ForPatients
by Roche

Non-Small Cell Lung Cancer (NSCLC)

A Phase 1b Study of Atezolizumab in Combination With Erlotinib or Alectinib in Participants With Non-Small Cell Lung Cancer (NSCLC)

Trial Status	Trial Runs In	Trial Identifier
Completed	6 Countries	NCT02013219 2013-004382-13 WP29158

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 1b Study of the Safety and Pharmacology of Atezolizumab (Anti-PD-L1 Antibody) Administered With Erlotinib or Alectinib in Patients With Advanced Non-Small Cell Lung Cancer

Trial Summary:

This open-label, multicenter study will assess the safety, tolerability, and pharmacokinetics of intravenous (IV) dosing of atezolizumab in combination with oral erlotinib or alectinib in participants with NSCLC. This study has two stages. In the erlotinib group, the combination treatment will be given to participants with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI)-treatment-naive, advanced (nonresectable) NSCLC in a safety-evaluation stage and to participants with previously untreated EGFR mutation-positive, advanced NSCLC in an expansion stage (Stage 2). In the alectinib group, for both the safety-evaluation and expansion stages (Stages 1 and 2), the combination will be given to participants who are treatment-naive with anaplastic lymphoma kinase (ALK)-positive advanced NSCLC. In Stage 1, erlotinib will be given at a starting dose of 150 milligrams (mg) by mouth (PO) once daily (QD) and the starting dose of alectinib will be 600 mg twice daily (BID), for 28 consecutive days during Cycle 1 and on Days 1 through 21 of each cycle thereafter. The starting dose of atezolizumab will be 1200 mg, administered every 3 weeks (q3W) starting on Day 8 of Cycle 1. If the starting regimen for a combination treatment is not tolerated, alternative doses and/or schedules of erlotinib and atezolizumab or alectinib and atezolizumab may be tested to determine potential recommended Phase 2 dose (RP2D) for that combination treatment. In Stage 2, a potential RP2D and schedule for each combination treatment will be investigated in an expansion cohort. For both stages, continuation of treatment beyond Cycle 1 will be at the discretion of the treating investigator. Study treatment will be discontinued in participants who experience disease progression or unacceptable toxicity, are not compliant with the study protocol, or, in their opinion or in the opinion of the investigator, are not benefiting from study treatment. However, in the absence of unacceptable toxicity, participants

with second-line or greater NSCLC who are still receiving atezolizumab at the time of radiographic disease progression may be permitted to continue study treatment.

Hoffmann-La Roche
Sponsor

Phase 1
Phase

NCT02013219 2013-004382-13 WP29158
Trial Identifiers

Eligibility Criteria:

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

Inclusion Criteria:

- Histologically or cytologically documented, locally advanced or metastatic NSCLC.
- Participants in Stage 1 (Safety Evaluation) receiving erlotinib: No limit to the number of prior therapies (except for EGFR TKIs).
- Participants in Stage 2 (Expansion) receiving erlotinib: i) sensitizing mutation in the EGFR gene and ii) consent to collection of tumor tissue samples before, during, and after treatment for biopsy and PD biomarker analyses.
- Participants receiving alectinib in either Stage 1 or Stage 2: must be ALK positive as assessed by Food and Drug Administration (FDA) approved test and must not have received prior treatment for their advanced NSCLC.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- Life expectancy of at least 12 weeks.
- Measurable disease, as defined by RECIST Version 1.1 (v1.1).
- Adequate hematologic and end-organ function.
- Use of highly effective contraception (as defined by protocol) and until 5 months after the last dose of atezolizumab and for 3 months after the last dose of alectinib or for 2 weeks after the last dose of erlotinib, whichever is longer; Males must also refrain from sperm donatation during this same time period. Participants must not be pregnant or breastfeeding.
- Archival tumor tissue specimen meeting protocol specifications or the participant will be offered the option of a pre-treatment biopsy to obtain adequate tissue sample.

Exclusion Criteria:

- For participants receiving erlotinib group: prior treatment with any EGFR mutant-targeting TKI
- Any approved anticancer therapy, including chemotherapy, or hormonal therapy (except hormone-replacement therapy or oral contraceptives) within 3 weeks of first dose.
- Treatment with any other test drug or participation in another clinical trial within 28 days of enrollment.
- Known symptomatic central nervous system (CNS) metastases. Participants with a history of treated or untreated asymptomatic CNS metastases may be eligible.
- Leptomeningeal disease.
- Uncontrolled tumor-related pain.
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring drainage at least once monthly.
- High levels of calcium requiring bisphosphonate therapy or denosumab.

- Malignancies other than NSCLC within 5 years prior to enrollment, with the exception of those with a negligible risk of metastasis or death (such as adequately treated carcinoma in-situ of the cervix, basal or squamous cell skin cancer, localized prostate cancer, or ductal carcinoma in situ).
- History of severe allergic, anaphylactic, or other 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.
- Participants with prior bone marrow or solid organ transplantation.
- History of lung inflammation or disease.
- Serum albumin less than (<) 2.5 grams per deciliter (g/dL).
- Positive for Human Immunodeficiency Virus (HIV).
- Liver disease.
- Current or active tuberculosis, hepatitis B, or hepatitis C.
- Participants with past or resolved hepatitis B virus (HBV) infection are eligible; participants positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction (PCR) is negative for HCV Riboxy Nucleic Acid (RNA).
- Signs or symptoms of infection within 2 weeks prior to first dosing.
- Received therapeutic oral or IV antibiotics within 2 weeks prior to first dosing.
- Significant cardiovascular disease.
- Major surgical procedure other than for diagnosis within 28 days prior to first dosing or during the course of the study.
- Administration of a live, attenuated vaccine within 4 weeks before first dosing or during the study.
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding that may reasonably prevent the participant from participating.
- Hypersensitivity to erlotinib or alectinib or to any of the excipients.
- Any significant ophthalmologic abnormality. The use of contact lenses is not recommended during the study.
- For participants receiving alectinib: baseline Fridericias corrected QT interval (QTcF) greater than (>) 470 milliseconds (ms) or symptomatic bradycardia.
- Prior treatment with 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 first dosing.
- Treatment with systemic immunosuppressive medications within 2 weeks prior to first dosing (inhaled corticosteroids and mineralocorticoids are allowed).
- Participants who received acute, low-dose systemic immunosuppressant medication or a one-time pulse dose of systemic immunosuppressant medication are elgible for study after discussion and approval by the Medical Monitor.