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Information for the public

related to the GMO Application submitted in Belgium

for the use of Surabgene Lomparvovec (ABBV- RGX- 314)

in Clinical Trial M24-528

EU Trial Number	2024-512298-28-00
Investigational Medicinal Product	ABBV-RGX-314 (also known as RGX-314)
Study Number	M24-528
Study Title	A Randomized, Controlled, Partially Masked, Phase 3b Study to Assess the Injection Burden, Efficacy, Safety, and Long-Term Preservation of Visual Acuity of Surabgene Lomparvovec (ABBV- RGX- 314) in a Real-World Context in Subjects with Neovascular Age-Related Macular Degeneration (nAMD)
Lay Protocol Title	A study of the safety and efficacy of surabgene lomparvovec (ABBV-RGX-314) compared to ranibizumab in patients with nAMD
Study Phase	Phase 3b
Sponsor	AbbVie Deutschland GmbH & Co. KG

1. Didactic description of the GMO

Genes are the substances in cells that carry the information that determines an organism's traits (features or characteristics, such as eye color). Some genes instruct the body to make certain proteins. In gene therapy, a gene is delivered to cells using a special virus that does not cause any diseases in people. These viruses are called vectors. The vector is designed to find certain cells in your body and deliver a gene that helps those cells to make a specific protein that may help treat the disease.
This process is called gene transfer and surabgene lomparvovec is considered a Genetically Modified Organism (GMO) because it can help cells make a protein to treat neovascular age-related macular degeneration (nAMD), also called wet AMD. The vector for this study is called adeno-associated virus (AAV) which is naturally occurring in humans and is not a known health risk.

The study treatment contains a gene that tells the cells to make a protein that blocks vascular endothelial growth factor (VEGF) in the eye. Blocking VEGF can help stop fluid from building up in the eye. Medicines that do this are called anti-VEGF treatments. The study treatment is designed to work in a similar way as other approved anti-VEGF therapies, like Lucentis®, (ranibizumab), Eylea® (aflibercept) and Beovu®

(brolucizumab). The use of these approved anti-VEGF treatments helps reduce the growth of new, abnormal blood vessels and keeps them from leaking fluid into the retina (light-sensitive tissue at the back of the eye). This may help restore lost vision and stop new vision loss. Anti-VEGF therapies have been shown to reduce the severity of wet AMD with regular use; however, there are many challenges to receiving regular, continuous treatment.

2. Nature and goal of the foreseen deliberate release

All patients will receive ranibizumab during the screening period (tests given to find out if a patient can join a study) to determine if they had an anatomic response (a change in the eye as a result of the study treatment). Patients that have the appropriate anatomic response will be randomized to receive:

- Single dose of surabgene lomparvovec Dose 1
- Single dose of surabgene lomparvovec Dose 2
- Ranibizumab as needed throughout the study

Ranibizumab will be given as an intravitreal injection (injection into the jelly-like tissue that fills the eyeball), and surabgene lomparvovec will be given as a subretinal injection (injection given between the retina and the back of the eye). This subretinal injection will be performed as a procedure in an operating room. After Week 6, patients may receive additional ranibizumab injections as determined by the study doctor. Patients will undergo physical exams, eye exams, blood tests, vision testing and will complete questionnaires throughout the study. Patients will participate in the study through Year 5.

3. Framework of research and/or development

Rationale

nAMD, also known as “wet” AMD, is the abnormal growth of new blood vessels in the light-sensitive tissue at the back of the eye called the retina. These new blood vessels can damage the macula, which is the part of the retina that allows for sharp, clear vision. This damage can block vision in the center of the eye and cause permanent vision loss. The primary cause of this breakdown of cells is an excess of a specific protein called VEGF in the eye. Proteins are complex molecules that do most of the work in the body’s cells. The current treatment for nAMD includes a group of medicines called anti-VEGFs. Anti-VEGFs are injected into the eye to stop the growth of abnormal blood vessels to improve vision, but these treatments require many injections and trips to the doctor’s office. Surabgene lomparvovec (ABBV-RGX-314) is a gene therapy which means that a small amount of genetic material is injected into the back of the eye. Surabgene lomparvovec

is a one-time treatment that works in a similar way to current anti-VEGFs to maintain vision but has the potential to last longer than current treatments.

Objective

The main goals of the study are to evaluate the safety and long-term efficacy (how well the medicine works) of a one-time treatment with surabgene lomparvovec compared to ranibizumab injections, that are given as needed, up to Year 3. Ranibizumab is an anti-VEGF currently approved in the European Union for the treatment of nAMD.

Trial design

This is a Phase 3b, randomized, assessor-masked study of surabgene lomparvovec compared to ranibizumab in patients with nAMD. Phase 3b studies test potential new treatments in a large number of patients with a condition or disease. A computer program is used to randomly (by chance) put the patients into 1 of 3 groups. This process is called randomization, which helps make the groups similar and reduces the differences between the groups. This study is assessor-masked which means that study personnel who evaluate how well treatment is working will not know who is given which study treatment, but the patients and study doctors will.

Trial population

This study will include patients 50 years of age and older, diagnosed with nAMD. Patients must have received at least 2 anti-VEGF injections in the past 6 months prior to the start of the study. Additional eligibility criteria will be discussed by the study doctor.

4. Potential advantages of the deliberate release

Patients with nAMD may benefit from treatment with surabgene lomparvovec because it is a gene therapy that leads to the production of an anti-VEGF protein and works to lessen the activity of VEGF in the eye to slow the growth of new blood vessels that impair vision. Gene therapies, like surabgene lomparvovec, have been evaluated in several studies but long-term risks of gene therapy are unknown.

5. Assessment of the potential risks for human health and the environment linked to the deliberate release

The main risks of treatment with surabgene lomparvovec include anti-VEGF proteins at levels higher than expected which may lead to ocular (eye) side effects. This study also includes treatment with ranibizumab, and patients should discuss potential risks with the study doctor.

Patient safety will be closely monitored in the study to lower risks. Patients may or may not receive direct medical benefit from participating in this study. Symptoms may get better, get worse, or stay the same. The information from this study could help other patients with nAMD or other similar conditions in the future. There may be a bigger responsibility for patients in this study compared to patients who receive standard of care treatment. Patients will attend regular visits during the study at a hospital or clinic. The effects of treatment will be checked by medical assessments, vision tests, checking for side effects, and completing questionnaires.
Regarding any potential risks for the environment: surabgene lomparvovec cannot help bacteria or other germs survive or grow, and it does not have the ability to make bacteria resistant to antibiotics or other treatments. Also, surabgene lomparvovec will not spread in the environment as it cannot replicate. Overall, the chance of surabgene lomparvovec causing any harm to people, animals, germs or the environment is negligible.

6. Proposed measures to limit the potential risks, to control and to ensure follow-up of the deliberate release

Healthcare providers and study personnel will be trained in best safety practices to be applied during handling, administration and disposal of ABBV-RGX-314.
Healthcare professionals will wear protective clothing when administering treatment, will have adequate equipment available to clean up any spills safely, and will properly dispose of medical waste.
ABBV-RGX-314 will be shipped to trial sites in line with standard recommendations for the safe transport of experimental gene therapies.
All study treatments must be stored in a secure and monitored area in accordance with the labelled storage conditions, with access limited to authorized site staff. Post-operative positioning instructions will be reviewed with the participant and provided in writing.

7. Conduct of the study in Belgium

Participating sites in Belgium:

Organisation Name:	UZ Leuven
Address Details:	Herestraat 49 3000 Leuven Belgium
Contact person:	Prof Julie Jacob (Principal Investigator), Lies Prové (Study Coordinator)

Organisation Name:	UZ Gent
Address Details:	Corneel Heymanslaan 10 9000 Gent Belgium
Contact person:	Dr Julie De Zaeytijd (Principal Investigator), Amber De Freyne (Study Coordinator)

Expected number of patients that will be enrolled in Belgium: 8

Expected start date of the study in Belgium: 05-Feb-2026

Expected end date of the study in Belgium: 06-Apr-2033