ForPatients
by Roche

CNS TumorsBrain TumorSolid TumorsCancer

A study to see how safe different doses of entrectinib are, how well they work and get to different parts of the body, and how the body gets rid of it in children and young people with brain tumours or solid tumours that have spread, cannot be removed with surgery or have no treatments available to them

Study of RXDX-101 in Children With Recurrent or Refractory Solid Tumors and Primary CNS Tumors, With or Without TRK, ROS1, or ALK Fusions

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	9 Countries	NCT02650401 CO40778 2023-505088-35-00 RXDX-101-03

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 1/2, Open-Label, Dose-Escalation And Expansion Study Of Entrectinib (Rxdx-101) In Pediatrics With Locally Advanced Or Metastatic Solid Or Primary CNS Tumors And/Or Who Have No Satisfactory Treatment Options

Trial Summary:

This is an open-label, Phase 1/2 multicenter dose escalation study in pediatric patients with relapsed or refractory extracranial solid tumors (Phase 1), with additional expansion cohorts (Phase 2) in patients with primary brain tumors harboring NTRK1/2/3 or ROS1 gene fusions, and extracranial solid tumors harboring NTRK1/2/3 or ROS1 gene fusions.

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Phase 1
Phase

NCT02650401 CO40778 2023-505088-35-00 RXDX-101-03
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#0 Years & # 18 Years	No

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1. Why is this study needed?

Solid tumours are cancer cells that grow in organ systems throughout the body, such as the lungs or brain. Some solid tumours are caused by sections of DNA (genes) changing or joining together.

New medicines are needed for children and young people with solid tumours with gene changes. This study is testing a medicine called entrectinib. It is being developed to treat people with solid tumours that have certain changes in the NTRK or ROS1 genes.

Entrectinib is approved by health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) for treating people who are older than 1 month of age with solid tumours that have changes in NTRK genes. It is also approved for treating adults with lung cancers that have changes in the ROS1 gene.

In this study, entrectinib is an experimental medicine. This means that some health authorities have not approved entrectinib for the treatment of children below the age of 12 with cancers that have changes in NTRK genes, or for treating people under the age of 18 with cancers that have changes in the ROS1 gene.

This study aims to test how safe entrectinib is at different doses and when given in different formulations (as capsules or minitablets to be swallowed, or using a feeding tube). Researchers will also aim to understand what happens to entrectinib once it is in the body, and how well it may work to treat children and young people with solid tumours that have changes in the NTRK or ROS1 genes. The study also looked at the effects of entrectinib in young people with changes in the ALK gene. This part of the study is now finished.

2. Who can take part in the study?

People less than 18 years of age with a solid tumour that cannot be removed with surgery, has spread to nearby tissue or to other parts of the body or is a brain tumour can take part in the study if the cancer cells have certain changes in the NTRK or ROS1 genes. They must also have no approved treatments available to them.

People may not be able to take part in this study if they have previously been given medicines similar to entrectinib, are being treated with certain epilepsy medicines, or have certain other medical problems such as heart problems or infections. 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.

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Everyone who joins this study will be given entrectinib once every day. The way entrectinib will be given will depend on whether participants have difficulty swallowing capsules or soft food. Entrectinib will be given as either:

- A capsule (to be swallowed)
- Minitablets taken with soft food
- Liquid - given through a feeding tube (nasogastric or a gastric tube) or with a syringe into the mouth

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 every week for the first month of treatment, then every 2 weeks. After 6 months of treatment they will be seen once a month or less if the study doctor decides it is safe to do so. The study doctor will see how well the treatment is working and any unwanted effects participants may have. Treatment will be given for as long as the participant agrees to it, or until their cancer worsens or they have unacceptable unwanted effects. After 2 years of treatment, participants who have no signs of cancer on tests or scans for the last 6 months may be given the option to pause treatment. Participants will have 1 follow-up visit 1 month after completing the study treatment, during which the study doctor will check on the participant's wellbeing. Participants will then receive follow-up telephone calls or have their medical records checked every 3 months, for as long as they agree to it. Total time of participation in the study will depend on how a participant responds to treatment, and could be more than 5 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 results measured in the study are:

- The highest amount of entrectinib that can be given safely, and the preferred dose to use
- The number of participants that have a positive response to the treatment

Other key results measured in the study include:

- The number and seriousness of unwanted effects
- How entrectinib gets to different parts of the body, and how the body changes and gets rid of it
- How much time there is between the participants starting treatment and their cancer first responding to treatment
- How much time there is between the participants' cancer first responding to treatment and the cancer getting worse

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- The number of participants whose tumours shrink or stay the same for at least 6 months with study treatment.
- How long participants live, and how long they live without their cancer getting worse
- The growth and development of the participants, as well as their brain and nerve function
- How acceptable participants find the different forms of entrectinib

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 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 entrectinib Participants may have unwanted effects of the drug 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.

Participants will be told about the known unwanted effects of entrectinib and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include feeling tired or weak, fever, throwing up, wanting to throw up, frequent watery stools, and pain in joints, muscles, back, neck, belly, arms or legs.

The study medicine(s) may be harmful to an unborn baby. Women of a child-bearing age, and men, must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Disease status:
- Phase 1 portion (closed): Participants must have measurable or evaluable disease, as defined by RECIST v1.1 * Phase 2 portion:
- Part B: Participants must have measurable or evaluable disease, as defined by RANO * Part C (closed): Participants must have measurable or evaluable disease, as defined by RECIST v1.1 ± Curie Scale * Part D: Participants must have measurable or evaluable disease, as defined by RECIST v1.1 * Part E (closed): Participants must have measurable or evaluable disease, as defined by RECIST v1.1 ± Curie Scale or RANO
- Tumor type:
- Phase 1 portion:

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- Part A: Relapsed or refractory extracranial solid tumors * Phase 2 portion
- Part B: Primary brain tumors with NTRK1/2/3 or ROS1 gene fusions; gene fusions are defined as those predicted to translate into a fusion protein with a functional TRKA/B/C or ROS1 kinase domain, without a concomitant second oncodriver as determined by a nucleic acid-based diagnostic testing method * Part D: Extracranial solid tumors (including NB) with NTRK1/2/3 or ROS1 gene fusions; gene fusions are defined as those predicted to translate into a fusion protein with a functional TRKA/B/C or ROS1 kinase domain, without a concomitant second oncodriver as determined by a nucleic acid-based diagnostic testing method
- Histologic/molecular diagnosis of malignancy at diagnosis or the time of relapse
- Archival tumor tissue from diagnosis or, preferably, at relapse
- Performance status: Lansky or Karnofsky score # 60% and minimum life expectancy of at least 4 weeks
- Prior therapy: Participants must have a disease that is locally advanced, metastatic, or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options for solid tumors and primary CNS tumors that are neurotrophic tyrosine receptor kinase (NTRK) or ROS1 fusion-positive
- Participants must have recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy prior to enrollment
- Adequate organ and neurologic function
- Females of childbearing potential must have a negative serum pregnancy test during screening and be neither breastfeeding nor intending to become pregnant during study participation. Agreement to remain abstinent or use use combined contraceptive methods prior to study entry, for the duration of study participation and in the following 90 days after discontinuation of study treatment.
- For male participants with a female partner of childbearing potential or a pregnant female partner: Agreement to remain abstinent or use a condom during the treatment period and for at least 3 months after the last dose of study drug

Exclusion Criteria:

- Receiving other experimental therapy
- Known congenital long QT syndrome
- History of recent (3 months) symptomatic congestive heart failure or ejection fraction #50% at screening
- Known active infections
- Familial or personal history of congenital bone disorders, bone metabolism alterations or osteopenia
- Receiving Enzyme Inducing Antiepileptic Drugs (EIAEDs) within 14 days of first dose.
- Prior treatment with approved or investigational TRK or ROS1 inhibitors
- Known hypersensitivity to entrectinib or any of the other excipients of the investigational medicinal product
- Patients with NB with bone marrow space-only disease
- Incomplete recovery from acute effects of any surgery prior to treatment.
- Active gastrointestinal disease or other malabsorption syndromes that would impact drug absorption.
- Other severe acute or chronic medical or psychiatric condition or lab abnormality that may increase the risk associated with study participation, drug administration or may interfere with the interpretation of study results.

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