Development of Anal Cancer Treatment selection model by Organoids (ACTOR)

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

Summary

ID

NL-OMON56888

Source
ToetsingOnline

Brief title
ACTOR

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
anal cancer, anal carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: KWF

Intervention

Keyword: (metastatic) analcancer, modelsystem, organoids, predictive value

Outcome measures

Primary outcome

To test the ability to function as predictive biomarker for the standard of

care therapies the following clinical endpoints are defined:

For the organoids the following endpoints will be evaluated:

• organoid establishment rate, time to establishment, time to screening.

• for in vitro drug/radiotherapy screening: Area Under the Curve (AUC), GR50,

GRmax.

To correlate organoid response to clinical outcomes in the patient, the

following endpoints will be evaluated:

Primary anal SCC:

Complete clinical response on clinical examination and pelvic MRI (CCR) versus

no CCR at 6-months follow-up. Pelvic MRI consists of anatomical T2 weighted

sequences and functional diffu-sion weighted imaging sequences (DWI); CCR on

MRI is defined as a hypointense scar tissue on T2 weighted imaging without

diffusion restriction.

Metastatic anal SCC:

The primary endpoint will be best radiological response by RECIST 1.1 within 6

months.

Secondary outcome

Primary anal SCC:

Secondary endpoints are progression-free and overall survival which will be defined as the time from start of treatment until documented progression or disease related death.

Metastatic anal SCC:

Secondary progression-free survival will be defined as the time from start of treatment until documented progression or disease related death.

Study description

Background summary

Anal squamous cell carcinoma (SCC) is a rare form of cancer affecting the anal canal. In the Netherlands, the prevalence of anal cancer has increased over the past decade. The standard of care treatment for non-metastatic anal SCC is definitive chemoradiotherapy. For patients with locally resistant or recurrent disease, salvage surgery is used and has been reported to be offered in up to 40% of patients. Complete response is achieved in approximately 80% after chemoradiotherapy with either 5-FU or capecitabine and mitomycin C. For patients with metastatic anal SCC, carboplatin plus paclitaxel combination chemotherapy is the current standard of care treatment with an objective response rate of 59%. New developments are hampered due to rareness of disease slowing done recruitment for clinical trials and testing novel agents. Furthermore, there is a lack of in vitro and in vivo models for anal SCC and no sufficiently good biomarkers are available to guide treatment in clinic. Patient-derived organoid models offer a unique opportunity to study anal SCC. These organoids can be derived from epithelial tumors, grown in 3D as miniature versions of the original patient tumor in vitro. Organoids have many advantages, the most prominent of which is the ability to recapitulate intratumor heterogeneity in vitro and accurately represent the tumors they are derived from both genetically and phenotypically. Additionally, compared to traditional 2D-cell lines and xenograft models, for the majority of tumor

types, organoid generation is very rapid (within 10-14 days of the tissue biopsy). This allows for fast establishment of a patient-derived organoid culture, with the potential to perform in vitro drug screening assays within a short timeframe to determine the sensitivities of a particular tumor to a particular drug or compound. Organoids can be used as a platform for in vitro drug screening to evaluate chemotherapy, radiotherapy as well as targeted therapy and immunotherapy.

Study objective

Aim of the ACTOR project is to develop organoid models for anal SCC, both in the non-metastatic and in the metastatic setting to:
1) learn about the biology of disease by characterising the organoids and original tissue, circulating immune cells and tumour infiltrating lymphocytes (TILs) in order to find new leads for therapeutic options;
2) test the ability organoids to function as predictive biomarker for standard of care therapies;
3) perform drug screens to investigate novel treatment options (organoids as patients in the lab).

Study design

This is an observational cohort study. Tumor tissue will be collected from either the primary tumor by a surgeon, or from a metastasis by a radiologist. The biopsy specimen will be used to culture tumor organoids and isolate tumor infiltrating lymphocytes(TILs). The tissue will also be used to enable RNA and DNA sequencing. Novel therapies will be evaluated in organoids by testing a panel of different agents targeting mutational pathways upregulated in anal SCC. Finally, co-cultures with immune cells will be performed to evaluate immunotherapy options Blood samples will be collected for germline DNA background variation and for PBMC isolation. The patient will be treated according to standard of care and clinical data of treatment type and survival outcomes will be collected.

Study burden and risks

For all included patient*s biopsies of the (metastatic) lesion(s) in the anal tumor, liver, lymph node or subcutaneous lesion will be performed taken in order to obtain material for organoid cultures. Ample experience exists with performing biopsies in patients with (metastatic) anal cancer and the procedure is considered to be safe. Alongside the tumor biopsies, during the study 4 times blood will be drawn (20ml in total per time-slot). Patients will be treated according to standard of care and clinical management of patients will be performed according to daily practice in participating institutions.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Patients with anal SCC who will start treatment with chemoradiotherapy, including:
Mitomycin C + Capecitabine + radiotherapy; or patients with metastatic anal SCC who will start treatment with either chemotherapy (e.g. carboplatin/paclitaxel) or immunotherapy.
2. Patient*s age older than 18 years, willing and able to comply with the protocol as judged by the investigator with a signed informed consent.

Exclusion criteria

1. Safely obtain biopsy: If a biopsy cannot be safely obtained as determined by either the surgeon or the radiologist and/or the treating physician, the patient will be excluded from the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-09-2024
Enrollment:	60
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	11-07-2024
Application type:	First submission
Review commission:	METC NedMec

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
CCMO	NL86168.041.24