Novartis reports one year results of Phase III MERLIN study evaluating BEOVU® every four week dosing and provides update on BEOVU clinical program

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- BEOVU (brolucizumab-dbll) met MERLIN's primary endpoint of non-inferiority in change in best corrected visual acuity from baseline and superiority on anatomical secondary endpoints at year one versus aflibercept when given every four weeks following the loading phase(1)
- In this study evaluating every four week dosing, BEOVU was associated with higher rates of IOI including retinal vasculitis and retinal vascular occlusion versus aflibercept(1)
- Patient safety is of paramount importance and led Novartis to decide on early termination of the MERLIN study
- Novartis has also decided on early termination of the RAPTOR and RAVEN studies, which assessed the efficacy and safety of brolucizumab in retinal vein occlusion, and included six initial monthly injections
- Novartis has proactively communicated these data to health authorities and will pursue an update to the BEOVU prescribing information globally regarding every four week dosing
- When used on a two- to three-month interval following the loading phase, BEOVU remains an important and effective treatment option for appropriate patients with wet AMD(2,3)

EAST HANOVER, N.J., May 28, 2021 - Today, Novartis reported the first interpretable year one results of the Phase III MERLIN study, a two-year study initiated in H2 2018, assessing the efficacy and safety of BEOVU® (brolucizumab-dbll) 6 mg versus aflibercept 2 mg given every four weeks following the loading phase in patients with wet age-related macular degeneration (AMD) who have persistent retinal fluid despite anti-VEGF therapy.

BEOVU met MERLIN's primary endpoint of non-inferiority in change in best corrected visual acuity from baseline and superiority on select anatomical secondary endpoints at year one versus aflibercept when given every four weeks following the loading phase[1]. However, given every four weeks in MERLIN, IOI including RV, and RO were reported with a higher frequency in the BEOVU 6 mg every four weeks arm when compared to aflibercept 2 mg every four weeks (IOI: 9.3% vs 4.5% of which RV: 0.8% vs 0.0%; RO: 2.0% vs 0.0%)[1]. The overall rate of vision loss (15 letters or more) due to all causes was 4.8% in the BEOVU arm and 1.7% in the aflibercept arm[1].

"Although longer dosing intervals may benefit many people living with wet AMD and other retinal diseases, some are in need of monthly dosing to address persistent fluid. We initiated MERLIN and other clinical programs to explore BEOVU for these patients," said John Tsai, MD, Global Head of Drug Development and Chief Medical Officer, Novartis. "These data help inform our trials moving forward, so we can best determine how appropriate patients can benefit most from this important medicine."

Novartis evaluated all ongoing brolucizumab clinical programs assessing studies with four week dosing intervals after the loading phase. In the interest of patient safety, Novartis has decided to terminate the MERLIN study and the RAPTOR and RAVEN studies, which were assessing the efficacy and safety of brolucizumab with six initial monthly injections in retinal vein occlusion. All other relevant ongoing trial protocols will be amended to discontinue four week dosing intervals after the loading phase. Clinical trial investigators have been informed and will appropriately follow up with their patients. Physicians should not treat patients with BEOVU 6 mg at intervals less than two months beyond the first three doses.

Novartis has proactively communicated these data to health authorities and will pursue an update to the BEOVU prescribing information globally.

When used on a two- to three-month interval following the loading phase, BEOVU continues to be an important and effective treatment option for appropriate patients with wet AMD[2,3]. Novartis remains committed to supporting the retina community with information regarding BEOVU. BEOVU is contraindicated in patients with ocular or periocular infections, active intraocular inflammation or known hypersensitivity to brolucizumab[4].

Further analysis of the clinical data from MERLIN is ongoing, and detailed data will be presented at an upcoming medical meeting. Novartis has a strong ongoing commitment to Ophthalmology and to bringing innovative treatments to patients with or at risk of developing eye conditions where there is a high unmet need.

About wet AMD

Wet AMD is the leading cause of severe vision loss and legal blindness in people over the age of 65 in North America, Europe, Australia and Asia, impacting an estimated 20 million people worldwide[5-7]. Wet AMD occurs when abnormal blood vessels form underneath the macula, the area of the retina responsible for sharp, central vision[8-10]. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage to the macula[8-10].

Early symptoms of wet AMD include distorted vision (or metamorphopsia) and difficulties seeing objects clearly[11]. Prompt diagnosis and intervention are essential. As the disease progresses, cell damage increases, further reducing vision quality[12]. This progression can lead to a complete loss of central vision, leaving the patient unable to read, drive or recognize familiar faces and potentially depriving them of their independence[12,13]. Without treatment, vision can rapidly deteriorate[14].

About BEOVU (brolucizumab-dbll)

BEOVU (brolucizumab-dbll, also known as RTH258) is approved for the treatment of wet age-related macular degeneration (AMD) in more than 60 countries, including in the US, EU, UK, Japan, Canada and Australia[4,15-18]. Additional trials, which study the effects of brolucizumab in patients with wet AMD, diabetic macular edema (DME), and proliferative diabetic retinopathy (PDR), are currently ongoing.

INDICATIONS AND USAGE

BEOVU® (brolucizumab-dbll) injection is indicated for the treatment of Neovascular (Wet) Age-related Macular Degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

BEOVU is contraindicated in patients with ocular or periocular infections, active intraocular inflammation or known hypersensitivity to brolucizumab or any of the excipients in BEOVU. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachment

Intravitreal injections, including those with BEOVU, have been associated with endophthalmitis and retinal detachment. Proper aseptic injection techniques must always be used when administering BEOVU. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

Retinal Vasculitis and/or Retinal Vascular Occlusion

Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of BEOVU. Patients should be instructed to report any change in vision without delay.

Increase in Intraocular Pressure

Acute increases in intraocular pressure (IOP) have been seen within 30 minutes of intravitreal injection including with BEOVU. Sustained IOP increases have also been reported. Both IOP and perfusion of the optic nerve head must be monitored and managed appropriately.

Thromboembolic Events

Although there was a low rate of arterial thromboembolic events (ATEs) observed in the BEOVU clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. Arterial thromboembolic events are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The ATE rate in the two controlled 96-week neovascular AMD studies (HAWK and HARRIER) during the first 96-weeks was 4.5% (33 of 730) in the pooled brolucizumab arms compared with 4.7% (34 of 729) in the pooled aflibercept arms.

ADVERSE REACTIONS

Serious adverse reactions including endophthalmitis, retinal detachment, retinal vasculitis and/or retinal vascular occlusion, increases in intraocular pressure, and arterial thromboembolic events have occurred following intravitreal injections with BEOVU.

The most common adverse events (≥5% of patients) with BEOVU were vision blurred, cataract, conjunctival hemorrhage, vitreous floaters and eye pain.

As with all therapeutic proteins, there is a potential for an immune response in patients treated with BEOVU. Anti-brolucizumab antibodies were detected in the pre-treatment sample of 36% to 52% of treatment naive patients. After initiation of dosing, anti-brolucizumab antibodies were detected in at least one serum sample in 53% to 67% of patients treated with BEOVU. Intraocular inflammation was observed in 6% of patients with anti-brolucizumab antibodies detected during dosing with BEOVU. The significance of anti-brolucizumab antibodies on the clinical effectiveness and safety of BEOVU is not known.

Please see full Prescribing Information.

About Novartis in Ophthalmology

At Novartis, our mission is to discover new ways to improve and extend people's lives. In ophthalmology, we develop and deliver life-changing medicines and therapies for diseases and conditions from front to back of the eye, enabled by data and transformative technologies. Our ophthalmic solutions reach more than 150M people per year, from premature infants to the elderly.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 16,000 people in the United States. For more information, please visit https://www.novartis.us.

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