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.

Published: 31-08-2017
Last updated: 12-04-2024

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...

Ethical review	Not approved
Status	Will not start
Health condition type	Autoimmune disorders
Study type	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 we 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 de proposed dose in children with JIA.

Study design

An open label, phase II study will be performed.

Intervention

Additional NAM therapy with 1,2g/m2/day or 1,8g/m2/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 minimalized 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

Public
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3584EA
NL
Scientific
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3584EA
NL

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 (>2x 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