# Dynamics of clonal hematopoiesis in pediatric stem cell transplantation recipients

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Haematological disorders NEC |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON57200

**Source**
ToetsingOnline

**Brief title**
Dynamics of clonal hematopoiesis after stem cell transplantation (DYNA-HIT)

### Condition

- Haematological disorders NEC
- Immune disorders NEC

**Synonym**
bone marrow transplantation, Clonal hematopoiesis

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Prinses Máxima Centrum voor Kinderoncologie
**Source(s) of monetary or material Support:** ZonMW Open Competitie; 09120232310091

## Intervention

**Keyword:** Bone marrow transplantation, Clonal hematopoiesis, Follow-up, Hematopoietic stem cell transplantation

## Outcome measures

### Primary outcome

The primary aim of this study is to determine the growth trajectories of

post-transplant clonal hematopoiesis, expressed as the changes in variant alele

frequencies, and depicted graphically as trajectories over time.

### Secondary outcome

We also aim to identify factors that may influence the chance of

post-transplant CH. To achieve this, we will compare clinical and clone-related

factors between HCT recipients with and without CH, one year after HCT.

Finally, using various laboratory technologies, we will investigate the

molecular processes that stimulate or inhibit the growth of CH clones.

# Study description

### Background summary

Hematopoietic cell transplantation (HCT) is a last-resort, potentially curative treatment for patients with from various, otherwise lethal diseases. As treatment strategies improve, the number of HCT survivors and their life expectancy continue to increase, We have recently shown that pediatric long-term HCT survivors are at increased risk of clonal hematopoiesis (CH) compared to age-matched controls. CH is an age-related disorder which, in the general population, is associated with an increased risk of hematologic and cardiovascular diseases, and a decreased risk of Alzheimer's disease.

It is yet unkonwn why hematopoietic cell transplanttaion leads to a higher incidence of CH. In addition, we don't know whether CH afte transplantation and CH in the general population have the same health consequences. Insight into clonal growth trajectories after HCT may identify critical periods during which

mutant stem cells preferentially expand, to identify potential modulating factors and to better predict the risk of future malignant transformation.

### Study objective

We aim to define the growth trajectory of clonal hematopoësis after allogeneic transplantation, and identify potential modulating factors.

### Study design

This is an observational, prospective, explorative study in children and adolescents/young adults undergoing allogeneic hematopoietic cell transplantation in the Princess Máxima Center. Study participants will donate one or multiple extra blood tubes, at various time points from before to long after HCT. Study blood sampling will be combined with planned blood collections for clinical care.

Clonal hematopoiesis will be assessed using a targeted sequencing panel of 38 CH driver mutations. The presence or absence of CH, and the size of the observed clones, will be studied over time and related to clinical factors (e.g., stem cell source). In addition, using various molecular technologies, we will study the fundamental mechanisms influencing the growth patterns of post-transplant CH.

### Study burden and risks

This study requires pediatric and young adult recipients, as their post-transplant survival exceeds that of older adult HCT recipients by several decades, posing unique challenges on the integrity and longevity of the engrafted HSCs. In addition, as clinical HCT regimens differ between children and adults (e.g. composition of the cell product, use of irradiation, chemotherapy dose), results obtained in adult HCT recipients cannot be translated directly to children.

This study will provide unique insights into the dynamics of clonal hematopoiesis after transpantation, while posing minimal risks to the participants. Results from this study may contribute to the development of therapeutic strategies to influence the growth of CH clones, after transplantation as well as in the general population.

## Contacts

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# 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)
Babies and toddlers (28 days-23 months)

## Inclusion criteria

Planned for first allogeneic HCT in the Princess Máxima Center.

## Exclusion criteria

- Failure of the HCT recipient and/or their legal representative to understand the patient information and informed consent form (either because of intellectual disability or language barriers).
- Recipients of pharma-sponsored, genetically modified cell products (e.g., Bluebird Bio)

# Study design

## Design

**Study type:** Observational invasive

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Basic science |

## Recruitment

NL

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|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-01-2025 |
| Enrollment: | 150 |
| Type: | Anticipated |

## Medical products/devices used

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|---|---|
| Registration: | No |

# Ethics review

Approved WMO

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|---|---|
| Date: | 24-12-2024 |
| Application type: | First submission |
| Review commission: | METC NedMec |

# 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 | NL87692.041.24 |