Neo-adjuvant chemotherapy followed by surgery versus surgery alone in high-risk patients with resectable colorectal liver metastases ;The CHARISMA randomized multicenter clinical trial

Published: 23-07-2014
Last updated: 19-03-2025

The primary study objective is to compare the efficacy, as assessed by overall survival, of surgery and neo-adjuvant chemotherapy to surgery alone in patients with resectable liver metastases of colorectal cancer and a high clinical risk score....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON44796

Source
ToetsingOnline

Brief title
CHARISMA

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified
- Gastrointestinal therapeutic procedures

Synonym
Liver metastases colorectal cancer

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: KWF subsidie Datamanagement Klinische Studies

Intervention

Keyword: Chemotherapy, High-risk, Liver metastases, Survival

Outcome measures

Primary outcome

Primary endpoint: overall survival (OS), calculated from the date of

randomization to the date of death from any cause of the patient

Secondary outcome

Besides OS, we will evaluate PFS of the patients included in the study. PFS

will be defined counting from the date of randomization to the first event

defined as local recurrence or progression, distant recurrence or death from

any cause. Furthermore:

* To determine quality of life in the two study arms

* To determine treatment response on neoadjuvant chemotherapy

* To compare morbidity of surgery and resection rate between the 2 arms

* To evaluate whether CEA can predict for treatment response, PFS and OS

Study description

Background summary

Efforts to improve the outcome of liver surgery by combining the resection with chemotherapy have failed to demonstrate overall survival (OS) benefit. This

may partly be due to the fact that these studies often involve strict study protocol inclusion criteria. Consequently, patients with a high Clinical Risk Score (CRS) - who might benefit the most from chemotherapy - are often underrepresented in these studies. Since genuine survival benefit has not yet been demonstrated, could this low impact of chemotherapy on survival then be explained by the relatively low risk of the patients in these trials? In view of the retrospective observations that pre-selection of patients by using prognostic characteristics may define the patient population most likely to benefit from chemotherapy, it was decided to take CRS stratification as the base for a randomized controlled trial in resectable patients.
This study will therefore evaluate the impact of neo-adjuvant chemotherapy in patients with high-risk (CRS 3-5) resectable colorectal liver metastases (CRLM) without extrahepatic disease. Our hypothesis is that adding neo-adjuvant chemotherapy to surgery will provide an improvement in OS in this high-risk patient group.

Study objective

The primary study objective is to compare the efficacy, as assessed by overall survival, of surgery and neo-adjuvant chemotherapy to surgery alone in patients with resectable liver metastases of colorectal cancer and a high clinical risk score. Secondary objectives are to investigate the progression free survival (PFS) in both arms and Quality of Life (QOL), to investigate morbidity of resection in both arms and to investigate whether CEA levels can predict for treatment response PFS

Study design

Randomized, prospective, phase III study

Intervention

Patients will be randomized into one of two groups. One group will be treated by surgery for the liver metastases only (standard treatment, arm 1). The other group will be treated by neo-adjuvant oxaliplatin-based chemotherapy, followed by surgery for the liver metastases (arm 2).

Study burden and risks

Patients who will participate in the study and randomize for arm B (neo-adjuvant chemotherapy + surgery) are expected to have a better overall survival compared to the current standard therapy (surgery only). However, the neo-adjuvant chemotherapy administered in arm B may cause systemic side effects. The chemotherapy regimen used in arm B is known to be well-tolerated as the regimen is used as a standard adjuvant treatment in stage 3 colorectal cancer patients. Unlike non-study patients, all patients participating in the

study will complete Quality of Life questionnaires (QLQ-C30 and MFI) at baseline and then every 3 months until 1 year after treatment completion.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075 EA
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Groene Hilledijk 301
Rotterdam 3075 EA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Age * 18 years.
* ECOG performance status 0 or 1
* Histologically confirmed primary colorectal carcinoma. Primary colorectal carcinomas to be included are:
* Previously resected histologically proven colorectal carcinoma
* Coloncarcinoma still in situ, deemed suitable for resection at the time of liver surgery
* Rectal carcinoma still in situ, requiring no neo-adjuvant radiotherapy, deemed suitable for resection at the time of liver surgery

* Rectal carcinoma still in situ, requiring short-course neo-adjuvant radiotherapy, deemed suitable for resection at the time of liver surgery
* Radiologically confirmed and resectable liver metastasis of colorectal cancer after surgery. Criteria for resectability are outlined in the study protocol.
* Clinical risk score of 3-5

Exclusion criteria

* Prior adjuvant chemotherapy for the primary colorectal carcinoma given <6 months prior to detection of the liver metastases.
* Prior non colorectal malignancies, except for patients with basal or squamous cell carcinoma of the skin, or patients with carcinoma in situ of the cervix.
* Presence of extrahepatic disease
* Locally advanced rectal cancer in situ requiring long-course pre-operative chemoradiotherapy
* Major surgical procedure <4 weeks prior to randomization.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-10-2014
Enrollment:	224
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Oxaliplatin
Generic name:	Oxaliplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xeloda
Generic name:	Capecitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	06-03-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 27498
Source: Nationaal Trial Register

Title:

In other registers

Register	ID
EudraCT	EUCTR2013-004952-39-NL
CCMO	NL47227.078.14
OMON	NL-OMON27498