Selecting cancer patients for treatment using Tumor Organoids, the SENSOR study

Published: 23-03-2016
Last updated: 21-04-2024

Primary: Evaluate the efficacy of patient-derived tumor organoids to successfully allocate patients for treatment with specific targeted agents.Secondary: Characterize safety and tolerability per experimental treatment regimen.

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

Summary

ID

NL-OMON46891

Source
ToetsingOnline

Brief title
SENSOR

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
colon cancer, Colorectal cancer, lung cancer, non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: Zwaartekracht subsidie

Intervention

Keyword: Colorectal cancer, Non-small cell lung cancer, Targeted treatment, Treatment selection, Tumor organoids

Outcome measures

Primary outcome

Overall clinical response rate (ORR) according to RECIST 1.1.

Secondary outcome

* Progression free survival (PFS) per RECIST 1.1.

* Progression free survival per RECIST 1.1 per compound or combination of compounds.

* Overall response rate (ORR) per RECIST 1.1 per compound or combination of compounds.

* Incidence and severity of adverse events per compound or combination of compounds.

Study description

Background summary

One of the most promising developments in oncology for the past two decades has been the introduction of targeted anti-cancer drugs. The main purpose of targeted therapy is to improve treatment efficacy and limit toxicity. Great results have been obtained by biomarker assisted patient selection, examples of which are trastuzumab in Her2 positive breast or gastric cancer and vemurafenib in BRAF V600E mutant melanoma. Nonetheless, actionable mutations and biomarkers for resistance have yet to be identified for the majority of targeted drugs and the process of drug development is still hampered by inadequate patient selection. Biomarker identification is a protracted and costly process and the complexity of genomic data generally prohibits a full understanding of drug sensitivity. Additional functional information of individual tumors would greatly improve our selection criteria in personalized cancer treatment. This could result in improved patient outcomes but will also greatly benefit the

process of drug development. Although tumor cell lines have been evaluated as in vitro predictive models, they have a limited success rate. A recent discovery by Sato et al. and Barker et al. offers an outlook on a new functional in vitro assay. They have established a culture system in which stem cells of various organs can be expanded and subsequently used for functional assays. Furthermore, it was demonstrated that these cultured cells are genetically stable over long periods of time and can regenerate the organ of origin when transplanted in mice. The in vitro expansion of stem cells is now possible for both normal and, importantly in this study, tumor tissue, giving us a potential in vitro model to screen for individual drug sensitivity.
By using tumor organoids for a comprehensive drug screen including a variety of targeted agents we have established a discovery pipeline that allows us to stratify patients for treatment with a (combination of) targeted agent(s). With the cooperation of the pharmaceutical industry we will have at our disposal a dynamic collection of targeted agents that will allow us to directly allocate patients to compound(s) best fit for their response profile. Pre-treatment stratification using this novel discovery pipeline holds the promise to not only improve patient outcomes, decrease the number of patients unnecessarily exposed to toxic agents and to promote cost-effectiveness but to also increase the number of potentially active targeted agents that become available.

Study objective

Primary:
Evaluate the efficacy of patient-derived tumor organoids to successfully allocate patients for treatment with specific targeted agents.

Secondary:
Characterize safety and tolerability per experimental treatment regimen.

Study design

This is a single center, interventional, open-label, clinical feasibility trial for patients with locally advanced (incurable) or metastatic colorectal cancer or NSCLC that have only one line of standard of care treatment left, or will start a study treatment. The primary aim of this study is to evaluate the efficacy of stratifying patients with locally advanced (incurable) or metastatic colorectal cancer or NSCLC for treatment with anticancer agents. This will be achieved by performing a comprehensive drug screen on every patient*s individual tumor organoids using a selected number of targeted agents supplied by the pharmaceutical industry. According to their individual organoid response profiles patients will be allocated to a particular treatment with an early phase (phase 1B or higher) or a currently registered compound that is consorted in this collective protocol.
Organoid response assays are currently estimated to take about 2-3 months. To bridge the analysis period, patients will receive standard of care treatment or

another study treatment after inclusion and the subsequent biopsy procedure. When progressive disease is observed on this treatment, our treatment stratification will be complete and patients will be allocated to a (combination of) targeted agent(s). Patients for whom it was not possible to identify an active agent or combination of agents will be referred back to standard of care treatment or another experimental treatment. Patients are asked to undergo a post-treatment biopsy after progressing on the intermittent treatment, this will allow us to evaluate if the intermittent treatment has conferred resistance to the allocated agent if a patient does not respond to the experimental treatment. The post-treatment biopsy will only be performed if the patient has signed consent for treatment with the selected experimental agent and has passed baseline screening.

A dynamic number of compounds is available. For each compound a separate supplemental will be constructed with information about sponsorship, data on the investigational product (including SPC, RP2D, dosage modification recommendations, method of administration, known preclinical and clinical data), agent specific inclusion and exclusion criteria and a compound specific additional patient information leaflet and informed consent form. Addition of each individual treatment regimen in this trial will be submitted to the ethics committee as an amendment.

Intervention

Treatment with one of the following compounds (if an active agent has been identified using organoid drug screens):
- Axitinib (VEGFR inhibitor)
- Palbociclib (CDK 4/6 inhibitor)
- PF-04449913 (SMO inhibitor)
- PF-05212384 (PI3K/mTOR inhibitor)
- Iressa (EGFR inhibitor)
- Selumetinib (MEK1/2 inhibitor)
- AZD2014 (mTOR inhibitor)
- AZD5363 (Akt inhibitor)

Study burden and risks

Patients will undergo a histological tumor biopsy and will subsequently be treated with standard of care until progression. Ample experience exists with performing biopsies in patients with locally advanced or metastatic lesions and the procedure is considered to be safe. At progression patients will undergo a second biopsy (in order to determine if the intermittent treatment has altered the drug sensitivity profile of the tumor) and are offered treatment based on tumor organoid drug sensitivity. Importantly, we will only treat patients with the recommended phase II or registered phase III dose, which limits the chance of unexpected toxicities. Safety data will be specified per treatment

regimen.

Contacts

Public
Nederlands Kanker Instituut

Plesmanlaan 121
Amsterdam 1066CX
NL
Scientific
Nederlands Kanker Instituut

Plesmanlaan 121
Amsterdam 1066CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients with locally advanced (incurable) or metastatic colorectal cancer or NSCLC that have only one line standard of care treatment left, or will start with a study treatment. Patients should have received a first line standard of care treatment.
2. No treatment options with curative intent
3. RECIST 1.1 measurable/evaluable disease
4. Safe biopsy of a metastatic lesion possible
5. Adequate organ function
6. WHO performance status 0-1
7. Age > 18 years and written informed consent;In- and exclusion criteria for each drug are

further determined by individual drug characteristics that are provided by pharmaceutical partners.

Exclusion criteria

1. Pregnant or lactating (nursing) women
2. Prior malignancy within 5 years.
3. Known infection with human immunodeficiency virus (HIV)
4. Leptomeningeal carcinomatosis
5. Symptomatic brain metastasis.
6. Other psychiatric or medical conditions that would make the patient unfit for participation.
7. Life expectancy of less than 3 months from tumor progression under standard of care. ;In- and exclusion criteria for each drug are further determined by individual drug characteristics that are provided by pharmaceutical partners.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-11-2016
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	-
Product type:	Medicine

Brand name:	Axitinib
Generic name:	-
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Palbociclib
Generic name:	-
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-03-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO	

Date:	02-03-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-11-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2014-003811-13-NL
CCMO	NL50400.031.14

Study results

Date completed: 16-04-2019

Actual enrolment: 61

Summary results
Trial is onging in other countries