Myeloid cell reprogramming in the context of radioiodine therapy in patients with non-medullary thyroid carcinoma

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Primary Objective: To assess the transcriptional, epigenetic and functional reprogramming of TAMs, circulating monocytes and BM myeloid progenitors cells in active and advanced metastatic TC and to assess the effect of RAI treatment on the…

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

Summary

ID

NL-OMON48852

Source
ToetsingOnline

Brief title
Myeloid cell reprogramming in thyroid carcinoma

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
thyroid carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: KWF

Intervention

Keyword: myeloid cell, Non-medullary thyroid carcinoma, radioactive iodide, reprogramming

Outcome measures

Primary outcome

Transcriptional and epigenetic signature and function of TAMs, BM myeloid

progenitors and circulating macrophages before and after treatment.

Secondary outcome

Presence of circulating tumor cells (CTC) and changes in circulating

metabolites (either tumor-derived or tumor-induced) concentrations

(metabolomics) associated with the functional reprograming of the immune cells.

Study description

Background summary

Non-medullary thyroid carcinoma (TC) is the most common endocrine malignancy and its incidence is one of the most rapidly increasing among the cancer types. For many patients with advanced and poorly differentiated tumors, treatment options are limited and the prognosis of advanced stage metastatic disease remains poor.
To improve the patients outcome and identify novel therapeutic targets, one needs a *systems understanding* of the pathophysiology of tumors, particularly the complex interaction of the malignant cells with other cell types in the tumor en the tumor environment (TME), especially immune cells. Tumor-associated macrophages (TAMs), the most dominant myeloid population in aggressive thyroid tumors, exhibit a distorted phenotype functioning predominantly as tumor enhancer. Despite the progress in understanding the importance of TAMs, the in-depth characterization of different TAMs populations is lacking and the mechanisms governing the functional polarization of TAMs are largely unknown. Understanding the interplay between TAMs and tumor cells represents a crucial step towards development of additional therapeutic strategies in cancer.

Hypothesis:

1. We first propose that in advanced TC, not only TAMs, but also circulating monocytes and bone marrow (BM) myeloid progenitors are functionally reprogrammed by tumor-derived metabolites even before their recruitment in the TME.
2. Radioactive iodide (I131)(RAI) is a very effective therapy for patients with TC, but is less effective in patients with advanced, metastatic tumors. We hypothesize that by exposing tumor antigens to the immune system, RAI might induce immunogenic effects at the level of the TME with reprogramming of both TAMs present in the TME and circulating monocytes, towards a tumor suppressive phenotype. This may further potentiate the effects of RAI. In addition this could be explored in the future as a basis for immunotherapy for tumors that are refractory to conventional treatment.

Study objective

Primary Objective:
To assess the transcriptional, epigenetic and functional reprogramming of TAMs, circulating monocytes and BM myeloid progenitors cells in active and advanced metastatic TC and to assess the effect of RAI treatment on the reprogramming of circulating monocytes.

Secondary Objectives:
To investigate whether the presence of circulating tumor cells (CTC) and changes in circulating metabolites (either tumor-derived or tumor-induced) concentrations (metabolomics) are associated with the functional reprograming of the immune cells.

Study design

investigator initiated, single-center explorative cross-sectional study at the Radboudumc Nijmegen

Study burden and risks

There are no risks associated with the study. There are no interventions other than those related to the regular patient care except for a BM aspiration that will take place during surgery. The burden for the patients will be maintained to a minimum. They will only be required to donate a limited number of blood samples (2-4 times for the patients and once for the healthy volunteers) and small samples of their removed thyroid tissue in case of surgery. To minimize the discomfort, BM samples will be collected during the same surgery under general anesthesia. For the same reason we have chosen not to collect BM from our healthy controls.

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

Group 1:
-newly diagnosed patients with TC that are therapy naïve and are planned to receive conventional treatment by surgery followed by RAI.
-no evidence of local or distant metastases
Group 2:
-patients with TC with evidence of distant metastases (either newly diagnosed patients who are therapy naïve or patients with persistent or recurrent disease) and are planned to receive conventional treatment by surgery followed by RAI.
-at least 4 months since the previous treatment with RAI (in the patients who have had this treatment in the past)
Group 3:

-patients with MNG in which the decision has been taken to undergo surgery because of obstructive symptoms or for cosmetic reasons
Group 4:
-patients with MNG in which the decision has been taken to undergo RAI because of obstructive symptoms.
Group 5:
-healthy individuals without evidence of thyroid disease.

Exclusion criteria

Excluded from participation in this study will be subjects who are/have:
Mentally incompetent;
Pregnant or breastfeeding;
Known inflammatory or infectious diseases or an immunosuppressive status;
Using medication interfering with the immune system;
Reduced platelets counts or other conditions associated with an increased risk of bleeding.
Severe comorbidities: other active malignancy (except for basal cell carcinoma), serious psychiatric pathology;
A self-reported alcohol consumption of >21 units per week.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-03-2018
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	18-10-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-01-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-06-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL62671.091.17