NOVARTIS

Novartis Phase III BEOVU® data show potential for fluid resolution in more diabetic macular edema patients with fewer injections versus aflibercept

May 01, 2021

- In KESTREL and KITE, BEOVU (brolucizumab-dbll) 6 mg met the primary endpoints of non-inferiority in change in best corrected visual acuity from baseline versus aflibercept 2 mg at year one in diabetic macular edema (DME) patients[1]
- More patients treated with BEOVU 6 mg experienced fluid (IRF/SRF) resolution at week 32 and week 52 versus aflibercept; fluid is a key marker of disease activity in DME[1]
- BEOVU demonstrated an overall well-tolerated safety profile in KESTREL and KITE[1]
- Phase III KESTREL and KITE trials are the first pivotal trials to assess an anti-VEGF on six-week dosing intervals in the loading phase, suggesting BEOVU may offer fewer injections from the start of treatment[1]
- Novartis is committed to bringing BEOVU 6 mg to DME patients and will submit data from KESTREL and KITE to global health authorities in H1 2021

EAST HANOVER, N.J., May 1, 2021 -- Novartis today announced positive one-year results of the Phase III KESTREL and KITE* studies, evaluating the efficacy and safety of BEOVU® (brolucizumab-dbll) 6 mg in diabetic macular edema (DME). Both studies met their primary endpoints of non-inferiority in change in best corrected visual acuity (BCVA) from baseline for BEOVU 6 mg versus aflibercept 2 mg at year one[1]. In KESTREL, patients on BEOVU 6 mg gained a mean of 9.2 letters versus 10.5 letters for patients on aflibercept 2 mg[1]. In KITE, patients on BEOVU 6 mg gained a mean of 10.6 letters versus 9.4 letters for patients on aflibercept 2 mg[1]. These results will be presented at the Association for Research in Vision and Ophthalmology (ARVO) 2021 Annual Meeting.

In pre-specified secondary endpoints, fewer eyes treated with BEOVU had intraretinal and/or subretinal fluid (IRF/SRF) at week 32 (first assessment of disease activity) and week 52 versus eyes treated with aflibercept[1]. More eyes treated with BEOVU 6 mg than eyes treated with aflibercept achieved central subfield thickness (CSFT) levels below 280 µm at weeks 32 and 52[1]. Fluid is a key marker of disease activity in DME and CSFT is a key indicator of fluid in the retina[1].

"Treatment for diabetic macular edema is a high unmet medical need in the US and globally. Our goal as physicians is to work on preventing blindness for the significant proportion of diabetics affected by this condition," said David M Brown MD FACS, Director of Clinical Research at the Retina Consultants of Texas and principal investigator of the KESTREL clinical trial. "DME patients often struggle with adherence due to the need to manage multiple comorbidities related to diabetes. The KESTREL and KITE clinical trials - the first pivotal trials to examine a longer dosing interval in the loading phase - confirm BEOVU's potential to be an important therapy for these patients."

To study its potential in reducing treatment burden, BEOVU was given at six-week dosing intervals during the loading phase versus aflibercept, which was given at the standard four-week dosing intervals, in line with its label[1,2]. Following the loading phase, over half of patients in the BEOVU 6 mg arm (55.1% in KESTREL and 50.3% in KITE) remained on a three-month dosing interval through year one, based on a treatment approach determined by disease activity assessment[1]. If disease activity was detected, BEOVU 6 mg patients were switched to two-month intervals through the end of the trial[1]. All aflibercept patients were on a two-month interval after the loading phase[1].

"We are pleased to share these data, which underscore BEOVU's potential to address an unmet need in the DME landscape," said Jill Hopkins, Global Development Unit Head, Ophthalmology, Novartis Pharmaceuticals. "With these data demonstrating vision gains, fluid resolution and the potential for less frequent injections for eligible patients, we are one step closer to providing DME patients with a potential new treatment option."

The Phase III KESTREL and KITE studies enrolled a total of 926 patients in 36 countries. BEOVU 6 mg is the commercialized dose in wet age-related macular degeneration (AMD)[3]. The brolucizumab 3 mg arm, which was only included in KESTREL, did not meet the primary endpoint[1].

BEOVU was overall well-tolerated in KESTREL and KITE[1]. The most common ocular and non-ocular adverse events (≥5%) in KESTREL and KITE were conjunctival hemorrhage, nasopharyngitis and hypertension[4]. IOI rates in KESTREL were 4.7% for brolucizumab 3 mg (including 1.6% retinal vasculitis), 3.7% for BEOVU 6 mg (including 0.5% retinal vasculitis), and 0.5% for aflibercept 2 mg[1]. IOI rates in KITE were equivalent (1.7%) between the BEOVU 6 mg and aflibercept 2 mg arms with no retinal vasculitis reported[1]. Retinal vascular occlusion was reported in KESTREL for brolucizumab 3 mg (1.1%) and 6 mg (0.5%), and in KITE for brolucizumab and aflibercept (0.6% each)[1]. The majority of these events were manageable and resolved with or without treatment[1].

Novartis is committed to bringing BEOVU 6 mg to market for DME patients, subject to regulatory approvals, and will be submitting these one-year data from the KESTREL and KITE trials to global health authorities in H1 2021. Novartis anticipates two-year results from KESTREL and KITE later in 2021.

About Diabetic Macular Edema

Diabetic macular edema (DME) is the leading cause of blindness in adults in developed countries, affecting 12% of people with type 1 diabetes and 28% of those with type 2 diabetes[5]. Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid[6]. This damage leads to an excess of vascular endothelial growth factor (VEGF)[5,6]. VEGF is a protein that stimulates the growth of blood vessels[5,6]. At elevated levels in DME, VEGF stimulates the growth of abnormal, leaky blood vessels[5,6]. The resulting accumulation of fluid (known as edema) in the macula can lead to vision loss[5,6]. The macula is the area of the retina responsible for sharp, central vision[6]. 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[6,7].

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[3,8-11]. Additional trials, which study the effects of brolucizumab in patients with wet AMD, DME, retinal vein occlusion (RVO) 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.

*Kite Pharma, Inc. is neither a sponsor nor associated with Novartis' KITE trial.

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

Eric Althoff	Jamie Bennett
Head, US Corp & Country External Comms,	Director, US Media Relations
Global Media & Corp Communications	+1 862 217 3976

+1 646 438 4335 jamie.bennett@novartis.com
eric.althoff@novartis.com

Novartis Investor Relations
E-mail: investor.relations@novartis.com

North America

Sloan Simpson +1 862 778 5052

References

1. 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 (ARVO) 2021 Annual Meeting. May 2021.
2. Eylea [prescribing information] Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2018.
3. Beovu [US prescribing information] East Hanover, NJ. Novartis: 2020.
4. Data on file. KESTREL and KITE Clinical Study Report. Novartis, 2021.
5. Romero-Aroca P. Managing diabetic macular edema: The leading cause of diabetes blindness. World J Diabetes. 2011;2(6):98-104.
6. National Eye Institute. Macular Edema. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema. Accessed April 2021.
7. National Eye Institute. Diabetic Retinopathy. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy. Accessed April 2021.
8. Beovu [summary of product characteristics] Basel, Switzerland. Novartis: 2020.
9. Pharma Japan. National Health Insurance Pricing. Available at: 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 April 2021.
10. 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 April 2021.
11. Beovu [prescription medicine decision summary] Australia. Novartis: 2020.

Source URL: *https://qa1.novartis.us/us-en/news/media-releases/novartis-phase-iii-beovu-data-show-potential-fluid-resolution-more-diabetic-macular-edema-patients-fewer-injections-versus-aflibercept*

List of links present in page

1. https://qa1.novartis.us/us-en/us-en/news/media-releases/novartis-phase-iii-beovu-data-show-potential-fluid-resolution-more-diabetic-macular-edema-patients-fewer-injections-versus-aflibercept
2. https://qa1.novartis.us/us-en/us-en/sites/novartis_us/files/2022-03/beovu_0.pdf
3. https://qa1.novartis.us/us-en/us-en/home
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:jamie.bennett@novartis.com
10. mailto:eric.althoff@novartis.com
11. mailto:investor.relations@novartis.com
12. https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema
13. https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy
14. 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
15. 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
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