Trained immunity of myeloid cells and their progenitors in patients with non-medullary thyroid carcinoma, colon carcinoma and melanoma

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To assess the transcriptional, epigenetic and functional reprogramming of circulating monocytes and BM myeloid progenitor cells in TC, CC and melanoma before and after in vitro exposure to agents that induce trained immunity.

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

Summary

ID

NL-OMON53801

Source
ToetsingOnline

Brief title
Trained immunity in thyroid carcinoma, colon carcinoma and melanoma

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
colon carcinioma, thyroid carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Interne Geneeskunde

Source(s) of monetary or material Support: NWO

Intervention

Keyword: bone marrow, colon carcinoma, myeloid cell, thyroid carcinoma, trained immunity

Outcome measures

Primary outcome

Transcriptional, epigenetic and functional signature of circulating monocytes

and BM myeloid progenitors before and after in vitro exposure to trained

immunity inducing agents.

Secondary outcome

not applicable

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. Also the incidence of colon carcinoma (CC) has been increasing in the past decades. In 2020 more than 8400 were diagnosed with CC in the Netherlands. Although survival has improved in the last years, in 2011-2018 the 5-year survival rate was still only 67%. Likewise, the incidence of melanoma has significantly increased in the last decades. In 2021, more than 7500 patients were diagnosed with melanoma in the Netherlands. Survival is excellent in patients with localized disease, but poor for patients who develop distant metastases. In those patients, 5-year survival is only 30% in patients with stage IV disease.
Tumor-related inflammation is one of the hallmarks of cancers in general. Innate immunity specifically is a common denominator which is involved in the pathogenesis of both TC and CC. In a previous study (NL62671.091.17), changes in the programming of myeloid immune cells and a possible role of their bone marrow progenitors were identified in TC patients. To improve the patient*s outcome and identify novel therapeutic targets, one needs a deeper understanding of the tumor-induced changes in the bone marrow myeloid

progenitor cells. Furthermore, treatment of these cells by nanoparticles or other agents that induce a program of *trained immunity* may be a novel way to re-educate myeloid cells and their bone marrow progenitors in TC patients. Lastly, we expect that this approach could be effective also in other cancers of which CC and melanoma are here proposed as an additional model.
Hypothesis:
We hypothesize that by exposing myeloid cells or their progenitors to various agents that induce trained immunity (e.g. HDL-MDP nanoparticles, recombinant and synthetic cytokines), these immune cells will undergo functional reprogramming to induce a tumor-suppressive phenotype. In the future, this could be explored as a novel immunotherapy for tumors that are refractory to conventional treatment.

Study objective

To assess the transcriptional, epigenetic and functional reprogramming of circulating monocytes and BM myeloid progenitor cells in TC, CC and melanoma before and after in vitro exposure to agents that induce trained immunity.

Study design

investigator-initiated, single-center cross-sectional explorative study which will be performed in the Radboud UMC 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 bone marrow 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 one blood sample and a small sample of their during surgery removed tissue. ïo minimize the discomfort, the bone marrow sample will be collected during the same surgery under general anesthesia.

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

-Subjects should be at least 18 years old and mentally competent

-Newly diagnosed patients with TC, CC or melanoma or with newly diagnosed metastases and that are planned to receive conventional treatment by surgery

Exclusion criteria

-Mentally incompetent
-Pregnant or breastfeeding
-Using medication interfering with the immune system
-Reduced platelets counts or other conditions associated with an increased risk of bleeding
- Severe comorbidities; other active malignancies (except for basalcel carcinoma)
- Surgery of the primary tumor in the previous 4 months.
-Serious psychiatric pathology
-A self-reported alcohol consumption of >21 units per week

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):	19-09-2022
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	26-01-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-01-2023
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	NL79885.091.21