A Multi-center, Double-Blind, Randomized, Two-Arm, Parallel-Group, Placebo Controlled Study to Assess the Efficacy and Safety of ELGN-2112 on Intestinal Malabsorption in Preterm Infants

Published: 13-03-2023
Last updated: 11-07-2024

Primary objective: To assess the efficacy of treatment with ELGN-2112 as compared to placebo on intestinal malabsorption in preterm infants as measured by the time to full enteral feeding. Defined as first day of reaching three consecutive days of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53803

Source
ToetsingOnline

Brief title
FIT-PIV

Condition

- Other condition
- Malabsorption conditions

Synonym
feeding intolerance, intestinal malabsorption in preterm infants

Health condition

Prematurity - preterm birth

Research involving
Human

Sponsors and support

Primary sponsor: ELGAN Pharma
Source(s) of monetary or material Support: farmaceutisch bedrijf

Intervention

Keyword: enteral feeding, gastrointestinal malabsorption, insulin, preterm infants

Outcome measures

Primary outcome

Numbers of days to achieve full enteral feeding, defined as the first day of

ability of the preterm infant to achieve enteral feeding of at least 150

ml/kg/day for three consecutive days.

Secondary outcome

1. Number of days until wean off PN

2. Incidence of Necrotizing Enterocolitis (NEC) (modified Bell*s stage grade

>=2a) in infants born at 26-28 weeks GA.

3. Number of days to discharge from primary hospital

4. Distribution of severity of NEC according to modified Bell*s staging in

infants born at 26-28 weeks GA.

5. Incidence of Necrotizing Enterocolitis (NEC) (modified Bell*s stage grade

>=2a) in the entire study population.

6. Distribution of severity of NEC according to modified Bell*s staging in the

entire study population.

7. Percentage of infants reaching full enteral feeding within 6, 8, and 10 days

from initiation of treatment.

8. Number of days to 120 ml/kg/day for three consecutive days

9. Percentage of infants weaned off PN within 4, 6, and 8 days from initiation

of treatment

10. Percent enteral/ parenteral feedings from total nutrition over time

11. Percentage of infants with sepsis

12. Percentage of subjects experiencing one of the adverse events of relevance

(NEC, Infections, Death)

13. Number of days to discharge to home

14. Anthropometrics

15. Retinopathy of prematurity (ROP) activity score at 30-36 weeks PMA

Study description

Background summary

Premature infants have an underdeveloped gastrointestinal tract at the time of birth. As a result, nutritional intolerance is frequently seen, and these infants are dependent on parenteral nutrition for a relatively long time. However, there are also complications associated, such as sepsis or cholestasis. Necrotizing enterocolitis is also a potential dreaded intestinal complication. Breast milk - compared to formula - partly protects against these complications. Various biologically active substances in breast milk protect the premature neonate. One of these factors in breast milk is insulin, which serves as a growth factor of the intestinal epithelium.

However, the insulin concentration in breast milk is particularly high in colostrum; after a few days this concentration drops significantly, and after a few days premature neonates hardly receive any insulin anymore.

Study objective

Primary objective:
To assess the efficacy of treatment with ELGN-2112 as compared to placebo on intestinal malabsorption in preterm infants as measured by the time to full enteral feeding. Defined as first day of reaching three consecutive days of EN feeding >=150 ml/kg/day.

Secondary Objectives:
Secundaire doelstellingen:
1. Number of days until wean off PN
2. Incidence of Necrotizing Enterocolitis (NEC) (modified Bell*s stage grade >=2a) in infants born at 26-28 weeks GA.
3. Number of days to discharge from primary hospital.
4. Distribution of severity of NEC according to modified Bell*s staging in infants born at 26-28 weeks GA.
5. Incidence of Necrotizing Enterocolitis (NEC) (modified Bell*s stage grade >=2a) in the entire study population.
6. Distribution of severity of NEC according to modified Bell*s staging in the entire study population.
7. Percentage of infants reaching full enteral feeding within 6, 8, and 10 days from initiation of treatment
8. Number of days to 120 ml/kg/day for three consecutive days
9. Percentage of infants weaned off PN within 4, 6, and 8 days from initiation of treatment
10. Percent enteral/ parenteral feedings from total nutrition over time
11. Percentage of infants with sepsis
12. Percentage of infants experiencing one of the adverse events of relevance (NEC, Infections, Death)
13. Number of days to discharge to home.
14. Anthropometrics
15. Retinopathy of prematurity (ROP) activity score at 30-36 weeks PMA.

Safety Objective:
To compare the safety of treatment of ELGN-2112 to placebo in preterm infants.

Study design

Multi-center, double-blind, randomized, two-arm, parallel-group, placebo-controlled.

The study physician will follow a recommended feeding protocol. The final feeding scheme is subject to the physician*s clinical evaluation.

Screening procedures:
After the parents or guardian signs the Informed Consent Form (ICF), all

inclusion/exclusion criteria will be checked for eligibility. A complete medical history and physical examination will be performed. Within 24 hours of the screening procedures, eligible infants will be randomly assigned to one of the two treatment groups.

Treatment procedure:
During the treatment period, the infants will receive study medication with their enteral feeding until discharge from the hospital or up to 28 days, whichever occurs first. The daily drug dose will be administered preferably divided over at least four times each day with enteral feedings. Treatment should commence at postnatal age of up through and including Day 5 (up to 120 hours post birth).

Follow up period:
The infants will return to the clinical site for a follow-up visit at 6 months, 12 months, and 24 months corrected age and 6 years. If additional follow up visits take place as standard-of-care, these will be recorded as well (up to age 12). Unblinding will take place 1 year after randomization of last subject.

Intervention

The study will be comprised of 180 infants per arm, in two strata (26+0-28+6 & 29+0-32+0 GA) or at least 360 infants in all, with at least 140 (70 per arm) in the younger strata. Each infant will be randomly assigned in a 1:1 ratio to the study medication (ELGN-2112) or placebo. In the event of twin pregnancies, if both twins are eligible to be included in the study, the firstborn will be randomized, and the other sibling will be automatically allocated to the same treatment group as the firstborn.

Study burden and risks

Except for the risks already mentioned in E9 no ther risks are foreseen. The additional burden comparded to standard of care is minimal.

Contacts

Public
ELGAN Pharma

13 Wadi El Haj 13 Nazareth 13
Nazareth 13
IL
Scientific
ELGAN Pharma

13 Wadi El Haj 13 Nazareth 13
Nazareth 13
IL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

1. Male or female preterm infant 26 and up to 32 weeks gestation (32 weeks + 0 day maximum). Gestational age matching (±2 weeks) between maternal dates and/or early antenatal ultrasound * 2. Birth weight >= 500 g 3. Singleton or twin birth 4. Postnatal age up through and including Day 5 (up to 120 hours post birth) 5. Fraction of inspired oxygen <= 0.60 at enrolment 6. Infants must demonstrate cardiovascular stability at time of enrolment and would be considered unstable if they require blood pressure support via a central line 7. Infant is able to tolerate enteral feeds 8. Infant is expected to wean off parenteral nutrition (PN) at the primary hospital 9. Informed consent form signed by parents or legal guardian 10. In the Investigator*s opinion, the infant is sufficiently stable to partake in the trial to completion * If both exist and difference > 2 weeks, based on early antenatal ultrasound

Exclusion criteria

1. Infant is consuming more than 100 ml/kg/day enterally at study entry
2. Infant is not dependent on any parenteral amino acids/lipids as nutrition
3. Major congenital malformation (e.g., infants with genetic, metabolic, and/or endocrine disorder diagnosed before enrolment)
4. Intra-uterine growth restriction (IUGR) defined as either weight for gestational age less than the third percentile according to Fenton preterm growth chart.
5. Confirmed necrotizing enterocolitis (NEC)
6. Maternal diabetes (Type I/II or gestational) requiring insulin during

pregnancy or in mothers past medical history.
7. Suspected or confirmed hyperinsulinemia requiring glucose administration of more than 12 mg/kg/min at randomization.
8. Any systemic insulin administration at randomization.
9. Nothing per os (NPO) at study entry and enteral/oral supplements are not allowed.
10. Heart and chest compression or any resuscitation drugs given to the infant during delivery
11. Subjects at risk for significant GI complications such as twin-to-twin transfusion syndrome (TTTS) or monochorionic monoamniotic twins.
12. Participation in another interventional clinical study that may interfere with the results of this trial**
13. Hypersensitivity to any of the drug components- Recombinant Human Insulin (rh-Insulin), Maltodextrin, Sodium Chloride
** Participation in another interventional clinical study that may interfere with results of this trial is not allowed until discharge from the hospital

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2023
Enrollment:	70
Type:	Anticipated

Ethics review

Approved WMO Date:	13-03-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2024
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	EUCTR2021-004890-29-NL
ClinicalTrials.gov	NCT05670951
CCMO	NL82850.018.22