Pilot study to determine the intraTUMORal OsImertinib concentration in patients with peritoneal metastasizeD colorectal cancer (TUMOROID study)

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON51641

Source
ToetsingOnline

Brief title
TUMOROID study

Condition

- Gastrointestinal neoplasms malignant and unspecified
- Gastrointestinal therapeutic procedures

Synonym
Colorectal cancer; colon cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: colorectal cancer, intratumoral, osimertinib, peritoneal metastasis

Outcome measures

Primary outcome

intratumoral osimertinib concentration in peritoneal metastasis and liver

metastasis

Secondary outcome

Intra- and interpatient variability in intratumoral osimertinib concentrations.

Relation between osimertinib concentration in ascites, plasma and healthy

tissue vs intratumoral osimertinib concentration. Safety and tolerability of

pre-operative osimertinib treatment.

Study description

Background summary

Patients with peritoneal metastasis (PM) from colorectal cancer (CRC) have reduced benefit from systemic chemotherapy compared with metastases to other sites. The mechanism underlying this site-dependent variation is unknown, but it is often explained as reduced drug exposure due to the peritoneal plasma barrier. The poorly permeable peritoneal plasma barrier is the rational for local administration of chemotherapy, which is routinely applied as hyperthermic intraperitoneal chemotherapy (HIPEC) immediately after cytoreductive surgery (CRS). However, the clinical evidence for this complex procedure is lacking. A recent randomized controlled trial failed to show an effect of CRS+HIPEC over CRS alone which further questions the role of HIPEC in routine clinical practice. Although HIPEC is performed with curative intent, two third of patients show recurrent disease of whom 50% have recurrence within 1 year after surgery. Recent findings demonstrate an enrichment of consensus

molecular subtype 4 (CMS4) in peritoneal metastasis. This could be an alternative explanation for reduced efficacy of chemotherapy in patients with peritoneal metastasis. Since HIPEC is a complex, invasive and costly application, being performed without convincing clinical evidence, there is an urgent need for new treatment strategies for patients with PM of CRC. One promising strategy is the use of targeted drugs in alternative dosing schedules, e.g. intermittent high-dose. Although preclinical studies with tyrosine kinase inhibitors (TKIs) are promising, the efficacy in patients with CRC is disappointing so far. It is unknown if this is a result of intrinsic resistance or suboptimal tumor tissue exposure which in the case of PM can be a result of the peritoneal plasma barrier. Patient-derived tumor organoids (PDTOs) can be used to select the most promising TKIs for further investigation. Drug experiments in organoid models can be used for translation from the preclinic to the clinical setting. Preclinical experiments showed promising efficacy for the TKI osimertinib in PDTOs from CRC. With the development of an LC/MS-MS assay we are able to determine the drug concentrations that inhibit proliferation or induce cell death in organoid tissue. However, to determine whether these preclinical findings can be translated to the clinical setting, it is of importance to gain knowledge about osimertinib exposure at the target site in patients with metastasis from colorectal cancer.

Study objective

The main objective of this pilot study is to determine the intratumoral concentrations of osimertinib upon 1 week of treatment in peritoneal metastasis of patients who are candidate for CRS-HIPEC treatment (group 1) and in liver metastasis of patients undergoing primary liver resection surgery (group 2).

Study design

Multi-center, non-randomized, interventional pilot study

Intervention

Patients of both groups will be treated with osimertinib in the registered dosing schedule (80mg OD) for a period of 1 week prior to CRC-HIPEC (group 1) or liver resection (group 2). Five patients will be included in both groups. Intratumoral osimertinib concentrations will be measured from tumor resection material that is removed as part of routine clinical care. Since the tumor material is resected with tumor-free margins, it is also possible to measure osimertinib concentrations in this tumor-free healthy tissue. If ascites is present a sample is collected during surgery to determine osimertinib concentration in ascites. Finally, a blood sample will be collected prior to surgery to determine the osimertinib concentration in plasma.

Study burden and risks

Enrolment in this study will require 1 week of treatment with osimertinib prior to cytoreductive surgery or liver surgery (depending on study group). Osimertinib is registered for the treatment of non-small cell lung cancer. Adverse events as a result of the use of osimertinib may occur, but are expected to be limited upon only one week of treatment. Resection of tumor tissue is part of routine clinical care and no additional intervention is required to obtain tumor samples. The collection of ascites during surgery and blood is considered risk-free. A burden for the patient is the extra visit including physical examination and laboratory analysis one week after the start of osimertinib to evaluate the treatment. There is no benefit for individual patients who participate in this pilot study. The benefit is mainly of scientific value. Preclinical studies investigating osimertinib antitumor efficacy in CRC cell lines demonstrate a possible enhancement of the effect of chemotherapy. However, it cannot be expected that osimertinib will significantly induce antitumor activity in only one week of treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Diagnosed with PM of CRC and candidate for CRS-HIPEC (GROUP 1)
- Diagnosed with liver metastasis of CRC and candidate for primary resection of at least one liver metastasis (GROUP 2)
- 18 years or older
- WHO performance status 0 or 1
- Adequate haematologic and organ function
- Written informed consent
- Able to swallow oral medication

Exclusion criteria

- Not fit to undergo surgery
- The use of concomitant drugs that interact with osimertinib according to the SPC
- An active contraindication for the use of osimertinib
- Mean resting corrected QT interval (QTc) > 470 msec at screening
- Medical history of interstitial lung disease
- Medical history of any skin disease

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-02-2024
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tagrisso
Generic name:	Osimertinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	21-11-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-02-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2022-003460-24-NL
CCMO	NL82914.091.22