Determination of the rhIGF-I/rhIGFBP-3 Dose; Administered as a Continuous Infusion, Required to Establish and Maintain Longitudinal SErum IGF-I Levels within Physiological Levels in Premature Infants, to prevent Retinopathy of Prematurity;A Phase II, Randomized Controlled, Assessor-Blind, Dose-Confirming, Pharmacokinetic, Safety and Efficacy, Multicenter Study

Published: 06-05-2014
Last updated: 20-04-2024

To compare the severity of retinopathy of prematurity (ROP) among treated infants with an untreated control population, matched for GA at birth while confirming the dose of rhIGF 1/rhIGFBP-3 is safe and efficacious.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Interventional

Summary

ID

NL-OMON42210

Source
ToetsingOnline

Brief title
ROP Phase-II

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
premature retinopathy; abnormal vasculair grow in the retina

Research involving
Human

Sponsors and support

Primary sponsor: MediServ
Source(s) of monetary or material Support: sponsor Premacure

Intervention

Keyword: Prematures, Retinopathy

Outcome measures

Primary outcome

*To determine the effect of rhIGF-1/rhIGFBP-3 on the severity of ROP as

compared to the severity of ROP in an untreated control population.

*To evaluate the dose of rhIGF-1/rhIGFBP-3, administered by continuous IV

infusion, required to reach and maintain a physiological range of serum IGF-1

of 28 to 109 µg/L, defined as the in utero levels of IGF-1 for corresponding GA

in a normal population as described in Shire Reports 725-ROP-13-2103 and 725

ROP 13-2113.

*To determine serum concentrations of IGF-1 and associated pharmacokinetic

parameters after continuous IV infusion of rhIGF-1/rhIGFBP-3.

*To determine serum concentration of insulin-like growth factor binding protein

3 (IGFBP-3) and acid labile subunit (ALS) after continuous IV infusion of rhIGF

1/rhIGFBP-3.

Secondary outcome

To determine the effect of rhIGF-1/rhIGFBP-3 on other efficacy parameters and

determine the safety profile of rhIGF-1/rhIGFBP-3 when compared with standard

neonatal care in preterm infants.

Study description

Background summary

When preterm infants are deprived of their natural intrauterine environment they lose access to important factors, normally found in utero, such as proteins, growth factors, and cytokines. It has been demonstrated that insulin-like growth factor-1 (IGF-1) is one such factor, but it is likely there are others. In utero these biological factors are introduced to the fetus via placental absorption or ingestion from amniotic fluid. Deprivation of such factors is likely to cause inhibition or improper stimulation of important pathways, which in the case of the eye may cause abnormal retinal vascular growth, the hallmark of retinopathy of prematurity (ROP). Understanding which factors are lost with preterm birth and evaluating their impact on the development of ROP as well as for the growth and development of other organ systems (brain, lungs, gut, and bones) is an important aim for this patient population. Therefore, research in this field is of great importance for the understanding of normal development of immature infants and for the prevention of many complications of preterm birth.

Study objective

To compare the severity of retinopathy of prematurity (ROP) among treated infants with an untreated control population, matched for GA at birth while confirming the dose of rhIGF 1/rhIGFBP-3 is safe and efficacious.

Study design

A Phase 2, Randomized Controlled, Assessor-blind, Dose-confirming, Pharmacokinetic, Safety and Efficacy, Multicenter Study

Intervention

Recombinant human insulin-like growth factor-1 (rhIGF-1)/recombinant human insulin like growth factor binding protein-3 (rhIGFBP-3) administered by IV

infusion will be compared to standard of care.
The dose will be 250 µg/kg/24 hours via continuous IV infusion. Once initiated, the IV infusion will be continued up to PMA 29 weeks + 6 days.

Study burden and risks

IGF-1 is an important growth factor needed for the body*s tissues and organs to develop normally. Abnormally high levels of IGF-1 for a protracted period have been associated with a risk of increased cell growth. The aim of this study is to achieve normal levels of IGF-1 during the limited period of time when the risk of developing ROP is greatest. Previous studies of children and adults have shown that the blood sugar level can fall slightly when one is given IGF-1. The blood sugar level will be monitored closely throughout the study. In previous studies of premature infants, no safety risks have been discovered and it has not been seen that mecasermin rinfabate has had any negative effects on the blood sugar level. A drop in polyuria and one case of patent ductus arteriosus that may be related to the study medicine have nevertheless been found.

Even though the study medicine is a substitute for a protein that the body itself produces, there is a small risk that antibodies are developed against the product.

Contacts

Public
MediServ

De Stadspoort 32
Eindhoven 5611 GZ
NL
Scientific
MediServ

De Stadspoort 32
Eindhoven 5611 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Each subject must meet the following criteria to be enrolled in this study:;1- A signed written informed consent from the subject's parents/guardians prior to any study-related procedures that has been approved by the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) ;2- Subject must be between GA of 26 weeks + 0 days and 27 weeks +6 days (Study Section A) or between GA of 23 weeks + 0 days and 27 weeks + 6 days (Study Sections B, C, and D), inclusive

Exclusion criteria

Subjects who meet any of the following criteria will be excluded from the study:;1- Subjects born small for gestational age (SGA), ie, weight at birth <-2 SDS (Study Section A only);2- Detectable gross malformation;3- Known or suspected chromosomal abnormality, genetic disorder, or syndrome, according to the investigator*s opinion;4- Persistent plasma glucose level <2.5 mmol/L or >10 mmol/L at Study Day 0 to exclude severe congenital abnormalities of glucose metabolism;5- Anticipated need of administration of erythropoietin (rhEPO) during treatment with study drug;6- Maternal history of gestational diabetes or any diabetes requiring insulin while pregnant;7- Clinically significant neurological disease according to the investigator*s opinion (Stage 1 IVH allowed);8- Any other condition or therapy that, in the investigator*s opinion, may pose a risk to the subject or interfere with the subject*s ability to be compliant with this protocol or interfere with interpretation of results;9- Monozygotic twins ;10- Subject participating or plans to participate in a clinical study of another investigational study drug

Study design

Design

Study phase: 2

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	mecasermin rinfabate

Ethics review

Approved WMO Date:	06-05-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-09-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-04-2015

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
Other	ClinicalTrial.gov ROPP-2008-01
EudraCT	EUCTR2007-007872-40-NL
CCMO	NL48773.029.14