Costimulatory and -inhibitory molecules on tumor-infiltrating lymphocytes from colorectal carcinoma and its metastases

Published: 16-01-2017
Last updated: 14-04-2024

To determine which costimulatory and co-inhibitory molecules are expressed on tumor-infiltrating lymphocytes (TIL) derived from patients with CRC (including metastasized CRC), and to study the effects of targeting these molecules on their function…

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

Summary

ID

NL-OMON43140

Source
ToetsingOnline

Brief title
Costimulatory and -inhibitory molecules in CRC

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
bowel cancer, colorectal carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Leveronderzoek
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: co-inhibitory molecules, colorectal carcinoma, costimulatory molecules, T cell

Outcome measures

Primary outcome

The main study parameters are:

1) Frequencies and absolute numbers of different lymphocyte populations that together compose the tumor-infiltrating lymphocyte pool

2) Expression of costimulatory and co-inhibitory molecules on TIL versus lymphocytes isolated from tumor-free tissue versus circulating lymphocytes

3) Effect of blocking co-inhibitory molecules or stimulating costimulatory molecules expressed by TIL on their function (proliferation and cytokine production) in ex vivo culture experiments

Secondary outcome

Depending on the co-inhibitory molecules detected on TIL, immunohistochemistry will be performed on residual formalin-fixed paraffin-embedded tumor tissue that is regularly stored to identify the expression of the ligands of these co-inhibitory molecules (e.g. PDL-1+2, GAL-9) on tumor (infiltrating) cells. If possible, lymph node (when part of excision preparation) will be analyzed.

Study description

Background summary

Colorectal carcinoma (CRC) is the most common malignancy, and is a cause of substantial morbidity and mortality. Curative treatment is possible, but strongly depends on the stage of the disease. Surgical resection, possibly supported by chemotherapy, is applied when the disease is contained in colon

or rectum (stage I, II) or has metastasized to the lymph nodes (stage III). When the tumor has metastasized to other tissues (mostly lung or liver; stage IV), chemotherapy and monoclonal antibodies are applied, sometimes combined with surgical resection. Treatment of metastasized disease has only limited life-extending effect, with less than 5% five year survival of patients. Immunotherapy represents an attractive alternative treatment option, because it is highly specific and can induce long-lasting immunological memory that may permanently prevent tumor recurrence. It is our ultimate goal to design effective immunotherapy for CRC patients. In the present study we aim to identify targets for immunotherapy by focusing on the tumor-infiltrating lymphocytes.
We hypothesize that costimulatory or co-inhibitory molecules on the surface of lymphocytes can be targeted to affect lymphocyte function as an immunotherapeutic strategy to combat CRC.

Study objective

To determine which costimulatory and co-inhibitory molecules are expressed on tumor-infiltrating lymphocytes (TIL) derived from patients with CRC (including metastasized CRC), and to study the effects of targeting these molecules on their function in ex vivo assays.

Study design

Cohort study in CRC patients in our centers that are undergoing resection of CRC or other tissue to which CRC has metastasized. Tumor-infiltrating lymphocytes will be isolated from residual tumor tissue and adjacent tumor-free tissue not needed for histological evaluation (*restmateriaal*). Their phenotype will be evaluated by flow cytometry and their function, including effects of targeting costimulatory and co-inhibitory surface molecules, in cell culture experiments. Blood is needed for comparison and to provide sufficient antigen presenting cells for in vitro T cell assays. In addition, leukocytes and plasma will be stored in a biobank for future studies.

Study burden and risks

Intervention: invasive measurement of 80 mL of blood collected during surgery. No benefit and negligible risk for the patients. Blood is taking once during surgery and so no additional intervention is needed. Hopefully, the results of the study will benefit CRC patients in the near future.

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

Adult colorectal carcinoma (CRC) patients that will undergo surgery for CRC or its metastases

Exclusion criteria

Patients who refuse blood donation/participation in the study
Patients with a severe immunocompromised condition, or patients taking immunosuppressive medication

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-04-2017
Enrollment:	677
Type:	Actual

Ethics review

Approved WMO

Date:	16-01-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL58534.078.16