A randomised, double-blind study evaluating the safety, tolerability, protein accretion, amino acid plasma levels and long-term outcome of Neoven compared to Vaminolact in premature very low birth weigth (VLBW) infants.

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To evaluate the safety, tolerability, protein accretion, amino acid plasma levels and long-term outcome of Neoven compared to Vaminolact in preterm infants with a birth weight from 800 g to less than 1500 g and with a gestational age from 25 weeks...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Protein and amino acid metabolism disorders NEC
Study type	Interventional

Summary

ID

NL-OMON34823

Source
ToetsingOnline

Brief title
NEOVEN-002 (05-NEOV-002)

Condition

- Protein and amino acid metabolism disorders NEC

Synonym
need for parenteral food, need of food through infusion when feeding through the mouth is not posible

Research involving
Human

Sponsors and support

Primary sponsor: Fresenius Kabi Deutschland GmbH
Source(s) of monetary or material Support: Fresenius-Kabi Deutschland GmbH

Intervention

Keyword: Neoven, Parenteral Nutrition, Vaminolact, VLBW infants

Outcome measures

Primary outcome

a) Hyperammonemia

b) Metabolic acidosis

c) Azotemia

d) Hyperaminoacidemia

e) Hyperglycemia

Secondary outcome

a) Anthropometry (weight, crown-heel length, head circumference)

b) Time to full enteral feeding defined as > 120 ml / kg / day

c) Length of ICU stay

d) Mortality rate

e) Adverse events

f) Infection rate including sepsis, for definition see appendix 3

g) Incidence of Necrotising Enterocolitis (NEC), BELL stage > grade II defined

by Bell et al 1978

h) Incidence of Broncho-Pulmonary Dysplasia (BPD) at 28 days and at 36 weeks of

corrected age as defined in appendix 7

(Jobe et al 2001)

i) Amino acid profiles

j) Mental and psychometric assessments including audiometry for otological

disorders evaluation

k) Incidence of visual disorders especially fundoscopy for retinopathies,

retinopathy of prematurity > grade III

Study description

Background summary

This study should give information on the safety, tolerability, protein accretion, amino acid plasma levels and long-term outcome of Neoven compared to Vaminolact in premature very low birth weight (VLBW) infants.

The main focus of the study will be to examine a variety of laboratory parameters evaluating azotemia, metabolic acidosis, hyperammonemia, hyperaminoacidemia and hyperglycemia. The secondary variables are important for both evaluation and comparison of the clinical condition of the patients and can be regarded as related to the administration of amino acids.

Vaminolact has been chosen as comparator not only in this trial but in all currently planned clinical trials with Neoven. Vaminolact is a well-established paediatric AA solution in many countries and it will help to standardise the overall safety evaluation of Neoven. At the end of the clinical development program, the data obtained from all Neoven trials will be pooled within an Overall Safety Analysis (OSA). In addition, as Neoven has compositional similarities to Vaminolact (e.g. mostly identical composition of essential AAs), the proof-of-concept of new compositional design elements (e.g. glutamine) can be better evaluated.

Dosing principles * start dose, staggering and full-dose as well as daily continuous infusion over at least 20 hours/day * are in accordance with accepted guidelines on nutrition and the clinical routine of the investigational sites.

Study objective

To evaluate the safety, tolerability, protein accretion, amino acid plasma

levels and long-term outcome of Neoven compared to Vaminolact in preterm infants with a birth weight from 800 g to less than 1500 g and with a gestational age from 25 weeks to less than 32 weeks

Study design

see page 16 of protocol : study schedules

Intervention

Investigational drug: Neoven (a 10% paediatric amino acid solution for intravenous infusion in parenteral nutrition)

Control drug: Vaminolact (a 6.5% paediatric amino acid solution for intravenous infusion in parenteral nutrition)

Dosage: 1.0 - 2.0 g AA/kg bw/d on day 1 of life*
1.5 - 2.5 g AA/kg bw/d on day 2 of life*
2.0 - 3.0 g AA/kg bw/d on day 3-5 of life*
as clinically needed on day 6-28 of life
* In case treatment with study drug starts on day 2 of life and the dosage of 1.5 g AA/kg bw/day is too high in the Investigator*s opinion the dosage regimen can refer to days of treatment instead of days of life, thus the Investigator can start with the lowest dosage of 1.0 g AA/kg bw/d on day 2.

Infusion time: At least 20 hours per day

Duration of Infusion: At least 5 consecutive days, infusion may continue if required until patient*s discharge for a maximum of 28 days.

Study burden and risks

The blood samples, which will be taken during this study may cause discomfort, pain and/or bruising. When a needle is placed in the skin and vein to take blood, there is a very small chance that an infection may occur.
All medicines may have side effects. A very limited number of side effects have been seen with the type of amino acid liquid which will be used in the study. Reactions that may occur because of the solution or the way it is given include fever, venous thrombosis or phlebitis, extravasation and hypervolemia.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

a) Sex: Male or female
b) Birth weight: 800 g - less than 1500 g
c) Gestational age: 250/7 - 316/7 weeks
d) Age: < 48 hours after birth
e) Life expectation should be at least 5 days as of start of PN
f) Estimated requirement of parenteral nutrition (PN) including amino acids for at least 5 days
g) Legal representative(s) signed and dated Informed Consent

Exclusion criteria

a) Severe congenital malformations [like gastroschisis, omphalocele, a syndrome associated with (suspected) chromosomal anomalies, severe hydrops fetalis]
b) Insufficient renal function with serum creatinine of * 2.0 mg/dl (* 120 µmol/L) or receiving dialysis/hemofiltration therapy.
c) Severe liver dysfunction with either ammonia levels >150 *mol/l or direct bilirubin > 8 mg/dl and ALT >200 IU/l
d) Severe congenital heart disease
e) Haematolytic disease and hyperbilirubinemia requiring exchange infusion

f) Oxygen saturation SpO2 < 80% for longer than two hours
g) Severe thrombocytopenia: platelets < 30x109/L
h) Administration of catecholamines except
- low dose dopamine * 10 µg/kg bw/min and/or
- dobutamine * 10 µg/kg bw/min or
- adrenaline * 0.2 µg/kg bw/min
i) Congenital metabolic and/or endocrinologic disorders that affect energy and nutrient metabolism (e.g. errors of amino acid metabolism)
j) Severe metabolic acidosis (pH < 6.9 and base excess (BE < -15 mmol/L) after 6 hours of life
k) Oral/enteral nutrition with more than 20% of total energy intake at the beginning of amino acid supplementation
l) Participation in another interventional clinical trial since birth

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-06-2010
Enrollment:	110
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Neoven
Generic name:	amino acid solution

Product type:	Medicine
Brand name:	Vaminolact
Generic name:	amino acid solution
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-03-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-03-2011
Application type:	Amendment
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
EudraCT	EUCTR2009-012602-39-NL
CCMO	NL31506.029.10