Immunological and molecular effects of MR-guided stereotactic radiotherapy in adrenal metastases - A hypothesis generating trial (IM-SABR)

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Objectives: The immunogenic effects of adrenal SMART schemes may vary even though the local tumor control rates are high. Our objective is to study the dose-related immunological signals accompanying the delivery of SMART to adrenal metastases using...

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

Summary

ID

NL-OMON51261

Source
ToetsingOnline

Brief title
IM-SABR

Condition

- Metastases

Synonym
adrenal metastases

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: beursaanvraag ,beursaanvraag Viewray is ingediend

Intervention

Keyword: adrenal, immunology, radiotherapy, SABR

Outcome measures

Primary outcome

Main study parameters/endpoints: This hypothesis generating study aims to characterize the immunological effects of different well-tolerated risk-adapted SMART schedules. The primary study endpoints will be the immune responses in the peripheral blood. The endpoints will be assessed by examination liquid biopsies and FACS analysis on peripheral blood to detect immune modulation.

Secondary outcome

Secondary endpoints will be local tumor control rates and correlation of measured immune parameters with PTV coverage and rates of tumor regression.

Study description

Background summary

Rationale: A meta-analysis revealed that the local control rates with SABR make it a good alternative to surgery for adrenal metastases (Chen et al., IJROBP 2020). Ablative SABR doses were not uniformly used due to concerns about toxicity. An explanation for the favorable outcomes with SABR may be a radiation-induced immunological response against tumor cells, which can enhance systemic immune responses. However, this so-called abscopal response appears to be dose/schedule dependent. SMART was introduced at our center in 2016, allowing for a safe delivery of high dose SABR. SMART is now the most frequently used local modality for adrenal metastases at our center [van Vliet C, ESTRO submission]. We propose an exploratory study of MR-guided SABR in patients with adrenal metastases to evaluate: 1) the immune responses induced by different SABR schemes used to treat adrenal metastases and 2) SABR schemes that may be preferred for use in trials of oligometastastic disease. We believe

this information will provide a basis for future study designs in which the immunological response resulting from a certain fractionation schedule of SABR could be leveraged to improve outcome further, e.g. by combination therapy of radiotherapy and immunotherapy.

Study objective

Objectives: The immunogenic effects of adrenal SMART schemes may vary even though the local tumor control rates are high. Our objective is to study the dose-related immunological signals accompanying the delivery of SMART to adrenal metastases using standard SABR schedules. Specifically, we will explore the pre- during- and post- SABR immune status in blood using FACS analyses, NanoString PlexSet* analyses of IFN type-I related response genes in peripheral blood mononuclear cells (PBMC) and Tumor Educated Platelet (TEP) analyses

Study design

Study design: Single-arm, non-randomized, exploratory trial evaluating immunological and molecular effects of SABR for adrenal metastases

Study burden and risks

Burden and risks are limited, since we ask only for peripheral blood samples 3-4 times during this trial.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081 HV
NL

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. Have adrenal metastases, for which MR-guided SABR has been recommended following dis-cussions within a multi-disciplinary tumor board.
2. Be willing and able to provide written informed consent for the trial.
3. Be 18 years of age on day of signing informed consent.

Exclusion criteria

1. Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 30 days prior to the MR-guided SABR.
2. Has had prior chemotherapy, targeted small molecule therapy, or radiotherapy within 30 days prior to MR-guided SABR.
3. Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy.
4. Has an active autoimmune disease requiring systemic treatment within the past 3 months or a syndrome that requires systemic steroids or immunosuppressive agents. Subjects that require intermittent use of bronchodilators or local steroid injections would not be excluded from the study. Subjects with hypothyroidism stable on hormone replacement will not be excluded from the study.
5. Has an active infection requiring systemic therapy.
6. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject*s participation for the full du-ration of the trial, or is not in the best interest of the subject to participate, in the opinion of the treating investigator.
7. Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2

antibodies) or a known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative] is detected).

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):	04-04-2022
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	24-01-2022
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	NL77647.029.21