ForPatients
by Roche

Urothelial CarcinomaBladder Cancer

A clinical trial to look at how well atezolizumab works when taken with other drugs, compared to atezolizumab alone, in people with bladder cancer

Study Evaluating the Efficacy and Safety of Multiple Immunotherapy-Based Treatments and Combinations in Patients With Urothelial Carcinoma (MORPHEUS-UC)

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	7 Countries	NCT03869190 WO39613

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 Umbrella Study Evaluating the Efficacy and Safety of Multiple Immunotherapy-Based Treatments and Combinations in Patients With Urothelial Carcinoma (MORPHEUS-UC)

Trial Summary:

A Phase Ib/II, open-label, multicenter, randomized, umbrella study in participants with MIBC and in participants with locally advanced or metastatic Urothelial Carcinoma (UC) who have progressed during or following a platinum-containing regimen. The study is designed with the flexibility to open new treatment arms as new treatments become available, close existing treatment arms that demonstrate minimal clinical activity or unacceptable toxicity, or modify the participant population (e.g., with regard to prior anti-cancer treatment or biomarker status). Participants in the mUC Cohort who experience loss of clinical benefit or unacceptable toxicity during Stage 1 may be eligible to continue treatment with a different treatment regimen for Stage 2.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT03869190 WO39613
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

All	#18 Years	No

How does the WO39613 clinical trial work?

This clinical trial is recruiting people who have bladder cancer that has spread to the muscle layer of the bladder (muscle invasive bladder cancer or MIBC).

The purpose of this clinical trial is to compare the effects, good or bad, of atezolizumab when taken with other drugs, compared to atezolizumab alone, in participants with MIBC. Patients will also have surgery during the study to remove the bladder, which is a standard treatment for MIBC.

Atezolizumab is an antibody that may help your immune system stop or reverse the growth of tumours. Atezolizumab is approved in some countries for the treatment of bladder cancer, lung cancer, breast cancer, liver cancer, and skin cancer. Participants who join this clinical trial will be given either atezolizumab alone or atezolizumab with another drug called tiragolumab. Tiragolumab is also an antibody that may help your immune system stop or reverse the growth of tumours. Patients who are healthy enough to receive chemotherapy (a standard treatment for MIBC) will receive cisplatin and gemcitabine in addition to atezolizumab/tiragolumab.

How do I take part in this clinical trial?

To be able to take part in this clinical trial, you must have been diagnosed with MIBC and be at least 18 years old. You must not have previously been given any of the medicines being tested in this clinical trial and you cannot join the trial if you are pregnant or breastfeeding.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in the clinical trial, women who can become pregnant will need to either avoid heterosexual intercourse or use contraception for safety reasons. Men that have a female partner who can become pregnant may need to follow the same restrictions.

What treatment will I be given if I join this clinical trial?

Participants will receive treatment based on their ability to receive cisplatin-containing chemotherapy. Participants will then be split randomly to receive atezolizumab or atezolizumab plus at least one other drug:

For participants who cannot be given cisplatin:

- **Atezolizumab** alone, given as an infusion into your vein on the first day of each treatment cycle, which lasts for 21 days, for 3 cycles **before surgery** and 14 cycles **after**
- OR **atezolizumab** and **tiragolumab**, both given as an infusion into your vein on the first day of each treatment cycle, for 3 cycles **before surgery** and 14 cycles **after**

For participants who can be given cisplatin:

- **Atezolizumab** given as an infusion into your vein every 3 weeks for 3 treatment cycles **before surgery** and 14 cycles **after**, plus
- **Cisplatin** given as an infusion into your vein every 3 weeks for 3 cycles **before surgery**, and
- **Gemcitabine** given as an infusion into your vein on the first and eighth day of each treatment cycle (lasting 21 days), for 3 cycles **before surgery**

OR

- **Atezolizumab** and **tiragolumab**, both given as an infusion into your vein every 3 weeks for 3 treatment cycles **before surgery** and 14 cycles **after**, plus
- **Cisplatin** given as an infusion into your vein every 3 weeks for 3 cycles **before surgery**, and
- **Gemcitabine**, given as an infusion into your vein on the first and eighth day of each treatment cycle (lasting 21 days), for 3 cycles **before surgery**

How often will I be seen in follow-up appointments and for how long?

You will be given the clinical trial treatment (atezolizumab alone or with another drug/ drugs) every 3 weeks for approximately 1 year. You are free to stop this treatment at any

time. After being given your final treatment, you will still be seen by the clinical trial doctor within 1 month and then every 3 months after that. These visits will include checks to see how you are responding to the treatment and any side effects that you may be having. In some cases, these visits may take place over the phone.

What happens if I am unable to take part in this clinical trial?

If this clinical trial is not suitable for you, you will not be able to take part. Your doctor may suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov

Trial-identifier: NCT03869190

Inclusion Criteria:

Inclusion Criteria for mUC Cohort:

- Histologically documented, locally advanced or metastatic UC (also termed TCC or urothelial cell carcinoma of the urinary tract; including renal pelvis, ureters, urinary bladder, and urethra)
- Availability of a representative tumor specimen that is suitable for determination of PD-L1 and/or additional biomarker status by means of central testing
- Disease progression during or following treatment with no more than one platinum-containing regimen for inoperable, locally advanced or metastatic UC or disease recurrence
- ECOG Performance Status of 0 or 1
- Measurable disease (at least one target lesion) according to RECIST v1.1
- Adequate hematologic and end-organ function
- Negative HIV test at screening
- Negative total hepatitis B core antibody (HBcAb) test and hepatitis C virus (HCV) antibody at screening
- Tumor accessible for biopsy
- For women of childbearing potential: agreement to remain abstinent or use contraceptive measures and agreement to refrain from donating eggs
- For men: agreement to remain abstinent or use contraceptive measures, and agreement to refrain from donating sperm

Inclusion Criteria for MIBC Cohorts:

- ECOG PS of 0 or 1
- Fit and planned-for cystectomy
- Histologically documented MIBC (pT2-4, N0, M0), also termed TCC or urothelial cell carcinoma of the urinary bladder
- N0 or M0 disease by CT or MRI
- Adequate hematologic and end-organ function
- Availability of TURBT specimen
- Negative HIV, HBcAb, and HCV test at screening

- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures and agreement to refrain from donating eggs as outlined for each specific treatment arm
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm, as outlined for each specific treatment arm

Exclusion Criteria:

Exclusion Criteria for mUC Cohort:

- Prior treatment with a T-cell co-stimulating therapy or a CPI including anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Prior treatment with any of the protocol-specified study treatments including treatment with poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP) inhibitor, nectin-4 targeting agents, signal regulatory protein alpha-targeting agents, or TIGIT-targeting agents, Trop-2 targeting agents, FAP-directed therapies, 4-1BB (CD137)-directed therapies, or topoisomerase 1 inhibitors
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Any approved anti-cancer therapy, including chemotherapy or hormonal therapy, within 3 weeks prior to initiation of study treatment
- Eligibility only for the control arm
- Prior allogeneic stem cell or solid organ transplantation
- Treatment with systemic immunostimulatory agents within 4 weeks or 5 half-lives of the drug (whichever is longer) prior to the initiation of study treatment
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment or anticipation of need for systemic immunosuppressant medication during study treatment
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during atezolizumab treatment or within 5 months after the last dose of atezolizumab
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures
- Uncontrolled tumor-related pain
- Uncontrolled or symptomatic hypercalcemia
- Symptomatic, untreated, or actively progressing CNS metastases
- History of leptomeningeal disease
- 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
- History of malignancy other than UC within 2 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death
- Active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- Significant cardiovascular disease
- Uncontrolled hypertension
- Grade 3 or greater hemorrhage or bleeding event within 28 days prior to initiation of study treatment
- Major surgical procedure, other than for diagnosis, within 4 weeks prior to initiation of study treatment
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study
- Additional drug-specific exclusion criteria might apply

Exclusion for MIBC Cohorts:

- Prior treatment with systemic immunostimulatory agents prior to the initiation of study treatment
- Eligibility only for the control arm

- Prior allogeneic stem cell or solid organ transplantation
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressant medication during study treatment, with the following exceptions: Patients who received acute, low-dose, systemic immunosuppressant medications, or a one-time pulse dose of systemic immunosuppressant medication are eligible for the study after Medical Monitor approval has been obtained. Patients who received mineralocorticoids, corticosteroids for chronic obstructive pulmonary disease or asthma, or low-dose corticosteroids for orthostatic hypotension or adrenal insufficiency are eligible for the study.
- Severe infection within 4 weeks prior to initiation of study treatment
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study
- Also includes all the mUC exclusion criteria

Additional Exclusion Criteria for Atezo+Tira and Atezo (Atezolizumab) +Tira+Cis (Cisplatin)+Gem (Gemcitabine) in the MIBC Cohorts:

- Active Epstein-Barr virus (EBV) infection or known or suspected chronic active EBV infection at screening.

Additional Exclusion Criteria for the Cisplatin-Eligible MIBC Cohort:

- Patients who decline neoadjuvant cisplatin-based chemotherapy or in whom neoadjuvant cisplatin-based therapy is not appropriate.
- Impaired renal function.