A Phase 2b, Multicenter, Randomized, Open-label, Two-Arm Study to Evaluate the Clinical Efficacy and Safety of OHB-607 Compared to Standard Neonatal Care for the Prevention of Bronchopulmonary Dysplasia, the Most Common Cause of Chronic Lung Disease of Prematurity

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This study has been transitioned to CTIS with ID 2024-515914-41-00 check the CTIS register for the current data. The primary objective of this study is to assess the effect of OHB-607 on reducing the burden of CLD, as indicated by a reduction in the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Neonatal respiratory disorders
Study type	Interventional

Summary

ID

NL-OMON52648

Source
ToetsingOnline

Brief title
OHB-607-202

Condition

- Neonatal respiratory disorders

Synonym
bronchopulmonary dysplasia, Chronic lung disease

Research involving
Human

Sponsors and support

Primary sponsor: OHB Neonatology Ltd
Source(s) of monetary or material Support: OHB Neonatology Ltd.

Intervention

Keyword: Chronic Lung Disease, OHB-607, Phase 2b, Premature Infants

Outcome measures

Primary outcome

Incidence of severe BPD (as defined by the modified NICHD severity grading) or death for all subjects at or before 36 weeks (±3 days) PMA. The definitions for BPD are based upon the modified NICHD guidelines for preterm infants born at <32 weeks GA:

• No BPD: oxygen for <28 days or none.

• Mild BPD: a need for oxygen for >=28 days but on room air at 36 weeks PMA.

• Moderate BPD: oxygen for >=28 days plus treatment with <30% oxygen at 36 weeks PMA.

• Severe BPD: oxygen for >=28 days plus oxygen >30% or positive pressure ventilation (CPAP, IMV, NNIMV), or high flow nasal cannula >=2 L/minute at 36 weeks PMA.

Secondary outcome

• Time to final weaning off of RTS from Day 1 of randomization through 12 months CA. The final weaning off of RTS is defined as the 7th consecutive day

that the subject is off RTS.

• Incidence of Grade 2 and Grade 3 (severe) BPD (as defined by the modified Jensen severity grading) or death for all subjects at 36 weeks PMA. The definitions for BPD are based on the classification according to Jensen et al., 2019:

- No BPD: no support.

- Grade 1: supplemental oxygen <2 L/min without positive pressure (including nasal cannula).

- Grade 2: positive pressure support (including CPAP, nasal cannula oxygen >=2 L/min, NIPPV).

- Grade 3: positive pressure ventilation (high-frequency oscillation ventilation and technologies with positive pressure tidal volume breaths, such as IMV).

• Incidence of severe (Grade 3 and 4) IVH before 40 weeks PMA (or discharge from/transfer from the NICU, whichever comes first) as assessed by central blinded reviewers and classified according to the Volpe:

- Grade 1: blood in the germinal matrix with or without IVH <10% of ventricular space.

- Grade 2: IVH occupying 10 to 50% of ventricular space on parasagittal view.

- Grade 3: IVH occupying >50% of ventricle with or without periventricular echo densities.

- Grade 4: evidence of posthemorrhagic infarction or periventricular echo densities.

• Incidence of severe ROP (Stage 3 and above) up to 40 weeks PMA according to

International Classification (International Committee for the Classification of

Retinopathy of Prematurity, 2021) by local blinded reviewer.

• Respiratory severity scoring will be determined from information captured

during follow-up telephone calls and clinical site visits at intervals

specified until 12 months CA using CLDPSS.

• Neurodevelopmental impairment as determined by the separate BSID III scales

at 24 months CA.

- Motor composite score

- Cognitive composite score

- Language composite score

Study description

Background summary

Extremely premature infants are at very high risk for developing morbidities such as BPD, intraventricular hemorrhage (IVH) and retinopathy of prematurity (ROP), often resulting in preterm infants with extremely low birth weight and has been shown to strongly predict the risk of later death or neurocognitive impairment. In a retrospective analysis of 12,050 extremely preterm infants in the US, the frequent co-occurrence of these three morbidities is associated with an incremental increase in mortality, readmissions, length of hospital stay and costs. Although the survival rates have greatly improved in recent years for infants of borderline viability, these infants remain at risk of developing a wide array of neonatal and long-term complications.

When preterm infants are deprived of their natural intrauterine environment, they lose important factors normally found in utero, such as proteins, growth factors and cytokines. It has been demonstrated that IGF-1 is one such factor that is introduced through placental absorption or ingestion from amniotic fluid. Thus, agents such as IGF-1 that promote organ development and drive growth in extremely preterm infants have the potential to address multiple complications of prematurity

OHB-607 (Mecasermin rinfabate; rhIGF-1/rhIGFBP-3 [formerly known as SHP607]) is the recombinant human version of the naturally occurring protein complex of insulin-like growth factor 1 (IGF-1) and its most abundant binding protein, insulin-like growth factor binding protein 3 (IGFBP-3). An increase of serum IGF-1 levels provided by OHB-607 administration may reduce the incidence of BPD and other complications of extreme prematurity. This would be the only available preventive pharmacological therapy leading to an absolute decrease in the incidence of moderate or severe BPD and an absolute decrease in the incidence of IVH for extremely premature babies translating to an improvement in long-term pulmonary and neurodevelopmental outcomes in these patients.

Study objective

This study has been transitioned to CTIS with ID 2024-515914-41-00 check the CTIS register for the current data.

The primary objective of this study is to assess the effect of OHB-607 on reducing the burden of CLD, as indicated by a reduction in the incidence of severe BPD (as defined by the modified NICHD severity grading) at 36 weeks (±3 days) PMA, or death at or before 36 weeks PMA, whichever comes first as compared to the SNC group.

Secondary objectives are:
• To assess the effect of OHB-607 on reducing the burden of CLD, as indicated by a reduction in time to final weaning off of RTS through 12 months CA, as compared to the SNC group.
• To assess the effect of OHB-607 on reducing the burden of CLD, as indicated by a reduction in the incidence of Grade 2 and Grade 3 (severe) BPD at 36 weeks (±3 days) PMA, or death, whichever comes first as compared to the SNC group, as classified according to Jensen et al., 2019.
•To assess the effect of OHB-607 on the occurrence of severe (Grade 3 and 4) IVH before 40 weeks PMA, as assessed by CUS as compared to the SNC group.
•To assess the effect of OHB-607 on occurrence of severe ROP (Stage 3 and above) up to 40 weeks PMA as compared to the SNC group.
•To assess the effect of OHB-607 on chronic respiratory outcomes as measured by the CLDPSS as compared to the SNC group at 12 months CA.

Study design

The subjects will be randomized to receive either 400 µg/kg/24 hoursOHB-607, or Standard Neonatal Care in a 1:1 ratio on an open-label basis. Standard Neonatal Care is determined based upon the individual premature infant*s condition and clinical judgment of the treating physician and may include interventions for thermoregulation, blood pressure support, respiratory/ventilatory support, nutritional support, treatment

for infections, etc. Recognizing that medical care required for each premature infant may vary, other than those specific parameters outlined in the protocol, local standards of clinical practice and investigator judgement will guide care decisions for study subjects.

Subjects randomly assigned to treatment with OHB-607 will receive continuous IV infusion of OHB-607 commencing within 24 hours of birth, once all baseline assessments have been completed. The infusion of study treatment will continue until 29 weeks +6 days PMA, when the subjects* endogenous production of IGF-1 is considered sufficient to maintain physiologic serum IGF-1 levels for corresponding GA. Infusion of study treatment may be discontinued before 29 weeks +6 days PMA if IV access is not possible according to the clinical judgment of the investigator or when the responsible physician, for other medical reasons, decides that infusion of study treatment should be discontinued or that the central line should be removed.

Under Protocol Amendment 2.1 dated 30Aug2022, all subjects randomized to receive OHB-607 will now receive the 400 µg/kg/24 hours dose. The rationale for selecting the higher dose is provided in Section 6.2.6. Stratification will be employed to enroll lower GA and higher GA subjects in approximately a 60:40 ratio.A 60:40 enrollment strategy will take advantage of the higher incidence of severe BPD among the lower GA subgroup hence favorably reducing the total number of subjects needed to demonstrate a 20% reduction in severe BPD in subjects receiving OHB 607 relative to SNC. Sites who cannot perform FAST IGF-1 measurements may not enroll subjects of lower GA until after the DSMB have reviewed IGF-1 levels measured through FAST IGF-1 when the twentieth subject in the lower GA group has been treated with OHB-607 for 14 days and 20 subjects have been treated with Standard Neonatal Care.

The study will be conducted in two parts (Parts A and B). Part A will complete when all subjects reach 40 weeks PMA, or are discharged from, or transferred from, the newborn, neonatal or equivalent hospital medical or intensive care unit or to a nonaffiliated medical care unit or facility, withdraw from the study, or die, whichever comes first. Safety and efficacy analyses will be conducted, and a clinical study report prepared based on these data.

Following discharge, clinical site visits in Part B will take place 6, 12 and 24 months CA (all ±4 weeks). In addition, follow-up telephone calls will be performed monthly for the first 3 months (each ±1 week) and at 9, 15, 18 and 21 months (all ±4 w eeks) CA (assessments can alternatively be completed in person if coincident with a routine hospital appointment). Part B will complete when all subjects have reached 24 months CA, withdraw from the study, die, or are lost to follow-up, whichever comes first.

The independent DSMB will provide periodic, independent review and assessment of safety data, to safeguard the interests and safety of the subjects participating in the study.An ad hoc meeting will be called to review analysis of IGF-1 levels measured through FAST IGF-1 when the twentiethsubject in the lower GA group has been treated with OHB-607 for 14 days and approximately 20 subjects have been enrolled in SNC. Only sites that can perform FAST IGF-1 will be included in advance of this review. In addition, an interim analysis will be conducted for futility by an Interim Analysis Review Committee (IARC) after 50% randomized subjects have reached 36 weeks PMA.

Intervention

OHB-607 doses will be administered at a dose of400 µg/kg/24 hours via continuous intravenous (IV) infusion from birth up to 29 weeks +6 days post-menstrual age (PMA).

Study burden and risks

Extremely premature infants are at high risk of complications from extreme preterm birth, which can lead to lower life expectancy and long-term disabilities. Despite recent increases in the survival rates of premature infants with minimal viability, the need for prevention of these complications due to extreme preterm birth is high. In this study, the subjects are subjected to different study procedures to determine the effect of OHB-607. The study activities are mainly non-invasive (eg questionnaires) or are an extension of the invasive actions that are already performed for the standard care (eg collecting blood more often). Results from previous studies with OHB-607 show a positive risk-benefit profile. Therefore, the sponsor believes that the available safety information from non-clinical and clinical studies with OHB-607 support the continuation of research in extremely preterm infants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

1. Written informed consents and/or assents must be signed and dated by the subject's parent(s) prior to any study-related procedures. The informed consent and any assents for underage parents must be approved by the IRB/IEC (in accordance with local regulations).
2. Written informed consents and/or assents must be signed and dated by the subject's birth mother prior to providing study-related information related to birth mother medical history, pregnancy and the birth of the subject. The informed consent and any assents for underage birth mothers must be approved by the IRB/IEC (in accordance with local regulations).
3. Subjects must be between 23 weeks +0 days and 27 weeks +6 days.

Exclusion criteria

Incidence of severe BPD (as defined by the modified NICHD severity grading) for all subjects at 36 weeks PMA. The definitions for BPD are based upon the modified NICHD guidelines for preterm infants born at <32 weeks GA:
• No BPD: oxygen for <28 days or none.
• Mild BPD: a need for oxygen for >=28 days but on room air at 36 weeks PMA.
• Moderate BPD: oxygen for >=28 days plus treatment with <30% oxygen at 36 weeks PMA.
• Severe BPD: oxygen for >=28 days plus oxygen >30% or positive pressure, or high flow nasal cannula >=2 L/minute at 36 weeks PMA.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	OHB-607
Generic name:	Mecasermin rinfabate

Ethics review

Approved WMO Date:	03-07-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-08-2020
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-11-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-02-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-02-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-06-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-07-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	

Date:	10-02-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-10-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-11-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-05-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EU-CTR	CTIS2024-515914-41-00
EudraCT	EUCTR2018-001393-16-NL
ClinicalTrials.gov	NCT03253263
CCMO	NL68744.068.19