A RANDOMIZED, CONTROLLED, DOUBLE-BLIND, MULTICENTER CLINICAL TRIAL ON HOME PARENTERAL NUTRITION USING AN OMEGA-3 FATTY ACID ENRICHED MCT/LCT LIPID EMULSION

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Primary Objective: Proof of safety and tolerability of home parenteral nutrition (HPN) with an Omega-3 fatty acid enriched MCT/LCT lipid emulsion in adult patients with chronic intestinal failure (CIF) in need of long-term HPNSecondary Objectives:...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malabsorption conditions
Study type	Interventional

Summary

ID

NL-OMON55393

Source
ToetsingOnline

Brief title
The HOME Study (HPN WITH OMEGA-3)

Condition

- Malabsorption conditions

Synonym
chronic bowel failure, chronic intestinal failure

Research involving
Human

Sponsors and support

Primary sponsor: B.Braun Melsungen AG
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Home Parenteral Nutrition, Lipid emulsion, Omega-3 Fatty Acid

Outcome measures

Primary outcome

The primary endpoint of the study is the change of liver function parameters

defined as the sum of the N(0,1)-transformed differences in

bilirubin, Alanine transaminase (ALT) and Aspartate transaminase (AST) from

baseline to visit 2.

Secondary outcome

Variables indicated with * are calculated values

Safety

Hepatic function

* Bilirubin

* Alanine transaminase (ALT)

* Aspartate transaminase (AST)

* AST/ALT ratio*

* Alkaline phosphatase (ALP)

* Gamma-glutamyl transpeptidase (GGT)

Blood count and coagulation

* White blood cells (WBCs)

* Red blood cells (RBCs)

* Hemoglobin (Hb)

* Hematocrit (Hct)

* Platelets

* International normalized ratio (INR) (if not possible prothrombin time [PT =

Quick-value] is accepted)

* Activated partial thromboplastin time (aPTT)

Other biochemical parameters

* Blood glucose

* Electrolytes (Na, Cl, K, Ca, Mg, P)

* Serum creatinin

* Triglycerides

* Cholesterol

* High-density lipoprotein (HDL)

* Low-density lipoprotein (LDL)

* C-reactive protein (CRP)

* α-Tocopherol/Vitamin E (facultative if routinely assessed)

* Triene:tetraene ratio* obtained from fatty acid pattern in serum

Adverse events (AEs)

Efficacy

• Fatty acid pattern in serum and RBCs

• BMI*

Other variables

• Demographic data

o Age

o Gender

o Ethnic origin

o Body height

o Body weight

Anamnesis

• Medical history relevant with regard to HPN

o Pathological classification of IF

o Underlying diseases

• Concomitant disease(s)

• Ongoing medications

• Lipid emulsion(s) during the last 6 months

• Anamnestic peculiarities

• Physical examination

• Vital signs

• Body weight change*

• Quality of life (EQ-5DTM)

• Concomitant medication

• Energy requirements

• PN regimen prescription

• Treatment compliance*

• Intake of oily fish meals

• Study termination

Study description

Background summary

Several studies have demonstrated beneficial effects of modern LEs containing Omega-3 FA in various patient groups, e.g. in critically-ill and gastrointestinal surgery patients. Thus far, the evidence on the use of Omega-3-PUFA LEs in HPN patients is still low. Due to this low evidence the recommendation for use of the n-3 enriched LE Lipidem is limited to 7 days. If medically indicated the lipid emulsion may be administered over longer periods with appropriate metabolic monitoring. Since most patients in need of long-term/life-long HPN receive lipids, it is of great importance to use a LE that provides sufficient amounts of EFA but without straining liver function. Studies on pediatric and adult HPN patients demonstrated that the use of a novel combination LE containing fish-oil is safe and yielded lower levels of bilirubin and/or transaminases compared to soybean-based lipid. Although the results are promising, their explanatory power is limited with only 4 weeks of treatment.
In this study, we want to compare Lipidem with a LCT/MCT LE (Lipofundin MCT) with regard to integrity of liver function in HPN patients with extended treatment duration. In line with the available literature we will consider biochemical markers for the assessment of
liver function, in particular AST, ALT and bilirubin for the primary analysis (Cavicchi et al., 2000; Klek et al. 2013; Tillman 2013). In this study HPN patients with CIF (IF Type III) will be considered and cancer patients will be excluded in order to have a largely homogenous patient population. This is because the medical instability of cancer patients related to their disease and/or anti-cancer treatment might tamper possible
nutrition related findings.
Aim of the study is to demonstrate non-inferiority of Lipidem against

Lipofundin MCT and consequently to proof of its safety and tolerability in the treatment of HPN patients for a projected period of 8 weeks.

Study objective

Primary Objective: Proof of safety and tolerability of home parenteral nutrition (HPN) with an Omega-3 fatty acid enriched MCT/LCT lipid emulsion in adult patients with chronic intestinal failure (CIF) in need of long-term HPN
Secondary Objectives: Further safety and efficacy evaluation

Study design

This is a prospective, randomized, controlled, double-blind, multicenter phase IV clinical trial performed in two parallel groups.

Intervention

Comparison will be made of an Omega-3-FA enriched MCT/LCT lipid emulsion (Lipidem) with a MCT/LCT lipid emulsion (Lipofundin MCT). The IP will be administered intraveniously.
Patients will be randomized at a 1:1 ratio to receive either the investigational test product or the investigational reference product.
The IP will be delivered as the lipid part of the PN and will be administered according to the individual patient*s normal prescription. The projected duration of IP treatment will be 8 weeks. Assessments will be done at baseline, visit 1 and visit 2. Thereafter, the study is terminated for the individual patient.

Study burden and risks

Both investigational products (IPs) have market authorization in various countries worldwide.
With regard to dosage and infusion rates the proposed use of IPs will be according to the registered Summaries of Product Characteristics (SmPCs). However, for the investigational test product Lipidem the evidence for long-term use is yet only low, whereby the recommendation for use is limited to 7 days.
The reference product Lipofundin MCT - as well as other LCT and LCT/MCT lipid emulsions - is used for the treatment of HPN patients since many years.
For both IPs there are potential undesirable effects, of which most are very rare under conditions of correct use in terms of dosage, monitoring, observation of safety restrictions and instructions. Given that patients of the intended population are dependent on nutritional treatment and the supply of lipids, the risks associated with the participation in the study are not higher than those that are assumed when lipids are administered in regular treatment.

Stable HPN patients usually visit their discharging hospital (HPN center) every 2-4 months for regular monitoring, which includes laboratory blood sample analysis. In the course of the study the monitoring intervals will be shorter, which necessitates two extra visits. During those extra visits, blood samples will be obtained for analysis of routine laboratory parameters as well. Furthermore, blood samples for special
laboratory analysis, i.e. fatty acid pattern analysis, will be taken at baseline and visit 2.
In total 70 ml blood will be obtained from the patient for the entire study. Due to the two extra study visits, participation might enhance the risks that are related with travelling activities.
All assessments that are performed during this study are corresponding to clinical practice and are carried out by trained personnel with proper equipment. The correlated risks are regarded as minimal. Moreover, the closer monitoring during the study course ensures the optimal supervision of the clinical status and the nutritional support of the patient, which can be regarded as benefit.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed informed consent available
2. Male or female patients >= 18 years of age
3. Patients with chronic intestinal failure receiving HPN including lipids in whom
the parenteral macronutrients have not been changed by more than 10% for at least 3 months
4. Patients receiving >= 3.0 g lipids/kg body weight per week

Exclusion criteria

1. Persistent high total bilirubin values in medical history of the last 6 months
(> 40µmol/l)
2. Patients in whom PN was interrupted for longer than 4 continuous weeks in the preceding 6 months
3. Patients with history of cancer and anti-cancer treatment within the last 2 years
4. Hypersensitivity to egg, fish or soya-bean protein or to any of the active substances or excipients
5. Patients treated in the past or currently with Teduglutide
6. Contraindications to investigational products (if available from medical records) including:
- Severe hyperlipidemia, including severe hypertriglyceridaemia (>= 1000 mg/dl or 11.4 mmol/l)
- Severe coagulopathy
- Intrahepatic cholestasis
- Severe hepatic insufficiency
- Severe renal insufficiency in absence of renal replacement therapy
- Acute thromboembolic events
- Fat embolism
- Aggravating haemorrhagic diatheses
- Metabolic acidosis
7. General contraindications to parenteral nutrition (if available from medical records) including:
- Unstable circulatory status with vital threat (states of collapse and shock)
- Acute phase of cardiac infarction or stroke

- Unstable metabolic conditions (e.g. decompensated diabetes mellitus, severe sepsis, coma of unknown origin)
- Inadequate cellular oxygen supply
- Disturbances of the electrolyte and fluid balance (e.g. hypokalaemia and hypotonic dehydration)
- Acute pulmonary edema
- Decompensated cardiac insufficiency
8. Positive test for HIV, Hepatitis B or C (from medical history)
9. Known or suspected drug or alcohol abuse
10. Patients who are unwilling or mentally and/or physically unable to adhere to study procedures
11. Participation in another interventional clinical trial in parallel or within three
months prior to the start of this clinical trial
12. Any medical condition that in the opinion of the investigator might put the subject at risk or interfere with patients participation
For women with childbearing potential (i.e. females who are not chemically or surgically sterile or females who are not post-menopausal)
13. Women of childbearing potential tested positive on standard pregnancy test (urine dipstick)
14. Lactation
15. Women of childbearing potential who do not agree to apply adequate contraception

Study design

Design

Study phase:	4
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):	08-01-2018

Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lipidem, 200 mg/ml, emulsion for infusion
Generic name:	lipid emulsion
Product type:	Medicine
Brand name:	Lipofundin MCT/LCT 20% (100 mg/ml + 100 mg/ml) emulsion for infusion
Generic name:	lipid emulsion
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-04-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-08-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-09-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-09-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-11-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2015-000849-23-NL
CCMO	NL59956.091.17