ForPatients
by Roche

Colorectal Cancer (CRC)Metastatic Colorectal Cancer

A study to look at how well different targeted therapies work to treat colorectal cancer that has spread to other parts of the body

A Study Evaluating the Safety and Efficacy of Targeted Therapies in Subpopulations of Patients With Metastatic Colorectal Cancer (Intrinsic)

Trial Status	Trial Runs In	Trial Identifier
Recruiting	11 Countries	NCT04929223 2021-001207-33 2023-505163-37-00 WO42758

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 I/Ib Global, Multicenter, Open-label Umbrella Study Evaluating the Safety and Efficacy of Targeted Therapies in Subpopulations of Patients With Metastatic Colorectal Cancer (INTRINSIC)

Trial Summary:

This open-label, exploratory study is designed to evaluate the safety and efficacy of targeted therapies or immunotherapy as single agents or combinations, in participants with metastatic colorectal cancer (mCRC) whose tumors are biomarker positive as per treatment arm-specific definition. Eligible participants with mCRC will be enrolled into specific treatment arms based on their biomarker assay results.

Hoffmann-La Roche	Phase 1
Sponsor	Phase

NCT04929223 2021-001207-33 2023-505163-37-00 WO42758
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Colorectal cancer (CRC) is a type of cancer that starts in the colon or rectum. CRC that has spread to other parts of the body is called ‘metastatic CRC’, or ‘mCRC’.

Standard treatment for mCRC includes ‘targeted therapy’. Targeted therapy is a type of treatment that treats abnormal cells (e.g. cancer cells) in the body. It causes less harm to the normal cells. Doctors can look at the genes inside cancer cells for features that can be targeted by therapy. But more types of targeted therapies are needed, and doctors need to understand how safe they are and how well they work on their own or in combination with other treatments.

This study is testing new targeted therapies. They are experimental medicines. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not yet approved the new targeted therapies for treating mCRC.

This study aims to test how well different targeted therapies work, how safe they are, and to understand what happens to them once in the body.

2. Who can take part in the study?

People of at least 18 years of age with mCRC that have certain genetic features can take part in the study. They must meet other criteria to join a particular treatment group, such as which treatments they have been given before, if any.

People may not be able to take part in this study if, for example, they have uncontrolled pain caused by their cancer, or cancer that has spread to the brain or spinal cord and causes symptoms. People who have certain medical conditions such as liver disease, or are taking certain treatments, are not able to take part. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

Participants 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 a group (known as a ‘cohort’) that they fit the criteria for. The cohort will depend on the genetic features of the participant’s mCRC and may depend on the treatments they have received before.

The cohort will be given an experimental targeted therapy that matches their mCRC type. If more than 1 experimental targeted therapy or combination is available to a cohort, the cohort will be split into smaller groups and each group will be given a different study treatment. The chance of being given a certain study treatment will depend on the number of treatments available to a participant. This will be explained by the study doctor.

Targeted therapy will be given either on its own or in combination with other medicines. The medicines in this study may be given as pills (to be swallowed), injections under the skin, or drips into a vein (infusions) in treatment cycles. A treatment cycle is the period of

treatment and recovery time before the next set of treatment is given – a cycle is usually 3 or 4 weeks.

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 regularly. They will see how well the treatment is working and any unwanted effects participants may have. The number of visits the participants will have will depend on which cohort they are in. Participants who have cancer that gets worse or who have unmanageable and unwanted effects while they are being given a particular study treatment, may be able to be given a different treatment in this study if one is available and they meet the criteria.

Participants' total time in the study could be more than 2 years and will depend on how they tolerate treatment and how their cancer responds to treatment. 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 many people have a reduction of their cancer after treatment.

Other key results measured in the study include:

- How much time there is between the person's cancer first responding to treatment and the cancer getting worse
- The number of people whose tumours didn't grow or actually shrank after receiving treatment
- The number and seriousness of unwanted effects
- How the study treatments get to different parts of the body, and how the body changes and gets rid of it

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 other 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 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.

Participants will be told about the known unwanted effects of the study medicines and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known common unwanted effects include loose watery stools, throwing up, wanting to throw up, or a reaction to the injection or infusion.

The study treatments will be given as pills (to be swallowed), injections under the skin, or infusions. Known unwanted effects of injections under the skin include redness, swelling or rash on the skin where it has been pricked with a needle to give a treatment. Known unwanted effects of infusions include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low or high blood pressure, fever, pain or discomfort in the head, frequent watery stools, shortness of breath, and cough.

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:

- Signed cohort-specific Informed Consent Form
- Age >= 18 years at time of signing Informed Consent Form
- Biomarker eligibility as determined by:
- A validated test approved by local health authorities for detection of the specified biomarkers/mutations.
- A validated test performed at a College of American Pathologists/clinical laboratory improvement amendments (CAP/CLIA) -certified or equivalently accredited diagnostic laboratory using a validated test for detection of the specified biomarkers.
- Prior test results completed before signing cohort-specific Informed Consent Form or local test results generated prior to or during screening, and availability of a full report of the testing results OR
- Blood-based FoundationOne Liquid CDx biomarker eligibility test result generated prior to or during screening or, in case of re-enrollment after treatment discontinuation, prior to starting a new anti-cancer therapy.
- Eastern Cooperative Oncology Group (ECOG) Performance Status of <= 1
- Life expectancy >= 3 months, as determined by the investigator
- Histologically confirmed adenocarcinoma originating from the colon or rectum
- Metastatic disease
- Prior therapies for metastatic disease
- Ability to comply with the study protocol, in the investigators judgment
- Measurable disease (at least one target lesion) according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1)
- Baseline tumor tissue samples will be collected from all participants for exploratory biomarker research
- Adequate hematologic and organ function within 14 days prior to initiation of study treatment
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures
- For men: agreement to remain abstinent or use contraceptive measures, and agreement to refrain from donating sperm

Exclusion Criteria:

- Current participation or enrollment in another interventional clinical trial. Participants who are participating in the follow-up period of an interventional clinical trial are eligible for the study.
- Any systemic anti-cancer treatment within 2 weeks or 5 half-lives (whichever is shorter) prior to start of study treatment
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Pregnant or breastfeeding, or intending to become pregnant during the study
- History of or concurrent serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in and completion of the study or confounds the ability to interpret data from the study
- Severe infection within 4 weeks prior to initiation of study treatment or any active infection that, in the opinion of the investigator, could impact patient safety
- Incomplete recovery from any surgery prior to the start of study treatment that would interfere with the determination of safety or efficacy of study treatment
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (once monthly or more frequently)
- Uncontrolled tumor-related pain
- Uncontrolled or symptomatic hypercalcemia
- Clinically significant and active liver disease
- Negative HIV test at screening, with the following exception: Participants with a positive HIV test at screening are eligible provided they are stable on anti-retroviral therapy for at least 4 weeks, have a CD4 count greater than or equal to 200/uL, have an undetectable viral load, and have not had a history of opportunistic infection attributable to AIDS within the last 12 months.
- Symptomatic, untreated, or actively progressing CNS metastases
- History of leptomeningeal disease or carcinomatous meningitis
- History of malignancy other than CRC within 2 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death
- Any other disease, unresolved toxicity from prior therapy, 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 participant at high risk from treatment complications
- Requirement for treatment with any medicinal product that contraindicates the use of any of the study treatments, may interfere with the planned treatment, affects participant compliance, or puts the patient at higher risk for treatment-related complications