'Specialist Infant Formulas for Non-IgE mediated Cow's Milk Allergy' study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal disorders
Study type	Interventional

Summary

ID

NL-OMON48638

Source
ToetsingOnline

Brief title
SInFoNIA study

Condition

- Gastrointestinal disorders
- Allergic conditions

Synonym
non-IgE mediated cow's milk allergy / gastro-intestinal allergy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: PPS-toeslag van Stichting LSH-TKI,Nutricia,Nutricia Research

Intervention

Keyword: AAF (amino acid formula), eHF (extensively hydrolyzed formula), Hypoallergenic formula, Non-IgE mediated cow's milk allergy

Outcome measures

Primary outcome

The main study endpoints of the study are time to symptom resolution and grade

of symptom resolution after 4 weeks of treatment. The data collected at the

phone call after 2 weeks of treatment will also be taken into account.

Secondary outcome

As secondary objectives we will assess:

- Parent-reported data on symptoms and formula intake during the elimination

period

- Number of failures and remissions in each study arm (based on the symptom

score)

- Time point of acquired tolerance

- Clinical effect markers; which subjects needed additional treatment with AAF

to resolve their symptoms?

- Biomarkers of (gut) inflammation

- Immune status

- Tolerance markers

- Microbiome

- Quality of Life (measured through the FAQLQ-PF: the food allergy related

quality of life questionnaire for parents of children aged 0 - 12 years)

Study description

Background summary

The guidelines used for the diagnosis and management of cow*s milk allergy (CMA) are largely based on research in children with the classical phenotype of IgE-mediated allergic disease. These guidelines do not focus on non-IgE-mediated CMA. In fact they may even be ineffective for this group. In IgE-mediated CMA, extensively hydrolysed formula (eHF) is considered an effective standard therapy for the majority of patients, with amino acid formula (AAF) being reserved for associated failure to thrive or insufficient treatment with eHF. However, in non-IgE-mediated CMA, literature and expert opinion suggest that this formula frequently fails to resolve the symptoms. AAF may be indicated in a large proportion of non-IgE mediated CMA. Currently, the pathophysiology of non-Ige mediated CMA and, as a result, the most suitable formula for these patients is not known. Preliminary data suggest that AAF has anti-inflammatory effects on the gastrointestinal tract and therefore could do better in comparison with eHF. The aim of this study is to compare the clinical outcomes of early introduction of eHF versus AAF in non-IgE-mediated CMA.

Study objective

Our primary objective is to compare the clinical outcome (time to and grade of symptom resolution) after 4-week-use of a whey based extensively hydrolysed formula (eHF) versus an amino acid-based formula (AAF) in children with nIgE-CMA. As secondary objectives biomarkers of (gut) inflammation, immune status, tolerance markers, and the microbiome will be assessed and compared between both study groups. Also, we will assess clinical characteristics of children failing to resolve symptoms on eHF.

Study design

This study is a phase III multicentre double-blind randomized controlled trial.

Intervention

One study group will receive whey-based extensively hydrolysed formula (eHF), the other group an amino acid-based formula (AAF). In case of insufficient symptom resolution after 4 weeks, the study subject will be deblinded. In case of treatment with eHF for this subject, a 4-week treatment with AAF will follow.

Study burden and risks

Subjects participating in this study will be treated at home with the allocated

formula during four weeks. Parents will have to fill in a diary during this treatment period. Study subjects will visit one of the study sites for the initiation visit and after four weeks. Two weeks after the start of the study, the coordinating investigator will make a phonecall to the parents, to evaluate the symptoms of their child. After the treatment period, they will undergo a double-blind placebo controlled food challenge (DBPCFC) at the hospital. Reintroduction of the cow*s milk into the diet will be done at home according to protocol. Follow-up visits will take place at the age of 6 and 12 months. Blood samples will be collected at the initiation visit, after four weeks of treatment and, dependent on the timing of the DBPCFC, at time of the food challenge. Two samples will be collected during follow-up. The study formulas are all approved treatments in the Netherlands and several other countries. The total study duration will be approximately 12 weeks for each participant, excluding the follow-up visits.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Infants *12 months of age.
- *Suspected non-IgE mediated CMA* as defined by a symptom score of at least 15 points and the pediatrician*s opinion of a possible benefit from an elimination diet.
- Symptoms are suspected to be related to cow's milk ingestion and not explained otherwise.
- A parental wish for formula feeding instead of a diet based on mother*s milk.
- Expected minimum *milk* intake (per day):
Birth up to 6 months: 500 ml
From 6 months to 8 months: 450 ml
From 9 months onwards: 350 ml
- Parents/Guardians are able to understand and comply with study instructions.
- Written informed consent provided by parents/ guardians, according to local law, to participate in this study, receive allocated treatment, fill out diaries and questionnaires and collect saliva, stool and blood samples.

Exclusion criteria

- Infants born <37 weeks gestation who require specific premature formula at time of study entry.
- Infants less than 2500 g at birth.
- Use of any hypoallergenic formulas (partially hydrolysed formula, eHF and/or AAF), <4 weeks prior to the first study visit, more than 1 bottle per week.
- An alternative diagnosis that is more probable than non-IgE mediated CMA (as decided by the expert team).
- Evidence of *severe concurrent illness* (as specified in protocol).
- The use of medication (as further specified in protocol) <4 weeks prior to the first study visit.
- Clinical history of allergy, hypersensitivity or intolerance to the excipients of the study formulas.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Double blinded (masking used)

Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-07-2019
Enrollment:	168
Type:	Actual

Ethics review

Approved WMO Date:	07-11-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-08-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 20308
Source: Nationaal Trial Register

Title:

In other registers

Register	ID
Other	Nederlands Trialregister, 7387
CCMO	NL65543.041.18
OMON	NL-OMON20308