ForPatients
by Roche

Renal Cell Cancer (RCC)Renal Cell Carcinoma

A Study of Immune Checkpoint Inhibitor Combinations With Axitinib in Participants with Previously Untreated Locally Advanced Unresectable or Renal Cell Carcinoma that has Spread from One Part of the Body to the Other

A Study of Immune Checkpoint Inhibitor Combinations With Axitinib in Participants With Untreated Locally Advanced Unresectable or Metastatic Renal Cell Carcinoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	9 Countries	NCT05805501 2023-505816-39-00 BO43936

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 Randomized Open Label Phase II Study of Immune Checkpoint Inhibitor Combinations With Axitinib in Patients With Previously Untreated Locally Advanced Unresectable or Metastatic Renal Cell Carcinoma

Trial Summary:

This study will evaluate the safety of tobemstomig (RO7247669) in combination with axitinib alone or with tiragolumab (anti-TIGIT) and axitinib as compared to pembrolizumab and axitinib in participants with previously untreated, unresectable locally advanced or metastatic clear-cell renal cell carcinoma (ccRCC).

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Sponsor

Phase 2
Phase

NCT05805501 2023-505816-39-00 BO43936
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

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Renal cell carcinoma (RCC) is the most common form of kidney cancer that originates in the cells lining the small tubes within the kidney, called renal tubules. In locally advanced or metastatic RCC, the cancer cells grow outside the kidneys and spread to other body parts. Sometimes RCC is ‘unresectable’ meaning it cannot be removed completely with surgery. Cancer treatment often includes a combination of drugs. However, these may not work for all patients, or at all times. Therefore, there is always a need to find new combinations of treatments.

This study is testing drugs called tobemstomig and tiragolumab, in combination with axitinib and comparing this to the combination of pembrolizumab with axitinib. The U.S. Food and Drug Administration (US FDA) have already approved the combination of pembrolizumab and axitinib as a standard of care in patients with RCC. However, in this study, tobemstomig in combination with axitinib, or tiragolumab in combination with tobemstomig and axitinib is experimental. This means health authorities (like the US FDA and European Medicines Agency) have not approved these combinations as a treatment for locally advanced unresectable or metastatic RCC.

This study aims to assess the safety of tobemstomig plus axitinib and tobemstomig plus tiragolumab plus axitinib as compared with pembrolizumab plus axitinib in people with previously untreated RCC that has spread to other parts of the body.

2. Who can take part in the study?

People who were at least 18 years old with RCC that could not be surgically removed or had spread to other parts of the body, took part in this study. People could not take part in this study if they had RCC that has spread to the brain and spinal cord, if they had certain other medical conditions, or had received any prior treatments for RCC. Women who were pregnant, or breastfeeding could not participate in the study.

3. How does this study work?

People were checked by the appropriate clinical staff to see if they were able to participate in the study. This review period took place for about 28 days before the start of treatment.

Everyone who joined this study was split into 3 groups (Groups A, B and a Control group) randomly (like flipping a coin). Participants received either tobemstomig plus axitinib (Group A) or tobemstomig plus tiragolumab plus axitinib (Group B) or pembrolizumab plus axitinib (Control group). Tobemstomig, tiragolumab and pembrolizumab were given as a drip into the vein (infusion) every 3 weeks and axitinib was given as tablets, to be taken by mouth twice a day (BID). Treatment may continue up to 24 months or until participants experience any unwanted side effects, their cancer worsens, or they withdraw from the study, whichever occurs first. Since the main results of this study showed reduced benefit and increased unwanted effects in Group A and B compared to the Control group with increased unwanted effects, all participants receiving treatment as a part of this study are

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recommended to stop the study treatment and take other cancer treatments outside of this study. However, the participant's study doctor, in consultation with the participant, may decide to allow the participant to continue to receive treatment as part of the study if the potential benefit of continuing treatment is greater than the potential risks.

Participants will be seen by the clinical trial doctor regularly. These visits will include checks to see how the participant is responding to the treatment and any unwanted effects they may be having. Participants will have follow-up visits up to 3 months after completion of 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 up to 28 months, depending on how the cancer responds to treatment. Participants have the right to stop study treatment and leave the study at any time if they wish to do so.

This was an open-label study. This means everyone involved, including the participant and the study doctor, knew the study treatment the participant had been given.

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

The main result measured in the study is to determine the number of participants with unwanted effects and its severity in Group A and B as compared to the Control group.

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. The study involves some risks to the participant. People interested in taking part were informed about the risks and benefits, as well as any additional procedures or tests they had to undergo. All details of the study were 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 side effects of the drugs used in this study. These unwanted side effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants are having regular check-ups to see if there are any unwanted side effects.

Participants were told about the known side effects and possible side effects of tobemstomig, tiragolumab, pembrolizumab, and axitinib based on human and laboratory studies or knowledge of similar medicines.

Tobemstomig Known side effects include allergic reactions; symptoms may include itching, difficulty breathing (dyspnoea), chest pain, rash, drop in heart rate (bradycardia), drop in blood pressure (hypotension), loss of consciousness, a blush of purplish discoloration of the skin.

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Tiragolumab Known side effects include inflammation of the liver, also called hepatitis, (with symptoms of yellowing of skin, pain in the stomach area, nausea, vomiting, itching, feeling tired or weak (fatigue), bleeding or bruising under the skin, and dark urine.

Pembrolizumab Known side effects include decrease in the number of red blood cells (anaemia), feeling less hungry, headache, cough, diarrhoea, nausea, vomiting, constipation, stomach pain, skin rash, fever, itching and high blood pressure (hypertension).

Axitinib Known side effects include high blood pressure (hypertension), increased levels of protein in urine (proteinuria), diarrhoea, bleeding (haemorrhage), increased or decreased thyroid function (hyperthyroidism or hypothyroidism), and inflammation of kidneys (nephritis).

Tobemstomig, tiragolumab, and pembrolizumab were given as a drip into a vein. Known side effects with infusion include irritation with symptoms of fever, chills, rash, swelling, itching, redness, pain, headache, changes in blood pressure, vomiting. The study medicines may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1
- International Metastatic RCC Database Consortium (IMDC) risk intermediate (score of 1 or 2) or poor (score of 3-6)
- Measurable disease with at least one measurable lesion
- Histologically confirmed ccRCC with or without sarcomatoid features
- Negative for HIV, hepatitis B, or hepatitis C virus (HCV)

Exclusion Criteria:

- Pregnant or breastfeeding, or intention of becoming pregnant during the study or within 90 days after the final dose of tiragolumab, 4 months after the final dose of tobemstomig (RO7249669) and pembrolizumab, or for 1 week after the final dose of axitinib, whichever occurs last
- Inability to swallow a tablet or malabsorption syndrome
- Prior treatment for localized and/or metastatic RCC with systemic RCC-directed therapy, including T-cell costimulating or immune checkpoint blockade therapies
- Ongoing use or anticipated need for treatment with a strong CYP3A4/5 inhibitor or inducer
- Major surgical procedure, other than for diagnosis, within 4 weeks prior to initiation of study treatment, or anticipation of need for a major surgical procedure during the study
- Uncontrolled or symptomatic hypercalcemia or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy or denosumab
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- History of leptomeningeal disease
- Uncontrolled tumor-related pain
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (once monthly or more frequently)

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- Moderate to severe hepatic impairment (Child-Pugh B or C)
- Uncontrolled hypertension
- Prior history of hypertensive crisis or hypertensive encephalopathy
- Significant cardiovascular/cerebrovascular disease within 3 months (12 months for UK participants) prior to randomization
- History of clinically significant ventricular dysrhythmias or risk factors for ventricular dysrhythmias
- History of congenital QT syndrome
- Resting heart rate (HR) > 100 bpm (or clinically significant tachycardia)
- Stroke (including transient ischemic attack), myocardial infarction, or other symptomatic ischemic event, or thromboembolic event (e.g., deep venous thrombosis [DVT], pulmonary embolism [PE]) within 3 months (12 months for UK participants) before randomization
- Significant vascular disease (e.g., aortic aneurysm or arterial dissection requiring surgical repair or recent peripheral arterial thrombosis) within 6 months prior to Day 1 of Cycle 1
- Tumors invading pulmonary blood vessels, cavitating pulmonary lesions or known endobronchial disease
- Tumor invading the gastrointestinal (GI) tract, including abdominal or tracheoesophageal fistulas
- Evidence of abdominal free air not explained by paracentesis or recent surgical procedure
- Active peptic ulcer disease, acute pancreatitis, acute obstruction of the pancreatic or biliary duct, appendicitis, cholangitis, cholecystitis, diverticulitis, gastric outlet obstruction
- Intra-abdominal abscess within 6 months before initiation of study treatment
- Clinical signs or symptoms of GI obstruction or requirement for routine parenteral hydration, parenteral nutrition, or tube feeding
- Evidence of bleeding diathesis or significant coagulopathy
- Grade # 3 hemorrhage or bleeding event within 28 days prior to initiation of study treatment
- Clinically significant hematuria, hematemesis, hemoptysis of > 0.5 teaspoon (2.5 mL) of red blood, coagulopathy, or other history of significant bleeding (e.g., pulmonary hemorrhage) within 3 months before initiation of study treatment
- Active or history of autoimmune disease or immune deficiency
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during study treatment
- Prior allogeneic stem cell or solid organ transplantation
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- History of another primary malignancy other than RCC within 2 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death (e.g., 5-year OS rate > 90%)
- Administration of a live, attenuated vaccine within 4 weeks before randomization or anticipation that such a live, attenuated vaccine will be required during the study
- Active tuberculosis (TB)
- Severe infection within 4 weeks prior to initiation of study treatment
- Participants with active Epstein-Barr virus (EBV) infection or known or suspected chronic active EBV infection at screening
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- Known hypersensitivity to Chinese hamster *ovary cell products or to any component of tobemstomig, tiragolumab, pembrolizumab, or axitinib

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