Clinical trial results:
EFFICACY, SAFETY, AND QUALITY OF LIFE OF A LONG-TERM HOME PARENTERAL NUTRITION REGIMEN WITH EITHER LIPIDEM® OR LIPOFUNDIN® MCT
A MONO-CENTER, RANDOMIZED, DOUBLE BLIND STUDY

Summary

EudraCT number	2005-001938-32
Trial protocol	DE
Global end of trial date	15 January 2014

Results information

Result version number	v1 (current)
This version publication date	07 March 2021
First version publication date	07 March 2021

Trial information

Trial identification

Sponsor protocol code	HC-G-H-0503

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00530738
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	B. Braun Melsungen AG, Division Hospital Care
Sponsor organisation address	Carl-Braun-Straße 1, Melsungen, Germany, 34212
Public contact	Medical Scientific Affairs Hospital Care / Clinical Development, B. Braun Melsungen AG, studies@bbraun.com
Scientific contact	Medical Scientific Affairs Hospital Care / Clinical Development, B. Braun Melsungen AG, studies@bbraun.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	30 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2014
Global end of trial reached?	Yes
Global end of trial date	15 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Proof non-inferiority of a home parenteral nutrition (HPN) regimen over 8 weeks prepared with a lipid emulsion containing fish-oil (FO) derived n-3 polyunsaturated fatty acids (Lipidem®) as compared to a conventional HPN regimen without FO with respect to nutritional efficacy.

Protection of trial subjects:

Treated in routine home parenteral nutrition.

Background therapy:

Investigational test and reference lipid emulsions were admixed to NuTRIflex® plus, a 2 chamber-bag containing amino acids and glucose. Additional components of parenteral nutrition, such as vitamins, trace elements and electrolytes were allowed to be applied according to the patient’s individual requirements.

Evidence for comparator:

Test and reference lipid emulsion (Lipidem® and Lipofundin® MCT) are 20% lipid emulsions with the same energy content but different lipid composition. The test lipid emulsion provides long-chain triglycerides (LCT), medium-chain triglycerides (MCT) and n-3 polyunsaturated fatty acids (n-3 PUFA) in a ratio of 4:5:1 while the reference lipid emulsion contains LCT and MCT in a 1:1 ratio but no n-3 PUFA. This allows assessing the impact of parenteral n-3 PUFA supplementation while providing equal amounts of fatty acids.

Actual start date of recruitment	08 February 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	29
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient in: 08.02.2008
Last patient out: 15.01.2014
Patients were recruited from the ambulatory nutritional service at the department of general, visceral, vascular, and thoracic surgery at the University Hospital of the Charité Berlin. Male and female patients aged between 18 and 80 years with a need of long-term HPN for at least 8 weeks.

Pre-assignment

Screening details:

43 patients recruited from the ambulatory nutritional service at the University Hospital of the Charité Berlin were screened for eligibility according to inclusion and exclusion criteria. One of these patients was not eligible (triglycerides > 300 mg/dL). The remaining 42 patients were enrolled into the study.

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:

Randomisation (1:1 ratio) via randomisation list (permuted block design, prepared by statistician not involved in final data analysis). IP-labelling according to randomisation list (label content: patient random number + 20 % lipid emulsion).Eligible patients received an enrollment number corresponding to the random number. Emergency envelopes ensured individual patient unblinding if necessary. The study was kept blinded until blind review meeting and final closure of the study database

Arms

Are arms mutually exclusive?	Yes
Arm title	Test group

Arm description:

Test group received HPN regimen prepared with the test lipid emulsion providing MCT/LCT/n-3 PUFA in a 5:4:1 ratio (Lipidem® 20%)

Arm type	Experimental
Investigational medicinal product name	Lipidem® 20%
Investigational medicinal product code	
Other name	Lipoplus
Pharmaceutical forms	Emulsion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mL Lipidem® 20% were added to a NuTRIflex®plus 2-chamber bag (1500 ml, 1190 kcal, containing amino acids and glucose). This all-in-one admixture was administered as continuous infusion overnight via a central venous catheter on 4 to 6 nights per week depending on individual caloric requirements (determined via indirect calorimetry or based on estimated needs of about 25 to 35 kcal/kg/day) in order to cover at least 70% of caloric needs.

Arm title	Control group

Arm description:

Control group received an HPN regimen prepared using Lipofundin® MCT 20% providing MCT and LCT in a 1:1 ratio.

Arm type	Active comparator

Investigational medicinal product name	Lipofundin® MCT 20%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mL Lipofundin® MCT 20% were added to a NuTRIflex®plus 2-chamber bag (1500 ml, 1190 kcal, containing amino acids and glucose). This all-in-one admixture was administered as continuous infusion overnight via a central venous catheter on 4 to 6 nights per week depending on individual caloric requirements (determined via indirect calorimetry or based on estimated needs of about 25 to 35 kcal/kg/day) in order to cover at least 70% of caloric needs.

Number of subjects in period 1	Test group	Control group
Started	21	21
Completed	15	18
Not completed	6	3
Consent withdrawn by subject	2	-
Adverse event, serious, non-fatal	4	2
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Test group
Reporting group description:	
Test group received HPN regimen prepared with the test lipid emulsion providing MCT/LCT/n-3 PUFA in a 5:4:1 ratio (Lipidem® 20%)	
Reporting group title	Control group
Reporting group description:	
Control group received an HPN regimen prepared using Lipofundin® MCT 20% providing MCT and LCT in a 1:1 ratio.	

Reporting group values	Test group	Control group	Total
Number of subjects	21	21	42
Age categorical Units: Subjects			
Adults (18-64 years)	15	14	29
From 65-84 years	6	7	13
Age continuous Units: years			
arithmetic mean	55.8	58.0	
standard deviation	± 15.1	± 13.0	-
Gender categorical Units: Subjects			
Female	7	9	16
Male	14	12	26
Body mass index Units: kg/m²			
arithmetic mean	21.4	20.8	
standard deviation	± 2.6	± 2.3	-

End points

End points reporting groups

Reporting group title	Test group
Reporting group description:	
Test group received HPN regimen prepared with the test lipid emulsion providing MCT/LCT/n-3 PUFA in a 5:4:1 ratio (Lipidem® 20%)	
Reporting group title	Control group
Reporting group description:	
Control group received an HPN regimen prepared using Lipofundin® MCT 20% providing MCT and LCT in a 1:1 ratio.	
Subject analysis set title	Intent to treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients who received the treatment at least once. This population is identical to the safety population.	
Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients who received the treatment at least once, were treated according to the protocol and a statement regarding the primary endpoint is possible. This population is identical to the full analysis set including all patients who received the treatment at least once and a statement regarding the primary endpoint is possible.	

Primary: Difference of bodymass index between baseline and 8 weeks of treatment

End point title	Difference of bodymass index between baseline and 8 weeks of treatment
End point description:	
The values for body weight which served as basis for the calculation of the BMI are presented as secondary endpoint.	
End point type	Primary
End point timeframe:	
Change of bodymass index after 8 weeks of treatment calculated based on bodymass index determined at Baseline and after 8 weeks.	

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	18		
Units: kg/m²				
arithmetic mean (standard deviation)	1.253 (± 1.060)	0.628 (± 0.903)		

Statistical analyses

Statistical analysis title	Assessment of non-inferiority

Statistical analysis description:

The primary efficacy endpoint (BMI change between Baseline and 8 weeks of treatment) was to be compared between groups using a parametric (t-statistic) one-sided 97.5% confidence interval for the treatment difference.

Comparison groups	Control group v Test group
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.0768
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.625
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-0.07

Notes:

[1] - Non-inferiority would be postulated if the lower bound of the confidence interval was above -1.1 kg/m² (non-inferiority margin). It was defined in the protocol, that the primary efficacy analysis would be performed within the per-protocol set of patients.

Secondary: Fatty acid pattern - Erythrocytes - Arachidonic acid

End point title	Fatty acid pattern - Erythrocytes - Arachidonic acid

End point description:

End point type	Secondary

End point timeframe:

Change of AA content in erythrocytes after 8 weeks of treatment calculated based on the fatty acid pattern in erythrocytes determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	-3.757 (± 2.230)	0.085 (± 2.176)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of AA - erythrocyte
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.93
upper limit	-1.76

Secondary: Fatty acid pattern - Erythrocytes - Eicosapentaenoic acid

End point title	Fatty acid pattern - Erythrocytes - Eicosapentaenoic acid

End point description:

End point type	Secondary

End point timeframe:

Change of EPA content in erythrocytes after 8 weeks of treatment calculated based on the fatty acid pattern in erythrocytes determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	2.184 (± 0.950)	0.067 (± 0.125)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of EPA -erythrocyes
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	2.79

Secondary: Inflammatory parameters - Interleukin-6

End point title	Inflammatory parameters - Interleukin-6

End point description:

End point type	Secondary

End point timeframe:

Change of IL-6 after 8 weeks of treatment calculated based on values determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: ng/l				
arithmetic mean (standard deviation)	3.673 (± 7.522)	-1.130 (± 2.956)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of IL-6
Comparison groups	Test group v Control group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	10.13

Secondary: Inflammatory parameters - Interleukin 10

End point title	Inflammatory parameters - Interleukin 10

End point description:

End point type	Secondary

End point timeframe:

Change of IL-10 after 8 weeks of treatment, calculated based on values determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: ng/l				
arithmetic mean (standard deviation)	0.000 (± 0.000)	0.030 (± 0.095)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of IL-10
Comparison groups	Test group v Control group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.03

Secondary: Inflammatory parameter - TNF-alpha

End point title	Inflammatory parameter - TNF-alpha

End point description:

End point type	Secondary

End point timeframe:

Change of TNF-alpha after 8 weeks od treatment calculated based on values determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: ng/l				
arithmetic mean (standard deviation)	-1.245 (± 3.788)	-2.160 (± 3.640)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of TNF-alpha
Comparison groups	Test group v Control group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.49
upper limit	4.32

Secondary: Inflammatory parameters - CRP

End point title	Inflammatory parameters - CRP

End point description:

End point type	Secondary

End point timeframe:

Change of CRP after 8 weeks of treatment calculated based on values determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: mg/dL				
arithmetic mean (standard deviation)	0.373 (± 1.346)	-0.232 (± 1.379)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of CRP
Comparison groups	Test group v Control group
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	1.6

Secondary: Fatty acid pattern - Platelets - Arachidonic Acid

End point title	Fatty acid pattern - Platelets - Arachidonic Acid

End point description:

End point type	Secondary

End point timeframe:

Change of AA content in platelets after 8 weeks of treatment calculated based on the fatty acid pattern in platelets determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	-3.181 (± 3.384)	-1.881 (± 1.189)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of AA- platelets
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	1.2

Secondary: Fatty acid pattern - Serum phospholipids - Arachidonic Acid

End point title	Fatty acid pattern - Serum phospholipids - Arachidonic Acid

End point description:

End point type	Secondary

End point timeframe:

Change of AA content in serum phospholipids after 8 weeks of treatment calculated based on the fatty acid pattern in serum phospholipids determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	-2.703 (± 1.495)	-0.006 (± 1.315)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes in AA - phospholipi
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.04
upper limit	-1.36

Secondary: Fatty acid pattern - Platelets - Eicosapentaenoic acid

End point title	Fatty acid pattern - Platelets - Eicosapentaenoic acid

End point description:

End point type	Secondary

End point timeframe:

Change of EPA content in platelets after 8 weeks of treatment calculated based on the fatty acid pattern in platelets determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	3.503 (± 1.927)	0.077 (± 0.220)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of EPA - platelets
Comparison groups	Test group v Control group

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	3.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.06
upper limit	4.79

Secondary: Fatty acid pattern - Serum phospholipids - Eicosapentaenoic acid

End point title	Fatty acid pattern - Serum phospholipids - Eicosapentaenoic acid

End point description:

End point type	Secondary

End point timeframe:

Change of EPA content in serum phospholipids after 8 weeks of treatment calculated based on the fatty acid pattern in serum phospholipids determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	3.497 (± 1.372)	0.020 (± 0.358)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of EPA -phospholipi
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	3.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.49
upper limit	4.47

Secondary: Fatty acid pattern - Erythrocytes - Docosahexaenoic acid

End point title	Fatty acid pattern - Erythrocytes - Docosahexaenoic acid

End point description:

End point type	Secondary

End point timeframe:

Change of DHA content in erythrocytes after 8 weeks of treatment calculated based on the fatty acid pattern in erythrocytes determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	2.206 (± 1.267)	0.030 (± 1.111)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of DHA -erythrocyte
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	3.31

Secondary: Fatty acid pattern - Platelets - Docosahexaenoic acid

End point title	Fatty acid pattern - Platelets - Docosahexaenoic acid

End point description:

End point type	Secondary

End point timeframe:

Change of DHA content in platelets after 8 weeks of treatment calculated based on the fatty acid pattern in platelets determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	1.878 (± 0.675)	0.119 (± 0.256)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of DHA - platelets
Comparison groups	Control group v Test group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.26

Secondary: Fatty acid pattern - Serum phospholipids - Docosahexaenoic acid

End point title	Fatty acid pattern - Serum phospholipids - Docosahexaenoic acid

End point description:

End point type	Secondary

End point timeframe:

Change of DHA content in serum phospholipids after 8 weeks of treatment calculated based on the fatty acid pattern in serum phospholipids determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: percent				
arithmetic mean (standard deviation)	2.698 (± 1.342)	0.074 (± 0.613)		

Statistical analyses

Statistical analysis title	Treatment comparison - changes of DHA -phospholipi
Comparison groups	Test group v Control group
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	3.64

Secondary: Bio impedance analysis – resistance

End point title	Bio impedance analysis – resistance

End point description:

End point type	Secondary

End point timeframe:

Change of resistance after 8 weeks of treatment calculated based on the resistance measured at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: ohm				
arithmetic mean (standard deviation)	-24.750 (± 37.816)	12.786 (± 42.320)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bio impedance analysis – reactance

End point title	Bio impedance analysis – reactance

End point description:

End point type	Secondary

End point timeframe:

Change of reactance after 8 weeks of treatment calculated based on the reactance measured at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: ohm				
arithmetic mean (standard deviation)	-0.917 (± 7.501)	1.714 (± 8.534)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bio impedance analysis – body cell mass

End point title	Bio impedance analysis – body cell mass

End point description:

End point type	Secondary

End point timeframe:

Change of body cell mass after 8 weeks of treatment calculated based on the body cell mass measured at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	15		
Units: kilogram(s)				
arithmetic mean (standard deviation)	0.775 (± 1.342)	0.780 (± 1.882)		

Statistical analyses

No statistical analyses for this end point

Secondary: Resting energy expenditure determined via indirect calorimetry

End point title	Resting energy expenditure determined via indirect calorimetry

End point description:

End point type	Secondary

End point timeframe:

Change of resting energy expenditure (REE) after 8 weeks of treatment calculated based on the REE determined via indirect calorimetry at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: kcal/day				
arithmetic mean (standard deviation)	85.2 (± 131.8)	10.0 (± 296.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Body weight

End point title	Body weight

End point description:

Change of body weight was not statistically analyzed. The values are solely presented since body weight served as the basis for calculation of the primary endpoint BMI

End point type	Secondary

End point timeframe:

Change of body weight after 8 weeks of treatment calculated based on the body weight determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	18		
Units: kilogram(s)				
arithmetic mean (standard deviation)	3.673 (± 3.128)	1.972 (± 2.896)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life - Global Health Status

End point title	Quality of Life - Global Health Status

End point description:

End point type	Secondary

End point timeframe:

Change of QoL "global health status" after 8 weeks of treatment calculated based on the QoL "global health status" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	5.83 (± 24.23)	9.44 (± 21.79)		

Statistical analyses

Statistical analysis title	Change of QoL "global health status"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.85
upper limit	15.63

Secondary: QoL - Functional Scale - cognitive functioning

End point title	QoL - Functional Scale - cognitive functioning

End point description:

End point type	Secondary

End point timeframe:

Change of functional scale "cognitive functioning" after 8 weeks of treatment calculated based on the function scale "cognitive functioning" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	8.33 (± 25.15)	0.0 (± 32.12)		

Statistical analyses

Statistical analysis title	Change of functional scale "cognitive functioning"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	8.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.66
upper limit	33.32

Secondary: QoL - Functional Scale - emotional functioning

End point title	QoL - Functional Scale - emotional functioning

End point description:

End point type	Secondary

End point timeframe:

Change of functional scale "emotional functioning" after 8 weeks of treatment calculated based on the functional scale "emotional functioning" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	4.17 (± 34.97)	-1.67 (± 26.20)		

Statistical analyses

Statistical analysis title	Change of functional scale "emotional functioning"
Comparison groups	Test group v Control group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	5.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.45
upper limit	31.12

Secondary: QoL - Functional Scale - physical functioning

End point title	QoL - Functional Scale - physical functioning

End point description:

End point type	Secondary

End point timeframe:

Change of functional scale "physical functioning" after 8 weeks of treatment calculated based on the functional scale "physical functioning" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	1.33 (± 15.65)	6.22 (± 9.58)		

Statistical analyses

Statistical analysis title	Change of functional scale "physical functioning"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.29
upper limit	5.51

Secondary: QoL - Functional Scale - role functioning

End point title	QoL - Functional Scale - role functioning

End point description:

End point type	Secondary

End point timeframe:

Change of functional scale "role functioning" after 8 weeks of treatment calculated based on the functional scale "role functioning" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	15.00 (± 31.87)	7.78 (± 38.25)		

Statistical analyses

Statistical analysis title	Changes of functional scale "role functioning"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	7.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.08
upper limit	37.53

Secondary: QoL - Functional Scale - social functioning

End point title	QoL - Functional Scale - social functioning

End point description:

End point type	Secondary

End point timeframe:

Change of functional scale "social functioning" after 8 weeks of treatment calculated based on the functional scale "social functioning" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	10.00 (± 23.83)	13.33 (± 29.68)		

Statistical analyses

Statistical analysis title	Changes of functional scale "social functioning"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.59
upper limit	19.92

Secondary: QoL - Symptom Scale - appetite loss

End point title	QoL - Symptom Scale - appetite loss

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "appetite loss" after 8 weeks of treatment calculated based on the symptom scale "appetite loss" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	3.33 (± 24.60)	6.67 (± 33.81)		

Statistical analyses

Statistical analysis title	Change of symptom scale "appetite loss"
Comparison groups	Test group v Control group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.12
upper limit	22.45

Secondary: QoL - Symptom Scale - constipation

End point title	QoL - Symptom Scale - constipation

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "constipation" after 8 weeks of treatment calculated based on the symptom scale "constipation" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	15		
Units: score				
arithmetic mean (standard deviation)	-3.70 (± 11.11)	0.0 (± 0.0)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "constipation"
Comparison groups	Control group v Test group
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.56
upper limit	2.16

Secondary: QoL - Symptom Scale - diarhoea

End point title	QoL - Symptom Scale - diarhoea

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "diarhoea" after 8 weeks of treatment calculated based on the symptom scale "diarhoea" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: score				
arithmetic mean (standard deviation)	-8.33 (± 23.57)	2.22 (± 29.46)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "diarhoea"
Comparison groups	Test group v Control group
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-10.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.72
upper limit	14.6

Secondary: QoL - Symptom Scale - dyspnoea

End point title	QoL - Symptom Scale - dyspnoea

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "dyspnoea" after 8 weeks of treatment calculated based on the symptom scale "dyspnoea" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	-3.33 (± 10.54)	4.44 (± 27.79)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "dyspnoea"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	7.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.92
upper limit	11.36

Secondary: QoL - Symptom Scale - fatigue

End point title	QoL - Symptom Scale - fatigue

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "fatigue" after 8 weeks of treatment calculated based on the symptom scale "fatigue" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	-10.00 (± 34.92)	-8.89 (± 23.46)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "fatigue"
Comparison groups	Test group v Control group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.92
upper limit	11.36

Secondary: QoL - Symptom Scale - financial problems

End point title	QoL - Symptom Scale - financial problems

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "financial problems" after 8 weeks of treatment calculated based on the symptom scale "financial problems" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	6.67 (± 21.08)	-2.22 (± 26.63)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "financial problems"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	8.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.89
upper limit	29.67

Secondary: QoL - Symptom Scale - insomnia

End point title	QoL - Symptom Scale - insomnia

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "insomnia" after 8 weeks of treatment calculated based on the symptom scale "insomnia" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	-3.33 (± 39.91)	2.22 (± 29.46)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "insomnia"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-5.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.21
upper limit	23.1

Secondary: QoL - Symptom Scale - nausea / vomiting

End point title	QoL - Symptom Scale - nausea / vomiting

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "nausea / vomiting" after 8 weeks of treatment calculated based on the symptom scale "nausea / vomiting" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	3.33 (± 35.83)	-3.33 (± 19.11)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "nausea/vomiting"
Comparison groups	Test group v Control group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	6.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.07
upper limit	29.4

Secondary: QoL - Symptom Scale - pain

End point title	QoL - Symptom Scale - pain

End point description:

End point type	Secondary

End point timeframe:

Change of symptom scale "pain" after 8 weeks of treatment calculated based on the symptom scale "pain" determined at Baseline and after 8 weeks.

End point values	Test group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: score				
arithmetic mean (standard deviation)	-15.00 (± 19.95)	0.00 (± 19.92)		

Statistical analyses

Statistical analysis title	Changes of symptom scale "pain"
Comparison groups	Test group v Control group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.83
upper limit	1.83

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 08Feb2008 - 15Jan2014	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Lipidem
Reporting group description: 20% Lipid emulsion containing long-chain triglycerides (soya oil), medium-chain triglycerides and omega-3 fatty acid triglycerides in a 4:5:1 ratio	
Reporting group title	Lipofundin
Reporting group description: 20 % Lipid emulsion containaining long-chain triglyceride and medium-chain triglyceride in a 1:1 ratio (but no n-3 PUFA)	

Serious adverse events	Lipidem	Lipofundin	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 21 (19.05%)	4 / 21 (19.05%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Investigation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Catheter placement			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Prerenal failure			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related sepsis			
subjects affected / exposed	3 / 21 (14.29%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 4	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	Lipidem	Lipofundin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 21 (52.38%)	12 / 21 (57.14%)	
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 21 (4.76%)	2 / 21 (9.52%)	
occurrences (all)	2	6	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	

Catheter site erythema			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	3	0	
Impaired healing			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
medical device complication			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 21 (0.00%)	3 / 21 (14.29%)	
occurrences (all)	0	10	
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	6	0	
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	
occurrences (all)	5	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	2	

Rash macular			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Skin haemorrhage			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Skin odour abnormal			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Stasis dermatitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 21 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 21 (4.76%)	3 / 21 (14.29%)	
occurrences (all)	1	6	
Neck pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	
occurrences (all)	1	0	

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	1 / 21 (4.76%) 1	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 21 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2007	Sample Size: Sample Size was increased from 73 to 74 to ease randomization in two groups. Exclusion criteria: Acute necrotizing pancreatitis was added as exclusion criterion because it is a contraindication for the administration of Lipofundin® MCT, it.
15 November 2007	Inclusion criteria: Need for HPN had not to be newly diagnosed
15 April 2008	Exclusion criteria: Change of restrictions regarding lab values for fasting triglycerides and serum creatinine to allow inclusion of patients that would be normally treated with HPN including lipids Patient Information Form: Inclusion of travel reimbursement
14 July 2008	Secondary variables: Patients were supplied with weighing logs for the nutrition bags to document the amount of PN used. Magnetic Resonance Tomography (MRT) was set as optional measurement Study duration: Since start of study was delayed, duration of recruitment period was prolonged accordingly.
15 February 2010	Study duration: Prolongation of recruitment period from 24 months to 38 months.
29 November 2010	Exclusion criteria: Change of restrictions regarding lab values of platelet count: The limit was lowered to 120.000/mm3 Secondary variables: Physical examinations on V1 and V2 were removed Optional variable MRT was completely removed Serum insulin measurements were deleted (no routine laboratory value, not determined at any time). Deletion of additional analyses of blood samples (Free Fatty Acids (FFA), EPA, AA, Leukotrienes B4/B5 (LTB4/5), Thromboxane B2 (TxB2)) for newly recruited patients Patient Information Form / Informed Consent Form: The patient information was changed to reflect the changed protocol (mainly deletion of MRT) and included also minor editorial changes.

20 July 2011	Sample size: Re-evaluation of sample size resulting in reduced sample size of evaluable patients Label: Instead of stating batch number and expiry date of each IP on one label a code number was used on the label
08 October 2012	Sample size: Correction of estimated drop-out rate Study duration: Prolongation of recruitment period from 38 months to 70 months

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported