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Novartis receives FDA approval for BEOVU®, offering wet AMD patients vision gains and greater fluid reductions vs aflibercept

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- In two head-to-head clinical trials, patients on BEOVU (brolucizumab-dbll) achieved vision gains that were non-inferior to aflibercept at year one with longer treatment intervals in a majority of patients[1,2]
- BEOVU demonstrated greater reductions in central subfield thickness (CST, a key indicator of fluid in the retina) as early as week 16 and at one year versus aflibercept[2]
- BEOVU is the only anti-VEGF in wet AMD recommended to maintain eligible patients on up to three-month dosing intervals immediately after the loading phase with no compromise in efficacy[1,2]
- In both clinical trials, at year one over half of patients were maintained on the three-month dosing interval (56% in HAWK and 51% in HARRIER)[1,2]
- Frequent injection intervals are a common reason patients drop off treatment for wet age-related macular degeneration (AMD), a leading cause of blindness, affecting more than 20M people worldwide[3-5]

EAST HANOVER, N.J., Oct. 8, 2019 /PRNewswire/ -- Novartis today announced that the U.S. Food and Drug Administration (FDA) approved BEOVU® (brolucizumab-dbll) injection, also known as RTH258, for the treatment of wet age-related macular degeneration (AMD)[1]. BEOVU is the first FDA-approved anti-VEGF to offer both greater fluid resolution versus aflibercept and the ability to maintain eligible wet AMD patients on a three-month dosing interval immediately after a three-month loading phase[1] with uncompromised efficacy.

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"BEOVU meets our goals in clinical practice for treating wet AMD: improving vision and drying retinal fluid," said Dr. Pravin U. Dugel, Managing Partner, Retinal Consultants of Arizona; Clinical Professor, Roski Eye Institute, Keck School of Medicine, University of Southern California; and principal investigator of the HAWK clinical trial. "With BEOVU, greater fluid reduction was demonstrated through larger decreases in retinal thickness and a higher proportion of patients with drier retinas. Coupled with the potential to treat patients with quarterly injections, this approval may change the way we approach the treatment of wet AMD."

The approval of BEOVU was based on findings from the Phase III HAWK and HARRIER clinical trials, in which BEOVU demonstrated non-inferiority versus aflibercept in mean change in best-corrected visual acuity (BCVA) at year one (week 48)[1,2]. In both clinical trials, approximately 30% of patients gained at least 15 letters at year one[1,2]. In HAWK and HARRIER, BEOVU showed greater reduction in central subfield thickness (CST) as early as week 16 and at year one, and fewer patients had intra-retinal (IRF) and/or sub-retinal fluid (SRF)[2]. Retinal fluid is a key marker of disease activity[6].

Wet AMD is a chronic, degenerative eye disease caused by an excess of VEGF, a protein that promotes the growth of abnormal blood vessels underneath the macula, the area of the retina responsible for sharp, central vision[7,8]. Fluid that leaks out of these abnormal blood vessels disrupts the normal retinal structure and ultimately damages the macula[8-10]. The BEOVU molecule is engineered to deliver the highest concentration of drug, providing more active binding agents than other anti-VEGFs[2]. By inhibiting VEGF, BEOVU suppresses the growth of abnormal blood vessels and the potential for fluid leakage into the retina[2].

"The approval of BEOVU delivers on the Novartis commitment to reimagining treatments for patients suffering from serious visual impairment," said Marie-France Tschudin, President, Novartis Pharmaceuticals. "The product labels of existing treatments state that they are not as effective when dosed every 12 weeks. BEOVU is the first to offer less frequent dosing in the first year of therapy while maintaining its effectiveness. This gives more time for wet AMD patients to focus on what's important in their lives."

In HAWK and HARRIER, eligible patients could be maintained on a three-month dosing interval immediately after the loading phase[1,2]. At year one, over half of patients were maintained on the three-month dosing interval (56% in HAWK and 51% in HARRIER)[1,2]. The remaining patients in the study were treated on a two-month dosing schedule[1,2].

BEOVU exhibited an overall safety profile comparable to aflibercept. BEOVU is contraindicated in patients with ocular or periocular infections, active intraocular inflammation or with known hypersensitivity to brolucizumab or any of the excipients in BEOVU[1]. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema or severe intraocular inflammation[1].

The most common adverse events (≥5% of patients) with BEOVU were vision blurred, cataract, conjunctival hemorrhage, vitreous floaters and eye pain[1,2].

Wet AMD distorts central vision and ultimately causes blindness and loss of independence[11,12]. Estimates suggest that in 2020, 1.75 million people in the U.S. will be living with wet AMD[13-15], making it a growing public health concern. Early symptoms of wet AMD include blurry or wavy vision[8].

As the disease progresses, patients lose central vision so it becomes difficult to see objects directly in front of them[8].

"As sight disappears, so does a person's connection to the world," said Dawn Prall, Founder and Executive Director, The Support Sight Foundation. "We welcome a new treatment that helps maintain vision and has the potential for quarterly treatments, which can reduce the burden on patients and their caregivers and help people with wet AMD keep doing what they love with the people they love."

With this approval, Novartis is offering BEOVU Your Way™ in the U.S. This program provides personalized, one-on-one support for patients and caregivers, with access to a care specialist committed to understanding patients' unique needs and preferences. Novartis is proud to be partnering with patient advocacy organizations to deliver educational materials for patients and caregivers, with the goal of empowering wet AMD patients to live safely and independently.

About BEOVU (brolucizumab-dbll)

BEOVU (brolucizumab-dbll) is the most clinically advanced humanized single-chain antibody fragment (scFv)[2,16]. Single-chain antibody fragments are highly sought after in drug development due to their small size, enhanced tissue penetration, rapid clearance from systemic circulation and drug delivery characteristics[16-18].

The proprietary innovative structure results in a small molecule (26 kDa) with potent inhibition of, and high affinity to, all VEGF-A isoforms[17]. BEOVU is engineered to deliver the highest concentration of drug, providing more active binding agents than other anti-VEGFs[2,16]. In preclinical studies, BEOVU inhibited activation of VEGF receptors through prevention of the ligand-receptor interaction[17-19]. Increased signaling through the VEGF pathway is associated with pathologic ocular angiogenesis and retinal edema[20]. Inhibition of the VEGF pathway has been shown to inhibit the growth of neovascular lesions and suppress endothelial cell proliferation and vascular permeability[20].

About the HAWK and HARRIER studies

With more than 1,800 patients across nearly 400 centers worldwide, HAWK (NCT02307682) and HARRIER (NCT02434328) are the first and only global head-to-head trials in patients with wet AMD that prospectively demonstrated efficacy at week 48 using an innovative q12w/q8w regimen, with a majority of patients on q12w immediately following the loading phase[2]. Both studies are 96-week prospective, randomized, double-masked multi-center studies and part of the Phase III clinical development of BEOVU[2]. The studies were designed to compare the efficacy and safety of intravitreal injections of brolucizumab 6 mg (HAWK and HARRIER) and 3 mg (HAWK only) versus aflibercept 2 mg in patients with wet AMD[2].

About wet age-related macular degeneration

Wet AMD is a 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[4,5,11]. It is estimated that 1.75 million people in the U.S. will be living with wet AMD in 2020[13-15]. 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[8,21]. Prompt diagnosis and intervention are essential[10]. As the disease progresses, cell damage increases, further reducing vision quality[8]. 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[8,12]. Without treatment, vision can rapidly deteriorate[22].

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.

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 Detachments

Intravitreal injections, including those with BEOVU, have been associated with endophthalmitis and retinal detachments. 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.

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 730) in the pooled aflibercept arms.

ADVERSE REACTIONS

Serious adverse reactions including endophthalmitis, retinal detachment, 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.

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

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 products reach more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Novartis Pharmaceuticals Corporation, a U.S. affiliate of Novartis, is located in East Hanover, NJ. Find out more at www.novartis.com.

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References

1. BEOVU [prescribing information] East Hanover, NJ. Novartis: 2019.
2. Dugel P, et al. HAWK and HARRIER: Phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration [published online ahead of print]. Ophthalmology. 2019.
3. Varano M, et al. Current barriers to treatment for wet age-related macular degeneration (wAMD): findings from the wAMD patient and caregiver survey. Clin Ophthalmol. 2015;9:2243–2250.
4. Wong WL, Su X, Li X, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a

systematic review and met analysis. Lancet Glob Health. 2014;2:106-16.
5. Singer M. Advances in the management of macular degeneration. F1000Prime Rep. 2014;6:29.
6. Arnold J, et al. 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.
7. Qazi Y, et al. Mediators of ocular angiogenesis. J. Genet. 2009;88(4):495-515.
8. National Eye Institute. Facts About Age-Related Macular Degeneration. Available at https://nei.nih.gov/health/maculardegen/armd_facts (link is external). Accessed September 2019.
9. World Health Organization. Priority eye diseases: Age-related macular degeneration. Available at http://www.who.int/blindness/causes/priority/en/index7.html (link is external). Accessed September 2019.
10. NHS Choices. Macular Degeneration. Available at http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Introduction.aspx (link is external). Accessed September 2019.
11. Schmidt-Erfurth U, et al. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). Br J Ophthalmol. 2014;98:1144-1167.
12. Mitchell J, Bradley C. Quality of life in age-related macular degeneration: a review of the literature. Health Qual Life Outcomes. 2006;4:97.
13. Friedman DS, O'Colmain BJ, Munoz B, et al. Prevalence of age-related macular degeneration in the United States. Arch Ophthalmol. 2004;122(4):564-72.
14. Klein R, Chou CF, Klein BE, Zhang X, Meuer SM, Saaddine JB. Prevalence of age-related macular degeneration in the U.S. population. Arch Ophthalmol. 2011;129(1):75-80.
15. American Academy of Ophthalmology. Age-related macular degeneration preferred practice patterns. Available at: https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp-2015 (link is external). Accessed September 2019.
16. Nimz EL, et al. Intraocular and systemic pharmacokinetics of brolucizumab (RTH258) in nonhuman primates. The Association for Research in Vision and Ophthalmology (ARVO) annual meeting. 2016. Abstract 4996.
17. Escher D, et al. Single-chain antibody fragments in ophthalmology. Oral presentation at EURETINA congress. 2015. Abstract.
18. Gaudreault J, et al. Preclinical pharmacology and safety of ESBA1008, a single-chain antibody fragment, investigated as potential treatment for age related macular degeneration. ARVO Annual Meeting abstract. Invest Ophthalmol Vis Sci. 2012;53:3025. http://iovs.arvojournals.org/article.aspx?articleid=2354604 (link is external). Accessed September 2019.
19. Tietz J, et al. Affinity and Potency of RTH258 (ESBA1008), a Novel Inhibitor of Vascular Endothelial Growth Factor A for the Treatment of Retinal Disorders. IOVS. 2015; 56(7):1501.
20. Kim R. Introduction, mechanism of action and rationale for anti-vascular endothelial growth factor drugs in age-related macular degeneration. Indian J Ophthalmol. 2007;55(6):413-415.
21. Healthline. What is metamorphopsia? Available at https://www.healthline.com/health/metamorphopsia (link is external). Accessed September 2019.
22. van Lookeren Campagne M, et al. Mechanisms of age-related macular degeneration and therapeutic opportunities. J Pathol. 2014; 232(2):151-64. doi: 10.1002/path.4266.

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