

MEDIA UPDATE

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

- *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) 6 mg demonstrated greater reductions in central subfield thickness, and fewer patients had intraretinal and/or subretinal fluid versus aflibercept¹*
- *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*
- *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%)*
- *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 profile³*
- *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*

Basel, August 17, 2021 — Novartis today announced positive results from two Phase III clinical trials assessing Beovu® (brolucizumab) 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 study¹. 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 weeks³. 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/SRF³.

In KITE, the most common ($\geq 5\%$) 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 ($\geq 5\%$) overall adverse events were COVID-19 and hypertension³. 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 aflibercept³. The majority of IOI events were manageable and resolved without any clinical complications³. 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 the KESTREL, KITE and KINGFISHER clinical trials

KESTREL, KITE and KINGFISHER are global, randomized, double-masked, Phase III, two-year studies comparing the safety and efficacy of Beovu and aflibercept in the treatment of DME⁶⁻⁸.

KESTREL and KITE involved 926 patients in 36 countries^{6,7}. In the loading phase of both trials, patients in the Beovu arms were treated every six weeks for a total of five doses; patients in the aflibercept arms were treated every four weeks for a total of five doses, in line with its label^{6,7}. Following the loading phase, patients in the Beovu arms were subsequently treated every 12 weeks, with those demonstrating disease activity moved to dosing every eight weeks for the remainder of the study^{6,7}.

At week 72 of KITE, Beovu patients dosed every 12 weeks could be extended to dosing every 16 weeks, and patients dosed every eight weeks could be extended to every 12 weeks⁷. As in year one, those demonstrating disease activity were moved to dosing every eight weeks for the remainder of the study⁷. Through the entirety of both two-year trials, patients in the aflibercept arms were treated every eight weeks^{6,7}.

KINGFISHER evaluated 517 patients at 115 centers over the course of one year⁸. Patients were treated with Beovu or aflibercept every four weeks through week 48, with a four-week follow-up period, for a total of 13 visits⁸.

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 blindness⁹. 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 diabetes⁹.

Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid¹⁰. 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 vision¹⁰. 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) 6 mg

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 Australia¹²⁻¹⁶. 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.

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 of nor associated with Novartis' KITE trial.*

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About Novartis

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