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A study to assess the effect of tiragolumab in presence of atezolizumab and bevacizumab in participants detected with lung cancer

Submission date
28/10/2022

Recruitment status
No longer recruiting

Registration date
08/11/2022

Overall study status
Ongoing

Last Edited
04/12/2023

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Non-squamous non-small cell lung cancer (nsq NSCLC) is the most common type of lung cancer. It usually grows and spreads more slowly than small cell lung cancer. Tiragolumab (formerly MTIG7192A) is a human antibody that is being studied as a potential therapy against various cancer types. An antibody is a protein in the blood that helps the body's defences by identifying and attaching to specific foreign substances including germs.
The aim of this study is to compare the effects, good or bad, of tiragolumab plus atezolizumab and bevacizumab in participants with nsq NSCLC.
Tiragolumab plus atezolizumab and bevacizumab are experimental drugs, which means health authorities have yet not approved the combination for the treatment of nsq NSCLC.

Who can participate?
Participants aged 18 years and above with previously untreated, locally advanced nsq NSCLC that has grown or spread and cannot be removed by surgery.

What does the study involve?
Participants will need to be a part of this study for about 3-5 years. This study will have three parts:
1. A screening visit, wherein certain tests would be done to determine if the participant is eligible to take part in the study.
2. The treatment period, when eligible participants will be given a single dose of tiragolumab plus atezolizumab and bevacizumab combination into the vein (infusion) every 3 weeks for a cycle of 21 days on a regular basis unless their cancer condition worsens. Participants will have to visit the clinic about every 3 weeks while they are receiving treatment and each visit may last 6 to 72 hours.
3. A follow-up period during which participants will have check-up visits every 3 months or more frequently till the end of the study. The participant will have to visit the clinic or will be contacted telephonically for the follow-up procedures.

What are the possible benefits and risks of participating?
Participants will not receive any direct medical benefit, but the information gained from this study may help other people with non-squamous non-small cell lung cancer in the future.
Participants will be paid renminbi (RMB) 100 as a transportation reimbursement for every clinic visit including the screening procedures.
Participants may have side effects from the drugs or procedures used in this study. These can be mild to severe and even life-threatening, and they can vary from person to person.
Tiragolumab has had limited testing in humans. Known potential side effects include fever, chills, shortness of breath, nausea, and changes in blood pressure. Participants may experience inflammation in the tumour but also in the healthy parts (normal tissue) of the body due to increased activity of the immune system. The affected parts of the body could be (but not limited to) the skin, eyes, nerves, gut, hormone system, kidneys, lungs, liver, muscles, blood vessels, and blood cells. Tiragolumab could also lower the number of certain white blood cells (lymphocytes).
Very common side effects of atezolizumab include back pain, cough, decreased appetite, loose stools, fatigue, fever, headache, itching of the skin (pruritus), joint pain (arthralgia), lack of energy (asthenia), muscle and bone pain (myalgia, musculoskeletal pain and bone pain), nausea, rash, shortness of breath (dyspnea), urinary tract infection, vomiting
Common side effects of atezolizumab include allergic reaction or intolerance to medication (hypersensitivity), chills, decreased level of potassium in the blood (hypokalemia), decreased level of sodium in the blood (hyponatremia), decreased oxygen supply in the body resulting in shortness of breath (hypoxia), difficulty swallowing (dysphagia), dry skin, flu-like illness, increased blood level of creatinine, a substance normally eliminated by the kidneys into the urine, increased blood sugar level (hyperglycemia), inflammation of the intestines (colitis), inflammation of the liver (hepatitis), inflammation of the lungs (pneumonitis), infusion-related reaction, low blood pressure (hypotension), a low platelet count in the blood, which may make you more likely to bruise or bleed (thrombocytopenia), mouth and throat pain (oropharyngeal pain), inflammation of the nose and throat (nasopharyngitis), stomach-area pain (abdominal pain), underactive thyroid gland (hypothyroidism)
Less common side effects of atezolizumab include decreased production of hormones by the adrenal glands (adrenal insufficiency), diabetes mellitus, inflammation of the brain and membrane surrounding the brain and spinal cord (meningoencephalitis), inflammation of the heart muscle (myocarditis), inflammation of the kidneys (nephritis), inflammation of the pancreas (pancreatitis), inflammation of the pituitary gland (hypophysitis), inflammation or damage of the muscles (myositis), nerve damage resulting in muscle weakness (myasthenic syndrome/myasthenia gravis), nerve damage that may cause muscle weakness and/or paralysis (Guillain-Barré syndrome), overactive thyroid gland (hyperthyroidism), red, dry, scaly patches of thickened skin (psoriasis), severe high levels of sugar and acids in the blood or urine (diabetic ketoacidosis), severe skin or mucosal reactions (severe cutaneous adverse reactions)
Very common serious side effects of bevacizumab include high blood pressure, numbness or loss of feeling in the fingers or toes, low numbers of white blood cells potentially associated with fever, low numbers of platelets, weakness, loss of energy, loose stools, with nausea, vomiting, and abdominal pain.
Very common non-serious side effects of bevacizumab include nausea and vomiting, pain, including headache and joint pain, constipation, mucosal inflammation or inflammation of the mouth, protein in the urine, bleeding in the moist lining of the digestive, respiratory, reproductive, or urinary tracts, loss of appetite, fever, runny nose, dry skin, flaking and inflammation of the skin, change in skin color, change in the sense of taste, problems with the eyes and tearing, cough.
Common serious side effects of bevacizumab include infection, presence of bacteria in the blood, collection of pus in tissue or organs, a tear or hole in the gut, an abnormal tube-like connection between the gastrointestinal tract and skin or other tissues that are not normally

connected, low number of red blood cells, bleeding, including bleeding associated with the tumour and nose bleeds, clogging of a vessel in the lung, blocking of the blood vessels (arteries) by a blood clot, including stroke or heart attack, heart failure, especially in participants who have taken certain chemotherapy, blood clots in the veins, abdominal pain, blockage in the intestine, body water loss, pain, tenderness, or blistering on the fingers or feet, reduced consciousness, sleepiness, feeling tired, fainting, allergic reaction, including allergic reaction to the drug during infusion, shortness of breath, low levels of oxygen in the blood, wound-healing problems.
Common non-serious side effects of bevacizumab include digestive system disorder, voice changes, hoarseness, muscular pain or muscular weakness.
Less common serious side effects of bevacizumab include an abnormal connection between internal organs (other than the digestive tract) and skin or other tissues not normally connected.
Other rare but potentially serious side effects of bevacizumab include reversible posterior leukoencephalopathy syndrome, which may include symptoms of impaired brain function (headaches, vision changes, confusion, or fit [seizures]), and, often, high blood pressure, hypertensive encephalopathy, which may include symptoms of impaired brain function (headaches, vision changes, confusion, or fit [seizures]) and, often, high blood pressure.
During tumour tissue sampling (biopsy) participants might experience pain, redness, swelling, excessive bleeding, bruising, or draining at the needle site. Abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site can also occur
Blood sampling: Drawing blood can cause pain, bruising, or infection where the needle is inserted. Some participants might experience dizziness, fainting, or an upset stomach when their blood is drawn.
Tumour assessment scanning procedures including computed tomography (CT) scan, positron emission tomography (PET)/CT scan, magnetic resonance imaging (MRI) scan, and Bone scan might include potential risks such as allergic reaction, nausea, constipation, diarrhoea, abdominal bloating, headaches, hives, temporary low blood pressure, chest pain, back pain, fever, weakness, and seizures to a tracer or a contrast agent. Although there are no known long-term harmful effects from the radiation of a single scan, the risk of harmful effects from multiple scans over a period is not known.
There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Participants who are pregnant, become pregnant or are currently breastfeeding cannot take part in this study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (USA)

When is the study starting and how long is it expected to run for?
January 2022 to December 2026

Who is funding the study?
F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?
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Contact information

Type(s)
Public

Contact name
Mr Clinical Trials

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Additional identifiers

Protocol serial number
ML43138

Study information

Scientific Title
A Phase II, single-arm study of tiragolumab plus atezolizumab and bevacizumab in patients with previously untreated locally advanced unresectable or metastatic PD-L1-positive non-squamous non-small cell lung cancer

Study objectives
The purpose of this study is to evaluate the efficacy of tiragolumab plus atezolizumab and bevacizumab treatment based on efficacy parameters i.e., objective response rate (ORR).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/06/2022, Cancer Institute and Hospital Chinese Academy of Medical Sciences Ethics Committee (No.17, Panjiayuan Nanli, Chaoyang District, Beijing City, 100021, China; cancergcp@163.com; +86 (0)10 87788495), ref: 22/199-3401

Primary study design
Interventional

Study design
Phase II open-label single-arm interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Non-squamous non-small cell lung cancer

Interventions

Participants will receive a single dose of tiragolumab, 600 mg, as an intravenous (IV) infusion, once every three weeks (Q3W) on Day 1 of each 21-day cycle. Participants will also receive a single-dose of atezolizumab, 1200 mg, as an IV infusion and a single dose of bevacizumab, 15 mg /kg, as an IV infusion, Q3W on Day 1 of each 21-day cycle in combination with tiragolumab, until disease progression, loss of clinical benefit or unacceptable toxicity.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Tiragolumab, atezolizumab, bevacizumab

Primary outcome(s)
Objective response rate (ORR), as determined by the investigator according to Response Evaluation Criteria in Solid Tumours, version 1.1 (RECIST v1.1) from baseline up to confirmed disease progression, loss of clinical benefit, death, or loss of follow-up (up to approximately 4.5 years)

Key secondary outcome(s)
1. Progression-free survival (PFS), determined by the investigator using RECIST version 1.1 from initiation of study treatment up to confirmed disease progression, loss of clinical benefit, death, or loss of follow-up (up to approximately 4.5 years)
2. Overall survival (OS) measured from initiation of study treatment up to confirmed disease progression, loss of clinical benefit, death, or loss of follow-up (up to approximately 4.5 years)
3. Duration of response (DOR), determined by the investigator using RECIST version 1.1 from initiation of study treatment up to first occurrence of a documented objective response to confirmed disease progression, loss of clinical benefit, death, or loss of follow-up (up to approximately 4.5 years)
4. Number of participants with adverse events and serious adverse events, with severity determined per National Cancer Institute Common Terminology Criteria For Adverse Events, version 5.0 (NCI CTCAE v4.0) toxicity grade, from baseline up to follow-up visits (up to approximately 4.5 years)
5. Number of participants with cytokine release syndrome (CRS) and severity of CRS determined according to the American Society For Transplantation And Cellular Therapy (ASTCT) CRS consensus grading scale from day 1 up to follow-up visits (up to approximately 4.5 years)

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Age ≥18 years at time of signing Informed Consent Form
2. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
3. Histologically or cytologically documented locally advanced unresectable non–small cell lung cancer (NSCLC) (i.e., Stage IIIB not eligible for definitive chemoradiotherapy), recurrent, or metastatic NSCLC (i.e., Stage IV) (per the Union Internationale Contre le Cancer/American Joint

Committee on Cancer [UICC/AJCC] staging system, 8th edition) of non-squamous histology
4. No prior systemic treatment for locally advanced unresectable or metastatic NSCLC
5. Tumour PD-L1 expression with a tumour cell (TC) ≥1%, as determined by the PD-L1 Immunohistochemistry (IHC) SP263 pharmDx assay performed by a central laboratory on previously obtained archival tumour tissue or tissue obtained from a biopsy at screening.
6. Confirmed availability of representative tumour specimens in formalin-fixed, paraffin embedded (FFPE) blocks (preferred) or at least 9 unstained serial slides, along with an associated pathology report. Measurable disease, as defined by RECIST v1.1
7. Life expectancy ≥12 weeks
8. Negative human immunodeficiency virus (HIV) test at screening
9. Negative hepatitis B surface antigen (HBsAg) test at screening
10. Negative hepatitis C virus (HCV) antibody test at screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Participants with non-squamous NSCLC known to have a sensitising mutation in the EGFR gene or an ALK fusion oncogene or ROS1 fusion oncogene
2. Participants with squamous NSCLC
3. Participants with the pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC
4. Prior treatment with CD137 agonists or immune checkpoint blockade therapies, including anti-cytotoxic T-lymphocyte-associated protein (CTLA)-4, anti-PD-1, anti-PD-L1 and anti-T cell immunoreceptor with immunoglobulin and ITIM domain (TIGIT) therapeutic antibodies
5. Current treatment with anti-viral therapy for HBV or HCV
6. Treatment with investigational therapy within 28 days prior to initiation of study treatment
7. Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
8. Uncontrolled tumour-related pain
9. History of malignancy other than NSCLC within 5 years prior to initiation of study treatment, with the exception of the cancer under investigation in this study and malignancies with a negligible risk of metastasis or death (e.g., 5-year OS rate >90%), such as adequately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localised prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer
10. Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the participants at high risk from treatment complications
11. Known allergy or hypersensitivity to any component of the study drugs or formulation
12. Prior allogeneic stem cell or solid organ transplantation
13. History of idiopathic pulmonary fibrosis, organising pneumonia (e.g., bronchiolitis obliterans),

drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
14. History of intra-abdominal inflammatory process within 6 months prior to initiation of study treatment, including but not limited to active peptic ulcer disease, diverticulitis, or colitis
15. Evidence of abdominal free air not explained by paracentesis or recent surgical procedure
16. Clear tumour infiltration into the thoracic great vessels is seen on imaging
17. Clear cavitation of pulmonary lesions is seen on imaging
18. Administration of a live, attenuated vaccine within 4 weeks prior to initiation of study treatment or anticipation that such a live attenuated vaccine will be required during the study
19. Pregnant, lactating, or breastfeeding women

Date of first enrolment
28/11/2022

Date of final enrolment
31/03/2024

Locations

Countries of recruitment
China

Study participating centre
Cancer Hospital Chinese Academy of Medical Sciences Shenzhen Center
China
518127

Study participating centre
Qingdao Central Hospital
China
266042

Study participating centre
Fudan Unviversity Shanghai Cancer Center
China
200032

Study participating centre
Ren Min Hospital Affiliated Wu Han University
China
430060

Study participating centre
Jiangsu Cancer Hospital
China
210009

Study participating centre
Shandong Cancer Hospital
China
250117

Study participating centre
Hubei Cancer Hospital
China
430079

Study participating centre
Tianjin Cancer Hospital
China
300060

Study participating centre
Harbin Medical University Cancer Hospital
China
150081

Study participating centre
Ningbo Medical treatment Center Lihuili Hospital
China
315046

Study participating centre
Cancer Institute and Hospital Chinese Academy of Medical Sciences
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100021

Study participating centre

Sir Run Run Shaw Hospital Zhejiang University
China
310016

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes