

# Modulating regulatory T cell function in Juvenile Idiopathic Arthritis with Vitamin B3 (nicotinamide): a phase I/II trial focusing on safety and feasibility aspects in children with JIA.

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NAM, well known as a dietary supplement, has also been extensively studied in humans in a variety of diseases in both children and adults. However, the safety, tolerability of NAM in children with JIA is yet unknown. Furthermore, studies performed...

<b>Ethical review</b>	Not approved
<b>Status</b>	Will not start
<b>Health condition type</b>	Autoimmune disorders
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON45620

### Source

ToetsingOnline

### Brief title

B-Vit in JIA trial

### Condition

- Autoimmune disorders

### Synonym

Juvenile idiopathic arthritis, juvenile rheumatoid arthritis

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Utrecht

**Source(s) of monetary or material Support:** Ministerie van OC&W, Vrienden WKZ en WKZ onderzoeksfonds

## Intervention

**Keyword:** JIA, NAM, Nicotinamide, Vit B 3

## Outcome measures

### Primary outcome

In this phase II trial essential information will be gained on safety, feasibility and tolerability of NAM as an additional treatment in JIA patients.

### Secondary outcome

Additionally, PK/PD data will be obtained which can be used to develop an optimal dosing scheme for a future phase III clinical trial. Next, preliminary data on the effect of NAM on the function of regulatory T cells will be acquired.

## Study description

### Background summary

In Juvenile Idiopathic Arthritis (JIA) there is a distortion in immunological balance between regulatory T cells (Treg) and effector T cells (Teff). Enhancing the suppressive function of regulatory T cells and thereby restoring this balance is therefore a promising novel therapeutic strategy. Current treatment, like DMARDs and biologicals, however focuses primarily on influencing effector T cells. Interestingly, in the past few years it was found that Vitamin B3, also known as nicotinamide (NAM) stabilizes FOXP3 expression via inhibition of the histone deacetylase SIRT1. Through this mechanism it has the potential to beneficially affect this immunological balance by positively influencing regulatory T cell function. In addition to the effect on regulatory T cells, NAM showed to have a down regulating effect on CD4+ and CD8+ cells and could therefore influence both sides of the equation. We envision that NAM

maintenance treatment, when combined with established immunosuppressive treatment, could help restore the immunological balance and hereby contribute to gaining and maintaining remission in JIA patients.

## **Study objective**

NAM, well known as a dietary supplement, has also been extensively studied in humans in a variety of diseases in both children and adults. However, the safety, tolerability of NAM in children with JIA is yet unknown. Furthermore, studies performed on pharmacokinetics of NAM have only been performed in adults. The primary objective of this study is therefore to assess safety, feasibility and tolerability of NAM in the proposed dose in children with JIA.

## **Study design**

An open label, phase II study will be performed.

## **Intervention**

Additional NAM therapy with 1,2g/m<sup>2</sup>/day or 1,8g/m<sup>2</sup>/day in either 2 or 3 doses a day during 3 months.

## **Study burden and risks**

Due to the study design the burden of participation of this study has been minimized by combining clinical visits and blood sampling with routine clinical care. Since JIA is a disease of childhood, this study can only be performed in minors. No serious adverse events are expected since extensive previous experience with use of high dose NAM in clinical trials in both children and adults. Participation could be beneficial, since it is hypothesized that additional NAM treatment could have a favourable effect on the immunological balance in JIA and maintaining remission in these patients.

## **Contacts**

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## **Trial sites**

### **Listed location countries**

Netherlands

## **Eligibility criteria**

### **Age**

Adolescents (12-15 years)

Adolescents (16-17 years)

Children (2-11 years)

### **Inclusion criteria**

- Patients with a diagnosis of oligo-articular or poly-articular JIA with active disease in 1 or multiple joints and an indication for intra-articular corticosteroid injection.
- Age between 4 to 18 years
- At the moment of inclusion, not on non-biological DMARD (Methotrexate) treatment or on stable DMARD treatment (at least 3 months of stable Methotrexate use).

### **Exclusion criteria**

- no informed consent possible by patient/parents or caregivers
- participation in other interventional trials
- Treatment with biological DMARD
- Recently started treatment with non-biological DMARD (Methotrexate). Defined as treatment for a period less than 3 months.
- Use of systemic corticosteroids
- Relevant co morbidity: raised liver enzymes ( $>2\times$  upper limit) and/or evidence of bone marrow failure (pancytopenia based upon full blood count).

## **Study design**

## Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

## Recruitment

NL	
Recruitment status:	Will not start
Enrollment:	45
Type:	Anticipated

## Medical products/devices used

Product type:	Medicine
Brand name:	Nicotinamide
Generic name:	Nicotinamide

## Ethics review

Approved WMO	
Date:	31-08-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved	
Date:	22-12-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

## 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
EudraCT	EUCTR2016-003643-10-NL
CCMO	NL61286.000.17
Other	volgt nog