INFORMATION FOR THE PUBLIC

AstriVax NV

LAV-YF17D/HBc

LAV-YF17D/HBc will be assessed in clinical study AVX37-101 called: "*A randomised, double-blind, placebo-controlled, multi-centre, Phase I study to evaluate the safety, reactogenicity and immunogenicity of AstriVax' investigational therapeutic hepatitis B virus (HBV) vaccine (AVX70371) in adult patients with chronic HBV (CHB) infection*"

Deliberate Release Reference Number
B/BE/24/BVW6

The release of genetically modified organisms (GMOs) in the environment is strictly regulated at European level by Directive 2001/18/EC and at Belgian level by the Royal Decree of 21 February 2005. To ensure safe use of GMOs, the provisions of the Royal Decree of 21 February 2005 stipulate that the release of GMOs for experimental aims is prohibited without prior consent from the competent Minister. The decision is based on a thorough evaluation of the biosafety of the planned release, which is conducted by the Biosafety Advisory Council, composed of different Scientific Committees grouping independent experts from Belgian universities and governmental institutes.

To acquire the necessary authorization from the competent Minister, AstriVax submitted an application dossier to the competent authority. On the basis of the advice of the Biosafety Council, the competent Minister could grant a permission to AstriVax to conduct the above-mentioned clinical study in which the genetically modified organism LAV-YF17D/HBc will be assessed, as stipulated in the application B/BE/24/BVW6.

In Belgium, the following hospital will take part in the clinical study:

- SGS Belgium N.V., Edegem (Antwerp)

It is possible that other hospitals will join in the future.

The clinical study is expected to start in March 2025 and to be completed by the end of 2026.

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GENERAL INFORMATION

Goal of the Genetic Modification

AstriVax is developing a vaccine (called AVX70371) to be part of a treatment for chronic hepatitis B virus infection. When the vaccine is given, it makes the genetically modified organism (GMO) in the body of the vaccinated person. The GMO is called live attenuated virus (or 'LAV' in short)-YF17D/HBc. It has the genetic code of the yellow fever vaccine strain 17D (YF17D) with that of the core protein of the hepatitis B virus (called HBc) inserted. The goal of this genetic modification is for the GMO to activate the body's natural defense mechanism to make immune cells against the hepatitis B virus. These immune cells should then recognize and destroy liver cells that are infected with the hepatitis B virus. The goal is for the vaccine to be given together with other drugs in the future, so that together they can work as a cure against chronic hepatitis B virus infection.

The hepatitis B virus can attack liver cells and cause long term (chronic) infection. People with chronic hepatitis B virus infection are at risk of death from liver damage (liver cirrhosis or cancer). In 2022, 254 million people worldwide were living with chronic hepatitis B infection and it caused about 1.1 million deaths. It is estimated that about 1.2 million new infections happen each year. There are drugs available that stop the hepatitis B virus from damaging the liver. However, these drugs cannot remove the hepatitis B virus from the liver, so they need to be taken life-long. That is why a cure for chronic hepatitis B infection is urgently needed.

Description of the Genetically Modified Organism (LAV-YF17D/HBc)

LAV-YF17D/HBc has the genetic code of YF17D with that of HBc inserted. YF17D is a weakened (or attenuated) form of the yellow fever virus. YF17D has been into use since the 1930s as the vaccine to protect against yellow fever. Because of this, a lot is known about YF17D, including that:

- After vaccination, YF17D multiplies in the body of the vaccinated person. After a few days, a low number of YF17D particles can be present in some bodily fluids (for instance in the blood). Once the person's natural defense mechanism kicks in, it will attack the YF17D particles and they disappear from the body.
- The YF17D particles do not spread from one person to another like the real yellow fever virus can. The real yellow fever virus spreads through mosquitoes that live in South and Central America or in Africa. The mosquitoes become infected when they bite someone who has yellow fever virus in their blood. While YF17D particles can sometimes be found in the blood of a vaccinated person, there are way too few particles for mosquitoes to become infected. On top of that, even if a mosquito were to become infected, YF17D is so weakened that the mosquito could not spread it further.
- The only way YF17D particles could spread from one person to another, is if the other person is in direct contact with a bodily fluid containing YF17D. This could for instance happen through breastfeeding, or by receiving a blood transfusion, or an organ transplant from a recently vaccinated person.
- The YF17D particles cannot survive outside the body.

Because the LAV-YF17D/HBc particles look and behave the same as the YF17D particles, all of the above is also true for the LAV-YF17D/HBc particles. On top of that, because of the genetic modification, each time the LAV-YF17D/HBc particles multiply, new HBc proteins are also made.

Description of the Vaccine (AVX70371)

The GMO, LAV-YF17D/HBc is not given as such to people. What is given instead is AVX70371. AVX70371 is a DNA vaccine that has the genetic code for LAV-YF17D/HBc. When AVX70371 is given, it makes LAV-YF17D/HBc particles in the body of the vaccinated person. AVX70371 itself does not spread in the body. It is cleared away at the location where it is given.

RESEARCH / DEVELOPMENT ACTIVITIES

Previous Development Activities

Up to now, only testing in animals has been done. In animals, LAV-YF17D/HBc particles can safely activate the natural defense system to make immune cells against the hepatitis B virus.

Future Activities: Clinical Study

LAV-YF17D/HBc will be tested for the first time in humans in a clinical study called "*A randomised, double-blind, placebo-controlled, multi-centre, Phase I study to evaluate the safety, reactogenicity and immunogenicity of AstriVax' investigational therapeutic hepatitis B virus (HBV) vaccine (AVX70371) in adult patients with chronic HBV (CHB) infection*"

The main goal of the study is to make sure that vaccination with AVX70371 is safe. Another goal of the study is to check if the LAV-YF17D/HBc particles can activate the natural defense system of people with chronic hepatitis B virus infection.

The people who take part in the study will get 2 injections with AVX70371, about 1 month apart. After the second injection, they will be followed up for 6 months. During the study, they will go to the clinic regularly for follow-up visits.

POTENTIAL BENEFITS

The vaccination with AVX70371 may not give a direct benefit for the people who take part in the study. Even if the vaccine works, we think that it will need to be given together with other drugs to work as a cure against chronic hepatitis B infection.

An indirect benefit is that the results of the study may help the development of a cure for chronic hepatitis B infection.

POTENTIAL RISKS

Potential Risks for Human Health Linked to the Spreading of the Genetically Modified Organism

The GMO, LAV-YF17D/HBc, may be present in some bodily fluids for a few days after each vaccination. The particles can most probably not naturally spread from one person to another. This means that the only way people outside the study could get infected with the particles is if:

- Personnel at the hospital taking part in the clinical study accidently self-administers AVX70371 (for instance through a needle stick injury). Or if they come directly into contact with bodily fluid containing LAV-YF17D/HBc particles (for instance if they take a blood sample from a person who takes part in the study, and accidently spill it on a skin cut).
- Someone gets a blood transfusion, an organ transplant, and egg / ovum or a sperm donation from someone who takes part in the study.
- If a woman who takes part in the study is breastfeeding her child, or if she is pregnant.

Even if one of the above would occur, it is still very unlikely that the person would actually get infected with LAV-YF17D/HBc particles. That is because only a low number of LAV-YF17D/HBc particles will be present for a short period of time in some of the bodily fluids of some of the vaccinated persons. Or in the case of a needle stick injury, the dose of AVX70371 will be much lower than what will be given to the people who take part in the study. On top of that, as described in the section below, measures will be put in place to avoid these situations. The risk that someone outside the clinical study will accidently get infected with LAV-YF17D/HBc particles is therefore low to negligible.

If someone still were to get infected with LAV-YF17D/HBc, the potential risks would be the same those for the people who are vaccinated with AVX70371 in the clinical study. These are:

- The risk of having side effects (for instance pain or redness at the place of the injection, or headache, feeling weak or unwell, muscle pain, fever, chills). Side effects could very rarely also be serious. The risk of having any side effect is low to moderate, while that of having serious side effects is low to negligible.
- A risk for the genetic material of the LAV-YF17D/HBc particles to slightly change (mutate) while they multiply in the body, which make that the particles cause more side effects. This risk is low to negligible because we know that this hardly ever happens with the YF17D vaccine (this has been seen once in the 800 million doses that have been given worldwide).
- A theoretical risk that the genetic material of the LAV-YF17D/HBc particles could mix with similar genetic material (for instance that of YF17D, of the real yellow fever virus, or of a similar virus). This can only happen if both are together in the same cell of the same person. In this case a new (mixed) virus could be made. The risk of this is negligible because not only is the mixing of genetic material very uncommon in this type of viruses, it is also very unlikely for a person to have the 2 types of genetic material present at the same time in the same cell. Indeed, the clinical study takes place in Europe, where viruses like yellow fever are not naturally present, and vaccination against this type of viruses is not routinely done.

If the body's natural defense system of the person who accidently gets infected with LAV-YF17D/HBc is weakened, or not fully developed yet (for young infants), the potential risks would be the same. However, the chance that the risks occur may be higher because their natural defense system cannot make immune cells against the LAV-YF17D/HBc particles so quickly.

Potential Risks for the Environment Linked to the Spreading of the Genetically Modified Organism

The LAV-YF17D/HBc particles cannot survive outside the body. The risk related to release of LAV-YF17D/HBc particles into the environment is therefore negligible.

CONTAINMENT, CONTROL AND MONITORING MEASURES

Measures to Limit the Risks for Human Health

While it is very unlikely that LAV-YF17D/HBc particles will accidently spread to people outside the clinical study, the following measures will be put in place to completely avoid this:

- AVX70371 will be stored in small containers that have a rubber stopper and a flip-off cap.
- Personnel at the hospital taking part in the clinical study will be trained. They will wear a lab coat and gloves when they handle AVX70371, or when they sample bodily fluids (for instance blood) from people who take part in the clinical study.
- All bodily fluids sampled from people in the clinical study will be stored in tubes that have a screw cap. If someone accidently spills a sample, the area will be thoroughly disinfected.
- All waste that may contain LAV-YF17D/HBc will be treated as hazardous medical waste.
- People who take part in the study cannot have a weakened natural defense mechanism.
- People who take part in the study cannot give blood or organs for 3 months after the last study vaccination, or donate eggs / ovum (for women) or sperm (for men) for 2 months after the last study vaccination.
- Women who are pregnant or breastfeeding cannot take part in the study. On top of that, women may not become pregnant during the first 2 months after the last study vaccination.
- Men who take part in the study must agree to use a condom when they have sexual intercourse with a woman, until 2 months after the last study vaccination.
- People who take part in the study cannot live with, or be the caregiver of a person with a weakened natural defense mechanism, or a very young infant, for up to 2 months after the last study vaccination.

Measures to Limit the Risks for the Environment

If a sample taken from people who take part in the clinical study is accidentally spilled, the surface will be thoroughly disinfected. No other measures will be put in place because the risk related to release of LAV-YF17D/HBc into the environment is negligible (as LAV-YF17D/HBc cannot survive outside the body).

Emergency Situations

If hospital personnel working on the clinical study accidently self-administers AVX70371, he / she will report this to the responsible person in the hospital.

GLOSSARY

Clinical Study. A research study to test an intervention (for instance a medicine or a vaccine) in people.

DNA. Genetic material. DNA is made of molecules which provide the code for making proteins.

Genetic code. The order of the molecules in DNA defining the composition of the proteins.

Genetically modified organism. An organism (microbe, plant or animal) whose genetic code has been changed using genetic engineering techniques.

Immune cells. The cells of the body's natural defense mechanism. Immune cells include antibodies and other cells that can fight off foreign organism such as viruses.

Vaccine. Vaccines teach the body's natural defense system to fight off organisms that can cause illness. Vaccines introduce the body to foreign substances. As a result, the body's natural defense mechanism is activated to make immune cells against the foreign substance. That way, the body's natural defense mechanism will recognize the substance as a target for attack. If the person gets infected with the real organism later in life, the natural defense mechanisms will recognize it and fight it off.

Virus. A very small (not visible for the naked eye) organism, which can infect and multiply in the cells of other organisms such as animals or humans.

CONTACT

If you have any comments on the public dossier or our activities or which to get additional information, you can contact us at:

AstriVax NV
Gaston Geenslaan 3
3001 Leuven
Belgium
Email: regulatory@astrivax.com