In vivo REsponse evaluation of colorectal liver metastases during systemic therapy using optical SPECTroscopy techniques: a pilot study

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The aim of the present pilot study is to assess whether percutaneous optical spectroscopy can serve as a novel tool for tumour response evaluation in patients with unresectable colorectal liver metastases receiving first line systemic therapy.

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

Summary

ID

NL-OMON38470

Source
ToetsingOnline

Brief title
RESPECT study

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified

Synonym
colorectal livermetastases

Research involving
Human

Sponsors and support

Primary sponsor: Philips Research
Source(s) of monetary or material Support: NKI-AVL

Intervention

Keyword: colorectal liver metastases, optical spectroscopy, systemic therapy

Outcome measures

Primary outcome

Primary Objective:

In this pilot study we aim to evaluate whether the results of the diffuse reflectance and fluorescence spectra can be used for response monitoring of first line systemic therapy in patients with colorectal liver metastasis.

Secondary outcome

Secondary Objectives:

To compare the accuracy of response monitoring using spectroscopy with standardized RECIST criteria. To correlate spectroscopic measurements with tissue characteristics from biopsies. During the measurement procedure, possible improvements of the measurement hardware will be recorded which can provide information for possible alterations of hardware design for improved clinical applicability in the future.

Study description

Background summary

Clinical problem:
Colorectal cancer is a major health problem with more than 12.000 newly diagnosed patients yearly in the Netherlands (Netherlands Cancer Registry -

www.ikc.nl). Approximately 20% of patients will present with liver metastases at initial diagnosis and eventually 50-60% of patients develop liver metastases during the course of the disease.
Only 20% of patients with synchronous or metachronous colorectal liver metastases are suitable for liver resection2. At best, these patients have a five-year survival of approximately 30-40%. The remaining patients undergo systemic therapy aimed at stabilizing or reducing metastatic disease. For systemic treatment with or without addition of targeted drugs the overall response rate is between 20 and 50%, the median survival is 12-20 months and five-year survival is 2-5%. When disease progression is observed during first line systemic therapy, a change to an alternative second line regimen is recommended. The response rate to second line systemic therapy is approximately 4-28%.
The actual response to systemic therapy is generally evaluated after 2-3 months by computed tomography (CT) imaging using standardized RECIST (response evaluation criteria in solid tumors) criteria. However, the response in patients receiving new targeted drugs such as bevacizumab that lack direct intrinsic cytotoxic activity, challenges the concept of tumour size alone (and thus RECIST-criteria) as a good indicator for response. Tumour shrinkage alone is not strongly correlated to response to bevacizumab-containing regimens and combination of tumour size and density might be a better predictor. Other modalities to assess the response to systemic therapy are under investigation. Experimental studies show that FDG-PET/CT could be of use for early outcome prediction in patients undergoing systemic therapy for metastatic colorectal cancer, although results are conficting. Contrast enhanced ultrasonography might also serve as a surrogate marker to predict treatment response in patients with metastasized colorectal cancer receiving bevacizumab.
In summary, response monitoring of patients undergoing systemic therapy for colorectal liver metastases, especially in the era of new targeted drugs, is troublesome and the development of novel monitoring tools are needed.

Study objective

The aim of the present pilot study is to assess whether percutaneous optical spectroscopy can serve as a novel tool for tumour response evaluation in patients with unresectable colorectal liver metastases receiving first line systemic therapy.

Study design

The study is designed as an observational pilot study.

Patients eligible for inclusion into this study are patients admitted to The Netherlands Cancer Institute (NKI-AvL) for first line systemic therapy for unresectable colorectal liver metastases.

In this pilot we investigate whether optical spectroscopy can be used to detect systemic therapy response after treatment. For that purpose optical spectroscopy results will be compared with standard pre- and post-systemic therapy CT imaging and with histopathological analysis of the tissue samples taken during the spectroscopic measurements.

Procedures
CT imaging is the gold standard procedure for response evaluation in patients with colorectal liver metastases undergoing systemic therapy. Prior to treatment, CT-imaging is performed to determine the size and shape of the liver lesions. After about three months a next CT-scan is performed to determine treatment response. In this pilot study optical measurements in combination with a tissue biopsy will be performed at the same interval as the CT-scans, thus prior to systemic treatment and after three months. The anticipated total time for the whole procedure will be about 10 minutes (twice).

Study burden and risks

Based on the extent of the planned intervention (optical spectroscopy and biopsy) as well as experiences with the optical spectroscopy system in vivo and ex vivo, the risk of SAE*s is comparable to that of a regular liver biopsy. Bleeding is generally considered the major complication after percutaneous liver biopsy. In literature, an overall bleeding rate between is described between 0.06 and 1.7%. The results of a multivariate analysis by Terjung et al. imply that the bleeding risk after a percutaneous liver biopsy can be effectively reduced by careful patient selection and by avoiding potentially hazardous co-therapy. Therefore, patients with a higher bleeding risk are excluded for this study.
In the future, patients could benefit from a better response monitoring system, laeding to an optimalized and if needed adapted systemic therapeutic regimen.

Contacts

Public
Philips Research

High Tech Campus 34 m/s 21
Eindhoven 5656 AE
NL
Scientific
Philips Research

High Tech Campus 34 m/s 21
Eindhoven 5656 AE

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Non-resectable colorectal liver metastases
- Liver metastases of which a histological biopsy can safely be obtained:
* Patients with safely accessible liver lesions according to an intervention-radiologist.
* Patients not known with bleeding disorders (such as hemophilia) or bleeding complications from biopsies, dental procedures or surgery.
* Patients not using any anti-coagulant medication at the time of biopsy: all aspirin derivatives, NSAID*s, coumarines, platelet function inhibitors, heparins (including LMWHs) and oral factor Xa inhibitors are not allowed, unless medication can either be safely stopped or counteracted.
* Adequate hematology and coagulation status as measured by:
* Hb > 6.0 mmol/L
* Platelet count > 100 x 109/L
* PT < 1.5 x Upper limit of normal (ULN)
* APTT < 1.5 x ULN
* PT-INR < 1.5 on the day of biopsy in patients using coumarines
- Patients not known with contraindications for lidocaine (or its derivatives)
- First line systemic treatment
- Written informed consent, >18y

Exclusion criteria

- Patients with suspected sensitivity to light; e.g. patients who have had photodynamic therapy
-Patients who have higher risk of bleeding, such as patients with coagulopathy or patients who receive anticoagulants

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-11-2013
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO

Date:	21-05-2013
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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: 22669
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL42902.031.12
OMON	NL-OMON22669