ForPatients
by Roche

Hepatocellular Carcinoma (HCC)

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

A Study Evaluating Atezolizumab and Bevacizumab, With or Without Tiragolumab, in Participants With Untreated Locally Advanced or Metastatic Hepatocellular Carcinoma (IMbrave152)

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	27 Countries	NCT05904886 2023-503422-39-00 CO44668

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official 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

Trial Summary:

The purpose of this study is to assess the efficacy and safety of tiragolumab, an anti-TIGIT monoclonal antibody, when administered in combination with atezolizumab and bevacizumab as first-line treatment, in participants with unresectable, locally advanced or metastatic HCC. Per amendment version 5, following a memo issued by the Sponsor, participants receiving treatment in the atezolizumab plus bevacizumab plus tiragolumab arm are recommended to discontinue tiragolumab treatment unless the investigator decides the benefit outweighs the risk. Participants receiving treatment in atezolizumab plus bevacizumab plus placebo arm must discontinue placebo treatment. Participants may continue receiving active treatment(s) per protocol until loss of clinical benefit or unacceptable toxicity, whichever occurs first.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT05904886 2023-503422-39-00 CO44668
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the IMbrave152 / SKYSCRAPER-14 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 / SKYSCRAPER-14 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 / SKYSCRAPER-14 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 ‘objective response rate’)

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- 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

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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.

Inclusion Criteria:

- Locally advanced or metastatic and/or unresectable HCC with diagnosis confirmed by histology/ cytology or clinically by American Association for the Study of Liver Diseases (AASLD) criteria in cirrhotic participants
- Disease that is not amenable to curative surgical and/or locoregional therapies
- No prior systemic treatment for locally advanced or metastatic and/or unresectable HCC-measurable disease according to RECIST v1.1
- Eastern cooperative oncology group (ECOG) performance status of 0 or 1 within 7 days prior to randomization
- Child-pugh Class A within 7 days prior to randomization
- Adequate hematologic and end-organ function
- Female participants of childbearing potential must be willing to avoid pregnancy within 5 months after the final dose of atezolizumab, within 6 months after the final dose of bevacizumab, and within 90 days after the final dose of tiragolumab/placebo
- Male participants with a female partner of childbearing potential or pregnant female partner must remain abstinent or use a condom during the treatment period and for 6 months after the final dose of bevacizumab and for 90 days after the final dose of tiragolumab/placebo to avoid exposing the embryo.

Exclusion Criteria:

- Pregnancy or breastfeeding within 5 months after the final dose of atezolizumab, within 6 months after the final dose of bevacizumab, and within 90 days after the final dose of tiragolumab/placebo

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- Prior treatment with cluster of differentiation 137 (CD137) agonists or immune checkpoint blockade therapies
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Treatment with locoregional therapy to liver within 28 days prior to initiation of study treatment, or non-recovery from side effects of any such procedure
- Treatment with systemic immunostimulatory agents
- Treatment with systemic immunosuppressive medication
- Untreated or incompletely treated esophageal and/or gastric varices with bleeding or that are at high risk for bleeding
- A prior bleeding event due to esophageal and/or gastric varices within 6 months prior to initiation of study treatment
- Active or history of autoimmune disease or immune deficiency
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- History of malignancy other than HCC within 5 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death
- Mixed histology or other subtypes/variants of HCC, including, but not limited to, known liver adenocarcinoma, fibrolamellar HCC, sarcomatoid HCC, other rare HCC variant, or mixed cholangiocarcinoma and HCC
- Co-infection with hepatitis B virus (HBV) and hepatitis C virus (HCV)
- Acute epstein-barr virus (EBV) infection or known or suspected chronic active EBV infection
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases.

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