LAY CLINICAL TRIAL DESCRIPTION / PROTOCOL SYNOPSIS in LAY LANGUAGE

General clinical trial information

Roche Trial Number / acronym: CO44668 / IMbrave152

National Clinical Trial Number / EU Clinical Trial Number: <TBD> / 2023-503422-39-00 Trial title: A phase III, randomized, double-blind, placebo-controlled study evaluating atezolizumab and bevacizumab, with or without tiragolumab, in patients with untreated locally advanced or metastatic hepatocellular carcinoma

Lay clinical trial title: A clinical trial to compare tiragolumab plus atezolizumab and bevacizumab with placebo plus atezolizumab and bevacizumab in people with untreated, advanced hepatocellular carcinoma

1. Why is the IMbrave152 clinical trial needed?

Hepatocellular carcinoma (HCC) is the most common type of liver cancer. Most people are first diagnosed with HCC once it has spread to surrounding tissues or lymph nodes (known as 'advanced HCC') or to other parts of the body (known as 'metastatic HCC'). The standard first treatment for advanced or metastatic HCC is a cancer immunotherapy (which helps the body's immune system to destroy cancer cells) called atezolizumab, given with another drug called bevacizumab. However, there is currently no cure for this disease. New treatment combinations are needed for advanced or metastatic HCC.

Tiragolumab is a type of immunotherapy that may boost anti-cancer activity when given with atezolizumab and bevacizumab. Tiragolumab is an experimental medicine, which means it has not been approved by health authorities for treating HCC. This clinical trial aims to compare the effects, good or bad, of tiragolumab plus atezolizumab and bevacizumab versus placebo plus atezolizumab and bevacizumab in people with HCC.

2. How does the IMbrave152 clinical trial work?

This clinical trial is recruiting people with HCC. People can take part if they have advanced or metastatic HCC and have not been treated for it. People who take part in this clinical trial (participants) will be given the clinical trial treatment tiragolumab plus the standard first treatment for HCC - atezolizumab plus bevacizumab, OR placebo plus atezolizumab plus bevacizumab. The clinical trial doctor will see them about every 3 weeks. These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. After the final dose of treatment, the clinical trial doctor will follow-up with participants about every 3 months for as long as they agree to it. The total time of participation in the clinical trial will depend how well a participant responds to treatment and could be up to more than 3 years. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the IMbrave152 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) are the length of time between the start of treatment and cancer getting worse (known as 'progression free survival') and how long participants live (known as 'overall survival').

The other clinical trial endpoints include:

- The number of participants who have either no detectable cancer or who have cancer that has reduced in size (known as 'overall response rate')
- The amount of time between cancer getting better from treatment and then getting worse (known as 'duration of response')
- Changes in quality of life
- The number and seriousness of side effects

- How the body breaks down and processes the clinical trial treatment
- Whether the participants' immune system tries to reject tiragolumab and atezolizumab

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old and have advanced or metastatic HCC, or HCC that cannot be removed with surgery. People may not be able to take part in this trial if they have previously received certain treatments, including those for advanced/metastatic HCC, or have certain medical conditions, such as problems with bleeding in the gut, other cancer types, auto-immune, lung or heart disease, certain infections, are pregnant or breastfeeding, or are planning to become pregnant shortly after the trial.

5. What treatment will participants be given in this clinical trial?

People who join this clinical trial will be split into 2 groups by chance (like flipping a coin) and given either:

- **Atezolizumab plus bevacizumab plus tiragolumab** given as an infusion (into the vein)

  OR
- **Atezolizumab plus bevacizumab plus placebo** given as an infusion (into the vein)

Treatment will be given every 3 weeks for as long as it can help them, and participants will have an equal chance of being placed in either group.

This is a 'placebo-controlled' clinical trial, which means that one of the groups will be given standard treatment plus a substance with no active ingredients (known as a 'placebo'); it looks like the drug being tested but does not contain any real medicine. Comparing results from the different groups helps the researchers know whether any changes seen result from the drug or occur by chance. This is a double-blinded trial, which means that neither the participant nor the clinical trial doctor can choose or know the group the participant is in, until the trial is over. This helps to prevent bias and expectations about what will happen. However, the participant's clinical trial doctor can find out which group the participant is in, if their safety is at risk.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. Participants will be told about the known side effects of **tiragolumab**, **atezolizumab** and **bevacizumab** and possible side effects based on human and laboratory studies or knowledge of similar drugs. Tiragolumab, atezolizumab, bevacizumab and placebo will be given as an infusion into the vein (intravenous infusion). Participants will be told about any known side effects of intravenous infusions.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.