ForPatients
by Roche

Unresectable Hepatocellular Carcinoma Hepatocellular Carcinoma (HCC)

A study to compare atezolizumab plus lenvatinib or sorafenib with lenvatinib or sorafenib alone in people with advanced and/or inoperable liver cancer (hepatocellular carcinoma) after previous treatment with atezolizumab plus bevacizumab

A Study of Atezolizumab With Lenvatinib or Sorafenib Versus Lenvatinib or Sorafenib Alone in Hepatocellular Carcinoma Previously Treated With Atezolizumab and Bevacizumab

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	30 Countries	NCT04770896 2023-503229-21-00 MO42541

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

Trial Summary:

This is a Phase III, open-label, multicenter, randomized, two-arm study designed to evaluate the efficacy and safety of atezolizumab plus either lenvatinib or sorafenib versus lenvatinib or sorafenib alone in participants with locally advanced or metastatic Hepatocellular Carcinoma (HCC) who have progressed on prior systemic treatment with atezolizumab plus bevacizumab combination.

Hoffmann-La Roche Sponsor	**Phase 3** Phase

NCT04770896 2023-503229-21-00 MO42541
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	>=18 Years	No

1. Why is this study needed?

Hepatocellular carcinoma (HCC) is the most common type of liver cancer. Standard first medicine for inoperable HCC includes atezolizumab and bevacizumab which are widely used cancer immunotherapies (CITs). They help the body’s immune system to destroy

cancer cells. Other treatments, such as sorafenib or lenvatinib are medicines that can block cancer growth. When first treatments do not work well, or stop working, treatment is switched to another therapy option. Currently, doctors do not know which medicines would work best as a next treatment for HCC after atezolizumab and bevacizumab stop working. This is why researchers are looking at new therapy options.

This study aims to compare the effects of atezolizumab plus lenvatinib or sorafenib versus lenvatinib or sorafenib alone in people with HCC.

2. Who can take part in this study?

People (males and females) of at least 18 years old and diagnosed with advanced, metastatic or inoperable HCC, can take part in this study if they have previously received atezolizumab plus bevacizumab as treatment for HCC and have good liver function.

People may not be able to take part in this study if they have had previous treatment with certain medications, have cancer that has spread to the brain or spinal cord and causes symptoms. People with certain medical conditions also may not be able to take part in the study, this includes a second type of cancer, autoimmune, heart, liver or lung diseases, or certain infections. Women who are pregnant or breastfeeding, cannot take part in this study.

3. How does this study work?

This clinical trial is recruiting people with HCC which has spread to surrounding tissues (called ‘advanced’), to other parts of the body (known as ‘metastatic’) or cannot be removed with surgery (called ‘inoperable’).

Participants will be screened to check if they are able to participate in the study. The screening period will take place 28 days before the start of treatment.

Everyone who joins this study will be split into two groups (Group A and Group B) randomly (like flipping a coin). Group A will be given atezolizimab, given as an infusion (into the vein) every 3 weeks, plus lenvatinib, given as pills which are taken every day OR sorafenib pills to be taken twice daily. Group B will be given lenvatinib, given as pills which are taken every day OR sorafenib pills to be taken twice daily. Participants will have an equal chance of being placed in either group. They will continue to receive treatment as long as there is clinical benefit. In both groups, whether participants get lenvatinib or sorafenib will depend on the study site, but all participants at each site will be given the same option.

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will see participants every 3 weeks while they are receiving treatment. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visits or telephone calls every 3 months, for 1 year after completing the study treatment, during which the study doctor will check on the participant's well being. Total time of participation in the study will be approximately 1 and a half years. It depends on the clinical benefit from the allocated study treatment. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main results measured in the study to assess if the medicine has worked how long participants live (overall survival) from the start of the study.

Other key results measured in the study include:

- The time between the start of the trial and cancer getting worse or loss of life for any reason (progression-free survival)
- How many participants have a reduction of their cancer after treatment (objective response rate)
- The duration between the start of a treatment and the point at which the cancer being treated progresses or worsens. (time to progression)
- How much time there is between the participant's cancer first responding to treatment and the cancer getting worse. (duration of response)
- The time between the start of the trial and to a worsening health-related quality of life
- The number, type, and seriousness of any side effects

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study drugs

Participants may have unwanted effects from the drugs used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to

person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Participants will be told about the known unwanted effects of atezolizumab, lenvatinib and sorafenib, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines.

Known unwanted effects of atezolizumab include inflammation as the medication is designed to increase the number of immune system cells in the body that can fight cancer. These cells may cause inflammation within the tumor, as well as in normal tissue, anywhere in the body. Other unwanted effects include back pain, cough, decreased appetite, diarrhea, fatigue, fever, headache, itching of the skin (pruritus), joint pain (arthralgia).

Known unwanted effects of lenvatinib include high or low blood pressure, loss of appetite or weight loss, feeling sick (nausea) and being sick (vomiting), constipation, diarrhea, abdominal pain, indigestion, feeling very tired or weak, hoarse voice, swelling of the legs, rash.

Known unwanted effects of sorafenib include diarrhea, feeling sick (nausea) and being sick (vomiting), feeling weak or tired (fatigue), pain (including mouth pain, abdominal pain, headache, bone pain, tumor pain), hair loss (alopecia).

The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.