# feasibility of immunotherapy in children with high-risk neuroblastoma

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Plasma cell neoplasms |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON33301

**Source**
ToetsingOnline

**Brief title**
Immunotherapy in children with HR NBL

### Condition

- Plasma cell neoplasms

**Synonym**
immunotherapy

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** KIKA

## Intervention

**Keyword:** BM, immuuntherapy, neuroblastoma, NK cells

## Outcome measures

### Primary outcome

If the BM sample is infiltrated by NBL cells, the expression of activating NK cell receptor ligands on the tumor itself; such as MIC (MICA/B) and ULBP (ULBP1-4) proteins and CD112/ -CD155 as well as the expression of HLA class I (inhibitory ligand), CD54/ -CD58 (adhesion) will be evaluated by FACS analysis using multiple markers.

NK cell sensitivity will be determined by labelling primary NBL cells with 51-Chromium or by chemo luminescent methods and adding resting and cytokine activated NK cells. Furthermore, if NK cell cytotoxicity occurs, activating NK cell receptors will be blocked by monoclonal antibodies (NKG2D, DNAM-1), thereby allowing analysis of the activating signals involved.

Peripheral blood samples of newly diagnosed, untreated NBL patients will allow analysis of NK cell phenotype and function in these patients at time of diagnosis.

### Secondary outcome

N/A

# Study description

### Background summary

The defining characteristics of high risk (HR) NBL include an age of more than one year, with regional or metastatic disease, unfavourable Shimada histology

or Myc-N amplification (NMA). Patients with HR NBL have a 5-year survival rate of only 30-40%, even if there is a favourable response to initial therapy.
For the majority of patients with relapsed refractory solid tumors, there are currently no further treatment options other than phase I/ II studies or palliation. Therefore, we aim to explore the feasibility of adoptive immunotherapy (AIT) as an additional treatment modality for this tumor, with a focus on natural killer (NK) cells.

### Study objective

In this research proposal, we aim to investigate the feasibility of NK cell immunotherapy by evaluating the expression of activating and inhibitory NK cell receptor ligands on primary tumor cells. Furthermore, we aim to evaluate the cytotoxic potential of unstimulated and cytokine stimulated NK cells towards primary NBL tumor cells.
Cytotoxic activity of NK cells towards NBL cells in vitro and additional stimulation methods (cytokines, irradiation, tumor manipulation) would further substantiate a role for NK cell AIT of high risk NBL. This will encourage the development of novel AIT strategies as an additional treatment for high risk or relapsed NBL next to conventional or other novel therapies.

### Study design

Prospective analysis, in newly diagnosed high risk neuroblastoma patients, of bone marrow (BM) samples that are infiltrated with NBL cells and NK cells obtained from blood, in order to perform immunological analysis.

### Study burden and risks

No additional burden, risks, the patients will undergo a bone marrow aspirate and bloods will be taken as a routine procedure in an newly diagnosed patient (once).
In this study additional material will be taken during the same procedure: bonemarrow 3-5 ml and blood 10-20 ml

## 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)
Elderly (65 years and older)

## Inclusion criteria

High risk neuroblastoma, between 1 and 21 years at diagnosis.
Neuroblastoma histological proven diagnosis
informed consent
Initial staging of the tumor
No pregnancy

## Exclusion criteria

Any prior or concomitant non-protocol anticancer treatment

# Study design

## Design

**Study type:** Observational non invasive

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 19-10-2010 |
| Enrollment: | 20 |
| Type: | Actual |

# Ethics review

Approved WMO

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| Application type: | First submission |
| 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 | NL28524.018.09 |