ForPatients
by Roche

Colorectal Cancer (CRC) Metastatic Colorectal Cancer

A clinical trial to look at how well different targeted therapies work to treat metastatic colorectal cancer (mCRC)

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	12 Countries	NCT04929223 2021-001207-33,2023-505163-37-00 WO42758

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

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 Sponsor	**Phase 1** 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 the INTRINSIC clinical trial needed?

Metastatic colorectal cancer (mCRC) is a type of colorectal cancer that has spread to other parts of the body outside of the colorectal area. This trial aims to test the safety and effectiveness of multiple therapies for the treatment of mCRC and to understand how the body responds to these treatments. These new therapies target specific changes or genetic alterations (changes in a person's DNA) in an individual's tumour. As the trial

progresses, the safety and effectiveness of other new treatment options may be tested in individuals with mCRC with different changes or genetic alterations.

2. How does the INTRINSIC clinical trial work?

This clinical trial is recruiting people who have been diagnosed with metastatic colorectal cancer. People who take part in this clinical trial will be given the clinical trial treatment for as long as it can help them. The clinical trial doctor will see participants regularly. The number of visits the participants will have will depend on which treatment group they are in. These hospital visits will include checks, such as a tumour assessment scan, to see how the participant responds to treatment and any side effects they may have. The tumour assessment scans will occur every 6 or 8 weeks for the first 48 weeks of the trial and then every 8 or 12 weeks after that. Participants' total time in the clinical trial will depend on how they tolerate treatment and how their cancer responds to treatment, this could be as long as 2 years or more. Participants can stop trial treatment and leave the clinical trial at any time.

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

The main clinical trial endpoint (the main result measured in the trial to see if the drug has worked) is to determine how many participants have a reduction in the size of their tumour (known as the "objective response rate"). The other clinical trial endpoints include:

- How much time there is between the participant's cancer first responding to treatment and the cancer getting worse (known as "duration of response")
- How many participants have tumours that stay the same or reduce in size for at least 12 weeks (known as "disease control rate")
- The number and seriousness of any side effects, and
- How the body processes the different therapies

4. Who can take part in this clinical trial?

People can take part in this trial if they have been diagnosed with mCRC that has certain genetic features and are at least 18 years old. People may not be able to take part in this trial if they have received anti-cancer treatment within 2 weeks of starting the clinical trial, or another clinical trial treatment within 28 days of starting this clinical trial. People who are pregnant or breastfeeding, are intending to become pregnant during the clinical trial or up to about 6 months after treatment, or who have certain other medical conditions or are taking certain treatments, are not able to take part. There are other specific criteria that participants may need to meet for each treatment in this clinical trial.

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

Everyone who joins this clinical trial will enter one of seven trial cohorts:

- **Cohort 1**: **If a participants' mCRC has a specific genetic alteration in the KRAS gene**, and they have not previously had chemotherapy that contained oxaliplatin, they will be given divarasib as a pill (to be swallowed) once every day, as well as cetuximab plus FOLFOX, each given as an infusion once every 2 weeks
- **Cohort 2: If a participants' mCRC has a specific genetic alteration in the KRAS gene,** and their cancer was not effectively controlled by, they did not tolerate, or they refused to be given oxaliplatin-and/or irinotecan-containing chemotherapy, they will be given divarasib as a pill (to be swallowed) once every day, as well as cetuximab as an infusion once every 2 weeks
- **Cohort 3: If a participants' mCRC has a specific genetic alteration in the KRAS gene,** and they have not previously had chemotherapy that contained irinotecan, they will be given divarasib as a pill (to be swallowed) once every day, as well as cetuximab plus FOLFIRI each given as an infusion once every 2 weeks
- **Cohort 4: If a participant has "microsatellite instability-high" (MSI-H) mCRC**, which means that a lot of instability has been detected in their mCRC (due to defects in the proteins responsible for repairing DNA), they will be split into two groups randomly (like flipping a coin) and given either atezolizumab plus tiragolumab plus bevacizumab, each given as an infusion (into a vein) once every 3 weeks OR atezolizumab plus tiragolumab, both given as an infusion once every 3 weeks
- **Cohort 5 (participants in the United States only): If a participants' mCRC has specific genetic alterations in the BRAF gene**, they will be given SY-5609 as a pill (to be swallowed) once every day for 7 days, followed by 7 days off, as well as atezolizumab as an infusion once every 4 weeks
- **Cohort 6: If a participants' mCRC has genetic alterations in the PIK3CA gene**, they will be given inavolisib as a pill (to be swallowed) once every day, as well as cetuximab as an infusion once every week
- **Cohort 7: If a participants' mCRC has genetic alterations in the PIK3CA and RAS genes** *,* they will be given inavolisib as a pill (to be swallowed) once every day, as well as bevacizumab as an infusion once every 3 weeks

This is an open-label 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).

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, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial and safety assessments will be performed regularly. Participants will be told about the known side effects of **atezolizumab, tiragolumab, bevacizumab, SY-5609, inavolisib, divarasib, cetuximab, FOLFOX, and FOLFIRI**, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Atezolizumab, tiragolumab, bevacizumab, cetuximab, FOLFOX, and FOLFIRI will each be given as an intravenous infusion (injection into a vein). Participants will be told about any known side effects of intravenous infusion. SY-5609, inavolisib, divarasib will each be given as a pill (to be swallowed). Participants will be told about any known side effects of oral administration.

Potential benefits associated with the clinical trial

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.