Novartis announces positive results from Phase III trials of BEOVU® in diabetic macular edema, including dosing intervals up to 16 weeks

Aug 17, 2021

- *Results from year two of the pivotal Phase III KITE clinical trial reaffirmed visual acuity gains and fluid reduction findings as well as safety profile from year one*[1,2]
- *In key fluid-related secondary endpoints from KITE at year two, BEOVU® (brolucizumab-dbll) 6 mg demonstrated greater reductions in central subfield thickness, and fewer patients had intraretinal and/or subretinal fluid versus aflibercept*[1]
- *A majority of patients who successfully completed an initial 12-week cycle following the loading phase were maintained on a 12- or 16-week dosing interval through year two of the KITE study*[1]
- *In KITE, IOI rates were 2.2% for BEOVU vs. 1.7% for aflibercept, no retinal vasculitis reported in either arm; equivalent rates of retinal vascular occlusion for both treatments (0.6%)*[1]
- *Additionally, KINGFISHER, a one-year Phase III study, demonstrated that BEOVU was non-inferior to aflibercept in mean change from baseline in best-corrected visual acuity when dosed every four weeks with an overall well-tolerated safety profile*[3]
- *Novartis has submitted its applications for BEOVU in the treatment of DME to both the FDA and the EMA, supported by findings from KESTREL and KITE pivotal trials, and plans to submit applications in other markets in due course*

East Hanover, August 17, 2021 - Novartis today announced positive results from two Phase III clinical trials assessing BEOVU® (brolucizumab-dbll) 6 mg versus aflibercept 2 mg in patients with diabetic macular edema (DME). Year two of the pivotal KITE* trial evaluated BEOVU on up to 16-week dosing intervals, and the one-year KINGFISHER study evaluated BEOVU dosed every four weeks[1,3]. Both trials demonstrated an overall well-tolerated safety profile.

Results from year two (week 100) of KITE demonstrated that a majority of patients who successfully completed an initial 12-week cycle following the loading phase were maintained on a 12- or 16-week dosing interval through the end of the study[1]. As previously reported, KITE met its primary endpoint of non-inferiority to aflibercept in best-corrected visual acuity (BCVA) from baseline at year one (week 52). At year one, BEOVU showed greater reductions versus aflibercept in central subfield thickness (CSFT) and in number of eyes with intraretinal fluid and/or subretinal fluid (IRF/SRF), which were key fluid-related secondary endpoints. Year two results were consistent with those seen at year one, including maintenance of BCVA and greater reductions in CSFT and in number of eyes with IRF/SRF treated with BEOVU versus aflibercept[1,2]. CSFT is a key indicator of fluid in the retina, and fluid is a key marker of disease activity[4,5]. Year two findings from KESTREL, another pivotal Phase III trial of BEOVU in DME, are due to read out in Q4 of this year.

“Patients with DME often struggle to adhere to burdensome treatment schedules as they manage various comorbidities related to diabetes,” said Prof. Dr. Justus Garweg, Clinic Director, Berne Eye Clinic at Lindenhof Hospital, Switzerland. “The extended dosing and fluid resolution observed in the KITE clinical trial suggest BEOVU has the potential to manage the disease in appropriate patients with a relaxed loading phase every six weeks, and dosing intervals as infrequent as every twelve or sixteen weeks.”

Another Phase III trial, KINGFISHER, met its primary endpoint of non-inferiority to aflibercept in change in BCVA from baseline at year one (week 52) when dosed every four weeks[3]. BEOVU also demonstrated superiority versus aflibercept in key fluid-related secondary endpoints at year one, including reductions in CSFT and in number of eyes with IRF/SRF[3].

In KITE, the most common (≥5%) overall adverse events were cataract and dry eye. Rates of intraocular inflammation (IOI) in KITE were 2.2% for BEOVU and 1.7% for aflibercept, and no retinal vasculitis (RV) was reported in either arm. Rates of retinal vascular occlusion (RO) were 0.6% for BEOVU versus 0.6% for aflibercept. In KITE, the majority of IOI events were manageable and resolved without any clinical complications. No RO events were associated with inflammation or vasculitis.

In KINGFISHER, the most common (≥5%) overall adverse events were COVID-19 and hypertension[3]. Rates of IOI were 4.0% for BEOVU (including 0.9% RV) and 2.9% for aflibercept (including 0.6% RV)[3]. RO rates were 0.3% for BEOVU versus 0.6% for aflibercept[3]. The majority of IOI events were manageable and resolved without any clinical complications[3]. No RO events were associated with inflammation or vasculitis.

“The year two KITE results reaffirm that BEOVU may meet an important need to extend dosing intervals for patients with diabetic macular edema, who are often overburdened with medical appointments,” said Jill Hopkins, Global Development Unit Head, Ophthalmology, Novartis Pharmaceuticals. “Along with the top-line results from KINGFISHER, the KITE findings add to the growing body of data supporting our understanding of where BEOVU may potentially fit into the DME treatment landscape. We look forward to continuing discussions with global health authorities about the findings from the KESTREL and KITE clinical trials, and we will continue to assess the clinical relevance of the positive KINGFISHER findings.”

Further details of KITE and KINGFISHER will be presented at upcoming medical meetings.

About diabetic macular edema (DME)

DME is a common microvascular complication in patients with diabetes that may have a debilitating impact on visual acuity, eventually leading to blindness[9]. DME is the leading cause of blindness in adults in developed countries, affecting 12% of patients with type 1 diabetes and 28% of those with type 2 diabetes[9].

Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid[10]. This damage leads to an excess of vascular endothelial growth factor (VEGF)[9,10]. VEGF is a protein that stimulates the growth of blood vessels[9,10]. At elevated levels in DME, VEGF stimulates the growth of abnormal, leaky blood vessels[9,10]. The resulting accumulation of fluid (known as edema) in the macula can lead to vision loss[9,10]. The macula is the area of the retina responsible for sharp, central vision[10]. Early symptoms of DME include blurry or wavy central vision and distorted color perception, although the disease can also progress without symptoms at early stages[10,11].

About BEOVU (brolucizumab-dbll)

BEOVU (brolucizumab, also known as RTH258) 6 mg is approved for the treatment of wet age-related macular degeneration (AMD) in 70 countries, including in the US, EU, UK, Japan, Canada and Australia[12-16]. 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.

Novartis and Novartis US is on Twitter. Sign up to follow @Novartis at https://twitter.com/novartisnews and @NovartisUS at https://twitter.com/NovartisUS.

For Novartis multimedia content, please visit https://www.novartis.com/news/media-library.

For questions about the site or required registration, please contact media.relations@novartis.com.

# # #

Novartis Media Relations

E-mail: media.relations@novartis.com

Amy Wolf	**Vicki Crafton**
Novartis External Communications	Novartis US Division Communications
+ 41 79 57607 23	+1 201 213 6338
amy.wolf@novartis.com	vicki.crafton@novartis.com

Julie Masow
Head, US External Engagement
+1 862 579 8456
julie.masow@novartis.com

Novartis Investor Relations

E-mail: investor.relations@novartis.com

North America

Sloan Simpson
+1 862 778 5052

References

1. Data on file. KITE (year two) first interpretable results. Novartis Pharmaceuticals Corp; 2021.
2. Brown D, Wolf S, Garweg JG, et al. Brolucizumab for the treatment of visual impairment due to diabetic macular edema: 52-week results from the KESTREL & KITE studies. Presented at: The Association for Research in Vision and Ophthalmology 2021 Annual Meeting. May 2021.
3. Data on file. KINGFISHER first interpretable results. Novartis Pharmaceuticals Corp; 2021.
4. Kang SW, Park CY, Ham D-I. The correlation between fluorescein angiographic and optical coherence tomographic features in clinically significant diabetic macular edema. *Am J Ophthalmol*. 2004;137(2):313-322.
5. Arnold J, Markey CM, Kurstjens NP, Guymer GH. The role of sub-retinal fluid in determining treatment outcomes in patients with neovascular age-related macular degeneration--a phase IV randomised clinical trial with ranibizumab: the FLUID study. *BMC Ophthalmol*. 2016;143(4):679-680.
6. Data on file. KESTREL clinical trial protocol (CRTH258B2301). Novartis Pharmaceuticals Corp; 2021.
7. Data on file. KITE clinical trial protocol (CRTH258B2302). Novartis Pharmaceuticals Corp; 2021.
8. Data on file. KINGFISHER clinical trial protocol (CRTH258B2305). Novartis Pharmaceuticals Corp; 2021.
9. Romero-Aroca P. Managing diabetic macular edema: The leading cause of diabetes blindness. *World J Diabetes*. 2011;2(6):98-104.
10. National Eye Institute. Macular Edema. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema. Accessed August 13, 2021.
11. National Eye Institute. Diabetic Retinopathy. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy. Accessed August 13, 2021.
12. Beovu [US prescribing information] East Hanover, NJ. Novartis Pharmaceuticals Corp; 2020.
13. Beovu [summary of product characteristics] Basel, Switzerland. Novartis; 2020.
14. Pharma Japan. National Health Insurance Pricing. https://pj.jiho.jp/sites/default/files/pj/document/2020/05/New%20Drugs%20to%20Be%20Added%20to%20NHI%20Price%20List%20on%20May%2020_1.pdf. Accessed August 13, 2021.
15. Canadian Agency for Drugs and Technologies in Health. CADTH Canadian Drug Expert Committee Recommendation. Available at: https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%2025%2C%202020_for%20posting.pdf. Accessed August 13, 2021.
16. Beovu [prescription medicine decision summary] Australia. Novartis: 2020.

List of links present in page

1. https://prod1.novartis.com/us-en/us-en/news/media-releases/novartis-announces-positive-results-from-phase-iii-trials-beovu-diabetic-macular-edema-including-dosing-intervals-16-weeks
2. https://prod1.novartis.com/us-en/us-en/sites/novartis_us/files/2022-03/beovu_0.pdf
3. https://prod1.novartis.com/us-en/us-en/node/431
4. https://twitter.com/novartisnews
5. https://twitter.com/NovartisUS
6. https://www.novartis.com/news/media-library
7. mailto:media.relations@novartis.com
8. mailto:media.relations@novartis.com
9. mailto:amy.wolf@novartis.com
10. mailto:vicki.crafton@novartis.com
11. mailto:julie.masow@novartis.com
12. mailto:investor.relations@novartis.com
13. https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema
14. https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy
15. https://pj.jiho.jp/sites/default/files/pj/document/2020/05/New%20Drugs%20to%20Be%20Added%20to%20NHI%20Price%20List%20on%20May%2020_1.pdf
16. https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%2025%2C%202020_for%20posting.pdf