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Efficacy and safety of long-term growth hormone treatment In short children born small for gestational age above the age of 8 years

Submission date
20/12/2005

Recruitment status
No longer recruiting

Registration date
20/12/2005

Overall study status
Completed

Last Edited
12/09/2019

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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
231.731/2003/155; NTR299

Study information

Scientific Title
Efficacy and safety of long-term growth hormone treatment In short children born small for gestational age above the age of 8 years

Acronym
Dutch SGA study

Study objectives
This study aims to evaluate the baseline growth hormone (GH) status, body composition and insulin sensitivity in (pre-)pubertal short children born small for gestational age (SGA). It also evaluates the effects of GH treatment on GH levels, body composition and insulin sensitivity. Furthermore this study evaluates in a randomised trial pubertal growth during GH therapy 2 versus 1 mg/m^2/day and the effects on bone maturation, body composition, insulin sensitivity, and other safety parameters. In addition, this study will evaluate the effect of 2 versus 1 mg GH /m^2/day on final height in around 50% of the SGA children who will receive treatment with an LHRH analogue for 2 years due to the start of relatively early puberty at a height less than 140 cm.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Received from the local medical ethics committee

Study design
Multicentre randomised active-controlled parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Persistent short stature, small for gestational age (SGA)

Interventions

All children are treated with Genotropin® (recombinant human somatropine, Pharmacia Corp., Peapack, NJ, USA) 1 mg/m^2/day until final height. During puberty GH therapy 2 versus 1 mg /m^2/day will be evaluated. Children with a height less than 140 cm at the start of puberty will be treated with Lucrin®, an LHRH analogue in a monthly dose depot of 3.75 mg for 2 years.

Clinical measurements (height, weight, physical examination) every 3 months until final height (FH). Routine chemistry and haematology at t = 0, 6, 12 months, then 1-yearly until FH. Only in pubertal children with a height less than 140 cm at the start of study: overnight GH profile tests during 12 hours at t = 0, 3 and 12 months. Frequent sampling intravenous glucose tolerance tests (FSIGT) during 2 hours at t = 0 and 12 months. LHRH test (= LHRH or Lucrin test) at t = 0, 3, 6 months. Ultrasound of ovaries and uterus, at t = 0, 6, 12, 24 months. All children dual energy x-ray absorptiometry (DEXA) at t = 0, 6 months, 2 years, then 2-yearly. Bone age determination at t = 0, then yearly until final height.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Genotropin®, Lucrin®

Primary outcome measure
1. To assess the effect of doubling the GH dose from 1 to 26 mg\m^2\day versus continuation of treatment with 1 mg GH\m^2\day on final height, at onset of puberty in short SGA children who start puberty at a height above 140 cm
2. To determine the dose-response effect of 1 versus 2 mg GH\m^2\day in combination with LHRH analogue treatment for 2 years on final height in short SGA children who start puberty at a height below 140 cm
3. To determine before and during long-term growth hormone treatment: insulin sensitivity and body composition

Secondary outcome measures
To assess the safety of GH treatment by studying the short- and long-term effects on:
1. Blood pressure
2. Thyroid function
3. Fasting glucose and insulin and HbA1c levels

Overall study start date
01/07/2003

Completion date
01/07/2007

Eligibility

Key inclusion criteria
1. Children born with a birth length and/or weight less than -2 SD for gestational age
2. Short stature defined in prepubertal children as a height SD score below 2.5 according to the

Dutch National Growth References of 1997 or a predicted final height less than -2.5 SD score, calculated as the height at start of puberty plus 30 cm for boys and +20 cm for girls
3. Height velocity (cm/year) for chronological age less than P50 in pre-pubertal children
4. Chronological age at start of treatment: 8 years or older (boys and girls)
5. Well documented growth data from birth up to 2 years and at least 1 year before the start of the study
6. Informed consent

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
96

Total final enrolment
107

Key exclusion criteria
1. Turner syndrome in girls, known syndromes and serious dysmorphic symptoms suggestive for a syndrome that has not yet been described, except for Silver Russell Syndrome
2. Severe asphyxia (defined as Apgar score less than 3 after 5 minutes), and no serious diseases such as long-term artificial ventilation and oxygen supply, bronchopulmonary dysplasia or other chronic lung disease
3. Coeliac disease and other chronic or serious diseases of the gastrointestinal tract, heart, genito-urinary tract, liver, lungs, skeleton or central nervous system, or chronic or recurrent major infectious diseases, nutritional and/or vitamin deficiencies
4. Any endocrine or metabolic disorder such as diabetes mellitus, diabetes insipidus, hypothyroidism, or inborn errors of metabolism, except of GHD
5. Medications or interventions during the previous 6 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)
6. Use of medication that might interfere with growth during GH therapy, such as corticosteroids, sex steroids, LHRH analogue
7. Active or treated malignancy or increased risk of leukaemia
8. Serious suspicion of psychosocial dwarfism (emotional deprivation)
9. Expected non-compliance

Date of first enrolment
01/07/2003

Date of final enrolment
01/07/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
P/a Dutch Growth Foundation
Rotterdam
Netherlands
3001 KB

Sponsor information

Organisation
Dutch Growth Foundation (Netherlands)

Sponsor details
Westzeedijk 106
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Sponsor type
Research organisation

Funder(s)

Funder type
Not defined

Funder Name
Not provided at time of registration

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	01/04/2009		Yes	No
Results article	results	01/04/2012		Yes	No
Results article	results	01/01/2013		Yes	No
Results article	results	01/10/2015		Yes	No
Results article	results	01/11/2018	12/09/2019	Yes	No