ForPatients
by Roche

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

A Study to Compare the Efficacy and Safety of Entrectinib and Crizotinib in Participants With Advanced or Metastatic ROS1 Non-small Cell Lung Cancer (NSCLC) With and Without Central Nervous System (CNS) Metastases

Trial Status	Trial Runs In	Trial Identifier
Recruiting	19 Countries	NCT04603807 2019-003859-11 2023-507494-18-00 MO41552

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:

Randomized, Open Label, Multicenter, Phase III Study of Entrectinib Versus Crizotinib in Patients With Locally-Advanced or Metastatic Non-Small Cell Lung Cancer Harboring ROS1 Gene Rearrangements With and Without Central Nervous System Metastases

Trial Summary:

The study will compare the efficacy and safety of entrectinib with crizotinib in participants with advanced or metastatic ROS1 non-small cell lung cancer (NSCLC). The participants will self-administer oral entrectinib or crizotinib as described in the protocol and local prescribing information. Treatments will continue until progressive disease, unacceptable toxicity, death, or withdrawal from the study, whichever occurs first.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT04603807 2019-003859-11 2023-507494-18-00 MO41552
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

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Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. NSCLC usually develops in the tissues lining the lungs. It can spread to nearby lymph nodes and other organs. Cancers that have spread are known as ‘advanced’ cancers.

Some cancers have a change in a gene called *ROS1*. A gene is a section of DNA that has instructions for making the body. Cells that have a changed *ROS1* gene are able to survive and grow out of control. They become cancerous tumours. NSCLC with a certain change in *ROS1* are called ‘ *ROS1* rearrangement-positive NSCLC’ or ‘ *ROS1*-positive NSCLC’.

Crizotinib is a medicine approved worldwide by health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) for treating *ROS1*-positive NSCLC that has spread. Crizotinib does not work very well when cancer has spread to the brain. Better treatments are needed for *ROS1*-positive NSCLC that has spread. In particular, for people with cancer that has spread to the brain.

This study is testing a medicine called entrectinib. It is being developed to treat *ROS1*-positive NSCLC that has spread. Entrectinib is approved by health authorities in Europe and the U.S. for the treatment of *ROS1*-positive NSCLC that has spread. Entrectinib is not approved in other countries.

This study aims to compare the effects of entrectinib against crizotinib in people with *ROS1*-positive NSCLC that has spread.

2. Who can take part in the study?

People of at least 18 years of age with *ROS1*-positive NSCLC that has spread can take part in the study, This is only if they have not been treated or have only been given radiotherapy for their NSCLC. They must also be able to swallow pills.

People may not be able to take part in this study if they have certain conditions, such as heart, lung or stomach problems. People also cannot take part if they have an active infection or had another cancer within the past 3 years. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. The screening period will take place from 1 month before the start of treatment.

Everyone who joins this study will be placed into 1 of 2 groups randomly (by chance, like flipping a coin). Participants will be given either entrectinib OR crizotinib, as pills to be swallowed every day.

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Participants will have an equal chance of being placed in either group. This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will see participants once a month for the first 3 months. Then about every 2 months. They will see how well the treatment is working and check for any unwanted effects participants may have. Participants will have 1 follow-up visit at 1 month after completing the study treatment, during which the study doctor will check on the participant's wellbeing. Then, participants will have follow-up visits or telephone calls from the study doctor every 2 to 3 months for as long as they agree to it. Total time of participation in the study will depend on how participants' cancer responds to treatment and could be more than 2 years. 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 result measured in the study to assess if the medicine has worked is how long participants live without their cancer getting worse, in those with NSCLC that has spread to the brain when they start the study.

Other key results measured in the study include:

- How long participants live without their cancer getting worse in the brain or anywhere in the body
- How many participants have a positive response to the treatment
- How much time there is between the participant's cancer first responding to treatment and the cancer getting worse in the brain or anywhere in the body
- How long participants live
- How participants' health and any related medical conditions impact their daily life and their ability to function and enjoy life
- How much lung cancer symptoms (such as cough, chest pain and difficulty breathing) change over time compared with the start of the trial
- The number and seriousness of any unwanted effects
- The economic value of the study treatments (based on improved ability to function and enjoy life)

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.

It may not be fully known at the time of the study how safe and how well the study treatment works. 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 will be informed about the risks

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and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study medicines

Participants may have unwanted effects of the medicines 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 will have regular check-ups to see if there are any unwanted effects.

Entrectinib and crizotinib

Participants will be told about the known unwanted effects of entrectinib and crizotinib, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines.

Known unwanted effects of entrectinib include feeling tired or weak, having a low number of red blood cells, swelling, feeling less hungry than usual, throwing up or wanting to throw up and pain or discomfort in the head.

Known unwanted effects of crizotinib include feeling tired, having a low number of red blood cells, swelling, feeling less hungry than usual, and a feeling of spinning, being unsteady and losing balance.

The study medicine(s) 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:

- Histologically or cytologically-confirmed diagnosis of advanced or recurrent (Stage IIIB/C not amenable for radical treatment) or metastatic (Stage IV) NSCLC that harbors a documented ROS1 gene rearrangement.
- No prior treatment with a ROS1 tyrosine kinase inhibitor, chemotherapy or other systemic therapy for advanced or recurrent (Stage IIIB/C not amenable for radical treatment) or metastatic (Stage IV) NSCLC
- Prior radiotherapy is allowed if more than 14 days have elapsed between the end of treatment and randomization
- Measurable systemic disease according to RECIST v1.1
- Participants with measurable and non-measurable CNS lesions per RECIST v1.1, including leptomeningeal carcinomatosis
- Life expectancy of at least 12 weeks
- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2
- Adequate hematologic, renal, liver functions
- Participants must have recovered from effects of any major surgery or significant traumatic injury at least 28 days before the first dose of study treatment
- Ability to swallow entrectinib and crizotinib intact without chewing, crushing, or opening the capsules

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- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods with a failure rate of <1% per year during the treatment period and for up to 5 weeks after the last dose of entrectinib or for at least 90 days after the last dose of crizotinib
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm.

Exclusion Criteria:

- Prior treatment with a ROS1 tyrosine kinase inhibitor, chemotherapy or other systemic therapy for advanced or recurrent (Stage IIIB/C not amenable for radical treatment) or metastatic (Stage IV) NSCLC
- NCI-CTCAE v5.0 Grade 3 or higher toxicities due to any prior therapy (excluding alopecia, fatigue, nausea and lack of appetite), which have not shown improvement and are strictly considered to interfere with current study drug
- History of recent (within the past 3 months) symptomatic congestive heart failure or ejection fraction # 50% observed during screening for the study
- History of prolonged corrected QTc interval
- Peripheral sensory neuropathy # Grade 2
- Known interstitial lung disease, interstitial fibrosis, or history of tyrosine kinase inhibitor-induced pneumonitis
- Previous malignancy within the past 3 years
- Incomplete recovery from any surgery prior to the start of study treatment
- Active GI disease (e.g., Crohn's disease, ulcerative colitis or short gut syndrome) or other malabsorption syndrome that would reasonably impact drug absorption
- History of prior therapy-induced pneumonitis
- Any condition (in the past 3 months) e.g., myocardial infarction, unstable angina, coronary/peripheral artery bypass graft, cerebrovascular accident or transient ischemic attack, stroke, symptomatic bradycardia, or uncontrolled arrhythmias requiring medication
- Known active infections (bacterial, fungal or viral, including human immunodeficiency virus positive)
- History of hypersensitivity to any of the additives in the entrectinib and/or crizotinib drug formulations
- Pregnant or lactating women
- Known human immunodeficiency virus (HIV) positivity or acquired immunodeficiency syndrome (AIDS)-related illness
- Any clinically significant concomitant disease or condition that could interfere with, or for which the treatment might interfere with, the conduct of the study or the absorption of oral medications.

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