ForPatients
by Roche

Non-Small Cell Lung Cancer (NSCLC)

A study of tiragolumab in combination with atezolizumab plus pemetrexed and carboplatin/cisplatin versus pembrolizumab plus pemetrexed and carboplatin/cisplatin in patients with previously untreated advanced non-squamous non-small cell lung cancer

A Study of Tiragolumab in Combination With Atezolizumab Plus Pemetrexed and Carboplatin/Cisplatin Versus Pembrolizumab Plus Pemetrexed and Carboplatin/Cisplatin in Participants With Previously Untreated Advanced Non-Squamous Non-Small Cell Lung Cancer

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	21 Countries	NCT04619797 2022-502031-20-00 BO42592

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/III, Randomized, Double-Blind, Placebo-Controlled Study of Tiragolumab in Combination With Atezolizumab Plus Pemetrexed and Carboplatin/Cisplatin Versus Pembrolizumab Plus Pemetrexed and Carboplatin/Cisplatin in Patients With Previously Untreated Advanced Non-Squamous Non-Small-Cell Lung Cancer

Trial Summary:

The purpose of this study is to evaluate the efficacy, safety, and pharmacokinetics of tiragolumab in combination with atezolizumab plus pemetrexed and carboplatin/cisplatin (Arm A) compared with placebo in combination with pembrolizumab plus pemetrexed and carboplatin/cisplatin (Arm B) in participants with previously untreated, locally advanced unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC). Eligible participants will be randomized in a 1:1 ratio to receive one of the following treatment regimens during the induction phase: * Arm A: Tiragolumab plus atezolizumab plus pemetrexed and carboplatin or cisplatin * Arm B: Placebo plus pembrolizumab plus pemetrexed and carboplatin or cisplatin Following the induction phase, participants will continue maintenance therapy with either tiragolumab in combination with atezolizumab and pemetrexed (Arm A) or placebo in combination with pembrolizumab and pemetrexed (Arm B).

Hoffmann-La Roche	Phase 2/Phase 3
Sponsor	Phase

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Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer that usually develops in the tissues lining the lungs. Non-squamous NSCLC are commonly found towards the outer parts of the lungs. In advanced NSCLC, the cancer spreads to other parts of the body. Sometimes, NSCLC presents at a stage that cannot be removed surgically (unresectable). 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 testing a combination of tiragolumab and atezolizumab. It is being developed as a combination treatment for NSCLC. Previous studies have shown that tiragolumab and atezolizumab can be given to treat advanced NSCLC. Atezolizumab alone or in combination with platinum-based cancer medicines (chemotherapy) are approved by health authorities for treating advanced NSCLC and other cancer types. However, in this study, the combination of tiragolumab and atezolizumab is considered to be experimental. Health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved the combination of tiragolumab and atezolizumab for the treatment of non-squamous NSCLC. Pemetrexed and pembrolizumab are approved medicines for the treatment of NSCLC.

This study aims to compare the effects of tiragolumab plus atezolizumab with pemetrexed and chemotherapy versus placebo plus pembrolizumab and chemotherapy in people with non-squamous NSCLC. Placebo is a medicine without any active ingredients.

2. Who could take part in the study?

People who were at least 18 years old with advanced non-squamous NSCLC that could not be surgically removed and those who did not receive any prior treatment could take part in this study. People who were pregnant, or breastfeeding also 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 two groups (Groups A and B). They will receive either atezolizumab plus tiragolumab with pemetrexed and chemotherapy (Group A) or placebo plus pembrolizumab with pemetrexed and chemotherapy (Group B), as drip into the vein every 3 weeks. Treatment may continue up to 24 months or until the cancer worsens, or participants experience any unacceptable unwanted effects, or withdraw from the study, whichever occurs first. Since the main results of this study showed reduced benefit in Group A compared with Group B, participants receiving atezolizumab plus tiragolumab are recommended to stop the study treatment and take other cancer treatments outside of this study. Those receiving pembrolizumab and chemotherapy may continue receiving treatment as planned or discontinue from the study and seek treatment options outside of the study.

This was a double-blinded study. This means that neither the participants in the study nor the team running it would know which treatment is being given until the study is over. However, the study is no longer blinded, and both the participants and researchers are aware of the treatment that participants received.

During this study, the study doctor will meet the participants every 3 weeks to see how well the treatment is working and any unwanted effects participants may have. Total time of participation in the study will depend 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.

4. What are the main results measured in this study?

The main results measured in the study are to find out the number of participants whose cancer responded to the treatment. The approximate time from the start of treatment until the first occurrence of cancer worsening or participants dying due to any cause will also be measured. Other key results measured include:

- Time taken for the cancer to come back in a participant who was previously cancer-free after undergoing treatment.
- Change in participant’s physical health and quality of life over time
- Number of participants with unwanted effects
- How well the body processes tiragolumab and atezolizumab
- Number of participants whose bodies produce proteins that work against tiragolumab and atezolizumab

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.

The study results showed reduced benefit among participants treated with tiragolumab plus atezolizumab and chemotherapy compared with pembrolizumab plus chemotherapy.

It may not be fully known at this time how safe the study treatment is. 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 may have to undergo. All details of the study were described in an informed consent document. This included information about possible effects and other options of 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.

Tiragolumab Participants were told about the known unwanted effects of tiragolumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include inflammation of the liver (hepatitis) with symptoms of yellowing of the skin, pain in the stomach area, nausea, vomiting, itching, fatigue (feeling tired or weak), bleeding or bruising under the skin, and dark urine.
Atezolizumab Participants were told about the known unwanted effects of atezolizumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include back pain, cough, decreased appetite, weakness, fever, headache, itching of the skin (pruritus), rash, joint pain (arthralgia), lack of energy (asthenia), and shortness of breath (dyspnea).
Pembrolizumab Known unwanted effects include a decrease in red blood cells, white cells (neutrophils), and cells that help blood to clot (platelets), numbness, weakness, tingling or burning pain in arms and legs, feeling less hungry, trouble sleeping, muscle aches, and rash.

Tiragolumab, atezolizumab, pemetrexed, pembrolizumab, chemotherapy, and placebo are given as a drip into a vein. Known unwanted effects with infusion include irritation where the injection is given, fever, chills, swelling, rash, redness, itching, or pain. 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 0 or 1
- Histologically or cytologically documented locally advanced unresectable or metastatic non-squamous NSCLC that is not eligible for curative surgery and/or definitive chemoradiotherapy
- No prior systemic treatment for metastatic non-squamous NSCLC
- Known tumor programmed death-ligand 1 (PD-L1) status
- Measurable disease, as defined by Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1)
- Life expectancy >= 12 weeks
- Adequate hematologic and end-organ function
- Negative human immunodeficiency virus (HIV) test at screening

- Serology test negative for active hepatitis B virus or active hepatitis C virus at screening.

Exclusion Criteria:

- Mutations in epidermal growth factor receptor (EGFR) gene or anaplastic lymphoma kinase (ALK) fusion oncogene
- Pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- 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 NSCLC within 5 years prior to randomization, with the exception of malignancies with a negligible risk of metastasis or death
- Severe infection within 4 weeks prior to initiation of study treatment or any active infection that, in the opinion of the investigator, could impact patient safety
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Prior treatment with CD137 agonists or immune checkpoint blockade therapies, including anti-cytotoxic T lymphocyte-associated protein 4, anti-TIGIT, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Treatment with systemic immunostimulatory agents within 4 weeks or 5 drug-elimination half-lives (whichever is longer) 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
- Known allergy or hypersensitivity or other contraindication to any component of the chemotherapy regimen the participant may receive during the study
- Women who are pregnant, or breastfeeding
- Known targetable c-ROS oncogene 1 (ROS1) or BRAFV600E genomic aberration.