Standardized versus individualized growth hormone treatment of short children born small for gestational age: Effects on short-term and longterm efficacy, long-term psychosocial development, glucose metabolism and body composition.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Endocrine and glandular disorders NEC
Study type	Interventional

Summary

ID

NL-OMON38571

Source
ToetsingOnline

Brief title
National SGA study

Condition

- Endocrine and glandular disorders NEC

Synonym
dysmaturity, small for gestational age

Research involving
Human

Sponsors and support

Primary sponsor: Dutch Growth Research Foundation
Source(s) of monetary or material Support: De verschillende farmaceuten die groeihormoon produceren met een SGA-indicatie,Eli Lilly,Novo Nordisk,Pfizer

Intervention

Keyword: Growth Hormone, Individualized treatment, SGA

Outcome measures

Primary outcome

Primary objectives:

• To assess the effect of individualizing the growth hormone dose versus

standard treatment with 1 mg/m2/day on adult height SDS.

• To study whether treatment with individualizing the growth hormone dose

results in comparable adult height SDS as standard treatment with 1 mg/m2/day

(non-inferiorty)

Secondary outcome

Secondary objectives

• To assess the effect of individualizing the growth hormone dose versus

standard treatment with 1 mg/m2/day on the first and five year growth response.

• To assess the long term safety of growth hormone therapy on glucose

metabolism and body composition.

• To determine the effect of growth hormone therapy on psychosocial and

neurological development, and intelligence.

Study description

Background summary

Children born small for gestational age with persistent short stature can be effectively treated with growth hormone. Several studies have described the short-term and long-term growth response of different growth hormone dosages, but the optimal dose for individual short SGA children has not yet been established. De Ridder et al. developed a model to predict height at the onset of puberty and adult height for short children born SGA who will start with growth hormone treatment. The model developed by De Ridder et al. can be used for prediction of adult height for an individual child. This allows a better determination of the growth hormone dose that should be prescribed for each individual patient. Using this prediction model to determine individual GH dosages might make better individual treatment possible.

Study objective

The primary objective of this study is to assess the effect of individualizing the growth hormone dose versus standard treatment with 1 mg/m2/day on adult height. Secondly, we want to assess the first and five year growth response, the long term safety of growth hormone therapy on glucose metabolism and body composition, and to determine the effect of growth hormone therapy on psychosocial development and intelligence.

Study design

Randomised, open labelled multicenter growth hormone trial

Intervention

Patients are randomly assigned to one of the two GH dose regimens (1 mg/m2/day versus individualized dose) at the start of the study.

Study burden and risks

Since June 2005 growth hormone treatment is licensed for short children born SGA (EMEA). Studies on growth hormone treatment did not reveal any deleterious effects of this therapy so far. Subjects will visit the local outpatient clinic on a three monthly basis. Yearly, blood samples will be drawn and bone age will be determined using X-rays of the left hand and wrist. These visits and measurements are in accordance with the national guidelines on treatment of short SGA children. A subgroup will have a two-yearly, more extensive investigation at the Erasmus MC / Sophia.

Contacts

Public
Dutch Growth Research Foundation

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• Children born with a birth length and/or weight <-2 SD for gestational age (Usher and McLean)
• Short stature defined as height SD score <-2.5 according to the Dutch National Growth References of 1997
• Height of <=1 SD score below target height SD score (TH SDS).
• Height velocity (cm/year) for chronological age <=0 SDS in prepubertal children
• Chronological age at start of treatment between 4 and 11 years for boys and between 4 and 9 years for girls
• Bone age (G&P) <=13 years for girls and <=15 years for boys
• Well documented growth data from birth up to 2 years and at least 1 year before the start of the study.

• Informed consent.

Exclusion criteria

• Syndromes (except for Silver Russell Syndrome), chromosomal abnormalities and serious dysmorphic symptoms suggestive for a syndrome that has not yet been described
• Severe psychomotor retardation according to the DSM IV
• Complicated neonatal period, including signs of severe asphyxia (defined as an Apgar score <3 after 5 minutes, severe sepsis with multiple organ failure (MOF), long term artificial ventilation and oxygen supply and/or bronchopulmonary dysplasia
• Celiac disease and other chronic or serious diseases of the gastro-intestinal tract, heart, genito-urinary tract, liver, lungs, skeleton or central nervous system, or chronic or recurrent major infectious diseases, nutritional and/or vitamin deficiencies
• Any endocrine or metabolic disorder such as diabetes mellitus, diabetes insipidus, hypothyroidism, or inborn errors of metabolism, except for growth hormone deficiency (GHD)
• Genetic alterations (e.g. mutations, deletions) in the IGF-I receptor gene
• Medications or interventions during the previous 6 months that might have interfered with growth, such as corticosteroids (including high dose of corticosteroids inhalation), sex steroids, growth hormone, or major surgery (particularly of the spine and extremities)
• Use of medication that might interfere with growth during GH therapy, such as corticosteroids and sex steroids
• Active or treated malignancy or increased risk of leukaemia
• Serious suspicion of psychosocial dwarfism (emotional deprivation)
• Expected non-compliance

Study design

Design

Study phase:	4
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):	01-01-2014
Enrollment:	300
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Genotropin
Generic name:	Somatropin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Humatrope
Generic name:	Somatropin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Norditropin
Generic name:	Somatropin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	14-08-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-11-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2013-003100-39-NL
CCMO	NL45651.078.13