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Efficacy and safety of growth hormone treatment in short children born small for gestational age; effects of growth hormone levels on growth, insulin sensitivity and body composition

Submission date	Recruitment status	[_] Prospectively registered
19/07/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/07/2006	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/12/2016	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Efficacy and safety of growth hormone treatment in short children born small for gestational age; effects of growth hormone levels on growth, insulin sensitivity and body composition

Acronym
IUGR-3 study

Study objectives
Children born small for gestational age (SGA) might be at increased risk for developing hypertension, cardiovascular disease and diabetes mellitus type 2. It has been shown that those SGA children with relatively higher growth hormone (GH) levels during an overnight GH-profile had more signs of insulin resistance. GH treatment does not seem to increase the risk of these diseases, but insulin sensitivity has not yet been evaluated in detail and has not yet been studied in relation to age, body composition, and baseline serum levels of GH, insulin-like growth factor (IGF)-1 and IGF-binding proteins. This type of research is very important since it might give clues which children are more prone to developing metabolic syndrome in later life and whether GH treatment during childhood and puberty has any effect on the development of this metabolic syndrome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised, parallel group, multicentre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Small for gestational age (SGA), children with persistent short stature

Interventions
Growth hormone treatment Norditropin SimpleXx 15 mg/1.5 ml.
The first 60 patients of five years and older who are included in the study, will undergo an overnight GH-profile, frequently sampled intravenous glucose tolerance test (FSIGT) and dual energy X-ray absorptiometry (DEXA). After stratification for gender, age, GH status, these patients will be randomised into two different groups: during the first six months, groups A and B will receive GH therapy in a dose of 1 and 2 mg/m^2/day, respectively. Subsequently, all patients will continue GH treatment with a dose of 1 mg/m^2/day.

Those patients of five years and older who will not undergo an overnight GH profile, FSIGT and DXA and all patients younger than 5 years will receive 1 mg GH/m2/day.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Norditropin

Primary outcome measure
1. To determine before, during and after treatment termination of long-term growth hormone treatment:
a. Insulin sensitivity (via frequent sampling intravenous glucose tolerance test)
b. Body composition: in relation to each other and baseline serum GH levels during an overnight GH profile and in relation with six months of treatment with two different GH doses
2. To assess the long-term efficacy of biosynthetic GH treatment in a dose of 3 IU/m^2/day on final height and other various auxological parameters

Secondary outcome measures
To assess the safety of GH treatment by studying the short- and long-term effects on:
a. Blood pressure
b. Thyroid function
c. Fasting glucose, insulin and haemoglobin HbA1c (HbA1c) levels

Overall study start date
01/03/2002

Completion date
01/10/2009

Eligibility

Key inclusion criteria
1. Children born with a birth length and/or weight <2 standard devations (SD) for gestational age (Usher McLean)

2. Neonatal period without signs of severe asphyxia (defined as Apgar score <3 after five minutes), and no serious diseases such as long-term artificial ventilation and oxygen supply, bronchopulmonary dysplasia or other chronic lung diseases
3. Short stature defined as a height SD score below 2.5 according to the Dutch National Growth references of 1997
4. Height velocity (cm/year) for chronological age
5. Chronological age at the start of treatment: 3.00 - 7.99 years (boys and girls)
6. Prepubertal signs defined as Tanner stage 1 or testicular volume <4 ml
7. Well documented growth data from birth up to two years and at least one year before the start of the study
8. Both growth hormone deficient and growth hormone insufficient patients
9. Informed consent

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
157

Key exclusion criteria
1. Chromosomal disorders, known syndromes and serious dysmorphic symptoms suggestive for a syndrome that has not yet been described, except for Silver Russell syndrome
2. Coeliac disease and other chronic or serious diseases of the gastrointestinal tract, heart, genitourinary tract, liver, lungs, skeleton, central nervous system, metabolic disease, chronic or recurrent major infectious diseases, nutritional and/or vitamin deficiencies
3. Any endocrine or metabolic disorder such as diabetes mellitus, diabetes insipidus, hypothyroidism, or inborn errors of metabolism, except for growth hormone deficiency (GHD)
4. Use of medications or interventions at this moment or during the previous six months that might have interfered with growth, such as corticosteroids (including high dose of corticosteroid inhalation), sex steroids, growth hormone, or major surgery (particularly of the spine or extremities)
5. Active malignancy or increased risk of leukaemia
6. Serious suspicion of psychosocial dwarfism (emotional deprivation)
7. Expected non-compliance

Date of first enrolment
01/03/2002

Date of final enrolment
01/10/2009

Locations

Countries of recruitment

Netherlands

Study participating centre
Erasmus Medical Center
Rotterdam
Netherlands
3000 CB

Sponsor information

Organisation
Erasmus Medical Center (The Netherlands)

Sponsor details
Sophia Children's Hospital
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Sponsor type
University/education

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Industry

Funder Name
Novo Nordisk

Alternative Name(s)
Novo Nordisk Global

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Denmark

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2017		Yes	No