issue to be confirmed
- NICE technology appraisal. Aflibercept solution for injection for treating wet age-related macular degeneration (TA 294). July 2013
- NICE technology appraisal. Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (TA155). May 2012
- NICE clinical guideline. Age-related macular degeneration (NG82). January 2018
- NICE interventional procedures guidance. Miniature lens system implantation for advanced age-related macular degeneration (IPG565). September 2016
- NICE interventional procedures guidance. Macular translocation with 360° retinotomy for wet age-related macular degeneration (IPG340). May 2010
- NICE interventional procedures guidance. Limited macular translocation for wet age-related macular degeneration (IPG339). May 2010

- NICE interventional procedures guidance. Transpupillary thermotherapy for age-related macular degeneration (IPG58). May 2004
- NICE interventional procedures guidance. Radiotherapy for age-related macular degeneration (IPG49). March 2004

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

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

OTHER GUIDANCE

- European Society of Retina Specialists (EURETINA). Guidelines for the Management of Neovascular Age-Related Macular Degeneration. September 2014[18]
- The College of Optometrists and The Royal College of Ophthalmologists. Commissioning better eye care: Age-related macular degeneration. November 2013.[19]

ADDITIONAL INFORMATION

Samsung Bioepis Co., Ltd. is a collaborator for this technology, and will be the Marketing Authorisation Holder for this technology.[a]

Biogen did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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[a] Information provided by Biogen Inc

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