ForPatients
by Roche

Muscle-invasive Bladder CancerBladder Cancer

A clinical trial to compare the effectiveness and safety of atezolizumab with placebo in people with bladder cancer

A Study of Atezolizumab Versus Placebo as Adjuvant Therapy in Patients With High-Risk Muscle-Invasive Bladder Cancer Who Are ctDNA Positive Following Cystectomy

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	24 Countries	NCT04660344 BO42843

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 III, Double-Blind, Multicenter, Randomized Study of Atezolizumab (Anti-PDL1 Antibody) Versus Placebo as Adjuvant Therapy in Patients With High-Risk Muscle-Invasive Bladder Cancer Who Are ctDNA Positive Following Cystectomy

Trial Summary:

This is a global Phase III, randomized, placebo-controlled, double-blind study designed to evaluate the efficacy and safety of adjuvant treatment with atezolizumab compared with placebo in participants with MIBC who are ctDNA positive and are at high risk for recurrence following cystectomy.

Hoffmann-La Roche
Sponsor

Phase 3
Phase

NCT04660344 BO42843
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

How does the IMvigor011 clinical trial work?

This clinical trial is recruiting people with a type of bladder cancer called muscle-invasive bladder cancer (MIBC), where the cancer has spread to the muscle layer of the bladder and the bladder has been surgically removed.

The purpose of this clinical trial is to compare the effects, good or bad, of atezolizumab against a placebo (with no active ingredient) in patients with MIBC who have had surgery to remove the bladder with no evidence of cancer on imaging but with confirmed circulating tumour DNA.

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 high-risk MIBC and been successfully treated with surgery to remove the bladder and the cancer within the last 6–14 weeks. A sample of the tumour will be tested for a protein called PD-L1.

If you have received certain treatments in the past, or within a particular timeframe, you may not be able to take part. You must not be pregnant or breastfeeding.

In order to be eligible for the clinical trial treatment, you must first take part in the ‘surveillance phase’ of the study, after which you may be invited to join the ‘treatment phase’.

During the surveillance phase, you will be monitored through regular blood tests every 6 weeks for up to 6 months (until 36 weeks from the date of surgery have passed) and then will continue with blood tests and scans every 12 weeks for up to 21 months. If the blood tests show you have fragments of genetic material from the tumour in your blood (known as circulating tumor DNA [or ctDNA]), and if your scans show no evidence that the bladder cancer has come back, you will be invited to join the treatment phase of the clinical trial. Finding cancer ctDNA in your blood after surgery might mean you are at a higher risk of having the cancer return.

You must have fully recovered from surgery before being allowed to enter the treatment phase.

If no ctDNA is detected in your blood at the end of the surveillance phase, you will not be able to continue in the study. Instead you will receive standard of care treatment outside of the study.

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 are not currently pregnant but can become pregnant will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

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

Everyone who is eligible to receive treatment will be split into 2 groups and given either:

- Atezolizumab, given as an infusion into the vein every 28 days for up to 12 rounds (1 year) of treatment
- OR placebo (non-active medicine) given as an infusion into the vein every 28 days for up to 12 rounds
  (1 year) of treatment

This is a ‘placebo-controlled’ clinical trial, which means that one of the groups will be given medicine with no active ingredients (also known as a ‘placebo’). A placebo is used to show that any effects (good or bad) are a result of the active treatment being tested and that the doctor or the participants cannot influence the results of the clinical trial.

You will have a 2 in 3 chance of being placed in the atezolizumab group and a 1 in 3 chance of being placed in the placebo group.

Neither you nor your clinical trial doctor can choose or know the group you are in. However, your clinical trial doctor can find out which group you are in, if your safety is at risk

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

You will be given the clinical trial treatment atezolizumab OR placebo for up to 12 rounds of treatment or up to 1 year (whichever occurs first). You are free to stop this treatment at any time.

During the treatment phase, you will have scans and blood tests every 9 weeks to see how you are responding to treatment and other regular checks for any potential side effects that you may be having.

If you need to leave the trial during treatment, you will be asked to return for a follow-up visit within 30 days of your last dose.

After completing treatment, you will still have scheduled assessments to check for signs of cancer every 9 weeks for the first year, every 12 weeks for the next year and every 24 weeks for the following 2 years, with one final visit after another 48 weeks.

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 will 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 **https://clinicaltrials.gov/ct2/show/record/NCT04660344**

Trial-identifier: NCT04660344

Inclusion Criteria:

Inclusion Criteria for the Surveillance Phase:

- Histologically confirmed MIUC (also termed TCC) of the bladder
- TNM classification (based on AJCC Cancer Staging Manual, 8th Edition; Amin et al. 2016) at pathological examination of surgical resection specimen as follows: For patients treated with prior NAC: tumor stage of ypT2-4a or ypN+ and M0. For patients who have not received prior NAC: tumor stage of pT2-4a or pN+ and M0
- Surgical resection of MIUC of the bladder
- Patients who have received prior platinum-based NAC.
- Patients who have not received prior platinum-based NAC, have refused, are ineligible ("unfit") for cisplatin-based adjuvant chemotherapy, or will not receive based on physicisan's decision.
- ctDNA assay developed based on tumor tissue specimen and matched normal DNA from blood.
- Tumor PD-L1 expression per IHC that is evaluable by central testing of a representative tumor tissue specimen.
- Absence of residual disease and absence of metastasis, as confirmed by a negative baseline computed tomography (CT) or magnetic resonance imaging (MRI) scan of the pelvis, abdomen, and chest no more than 4 weeks prior to enrollment.

- Full recovery from cystectomy and enrollment within 24 weeks following cystectomy. Minimum of 6 weeks must have elapsed from surgery.

Additional Inclusion Criteria for the Treatment Phase:

- Blood for plasma ctDNA sample evaluated to be ctDNA positive, defined as the presence of two or more mutations out of the 16 mutations identified based on patient's WES evaluable (ctDNA assay designability) report
- Absence of residual disease and absence of metastasis, as confirmed by a negative baseline CT or MRI scan of the pelvis, abdomen, and chest no more than 28 days prior to randomization, as assessed by the investigator
- ECOG Performance Status of <= 2
- Life expectancy >=12 weeks
- Adequate hematologic and end-organ function, investigator decision
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception and agreement to refrain from donating eggs

Exclusion Criteria:

General Medical Exclusion Criteria for the Surveillance Phase:

- Known PD-L1 IHC result for adjuvant therapy. The decision for the adjuvant therapy should not be based on the PD-L1 IHC result. If a cap is in effect limiting enrollment of PD-L1 negative patients, this exclusion criterion will not apply.
- Pregnancy or breastfeeding
- Positive test for HIV, with the following exception: Patients with a positive HIV test at screening are eligible provided they are stable on antiretroviral therapy, have a CD4 count >= 200/µL, and have an undetectable viral load
- Patients with active hepatitis B virus or hepatitis C. Patients with past HBV infection or resolved HBV infection are eligible. A negative HBV DNA test must be obtained in these patients prior to enrollment.

Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA.

- Active tuberculosis confirmed by a test performed within 3 months prior to treatment initiation.
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to biopharmaceuticals produced in Chinese hamster ovary cells or any component of the atezolizumab formulation
- History of autoimmune disease. Patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone may be eligible for this study. Patients with controlled Type I diabetes mellitus on a stable dose of insulin regimen may be eligible for this study.
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted.
- Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or greater), myocardial infarction within the previous 3 months, unstable arrhythmias, or unstable angina

Cancer-Specific Exclusion Criteria for the Surveillance Phase:

- Any approved anti-cancer therapy, including chemotherapy, or hormonal therapy within 3 weeks prior to study enrollment
- Adjuvant chemotherapy or radiation therapy for UC following cystectomy
- Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 28 days or 5 half-lives of the drug, whichever is longer, prior to enrollment
- Malignancies other than UC within 5 years prior to study enrollment

Additional Exclusion Criteria for the Treatment Phase:

- Any approved anti-cancer therapy, including chemotherapy, or hormonal therapy within 3 weeks prior to randomization to the treatment phase Hormone-replacement therapy or oral contraceptives are allowed.
- Adjuvant chemotherapy or radiation therapy for UC following cystectomy
- Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 28 days or 5 half-lives of the drug, whichever is longer, prior to randomization to the treatment phase
- Positive test for HIV, with the following exception: Patients with a positive HIV test at screening are eligible provided they are stable on antiretroviral therapy, have a CD4 count >= 200/µL, and have an undetectable viral load.
- Patients with active hepatitis B virus or hepatitis C
- Active tuberculosis confirmed by a test performed within 3 months prior to treatment initiation