

# Study of expression of and immunity against neoantigens in patients with constitutional mismatch repair deficiency (CMMR-D) syndrome

Published: 20-07-2020

Last updated: 27-04-2024

In this explorative study, we aim to: • Analyze neoantigens expressed on different tumors of CMMR-D patients, to identify possible target antigens for DC vaccination studies. • Investigate the presence of pre-existing immune responses against...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Congenital and hereditary disorders NEC
<b>Study type</b>	Observational invasive

## Summary

### ID

NL-OMON49277

### Source

ToetsingOnline

### Brief title

Immunity against neoantigens in CMMR-D

### Condition

- Congenital and hereditary disorders NEC
- Miscellaneous and site unspecified neoplasms malignant and unspecified

### Synonym

bi-allelic Lynch syndrome, Biallelic MisMatch Repair Deficiency (BMMRD)

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Radboud Universitair Medisch Centrum

**Source(s) of monetary or material Support:** KiKa

## Intervention

**Keyword:** CMMR-D, immunity, neoantigens

## Outcome measures

### Primary outcome

The primary endpoints of the study are the identification of neoantigens on different tumors of CMMR-D patients and the detection of pre-existing immune responses against neoantigens

### Secondary outcome

n.a.

## Study description

### Background summary

CMMRD

In 1999, a recessive paediatric tumor predisposition syndrome called Constitutional Mismatch Repair Deficiency (CMMR-D) syndrome was recognized. CMMR-D syndrome is caused by homozygous or compound heterozygous germline mutations in one of the DNA mismatch repair (MMR) genes. Mainly three types of malignancy characterize this syndrome: gastrointestinal tract cancer, haematological malignancies and brain tumors, which occur in childhood or adolescence. If patients survive the first malignancy, they have a high chance of developing a second or even a third malignancy. To date, patients with CMMR-D are intensively screened but this does not guarantee the detection of precancerous lesions or cancer at a curable stage. A preventive treatment modality would therefore be a major step forward.

Due to germline mutations in MMR genes coding for proteins involved in repair of nucleotide mismatches, truncated proteins with impaired function are formed. These aberrant proteins can be recognized by the immune system and they might

be excellent targets for immunotherapy since only tumor cells express them.

### DC vaccination

Dendritic cells (DCs) play a central role in the induction of immune responses. During an infection, DCs become activated and migrate to the lymph nodes where they stimulate specific killer T cells. Their decisive role in inducing immunity formed the rationale for DC immunotherapy: DCs loaded with tumor antigens are injected into cancer patients to stimulate T cells to eradicate tumors. In experimental clinical studies, DC vaccination has led to effective anti-tumor immune responses and increased survival in patients with melanoma. In healthy Lynch syndrome carriers, who have only a mono-allelic mutation in their DNA mismatch repair system, DC vaccination has led to induction of neoantigen-specific T cells, without inducing serious side effects.

### DC vaccination of CMMRD

In this study we want to develop a preventive treatment for children with CMMRD. We aim to induce immune responses against neoantigens with DC vaccines, to prevent the formation of new lesions. For this, we need more knowledge of the presence of neoantigens and immune responses in tumors of CMMRD patients. In this explorative study, we will make an inventory of neoantigens expressed by different tumors of patients with CMMRD syndrome, to select/identify possible target antigens for DC vaccination studies. In addition, we will investigate the presence and specificity of pre-existing immune responses against neoantigens in blood of CMMR-D patients. The results of this study will be translated into the development of a preventive DC vaccine for children with CMMRD in a follow-up study.

## Study objective

In this explorative study, we aim to:

- Analyze neoantigens expressed on different tumors of CMMR-D patients, to identify possible target antigens for DC vaccination studies.
- Investigate the presence of pre-existing immune responses against neoantigens in CMMR-D carriers.

## Study design

This study is a single arm exploratory, multi-centre study

## Study burden and risks

There are no additional risks to participation in this study other than that of regular blood collection. The burden for the participants is minimal, as blood collection for the study will take place during regular blood collection.

## Contacts

### Public

Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 28

Nijmegen 6525GA

NL

### Scientific

Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 28

Nijmegen 6525GA

NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adolescents (12-15 years)

Adolescents (16-17 years)

Adults (18-64 years)

Children (2-11 years)

Elderly (65 years and older)

### Inclusion criteria

- Patients with genetically proven Constitutional Mismatch Repair Deficiency (CMMRD)
- Signed informed consent

### Exclusion criteria

- Any form of comorbidity interfering with safe collection of blood

- Having objectives against coded storage of tissue

## Study design

### Design

**Study type:** Observational invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Treatment

### Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 11-03-2021

Enrollment: 10

Type: Actual

## Ethics review

Approved WMO

Date: 20-07-2020

Application type: First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date: 23-02-2021

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	NL73648.091.20

## Study results

Date completed:	17-04-2023
Actual enrolment:	10

### Summary results

Trial is ongoing in other countries