Integration of Whole-Genome Sequencing profiles and Immune Status in cancer - a molecular profiling protocol to broaden the view on drug targets and immune contexture in patients with melanoma and pancreatic cancer

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To analyse the relation between oncogenic signaling and the tumour immune contexture in patients with advanced melanoma and pancreatic cancer with resistance to (immuno)therapy, aiming to identify targets and approaches for future (combination)...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON53449

Source
ToetsingOnline

Brief title
SONATA

Condition

- Other condition
- Skin neoplasms malignant and unspecified

Synonym
malignant melanoma, PDAC, skin cancer; pancreatic (ductal) adenocarcinoma

Health condition

maligne neoplasmata pancreas

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: CCA Grant;Cancer Center Amsterdam (CCA 2020-1-30)

Intervention

Keyword: immunotherapy, melanoma, pancreatic cancer, whole-genome sequencing

Outcome measures

Primary outcome

The primary endpoint of this study is the number of patients for whom both

tumour WGS and immune profiles could be adequately obtained.

The co-primary endpoint is the frequency of *inflamed* vs *immune

excluded/desert* tumours (based on tumour infiltrating immune cells) in

patients with

o NRAS/KRAS mutant vs wild-type tumours

o High vs low mutational tumour load

Secondary outcome

Secondary endpoints of this study are:

• The percentage of patients with evaluable tumour DNA, RNA and (tissue and

peripheral) immune profiles

• The frequency of (potentially) actionable genomic alterations, including but

not limited to HER2 amplification and mutation, HRD signature, Microsatellite

instability, gene fusions

• The relation between tumour and peripheral immune profiles

• The percentage of patients with melanoma with evaluable (phospho)proteomic

profiles

• A database of all (coded) data and biobank of all (remaining) tissues and

PBMCs obtained in this study.

Study description

Background summary

The introduction of immune checkpoint inhibitors (ICI) as anticancer therapy have marked a therapeutic renaissance for patients with advanced melanoma and several other types of cancer. Still, not all patients benefit (long term) from current ICI-based cancer immunotherapy and, sometimes severe, immune related adverse events (irAE) occur frequently. Acquired and intrinsic resistance to immune checkpoint blockade is a major problem. Its underlying mechanisms are complex and incompletely understood. Genetic aberrations inherent to cancer development may directly or indirectly contribute to ICI resistance.
Tumour profiling based on whole-genome sequencing (WGS) may identify these aberrations, which sometimes represent molecular targets for which approved targeted therapies are available. Besides on tumour mutational load, WGS may potentially inform immunotherapy response or resistance as certain oncogenic driver mutations, e.g. KRAS, are linked to immune suppressive mechanisms that shape the tumour immune microenvironment and immune response.
Linking WGS profiles with immune status may thus widen the scope of therapeutic targets to include specific immunotherapy options besides, or in support of, immune checkpoint blockade. It is of interest to explore this option and obtain proof of concept in an immunogenic vs. poorly immunogenic tumour type, more specifically in melanoma vs pancreatic cancer. In the latter tumour type (chemo)resistance is probably related to low mutation levels resulting in lack of tumour lymphocyte infiltration and a tumour microenvironment (TME) with an abundance of non-cancer cell components.

Study objective

To analyse the relation between oncogenic signaling and the tumour immune contexture in patients with advanced melanoma and pancreatic cancer with resistance to (immuno)therapy, aiming to identify targets and approaches for

future (combination) treatment.

Study design

Investigator-initiated observational tumor profiling study with a one-time invasive procedure (biopsy protocol);
Patients undergo tumor biopsy and venipuncture once.

Study burden and risks

Patients will undergo a extra tumour biopsy once during a tumour biopsy procedure done performed as part of standard treatment of which in our opinion the possible benefits - tumour WGS profiling to obtain information on potential therapeutic targets and potential access to off-label molecular targeted treatment - outweigh the potential risk for individual patients. The procedure will encompass biopsy of a safely accessible metastatic lesion and will be performed according to routine (diagnostic) procedures. Generally, these biopsies will require CT- or ultrasound (US) guidance. Although frequently uncomfortable, tumour biopsy is generally safe and well tolerated with standard precautionary (including local anaesthetics) measures. For US-guided liver biopsies, there is a very small chance of bleeding. CT-guided lung biopsies bear the risk of (a small) pneumothorax which generally does not require intervention. As a whole, this protocol may significantly contribute to improved understanding of ICI resistance and the relation between the (oncogenic) signalling and immune context in patients with ICI resistant tumours.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Diagnosis of locally advanced or metastatic cutaneous/mucosal melanoma or pancreatic cancer, meeting the following characteristics:
a. Melanoma
i. Patients with histologically proven locally advanced or metastatic melanoma (stage IV), with intrinsic or acquired resistance to treatment with immune checkpoint inhibition (anti-PD1 antibody +/- ipilimumab)
ii. Patients with locoregional or distant recurrence either during, or within 3 months after completion or discontinuation of (neo)adjuvant anti-PD1-based immunotherapy for stage III melanoma.
b. Pancreatic cancer
i. Patients with histologically proven metastatic pancreatic cancer with progression under or after standard first-line chemotherapy (FOLFIRINOX or gemcitabine/nab-paclitaxel).
2. Patients must be willing and able to provide written informed consent and be willing and able to comply with the study protocol.
3. Patients must be >=18 years of age.
4. Metastatic or locoregional lesion of which a tumour needle biopsy can be safely obtained according to routine clinical practice.

Exclusion criteria

Patients with metastatic or locally advanced lesions which are not considered to be technically and/or safely biopsied

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):	31-07-2023
Enrollment:	180
Type:	Actual

Ethics review

Approved WMO

Date:	28-04-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL82542.029.22