ForPatients
by Roche

Urothelial Cancer

A Study Evaluating Different Immunotherapies (LAG-3 and PD-1 With or Without TGIT, Compared to PD-L1 Alone) in Participants With Untreated Locally Advanced or Metastatic Urothelial Cancer

A Study Evaluating Different Immunotherapies (LAG-3 and PD-1 With or Without TIGIT, Compared to PD-L1 Alone) in Participants With Untreated Locally Advanced Metastatic Urothelial Cancer

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	15 Countries	NCT05645692 2023-504027-78-00 BO44157

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 II, Randomized, Multicenter, Open-Label, Controlled Study of Tobemstomig Alone or in Combination With Tiragolumab Versus Atezolizumab in Patients With Previously Untreated Locally Advanced or Metastatic Urothelial Cancer Who Are Ineligible for Platinum-Containing Chemotherapy

Trial Summary:

This study will evaluate the safety of tobemstomig alone or in combination with tiragolumab compared with atezolizumab in participants with previously untreated, locally advanced or metastatic urothelial cancer (mUC) who are ineligible to receive a platinum containing chemotherapy.

Hoffmann-La Roche Sponsor	**Phase 2** Phase

NCT05645692 2023-504027-78-00 BO44157
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Urothelial cancer, also known as “bladder cancer” is a cancer that develops in the cells of the bladder lining. In ‘locally advanced’ bladder cancer the cancer cells grow outside the bladder or urinary tract but have not yet spread to other body parts. When the cancer spreads to other parts of the body it is called ‘metastatic’ cancer. 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 comparing the effects of tobemstomig alone or in combination with tiragolumab in comparison with atezolizumab in people with bladder cancer. Tobemstomig, an anti-PD-1 and ant-LAG-3 bispecific antibody, and tiragolumab, an anti-TIGIT monoclonal antibody, are experimental medicines, which means that they have not been approved by health authorities (like the US FDA and European Medicines Agency) for the treatment for bladder cancer that has spread to other parts of the body. Atezolizumab, an anti PD-L1 monoclonal antibody, is approved for the treatment of other types of cancers in several countries.

This study aims to assess the safety of tobemstomig alone or in combination with tiragolumab compared with atezolizumab in people with previously untreated, bladder cancer that has spread to other parts of the body and who are also not suitable to receive platinum-containing cancer medicines.

2. Who can take part in the study?

People who were at least 18 years old with bladder cancer that has spread to other parts of the body and who were not suitable to receive platinum-containing cancer medicines, took part in this study. People could not take part in this study if their cancer had spread to the brain and spinal cord, if they had certain other medical conditions, or if they had received any prior treatments for bladder cancer. Women who were pregnant, or breastfeeding could not participate in the study.

3. How does this study work?

People were screened to check if they were able to participate in the study. The screening period took place for about 28 days before the start of treatment.

Everyone who joined this study was split into 3 groups (Group A [Control group], B and C) randomly (like flipping a coin). Participants received either atezolizumab (Group A) or tobemstomig (Group B) or tobemstomig plus tiragolumab (Group C), as a drip into the vein (infusion) every 3 weeks. Treatment may continue as long as participants experience benefit from the treatment, or until their cancer worsens, or they experience any unacceptable unwanted effects, or they withdraw from the study, whichever occurs first. In September 2024, the Sponsor decided to stop the clinical development of tobemstomig, and all participants receiving treatment as a part of this study were recommended to stop the study treatment and take other cancer treatments outside of this study. Participants

for whom the study doctor has determined would clearly benefit from this treatment rather than another cancer treatment, can continue receiving it.

The study doctor will see the participants who choose to continue in this study every 3 weeks to check how well the treatment is working and any unwanted effects participants may have. Participants will have a follow-up visit 3 months after completion of treatment, during which the study doctor will check on the participant's well-being. Total time of participation in the study could be more than 30 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 is 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 the number of participants with any unwanted effects and its severity in Group B and C as compared to the Control group (A).

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 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 for treatment.

Risks associated with the study drugs Participants may have unwanted effects of 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 are having regular check-ups to see if there are any unwanted effects.

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

Tobemstomig Known unwanted effects are related to the infusion and include itching, difficulty breathing (dyspnoea), chest pain, rash, drop in heart rate (bradycardia) and/or drop in blood pressure (hypotension).

Tiragolumab Known unwanted effects include effects related to the infusion, such as fever, chills, shortness of breath, rash, nausea, and changes in blood pressure; and inflammation of the liver (hepatitis), symptoms might include yellowing of the skin, pain in the stomach area, nausea, vomiting, itching, feeling tired or weak (fatigue), bleeding or bruising under the skin, and dark urine.

Atezolizumab There are a range of known unwanted effects with atezolizumab, some of which are common and some less common but important to be aware of. Very common side effects, occurring in more than 10% of patients, include back pain, cough, decreased appetite, diarrhoea, fatigue, fever, headache, muscle and bone pain and an infection of any part of the urinary tract. There are also some serious side effects that occur less frequently but require attention, such as inflammation of various organs. Unwanted events relating to the infusion of atezolizumab could also include nausea, vomiting, skin reactions (hives or rash), difficulty breathing, or low blood pressure.

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 (ECOG) Performance Status of # 2
- Histologically or cytologically documented locally advanced or metastatic transitional cell carcinoma (TCC) of the urothelium. Participants with squamous, sarcomatoid, micropapillary, and glandular variant histologies are eligible for inclusion in the study, provided that a urothelial component is present in the tumor specimen. Participants with other variant histologies or pure variant histologies are not eligible for inclusion in this study
- Ineligible ("unfit") to receive platinum-based chemotherapy
- No prior chemotherapy for inoperable locally advanced or metastatic or recurrent urothelial carcinoma (UC)
- Measurable disease; at least one measurable lesion as defined by response evaluation criteria in solid tumors, version 1.1 (RECIST v1.1)
- Availability of a representative leftover tumor specimen that is suitable for determination of PD-L1 status as assessed by a central laboratory
- Adequate hematologic and end organ function
- Negative for hepatitis B and hepatitis C virus (HCV)
- Adequate cardiovascular function

Exclusion Criteria:

- Pregnancy or breastfeeding
- GFR <15 mL/min/1.73 m2
- 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
- Uncontrolled or symptomatic hypercalcemia
- 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
- Active tuberculosis (TB) or acute Epstein-Barr virus (EBV)
- Significant cardiovascular/cerebrovascular disease within 3 months prior to initiation of study treatment
- 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
- History of another primary malignancy other than urothelial carcinoma within 2 years prior to initiation of study treatment, with the exception of malignancies with a negligible risk of metastasis or death
- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic oral or intravenous antibiotics within 2 weeks prior to initiation of study treatment. Participants receiving prophylactic antibiotics (e.g., to prevent a urinary tract infection or chronic obstructive pulmonary disease [COPD] exacerbation), or who are receiving oral antibiotics to treat a urinary tract infection are eligible for the study
- Prior allogeneic stem cell or solid organ transplantation
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during treatment or within 5 months after the final dose of atezolizumab, 4 months after the final dose of tobemstomig, or 90 days after the final dose of tiragolumab
- Current treatment with anti-viral therapy for HBV
- Treatment with any approved anti-cancer therapy, including chemotherapy or hormonal therapy, within 3 weeks prior to initiation of study treatment
- Treatment with investigational therapy within 4 weeks or 5 drug-elimination half-lives (whichever is longer) prior to initiation of study treatment
- Prior treatment with CD137 agonists or immune checkpoint blockade therapies, including anti-TIGIT and anti-LAG3 therapeutic antibodies or pathways targeting agents
- Treatment with systemic immunostimulatory agents within 4 weeks or 5 drug-elimination half-lives prior to initiation of study treatment
- 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
- History of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins