Costimulatory and co-inhibitory molecules on tumor-infiltrating lymphocytes from hepatocellular carcinoma and cholangiocarcinoma

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

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

Summary

ID

NL-OMON53120

Source
ToetsingOnline

Brief title
Costimulatory and co-inhibitory molecules in HCC and CCA

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
hepatocellular carcinoma, liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Stichting Leveronderzoek

Intervention

Keyword: cholangiocarcinoma, co-inhibitory molecules, costimulatory molecules, hepatocellular carcinoma

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.

Study description

Background summary

Liver cancer is the second most common cause of cancer-related mortality worldwide. The most prevalent primary liver cancer is hepatocellular carcinoma (HCC), followed by cholangiocarcinoma (CCA). The current treatment options for

HCC and CCA are only curative for patients with early disease. Unfortunately, the majority of HCC and CCA patients are not eligible for curative procedures because of late diagnosis and thus have poor prognosis.
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 HCC and CCA 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 (a.o. T cell) as an immunotherapeutic strategy to combat HCC and CCA.

Study objective

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

Study design

Cohort study in HCC or CCA patients in our centers that are undergoing resection. 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 HCC and CCA patients in the near future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Adult hepatocellular carcinoma (HCC) or cholangiocarcinoma (CCA) patients that will undergo surgery for this disease

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):	03-01-2018
Enrollment:	272
Type:	Actual

Ethics review

Approved WMO Date:	27-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2022
Application type:	Amendment
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	NL58958.018.17