ForPatients
by Roche

Bladder Cancer

Safety and Pharmacology Study of Atezolizumab Alone and in Combination With Bacille Calmette-Guérin (BCG) in High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC) Participants

Trial Status	Trial Runs In	Trial Identifier
Terminated	1 Country	NCT02792192 WO29635

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 Study of the Safety and Pharmacology of Atezolizumab Administered With or Without Bacille Calmette-Guérin in Patients With High-Risk Non-Muscle-Invasive Bladder Cancer

Trial Summary:

This Phase Ib/II study is designed to assess the safety, tolerability, pharmacokinetics, immunogenicity, patient reported outcomes (PROs), and preliminary anti-tumor activity of atezolizumab administered by intravenous (IV) infusion alone and in combination with intravesical BCG in high-risk NMIBC participants. The study will be conducted in following cohorts: Cohort 1A, Cohort 1B, Cohort 2, and Cohort 3. Atezolizumab will be administered at a fixed dose of 1200 milligrams (mg) every 3 weeks (q3w) for a maximum of 96 weeks. BCG will be administered to evaluate dose-limiting toxicities (DLTs), maximum tolerated dose (MTD), or maximum administered dose (MAD). De-escalation will be allowed for up to three dose levels of BCG (full dose [50 mg], 66 percent [%] of a full dose, and 33% of a full dose [Cohort 1B only]). After the MTD or MAD is determined for Cohort 1B, this dose will be used for all subsequent participants enrolled into Cohorts 1B, 2, and 3, unless the MTD is determined to be 33% of a full BCG dose. If MTD is determined to be 33% of a full BCG dose, then, no participants will be enrolled into Cohorts 2 and 3 until an assessment of the safety and activity of the combination of atezolizumab plus 33% of a full BCG dose is completed.

Hoffmann-La Roche	Phase 1/Phase 2
Sponsor	Phase

NCT02792192 WO29635
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	**# 18 Years**	**No**

Inclusion Criteria:

- Histologically confirmed non-muscle-invasive transitional cell carcinoma (TCC) of the bladder with carcinoma in-situ (CIS)
- High-risk NMIBC defined by the following:

BCG-unresponsive NMIBC:

Persistence of high-grade CIS at 6 months following an adequate course of BCG; or Stage/grade progression at 3 months after induction BCG; or Recurrence of high-grade CIS after achieving a disease-free state (i.e., CR) following induction of an adequate course of BCG that occurs less than (<) 6 months after the last exposure to BCG

BCG-relapsing NMIBC:

Recurrence of high-grade CIS after achieving a disease-free state following induction of an adequate course of BCG that occurs greater than or equal to (>/=) 6 months after the last exposure to BCG

Very high-risk (VHR) BCG-naïve NMIBC:

VHR NMIBC, defined as having at least 1 of the following: Multiple and/or large (greater than [>] 3 centimeters [cm]) T1, (HG/G3) tumors; T1, (HG/G3) tumor with concurrent CIS; T1, G3 with CIS in prostatic urethra; Micropapillary variant of non-muscle invasive urothelial carcinoma

- For BCG-unresponsive and BCG-relapsing NMIBC, participants must have received an adequate course of BCG
- Resection of all pTa/pT1 papillary disease
- No prior radiation to bladder or pelvic region
- Eastern Cooperative Oncology Group (ECOG) performance status of less than or equal to (</=) 2;
- Life expectancy >/=12 weeks
- Adequate hematologic and end-organ function
- Creatinine clearance >/=30 milliliters per minute (mL/min) (calculated using the Cockcroft-Gault formula)
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of <1% per year during the treatment period and for at least 5 months after the last dose of study drug. Women must refrain from donating eggs during this same period.
- For men receiving BCG: Agreement to remain abstinent (refrain from sexual intercourse) or use a condom

- Tumor tissue biopsy within 60 days prior to study entry or availability of an archival specimen obtained within 60 days of study screening

Exclusion Criteria:

- Evidence of locally advanced, metastatic, muscle-invasive, and/or extravesical bladder cancer
- Any malignancy within 5 years prior to Cycle 1, Day 1
- History of autoimmune disease, idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, idiopathic pneumonitis, or active pneumonitis
- Signs or symptoms of infection within 2 weeks prior to the first dose of study treatment
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to the first dose of study treatment
- Treatment with any approved anti-cancer therapy within 3 weeks prior to the first dose of study treatment
- Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 4 weeks prior to the first dose of study treatment
- Pregnant or lactating women, or women intending to become pregnant during the study
- Prior allogeneic stem cell or solid organ transplantation
- Positive test for human immunodeficiency virus (HIV)
- Active hepatitis B or C and/or tuberculosis
- Severe infections within 28 days prior to the first dose of study treatment
- Significant cardiovascular disease
- Major surgical procedure other than for diagnosis within 4 weeks prior to the first dose of study treatment, or anticipation of need for a major surgical procedure during the course of the study
- Administration of a live/attenuated vaccine within 4 weeks prior to the first dose of study treatment, within 5 months following the administration of the last dose of study drug, or anticipation that such a live/attenuated vaccine will be required during the study
- History of prior significant toxicity or intolerance to BCG requiring discontinuation of treatment
- History of prior systemic BCG infection
- History of immunosuppression, or conditions associated with congenital or acquired immune deficiency
- Concurrent febrile illness, urinary tract infection, or gross hematuria
- Prior treatment with cluster of differentiation 137 (CD137) agonists or immune checkpoint blockade therapies
- Treatment with systemic immunostimulatory agents within 6 weeks or five half-lives of the drug, whichever is shorter, prior to the first dose of study treatment
- Treatment with systemic immunosuppressive medications within 2 weeks prior to the first dose of study treatment, or anticipated requirement for systemic immunosuppressive medications during the trial