A Multi-center, Double-Blind, Randomized, Two-Arm, Parallel-Group, Placebo Controlled Basket Study to Assess the Safety of ELGN-2112 in Populations of Interest

Published: 09-03-2023
Last updated: 11-07-2024

Primary objective: To compare the safety of treatment with ELGN-2112 to placebo in preterm infants born less than 26 weeks GA and IUGR infants<3rd percentile * born at 26-32 weeks GA. * According to Fenton preterm growth chart. Secondary…

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

Summary

ID

NL-OMON53321

Source
ToetsingOnline

Brief title
FIT-05

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, oral insulin formulation, preterm infants

Outcome measures

Primary outcome

Safety of ELGN-2112 as compared to placebo in preterm infants born under 26

weeks GA and IUGR infants born between 26-32 weeks GA.

Secondary outcome

1. Number 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.

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

stage grade >=2a of NEC)

3. Number of days until wean off PN (total cessation)

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

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

6. Percentage of infants reaching full enteral feeding at time points of

interest from initiation of treatment.

7. Percentage of infants weaned off PN at time points of interest from

initiation of treatment

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

9. Percentage of infants with sepsis

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

(NEC, Infections, Death)

11. Number of days to discharge from primary hospital.

12. Number of days to discharge home.

13. Anthropometrics

14. 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 compare the safety of treatment with ELGN-2112 to placebo in preterm infants born less than 26 weeks GA and IUGR infants<3rd percentile * born at 26-32 weeks GA. * According to Fenton preterm growth chart. Secondary objectives: 1. 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 2. To assess the effect of ELGN-2112 on Incidence of Necrotizing Enterocolitis (NEC) (modified

Bell*s stage grade >=2a) 3. To assess effect of ELGN-2112 compared to placebo on number of days until full wean off PN (total cessation) 4. To assess the effect of ELGN-2112 on Distribution of severity of NEC according to modified Bell*s staging 5. To assess the effect of ELGN-2112 on Number of days to 120 ml/kg/day for three consecutive days. 6. To assess the effect of ELGN-2112 on percentage of infants reaching full enteral feeding at time points of interest from initiation of treatment. 7. To assess the effect of ELGN-2112 on percentage of infants weaned off PN at time points of interest from initiation of treatment 8. To assess the effect of ELGN-2112 on Percent enteral/ parenteral feedings from total nutrition over time. 9. To assess the effect of ELGN-2112 on Percentage of infants with sepsis 10. To assess the effect of ELGN-2112 on Percentage of infants experiencing one of the adverse events of relevance (NEC, Infections, Death). 11. To assess the effect of ELGN-2112 on Number of days to discharge from primary hospital 12. To assess the effect of ELGN-2112 compared to placebo on number of days to discharge home. 13. To assess the effect of ELGN-2112 on Anthropometrics 14. To assess the effect of ELGN-2112 on Retinopathy of prematurity (ROP) activity score at 30-36 weeks PMA.

Study design

This basket study will evaluate the safety of ELGN-2112 as compared to placebo in several populations of interest.

ELGN-2112 is a powder for reconstitution containing human recombinant insulin, reconstituted in breast milk, infant formula, water, or normal and half-normal saline, and administered concomitantly with preterm infant's enteral nutrition for local gastrointestinal (GI) therapy.

The study will enroll preterm infants born under 26 weeks gestational age and Intra-Uterine Growth Restricted (IUGR) infants (below 3rd percentile*), born at 26-32 weeks GA , weighing at least 450 g who meet the inclusion and exclusion criteria.

Safety will be assessed by capturing of adverse events (AEs), PE, and vital signs during the treatment period.

The effect on intestinal malabsorption will be evaluated by comparing the ability of preterm infants to achieve full enteral (EN) feeding for three consecutive days.

Subjects will be treated for 42 days (6 weeks) or up to hospital discharge, whichever is the earliest. They will receive ELGN-2112 treatment according to their recorded weight (0.3IU/kg/day) or placebo.

During the treatment period, infants will undergo daily evaluation of AEs, concomitant medication, nutrition, general growth, and development progression.

Infants will be evaluated at day of discharge. Follow-up visits will be performed at 6 months, 12 months, and 24 months corrected age, and 6 years.

Intervention

Following screening procedures eligible infants will be randomly assigned to one of the two groups in a 1:1 ratio. Randomization should take place as close as possible to treatment initiation and within 24 hours of confirmation of eligibility.

Randomization will be balanced per country within each of the following:
• Preterm infants born less than 26 weeks GA (up to 25+6)
• Intra-Uterine Growth Restricted (IUGR) infants (below 3rd percentile), born between 26+0 to 28+6 GA.
• Intra-Uterine Growth Restricted (IUGR) infants (below 3rd percentile), born between 29+0 to 31+6 GA.

Randomization of infants (or, in the case of twins, families) within stratum, to arm A or B will be in a 1:1

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
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

1. Male or female preterm infant born less than 26 weeks GA (up to 25+6) or Intra-Uterine Growth Restricted (IUGR) infants (below 3rd percentile), born between 26+0 to 31+6 GA. *Gestational age matching (±2 weeks) between maternal dates and/or early antenatal ultrasound. 2. Birth weight >= 450g 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. For infants born under 26 weeks GA, Intra-uterine growth restriction (IUGR) defined as 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. 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 the results of this trial is not allowed until discharge from the hospital

Study design

Design

Study phase:	2
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:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	09-03-2023
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	EUCTR2022-004195-42-NL
CCMO	NL83530.018.23