ForPatients
by Roche

Non-Small Cell Lung Cancer (NSCLC)Non Small Cell Lung Carcinoma

A clinical trial to look at the safety and activity of divarasib at different doses in combination with other anti-cancer therapies in people with non-small cell lung cancer that have a KRAS G12C mutation and has spread, and who haven't previously been treated for this.

A Study Evaluating the Safety, Activity, and Pharmacokinetics of Divarasib in Combination With Other Anti-Cancer Therapies in Participants With Previously Untreated Advanced or Metastatic Non-Small Cell Lung Cancer With a KRAS G12C Mutation

Trial Status	Trial Runs In	Trial Identifier
Recruiting	18 Countries	NCT05789082 2022-003048-28 2023-507171-22-00 BO44426

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, multicenter study evaluating the safety, activity, and pharmacokinetics of divarasib in combination with other anti-cancer therapies in patients with previously untreated advanced or metastatic non-small cell lung cancer with a KRAS G12C mutation

Trial Summary:

The purpose of this study is to evaluate the safety, pharmacokinetics (PK), and activity of divarasib combined with other anti-cancer therapies in participants with previously untreated, advanced or metastatic non-small cell lung cancer (NSCLC).

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT05789082 2022-003048-28 2023-507171-22-00 BO44426
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the Krascendo 170 Lung clinical trial needed?

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. New treatments are needed that improve health outcomes for people living with locally advanced or metastatic NSCLC. 'Locally advanced' means the NSCLC has spread to nearby tissue, and 'metastatic' is spread to other parts of the body. Standard first treatment for locally advanced or metastatic NSCLC includes medicines that help the body's immune system to attack tumours (known as 'immunotherapy'), such as pembrolizumab, given with or without chemotherapy. Pembrolizumab treatment works better against cancer cells that have a protein called PD-L1 (known as a 'biomarker'). PD-L1 positive cancer cells are more difficult for the immune system to find and destroy. Pembrolizumab blocks the activity of PD-L1 to help the immune system fight cancer cells.

Around 1 in 10 people with NSCLC have cancer cells with a change (mutation) in the *KRAS* gene, called a *KRAS G12C* mutation, that makes the cancer cells grow out of control. Recent research has shown that NSCLC cells with a *KRAS G12C* mutation are often PD-L1 positive as well.

Divarasib is an experimental drug. This means it is not approved for treating NSCLC. Divarasib blocks the activity of the *KRAS G12C* mutation. In this clinical trial, researchers will test how safe and how well divarasib works against PD-L1 positive or negative NSCLC with the *KRAS G12C* mutation, when given with anti-cancer therapies.

2. How does the Krascendo 170 Lung clinical trial work?

This clinical trial is recruiting people who have not been treated before for locally advanced or metastatic NSCLC. Also, the NSCLC must have the *KRAS G12C* mutation .

Participants will be given the clinical trial treatment, divarasib, combined with pembrolizumab (Group A) or with pembrolizumab and chemotherapy (Group B) in 3-week treatment periods (called treatment 'cycles'). Participants will continue to receive the clinical trial treatment for as long as they receive benefit and do not have unacceptable side effects. Participants will be seen by the clinical trial doctor every week for the first 2 treatment cycles, then twice during Cycles 3 and 4, and then every 3 weeks for all remaining treatment cycles. These hospital visits will include treatment and checks to see how the participant is responding to the treatment and any side effects they may be having. Participants' total time in the clinical trial will depend on how their NSCLC responds to treatment. This could range from 1 day to more than 2 years. After the final dose of clinical trial treatment, the trial doctor will follow up with participants every 3 months for as long as they agree to it. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the Krascendo 170 Lung clinical trial?

The main endpoints (the main results that are measured in the trial) of this clinical trial are the number of side effects and how well different doses of divarasib in combination with other anti-cancer therapies are tolerated.

The other endpoints include:

- How many participants have a decrease in the size of their tumours (known as 'overall response rate')
- How much time passes between participants' cancer first responding to treatment and cancer getting worse (known as 'duration of response')
- How much time passes between the start of the trial and participants' cancer getting worse (known as 'progression-free survival')
- The seriousness of side effects and how they affect participants' daily lives
- How divarasib moves around the body
- What is the best (when looking at safety and how effective it is) dose of divarasib to use

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years of age and have locally advanced or metastatic NSCLC that has a *KRAS G12C* mutation (and PD-L1 positive NSCLC if they join Group A).

People may not be able to take part in this trial if they have:

- Previously received any medicine for locally advanced or metastatic NSCLC unless treatment for non-metastatic cancer was last given more than 6 months previously
- Received certain other treatments, including other *KRAS G12C* inhibitors
- Cancer that has spread to the brain or spinal cord and causes symptoms, and is untreated or is currently being treated with certain medicines
- Certain other medical conditions such as heart problems or hepatitis virus infection; they are pregnant or breastfeeding or are planning to become pregnant during or soon after the trial

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

Everyone who joins this clinical trial will be placed into 1 of 2 groups, and will be given:

- **Group A**: divarasib, as a tablet (taken by mouth), once a day AND pembrolizumab, given as an infusion (into the vein) every 3 weeks for up to 2 years (depending on local regulations)
- **Group B**: divarasib AND pembrolizumab in the same way as Group A, AND the clinical trial doctors' choice of carboplatin or cisplatin chemotherapy for approximately 3 months and pemetrexed for up to 2 years, each given as an infusion (into the vein) every 3 weeks

Participants will be placed into one of two treatment stages, depending on when they start the trial.
In the first stage, participants will be given either a low, or high dose of divarasib with other anti-cancer therapies. This is so researchers can test the safety and how well the body tolerates the treatment, with the lowest dose of divarasib being assessed first. If the doses of divarasib are acceptable, the second stage of the trial can begin.

In the second stage, Group A participants will be given a low or high dose of divarasib plus pembrolizumab. Participants will have an equal chance of being placed in either the low-dose or high-dose group. **Group B** participants will be given a high dose of divarasib plus pembrolizumab with chemotherapy. This is an open-label trial, which means everyone involved, including the participants and the doctors, will know which dose of divarasib is given with other anti-cancer therapies.

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

The safety or effectiveness of the experimental treatment may not be fully known at the time of the trial. The trial involves some risks to the participant, although it may not be greater than the risks related to routine medical care or the natural progression of the health condition. Potential participants 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. These will all be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for a clinical trial). Potential participants should also discuss these with members of the research team and with their usual healthcare provider.

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe and even life-threatening, and can vary from person to person. Potential participants will be told about the known side effects of carboplatin, cisplatin, divarasib, pemetrexed and pembrolizumab, and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs. Participants will also be told about any known side effects of taking tablets and receiving infusions.

Potential benefits associated with the clinical trial Participants' health may or may not improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

Inclusion Criteria:

- Confirmation of Biomarker eligibility

- Pre-treatment tumor tissue along with an associated pathology report is required for all participants enrolled on study. Representative tumor specimens must be in formalin-fixed, paraffin embedded (FFPE) blocks (preferred) or 15 unstained, freshly cut, serial slides. Although 15 slides are required, if only 10 slides are available, the participant may be eligible for the study following consultation with the Sponsor.
- Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1
- Histologically or cytologically documented locally advanced unresectable or metastatic NSCLC that is not eligible for curative surgery and/or definitive chemoradiotherapy
- No prior systemic treatment for advanced unresectable or metastatic NSCLC
- Measurable disease, as defined by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

Exclusion Criteria:

- Known concomitant second oncogenic driver with available targeted treatment
- Squamous cell histology NSCLC
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- Prior treatment with a KRAS G12C inhibitor
- Known hypersensitivity to any of the components of divarasib or pembrolizumab; or known hypersensitivity to pemetrexed, carboplatin, or cisplatin (Cohort B only)
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis, active tuberculosis, significant cardiovascular disease within 3 months prior to initiation of study treatment
- History of malignancy other than NSCLC within 5 years prior to initiation of study treatment, with the exception of malignancies with a negligible risk of metastasis or death (e.g., 5-year OS rate more >90%), such as adequately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localized prostate cancer, ductal breast carcinoma in situ, or Stage I uterine cancer
- Uncontrolled tumor related pain, pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures, uncontrolled or symptomatic hypercalcemia
- Co-morbid condition that is an absolute contraindication to treatment with corticosteroids
- Inability or unwillingness to take prophylactic treatments such as corticosteroids, anti-emetics, folic acid, or vitamin B12 supplementation.