# Co-stimulatory and -inhibitory molecules on tumor-infiltrating lymphocytes from cholangiocarcinoma

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

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

## Summary

### ID

NL-OMON43309

**Source**
ToetsingOnline

**Brief title**
Co-stimulatory and -inhibitory molecules in CCA

### Condition

- Hepatobiliary neoplasms malignant and unspecified

**Synonym**
bile duct cancer, cholangiocarcinoma

**Research involving**
Human

### Sponsors and support

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

## Intervention

**Keyword:** cholangiocarcinoma, co-inhibitory molecules, T cell

## Outcome measures

### Primary outcome

The main study parameters are:

1) Frequencies and absolute cell counts of different lymphocyte populations

that together compose the tumor-infiltrating lymphocyte pool.

2) Expression of co-stimulatory/co-inhibitory molecules on TIL vs lymphocytes

isolated from tumor-free liver tissue vs circulating lymphocytes

3) Effect of blocking co-inhibitory molecules or stimulating co-stimulatory

molecules expressed by TIL on their function (proliferation and cytokine

production) in ex vivo co-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 (for instance PDL1+2 and GAL9) on tumor (infiltrating)

cells.

# Study description

### Background summary

Rationale: Cholangiocarcinoma (CCA) is the most common primary malignancy of the biliary tract, and is a cause of substantial morbidity and mortality. Complete surgical resection is potentially curative, but it can only be achieved in the 10% of patients who present with localized disease without

vascular invasion. Patients with locally advanced, metastatic, or recurrent disease are typically offered chemotherapy and have a dismal 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 CCA patients. In the present study we aim to identify targets for immunotherapy by focussing on the tumor-infiltrating lymphocytes.
We hypothesise that co-stimulatory or -inhibitory molecules on the surface of T cells can be targeted to affect T cell function as an immunotherapeutic strategy to combat CCA.

### Study objective

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

### Study design

Study design: Cohort study in CCA-patients that are undergoing CCA resection in our center. Tumor-infiltrating lymphocytes will be isolated from residual tumor tissue and adjacent tumor-free liver tissue not needed for histological evaluation (*rest materiaal*). Their phenotype will be evaluated by flow-cytometry and their function, including effects of targeting co-stimulatory and *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 frozen in a bio-bank for future studies.

### Study burden and risks

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

## Contacts

**Public**
Stichting Leveronderzoek

s Gravendijkwal 230 Room HA-212

Rotterdam 3015CE
NL
**Scientific**
Stichting Leveronderzoek

s Gravendijkwal 230 Room HA-212
Rotterdam 3015CE
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Adult 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)

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| Control: | Uncontrolled |
| Primary purpose: | Other |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 01-09-2016 |
| Enrollment: | 102 |
| Type: | Actual |

## Ethics review

Approved WMO

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|---|---|
| Date: | 15-08-2016 |
| 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 | NL57895.078.16 |