ForPatients
by Roche

Metastatic MelanomaNon-Small Cell Lung Cancer (NSCLC)Solid TumorsEsophageal Squamous Cell CarcinomaNon Small Cell Lung Carcinoma

A clinical trial to look at how safe and how well different doses of RO7247669 work in people with solid tumours that have grown or spread, and how the body processes RO7247669

Dose Escalation Study of a PD1-LAG3 Bispecific Antibody in Patients With Advanced and/or Metastatic Solid Tumors

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	9 Countries	NCT04140500 2019-000779-18 NP41300

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:

An Open Label, Multicenter, Dose Escalation, Phase 1 Study to Evaluate Safety/Tolerability, Pharmacokinetics, Pharmacodynamics and Preliminary Anti Tumor Activity of RO7247669, a PD1-LAG3 Bispecific Antibody, in Patients With Advanced and/or Metastatic Solid Tumors

Trial Summary:

This is a first-in-human, open-label, multicenter, Phase I multiple-ascending dose (MAD) study of RO7247669, an anti PD-1 (programmed death-1) and LAG-3 (Lymphocyte-activation gene 3) bispecific antibody, for participants with advanced and/or metastatic solid tumors. This study aims to establish the maximum tolerated dose (MTD) and/or define the recommended phase 2 dose (RP2D) based on the safety, tolerability, pharmacokinetic (PK) and/or pharmacodynamic (PD) profile of RO7247669, and to evaluate preliminary anti-tumor activity in participants with solid tumors. An expansion part of the study is planned to enroll tumor-specific cohorts to evaluate anti-tumor activity of the MTD and/or RP2D of RO7247669 and to confirm safety and tolerability in participants with selected tumor types.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT04140500 2019-000779-18 NP41300
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the NP41300 clinical trial needed?

Solid tumours are cancer cells that grow in organ systems anywhere in the body. Standard treatment includes surgery, chemotherapy, radiotherapy, and medicines that help the body's immune system fight cancer (known as 'immunotherapy'), such as anti-PD-L1 or anti-PD-1. Usually, PD-L1/PD-1 help the immune system recognise healthy cells to prevent the body from attacking itself. But cancer cells with PD-L1 on the surface (known as 'PD-L1 positive' cells) can 'hide' from cancer-killing cells of the immune system. Anti-PD-L1/PD-1 treatments block this process and help the immune system 'see' and destroy cancer cells. However, treatment does not work for everyone or stops working after a time and so new combinations of immunotherapy are needed. RO7247669 is a type of anti-PD-1 immunotherapy. It blocks the activity of PD-1 and another element that cancer cells can use to hide from the immune system called 'LAG-3'. By blocking PD-1 and LAG-3 at the same time, researchers hope that RO7247669 may work when other treatments do not. RO7247669 is an experimental drug, which means is not approved by health authorities as a treatment for solid tumours. This clinical trial is the first time that RO7247669 will be given to people. This clinical trial aims to find out the highest, safest dose of RO7247669 that can be given, and to understand the side effects of RO7247669 at different doses and effects on the body.

2. How does the NP41300 clinical trial work?

This clinical trial is recruiting people with a solid tumour that requires treatment. People can take part if they have solid tumours that have grown (known as 'advanced') or spread in the body (known as 'metastatic'). The trial is in 2 parts. Part A will look at the effects of increasing doses of RO7247669 to select the best dose and schedule (every 2 or 3 weeks) for testing in Part B. Part B will look at the effect of RO7247669 on certain types of cancer. People who take part in this clinical trial (participants) will be given the clinical trial treatment RO7247669 for up to 2 years or longer if the treatment is benefiting them – known as 'extended treatment'. The clinical trial doctor will see them regularly throughout the trial. These clinic visits will include treatment, checks to see how the participant responds to the treatment, and any side effects they may have. Participants will be asked to attend a follow-up visit at the clinic 3 months after their last dose of RO7247669 and will be contacted every 3 months after that to check their health. The total time of participation in the clinical trial will be about 2 years and 4 months, or about 4 years for participants who are given extended treatment. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the NP41300 clinical trial?

The main clinical trial endpoints (the main results measured to see if the drug has worked) are:

- The number, type, and seriousness of any side effects at different doses
- The number of people with smaller tumours after treatment ('objective response') and with tumours that stay approximately the same size ('disease control')
- The amount of time between cancer getting better and then getting worse ('duration of response') and from the start of the trial to cancer getting worse ('progression-free survival')

The other clinical trial endpoints include how the body breaks down and processes RO7247669, how it affects the immune system, and how well RO7247669 sticks to PD-1 and LAG-3 on participants' cells in laboratory tests.

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old and have advanced or metastatic solid tumours. Parts A and B of the trial are divided into groups depending on the dose of RO7247669 that will be given and how often. People can join Part A or Part B (groups 5 and 6) if there is no standard treatment available for their cancer or their cancer has worsened after standard treatment or caused unacceptable side effects. People can join Part B (groups 1 to 4) if they have: had anti-PD-1 or anti-PD-L1 treatment that stopped working for advanced or metastatic skin cancer (melanoma) or non-small cell lung cancer (NSCLC), untreated NSCLC that is highly positive for PDL1, or cancer that starts in the flat cells inside the food pipe (oesophageal squamous cell carcinoma) that did not get better with one previous standard treatment. People may not be able to take part in this trial if they have cancer that has spread to the brain or spinal cord and causes symptoms, their cancer has certain changes (mutations), or they have certain other medical conditions, including a second type of cancer, diabetes, autoimmune, heart, liver or lung diseases, or certain infections. Women who are pregnant or breastfeeding, and people who have previously received certain treatments, including an anti-LAG 3, or who had severe side effects to previous immunotherapy, cannot take part in this trial.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given RO7247669 as an infusion (into the vein) every 2 or 3 weeks for up to 2 years (or longer in the extended treatment period), or until their cancer gets worse, they have unacceptable side effects, or they decide to leave the clinical trial. This is an openlabel trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial). Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drug used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. RO7247669 has not yet been tested in humans. For this reason, this drug's side effects are not known now. Participants will be told about the possible side effects based on laboratory studies or knowledge of similar drugs. RO7247669 will be given as infusions into a vein (intravenous infusions). Participants will be told about any known side effects of intravenous infusions. Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Patient must have histologically or cytologically confirmed advanced and/or metastatic solid tumor malignancies for which standard curative or palliative measures do not exist, are no longer effective, or are not acceptable to the patient
- Eastern Cooperative Oncology Group Performance Status 0-1
- Fresh biopsies may be required
- Women of childbearing potential and male participants must agree to remain abstinent or use contraceptive methods as defined by the protocol

Additional Specific Inclusion Criteria for Participants with Melanoma

- Histologically confirmed, unresectable stage III or stage IV melanoma
- Not more than 2 prior lines of treatment for metastatic disease are allowed prior to enrolling in the study
- Prior treatment with an approved anti-PD-1 or anti-PD-L1 agent

Additional Specific Inclusion Criteria for Participants with Non-Small Cell Lung Cancer who Previously Received Treatment for Metastatic Disease

- Participants with histologically confirmed advanced non-small cell lung cancer
- Not more than 2 prior lines of treatment for metastatic disease are allowed prior to enrolling in the study
- Previously treated with approved PD-L1/PD-1 inhibitors
- Tumor PD-L1 expression as determined by immunohistochemistry assay of archival tumor tissue or tissue obtained at screening

Additional Specific Inclusion Criteria for Participants with Esophageal Squamous Cell Carcinoma

- Participants whose major lesion was histologically confirmed as squamous cell carcinoma or adenosquamous cell carcinoma of the esophagus
- Participants who have previously received not more than 1 prior line of treatment for metastatic disease prior to enrolling in the study

Additional Specific Inclusion Criteria for Participants with Non-Small Cell Lung Cancer who Previously did not Receive Treatment for Metastatic Disease

- Participants with histologically confirmed advanced non-small cell lung cancer
- Tumor PD-L1 expression as determined by immunohistochemistry assay of archival tumor tissue or tissue obtained at screening

Exclusion Criteria:

- Pregnancy, lactation, or breastfeeding
- Known hypersensitivity to any of the components of RO7247669
- Active or untreated central nervous system (CNS) metastases
- An active second malignancy
- Evidence of concomitant diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the participant at high risk from treatment complications
- Positive HIV, hepatitis B, or hepatitis C test result
- Known active or uncontrolled bacterial, viral, fungal, mycobacterial, parasitic, or other infection
- Vaccination with live vaccines within 28 days prior to Cycle 1 Day 1
- Treatment with oral or IV antibiotics within 2 weeks prior to Cycle 1 Day 1
- Active or history of autoimmune disease or immune deficiency
- Prior treatment with adoptive cell therapies, such as CAR-T therapies
- Concurrent therapy with any other investigational drug < 28 days or 5 half-lives of the drug, whichever is shorter, prior to the first RO7247669 administration
- Regular immunosuppressive therapy
- Radiotherapy within the last 4 weeks before start of study drug treatment, with the exception of limited palliative radiotherapy
- Prior treatment with a lymphocyte activation gene-3 (LAG-3) inhibitor

Additional Specific Exclusion Criteria for Participants with Non-Small Cell Lung Cancer who Previously Received Treatment for Metastatic Disease

- Participants with the following muations, rearrangements, translocations are not eligible: EGFR, ALK, ROS1, BRAFV600E, and NTRK

Additional Specific Exclusion Criteria for Participants with Esophageal Squamous Cell Carcinoma

- Prior therapy with any immunomodulatory agents

Additional Specific Exclusion Criteria for Participants with Non-Small Cell Lung Cancer who Previously did not Receive Treatment for Metastatic Disease

- Prior therapy for metastatic disease is not permitted
- Neo-adjuvant anti-PD-1 or anti-PD-L1 therapy is not allowed