ForPatients
by Roche

Hepatocellular Carcinoma (HCC)

A clinical trial to look at how safe and effective different combinations of treatment that include an immunotherapy are to reduce tumour size before surgery in people with liver cancer (hepatocellular carcinoma)

A Study Evaluating The Efficacy and Safety of Neoadjuvant Immunotherapy Combinations in Patients With Surgically Resectable Hepatocellular Carcinoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	9 Countries	NCT05908786 2022-502840-11-00 GO44457

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 Ib/II, open-label, multicenter, randomized platform study evaluating the efficacy and safety of neoadjuvant immunotherapy combinations in patients with surgically resectable hepatocellular carcinoma (MORPHEUS-Neoadjuvant HCC)

Trial Summary:

This is a Phase Ib/II, open-label, multicenter, randomized platform study to evaluate neoadjuvant immunotherapy combinations in participants with resectable HCC. The study is designed with the flexibility to open new treatment arms as new agents become available, close existing treatment arms that demonstrate minimal clinical activity or unacceptable toxicity, or modify the participant population.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT05908786 2022-502840-11-00 GO44457
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the GO44457 clinical trial needed?

Hepatocellular carcinoma (HCC) is the most common type of liver cancer. For some patients, they may receive a type of surgery known as a liver resection as a form of treatment. This type of HCC is also known as ‘resectable’ or ‘operable’ HCC which means the tumour can be removed by surgery. Yet, 2 out of 3 people with HCC cannot have surgery, often due to the tumour being too big. Cancer cells can spread from the tumour and grow in other parts of the body – these are called ‘micrometastases’ when they are too small to be seen on scans. If people with HCC have micrometastases, the HCC can return after surgery. The risk of cancer returning after surgery is high for people with large tumours or micrometastases.

In other cancer types, treatments before surgery (known as ‘neoadjuvant treatments’) can shrink tumours and destroy micrometastases. Neoadjuvant treatments are needed for people with HCC so that people with larger tumours can have surgery and also lower the risk of cancer returning afterwards. Treatments that help the immune system destroy cancer cells (known as ‘cancer immunotherapies’, or CITs) have been shown to be effective against HCC that has grown or spread in the body. CITs may also work well as neoadjuvant treatments, and the anti-cancer activity may be boosted when different treatments are given at the same time – as CIT combinations.

This clinical trial aims to compare the effects, good or bad, of different combinations of CIT as neoadjuvant treatments in HCC. Health authorities have not approved the combinations as neoadjuvant treatments for HCC, so they are called experimental drug treatments in this trial.

2. How does the GO44457 clinical trial work?

This clinical trial is recruiting people with HCC. People can take part if they have been diagnosed with HCC, which can be removed with surgery, and they have not received any treatment for HCC. People who take part in this clinical trial (participants) will be given up to 3 rounds of treatment (once every 3 weeks, known as treatment ‘cycles’) with one of several CIT combinations (consisting of at least one CIT drug) unless participants have unacceptable side effects. About 1 month after the third treatment cycle, participants may have surgery. After they have fully recovered from surgery, participants may be given the option to continue to receive treatment with a CIT combination (starting 1–3 months after surgery) or to attend follow-up visits in the clinic with no further CIT treatment. During treatment, participants will be seen by the clinical trial doctor at clinic visits every 2–4 weeks for about 5 months, then follow-up visits every 4 months after the last treatment dose for the next 2 years. These visits are to see how participants respond to treatment and any side effects they may have. The total time in the clinical trial will be approximately 2–3 years, including the follow-up visits, depending on how well the treatment works and any side effects they may have. Participants can stop trial treatment and leave the trial at any time.

3. What are the main endpoints of the GO44457 clinical trial?

The main clinical trial endpoint (the main result measured in the trial to see if each CIT combination has worked) is the number of participants who have less than one-tenth of their cancer remaining after treatment, compared with before treatment (known as ‘major pathologic response’).

The other clinical trial endpoints include:

- The number of participants who have no cancer remaining (complete pathologic response)
- The time that passes between surgery and cancer coming back (relapse-free survival)
- The time that passes between the trial start and cancer getting worse (event-free survival)
- How long participants live (overall survival)
- The number of participants who have either no detectable cancer or who have cancer that has reduced in size before surgery (objective response rate)
- The number, type, and seriousness of any side effects

4. Who can take part in this clinical trial?

People can take part in this trial if they are over 18 years old and are willing to provide a tumour tissue sample (known as a ‘core needle biopsy’) at the start of the trial.

People may not be able to take part in this trial if they have:

- Rare types of HCC (such as fibrolamellar HCC and sarcomatoid HCC)
- Previously received certain treatments, including with CITs
- Certain other medical conditions, including liver conditions, high blood pressure, auto-immune diseases, infections, another cancer type within the last 5 years, pregnancy or breastfeeding, or people planning to conceive during or shortly after the trial

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

Participants will be given a combination of CITs (such as **atezolizumab** plus **bevacizumab** with or without **tiragolumab**, or **RO7247669** plus **bevacizumab**) as an infusion into a vein. Participants will be placed in a CIT combination treatment group randomly (by chance) depending on the safety criteria they meet and the number of groups available. If three CIT combinations are available, they will have a 1 in 3 chance of receiving any one of those CIT combinations. This is an open-label trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

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 delay surgery that could provide a cure, and have side effects (an unwanted effect of a 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 told about the known side effects of **CITs** and possible side effects based on human and laboratory studies or knowledge of similar drugs. **CITs** will be given as an infusion into a vein (intravenous infusion). Participants will be told about known side effects of intravenous infusion.

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:

- Diagnosis of HCC confirmed either histologically or clinically according to AASLD criteria for patients with cirrhosis. For participants without cirrhosis, histological confirmation is mandatory.
- HCC that is amenable to R0 surgical resection with curative intent in the opinion of the surgeons and oncologists or hepatologists involved in the care of the participant. Patients presenting with resectable HCC within or beyond Milan criteria (without extrahepatic spread or macrovascular invasion) are eligible.
- Measurable disease (at least one target lesion) according to RECIST v1.1 as determined by the investigator
- 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
- Negative HIV test at screening
- No prior locoregional or systemic treatment for HCC
- Adequate hematologic and end-organ function
- Documented virology status of hepatitis
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agreement to refrain from donating sperm

Exclusion Criteria:

General Exclusion Criteria:

- Presence of extrahepatic disease or macrovascular invasion
- Known fibrolamellar HCC, sarcomatoid HCC, mixed cholangiocarcinoma and HCC, or other rare variants of HCC
- History of hepatic encephalopathy if clinically significant within one year prior to initiation of study treatment
- Moderate or severe ascites
- Active co-infection with HBV and HCV
- Active co-infection with HBV and hepatitis D viral infection
- Prior treatment with CD137 agonists or immune checkpoint inhibitors, including anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- 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
- Inadequately controlled hypertension
- History of hypertensive crisis or hypertensive encephalopathy
- Significant vascular disease within 6 months prior to initiation of study treatment
- History of hemoptysis within 1 month prior to initiation of study treatment
- Evidence of bleeding diathesis or significant coagulopathy
- Current or recent (<= 10 days prior to initiation of study treatment) use of full-dose oral or parenteral anticoagulants or thrombolytic agents for therapeutic purposes
- History of abdominal or tracheoesophageal fistula, GI perforation or intra-abdominal abscesses within 6 months prior to initiation of study treatment
- History of intestinal obstruction and/or clinical sign or symptoms of GI obstruction
- Serious, non-healing or dehiscing wound, active ulcer, or untreated bone fracture
- Grade >= proteinuria
- Major surgical procedure, open biopsy, or significant traumatic injury, or abdominal surgery, interventions or traumatic injuries, or anticipation of need of major surgical procedure other than potentially curative liver resection
- Chronic daily treatment with a non-steroidal anti-inflammatory drug (NSAID)
- Serious infection requiring oral or IV antibiotics and/or hospitalization
- Active tuberculosis