EHVA T02/ANRS VRI07 Clinical Trial FAQ (English)

EHVA T02/ANRS VRI07 Clinical Trial: "A phase II randomised, placebo-controlled trial of vedolizumab with or without a therapeutic MVA-based HIV vaccine in individuals who started antiretrovirals during primary or chronic infection"

1. What is the goal of this trial?

This trial will evaluate a new experimental therapy for people living with HIV. Known as a phase II trial, it will evaluate a **therapeutic vaccine candidate** together with an antibody-based immunotherapy (a treatment aimed at stimulating immune responses). The trial has **two main objectives**:

- To **evaluate the safety and tolerability** of the experimental vaccine candidate in combination with the antibody, or the antibody alone.
- To evaluate if the experimental vaccine in combination with the antibody, or the antibody alone, can **control HIV infection** in participants who are on antiretroviral therapy, once this therapy is halted.

The trial seeks to determine if the vaccine and antibody, alone or in combination, can generate new immune responses against HIV and/or can boost the participant's existing immune responses to HIV. The immune responses of the vaccine and antibody will be evaluated in comparison with a placebo (a dummy vaccine/infusion that is inactive).

2. What products / therapies are being evaluated in the trial?

The trial will evaluate an experimental therapeutic vaccine together with an antibody. The experimental therapeutic vaccine is an MVA vaccine, known as ANRS MVA HIV-B, which was developed by the ANRS, a public HIV research agency based in France. This vaccine contains genetic sequences of the most common type of HIV in Europe, called Clade B; these sequences are called gag, pol and nef, and they are delivered in a viral vector based on Modified Vaccinia Virus Ankara (MVA). This virus-based vector cannot replicate in human cells but acts as a "carrier" for the HIV genes.

The trial will also evaluate a monoclonal antibody called vedolizumab. Monoclonal means that it is made by identical cells, all of them are clones of a cell of the immune system. Vedolizumab may reinforce the action of the immune system. Earlier studies suggest that vedolizumab may impede HIV replication and support the immune system in controlling the HIV infection even when antiretroviral treatment is halted. Vedolizumab is an immunotherapy approved in humans for the treatment of inflammatory bowel disease (Crohn's and Ulcerative Colitis).

3. What is a therapeutic HIV vaccine?

Vaccines can be prophylactic (preventative) or therapeutic. Preventative vaccines are administered to healthy individuals to prevent infection or disease. Such vaccines achieve this by teaching the immune system to fight a virus or other invader before the body is exposed to it. Therapeutic vaccines are vaccines that are administered to people who already have an infection of HIV. **The aim of therapeutic HIV vaccines is to help the immune system to control HIV infection and slow or halt progression to AIDS**. There are currently no therapeutic HIV vaccines available on the market.

4. Why are therapeutic HIV vaccines needed?

Therapeutic vaccines can be part of a strategy to control infection in people living with HIV beyond what antiretroviral treatment (ART) for HIV can achieve. People living with HIV who take ART can live long and healthy lives, but most of them must take their medicines every day, they may experience side-effects, and some people may find it difficult to take a drug every day for the rest of their life. Researchers are developing alternative approaches to increase the number of therapeutic options for people living with HIV. Therapeutic vaccination could potentially provide such an alternative option. The aim would be to develop vaccines that are able to control infection in people living with HIV, in the absence of ART.

5. How are therapeutic HIV vaccines tested?

Therapeutic vaccines are tested like other vaccines or drugs. They go through rigorous pre-clinical trials (not in people) and clinical trials to ensure that they are safe and work. All procedures require approval from ethics committees to ensure that the safety and rights of volunteers participating in the trial are protected and the trials follow ethical regulations. **Therapeutic HIV vaccines are evaluated with participation of people living with HIV.** The clinical trial will have a detailed protocol on how the vaccine candidate is evaluated against the standard of care (i.e. ART) and how the safety and rights of volunteers are protected.

6. What is involved during the vaccine trial?

People who are eligible to participate in the trial and that have provided informed consent for their participation will be randomly assigned to different groups. They will receive either the vaccine candidate in combination with the antibody, or the antibody alone. To find out whether observed responses are linked to the vaccine or antibody, a group is included in the trial who do not receive any active products: this is a control group that will receive placebo (dummy products). The placebos will be administered in the same way as the active products.

To find out whether the vaccine candidate in combination with the antibody, or the antibody alone, is able to generate immune responses and control HIV infection, all **participants will be asked to halt their HIV treatment for a short time**. This is known as analytic treatment interruption. **Halting treatment carries the risk that HIV rebounds and viral loads increase;** it is not recommended in treatment guidelines and is used only as part of a clinical study. **Participants who undergo treatment interruption as part of this trial will be carefully monitored and treatment will be re-instated if there are any symptoms due to HIV or signs that the viral loads increase**.

Participants in the trial will have to undertake **regular visits** to the clinical trial center during the period of the trial, which is **scheduled to run for 37.5 months** to receive the products being evaluated, to monitor their health and to provide blood samples for analysis. Participants will receive **two injections of the vaccine candidate or placebo** and receive **vedoluzimab or placebo by i.v. infusion seven times**.

7. Who is running the trial?

The trial is part of the work of the **European HIV Vaccine Alliance (EHVA).** The EHVA is a consortium of 42 partners, including scientists, civil society organisations, and academic and industrial research partners. The lead organisation and technical sponsor, with responsibility for the trial is Inserm-

ANRS in France. **ANRS** is a public agency, part of **Inserm (the French National Institute for Health and Medical Research)**, responsible for HIV research. You can find out more at www.anrs.fr/ . The **MRC Clinical Trials Unit** at the **University College London** in the UK is overseeing the management of the trial. You can find out more at www.ctu.mrc.ac.uk/.

The trial is scheduled to run in four European countries; in each country the trial will be managed by a national clinical research centre. All centres involved in this trial have extensive expertise in running clinical trials. The European AIDS Treatment Group serves as the community engagement partner and is represented at all levels of trial management including the oversight committees. Other members of the European HIV Vaccine Alliance will support with the analysis, data management and dissemination of trial information and results.

The study is funded by the European Commission Horizon 2020 Research and Innovation Programme (grant no. 681032), and the Swiss government through SERI (grant no. 15.0337).

8. Can participants in the trial be cured from HIV?

The participants of this trial are not expected to be cured from HIV. The vaccine regimen and immunotherapy in this trial is experimental and we do not yet know if in the future it will be used to improve the control of the HIV viral replication. The products will be tested for their ability to control viral replication over a relatively short period of time in the absence of anti-retroviral (ARV) therapy. If the results are positive – meaning if the regimen is found to be well tolerated and able to delay the time to viral replication over a significantly longer time period compared with the placebo – this would provide a signal for further research of the regimen.

9. Is there a risk of HIV transmission during HIV treatment interruption?

HIV may come back quickly when HIV treatment is interrupted, and it may reach high levels in between the routine weekly tests. The rebound in viral load might also be associated with a risk of viral transmission to sexual partner(s). This is why it is important to use alternative methods to reduce the risk of onward HIV transmission when HIV treatment is interrupted. This could be having no sex, or only with condoms, or having sex with partner(s) who take Pre-exposure Prophylaxis (PrEP).

During the treatment interruption phase of the study, participants will be asked to return every week for check-ups. This is in order to reduce any risk to participants' health as well as transmission to partners.

10. What type of volunteers is the study looking for?

The trial will enrol participants living with HIV. The aim is to enrol 69 eligible individuals across the six participating research centres. People are eligible for the trial participation if they are living with HIV, between 18 – 65 years of age, initiated antiretroviral therapy (cART) after 2009 and have been on treatment for at least one year prior to screening, with viral load below 50 copies/ml at screening and a CD4 count of at least 500 cells/mm3, willing to interrupt treatment for up to 24 weeks and to change treatment regimen if required.

11. Which safeguarding measures are implemented for trial participants to reduce health risks associated with COVID-19?

The EHVA team postponed the start of the trial in the spring to ensure that those interested in participating in the trial will have been able to complete their COVID-19 vaccination. The EHVA trial team anticipates, based on current national guidance, that people living with HIV will have had the opportunity to complete COVID-19 vaccinations and likely boosters towards the end of 2021 in all participating countries. Participation in the trial will require that the last vaccination will have taken place at least 28 days before receipt of the experimental HIV vaccine. In anticipation of a potential need for further COVID-19 booster vaccines as well flu vaccines during the trial, clinical investigators will safely time the trial injections by leaving a 28-day gap to avoid potential interference between authorised vaccinations and the experimental intervention.

12. I am interested in learning more – who can I contact for further information?

If you are interested in learning more about the EHVA T02 study, please contact the European AIDS Treatment Group to connect to local community contacts (projects@eatg.org) or the EHVA communications team for general inquiries (communication@ehv-a.eu).