Clinical trial results:
A randomised, double-blind study of the safety and efficacy of Neoven compared to Vaminolact® in infants and children requiring long-term parenteral nutrition

Summary

EudraCT number	2009-012604-92
Trial protocol	FR
Global end of trial date	01 February 2011

Results information

Result version number	v1 (current)
This version publication date	09 March 2019
First version publication date	09 March 2019

Trial information

Trial identification

Sponsor protocol code	05-NEOV-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fresenius Kabi Deutschland GmbH
Sponsor organisation address	Borkenberg 14, Oberursel, Germany, 61440
Public contact	Divisional Medical & Clinical Affairs Clinical Nutrition & Ketosteril, Fresenius Kabi Deutschland GmbH, trial-disclosure@fresenius-kabi.com
Scientific contact	Divisional Medical & Clinical Affairs Clinical Nutrition & Ketosteril, Fresenius Kabi Deutschland GmbH, trial-disclosure@fresenius-kabi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000042-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 December 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 February 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the safety of Neoven compared to Vaminolact in infants and children requiring long-term parenteral nutrition (PN).

Protection of trial subjects:

Subject protection was ensured by high medical and ethical standards in accordance with Declaration of Helsinki, Good Clinical Practice and applicable national and local laws and regulations. The signed informed consent was obtained from the legal representative of the patient prior to inclusion in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1
Children (2-11 years)	5
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 6 patients were enrolled in the study in 2 centers in France, thereof 3 patients in the Neoven group and 3 patients in the Vaminolact group.

Pre-assignment

Screening details:

Screened were male and female infants, aged from 1 month up to 11 years, with intestinal malabsorption requiring PN.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Study medication was provided as bulk products to the responsible laboratory for masking due to the different strengths of products: Neoven has strength of 10 % and Vaminolact of 6.5 %. Neoven was diluted to a strength of 6.5 %. The responsible pharmacist provided a blinded final PN product which did not reveal any treatment allocation. Additional independent unblinded study monitor checked adherence to pre-defined working procedures.

Arms

Are arms mutually exclusive?	Yes
Arm title	Neoven

Arm description:

Participants received Neoven to provide AA in the frame of a complete parenteral nutrition.

Arm type	Experimental
Investigational medicinal product name	Neoven
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Neoven was planned to be infused for 12 consecutive weeks over 4 days to 7 days per week for approximately 10 to 24 hours per day.
In children up to 2 years: 2.0 to 2.5 g AA/kg body weight (bw) per day
In children from 2 to 11 years: 1.5 to-2.0 g AA/kg bw per day.

Arm title	Vaminolact

Arm description:

Participants received Vaminolact to provide AA in the frame of a complete parenteral nutrition.

Arm type	Active comparator
Investigational medicinal product name	Vaminolact
Investigational medicinal product code	
Other name	Vaminolac, Vamin Infant
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vaminolact was planned to be infused for 12 consecutive weeks over 4 days to 7 days per week for approximately 10 to 24 hours per day.
In children up to 2 years: 2.0 to 2.5 g AA/kg body weight (bw) per day
In children from 2 to 11 years: 1.5 to-2.0 g AA/kg bw per day.

Number of subjects in period 1	Neoven	Vaminolact
Started	3	3
Completed	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Neoven
Reporting group description:	
Participants received Neoven to provide AA in the frame of a complete parenteral nutrition.	
Reporting group title	Vaminolact
Reporting group description:	
Participants received Vaminolact to provide AA in the frame of a complete parenteral nutrition.	

Reporting group values	Neoven	Vaminolact	Total
Number of subjects	3	3	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	1	0	1
Children (2-11 years)	2	3	5
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	1	2	3
Male	2	1	3

End points

End points reporting groups

Reporting group title	Neoven
Reporting group description:	
Participants received Neoven to provide AA in the frame of a complete parenteral nutrition.	
Reporting group title	Vaminolact
Reporting group description:	
Participants received Vaminolact to provide AA in the frame of a complete parenteral nutrition.	

Primary: Occurrence of hyperammonaemia

End point title	Occurrence of hyperammonaemia[1]
End point description:	
The primary variables were evaluated as safety parameters. The assessment of hyperammonaemia was based on the ammonia measurements.	
End point type	Primary
End point timeframe:	
In Week 4, Week 8 and Week 12 (± 3 days) or if patient dropped out prematurely, after completion of last study treatment. At the same time of day, preferably 2 to 12 hours after completion of weekly infusion and before start of next infusion.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the study, it was decided to produce an abridged statistical evaluation only. All planned inference statistics were dropped.

End point values	Neoven	Vaminolact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of Subjects with at Least 1 Event	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of metabolic acidosis

End point title	Occurrence of metabolic acidosis[2]
End point description:	
The primary variables were evaluated as safety parameters. Metabolic acidosis was assessed from pH	
End point type	Primary
End point timeframe:	
In Week 4, Week 8 and Week 12 (± 3 days) or if patient dropped out prematurely, after completion of last study treatment.	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the study, it was decided to produce an abridged statistical evaluation only. All planned inference statistics were dropped.

End point values	Neoven	Vaminolact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of Subjects with at Least 1 Event	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of azotaemia

End point title	Occurrence of azotaemia[3]

End point description:

The primary variables were evaluated as safety parameters. Azotaemia was assessed from blood urea nitrogen.

End point type	Primary

End point timeframe:

In Week 4, Week 8 and Week 12 (± 3 days) or if patient dropped out prematurely, after completion of last study treatment. At the same time of day, preferably 2 to 12 hours after completion of weekly infusion and before start of next infusion.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the study, it was decided to produce an abridged statistical evaluation only. All planned inference statistics were dropped.

End point values	Neoven	Vaminolact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of Subjects with at Least 1 Event	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of hyperaminoacidaemia

End point title	Occurrence of hyperaminoacidaemia[4]

End point description:

The primary variables were evaluated as safety parameters. Hyperaminoacidaemia was assessed based on measurements of AA.

End point type	Primary

End point timeframe:

In Week 4, Week 8 and Week 12 (± 3 days) or if patient dropped out prematurely, after completion of last study treatment. At the same time of day, preferably 2 to 12 hours after completion of weekly infusion and before start of next infusion.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the study, it was decided to produce an abridged statistical evaluation only. All planned inference statistics were dropped.

End point values	Neoven	Vaminolact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of Subjects with at Least 1 Event	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of hyperglycaemia

End point title	Occurrence of hyperglycaemia[5]

End point description:

The primary variables were evaluated as safety parameters. Hyperglycaemia was assessed based on measurements of blood glucose.

End point type	Primary

End point timeframe:

In Week 4, Week 8 and Week 12 (± 3 days) or if patient dropped out prematurely, after completion of last study treatment. At the same time of day, preferably 2 to 12 hours after completion of weekly infusion and before start of next infusion.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the study, it was decided to produce an abridged statistical evaluation only. All planned inference statistics were dropped.

End point values	Neoven	Vaminolact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of Subjects with at Least 1 Event	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of hepatic function/dysfunction

End point title	Occurrence of hepatic function/dysfunction[6]

End point description:

The primary variables were evaluated as safety parameters.
Hepatic function parameters were the following: ammonia levels, aspartate aminotransferase [AST], alanine aminotransferase [ALT], alkaline Phosphatase [AP], gamma-glutamyltranspeptidase [GGT], direct bilirubin and total bilirubin levels.

End point type	Primary

End point timeframe:

In Week 4, Week 8 and Week 12 (± 3 days) or if patient dropped out prematurely, after completion of last study treatment. At the same time of day, preferably 2 to 12 hours after completion of weekly infusion and before start of next infusion.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the study, it was decided to produce an abridged statistical evaluation only. All planned inference statistics were dropped.

End point values	Neoven	Vaminolact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of Subjects with at Least 1 Event	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From receipt of informed consent until the end of follow-up (7 days for AEs and 4 weeks for serious AEs after last treatment).

Adverse event reporting additional description:

All SAEs and all treatment-emergent AEs, occurred in the studies, are listed below.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Neoven

Reporting group description:

Participants received Neoven to provide AA in the frame of a complete parenteral nutrition.

Reporting group title	Vaminolact

Reporting group description:

Participants received Vaminolact to provide AA in the frame of a complete parenteral nutrition.

Serious adverse events	Neoven	Vaminolact	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Device breakage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Staphylococcal sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Neoven	Vaminolact	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	
Investigations			
Prealbumin decreased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	
occurrences (all)	1	2	
Haematocrit decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Red blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Heart rate increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
White blood cell count decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood pressure systolic increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
PCO2 increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood albumin decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Device leakage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hyperchlorhydria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Pharyngeal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Premature termination of the study.
Only abridged evaluation was performed without any summary tables or inferential statistical testing.
Only patient data listings based on all randomized patients were computed.

Notes: