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The safety and efficacy of growth hormone treatment in children born small for gestational age

Submission date	Recruitment status	[_] Prospectively registered
23/04/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/04/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
11/07/2014	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.medschl.cam.ac.uk/paediatrics/pages/nesgas.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2005-001507-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2261

Study information

Scientific Title
A randomized, multicentre, multinational trial to evaluate the safety and efficacy of Growth Hormone treatment at varying doses in short children, born small for gestational age (SGA)

Acronym
NESGAS

Study objectives
Several companies were recently awarded a product licence for the treatment with high dose growth hormone (GH) of short children born small for gestational age without based on two large studies showing improvements in final height. The recommended dose of growth hormone was 35 µg/kg/day but the product license also acknowledged that a larger dose of 67 µg/kg/day could be used during the first year of treatment to enhance catch-up growth. In the USA the larger dose is used routinely as approved by the FDA.

The British Society for Paediatric Endocrinology and Diabetes (BSPED), which represents consultants in the UK who prescribe growth hormone therapy, had concerns about the widespread use of GH in this indication without further study. In particular they were concerned that the use of the lower dose during the first year of treatment may lead to many non-responders to GH staying on treatment for much longer than necessary. Secondly they had concerns about whether the long term safety of the therapy had been proven and they wanted to gather further information on carbohydrate metabolism and levels of insulin-like growth factor 1 in the circulation. The Society felt that such information should be gathered for the likely NICE review, of this and other indications for GH therapy.

The novel features of the study are:
1. All subjects will be treated with the high dose of GH during the first year to identify responders from non-responders. Non-responders to the high dose of GH would not continue with GH therapy beyond the first year.
2. That all patients would have careful assessments of carbohydrate metabolism before starting treatment and would continue to be assessed annually with glucose tolerance tests and studies of body composition once treatment had started
3. All the children would have IGF-1 levels carefully monitored to determine the effects of different dosages and whether variable dose in the second year could lead to improved growth

Ethics approval required
Old ethics approval format

Ethics approval(s)
Eastern Multicentre Research Ethics Committee (now Cambridgeshire 4 REC), 10/06/2004, ref: 04/5/025

Study design
Randomised interventional treatment 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 listed on the study web page to request a patient information sheet: http://www.medschl.cam.ac.uk/paediatrics/pages/nesgas.html

Health condition(s) or problem(s) studied
Topic: Medicines for Children Research Network; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
All study participants were treated with 67 µg/kg/day growth hormone in the first year of the study to identify non-responders from responders. Non-responders would not continue with growth hormone treatment beyond the first year. Responders would be randomised to receive a dose of 35 µg/kg/day, 67 µg/kg/day or an IGF-1 titrated dose for the following 2 years at the end of which all study participants change to a dose of 35 µg/kg/day which they would continue to take until final height.

Follow up length: 60 months. Initially patients were followed up for 3 years, an amendment has now been approved to follow up participants who consent to participate in NESGAS Extension until they reach final height.
Study Entry: registration and one or more randomisations
Recruitment: Recruitment is now complete and total UK recruitment was 34 patients however lower dropout rates than anticipated mean that there are sufficient recruits for the study data to be statistically valid.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Growth hormone

Primary outcome measure
Height gain (HSDS) (3 yrs), measured when study participants reach final height; this has been taken to be 16 years of age at the latest some participants will reach final height before that age.

Secondary outcome measures

1. Insulin resistance (IVGTT)
2. IGF-related parameters
3. Genetic polymorphisms in the population

Measured when study participants reach final height; this has been taken to be 16 years of age at the latest some participants will reach final height before that age.

Overall study start date
30/09/2004

Completion date
31/12/2008

Eligibility

Key inclusion criteria
1. Small for gestational age (body weight [BW] less than -2 SD according to country specific references)
2. Gestational age at birth more than 28 weeks
3. Short at 4 years of age (Height SDS less than -2.5 according to country specific references)
4. Short for parental height (HSDS greater than 1 SD below parental adjusted HSDS (mid parental height SDS)
5. Age 4 - 8.99 years (girls) and 4 - 9.99 years (boys)
6. Prepubertal at start of treatment (largest testis volume less than 4 ml, breast stage 1)
7. Height records must be available for 6 months prior to inclusion into the study
8. Height velocity SDS less than 0 during last 6 months (according to country specific references)
9. Subjects must be naïve to growth hormone therapy

Participant type(s)
Patient

Age group
Child

Lower age limit
4 Years

Upper age limit
9 Years

Sex
Both

Target number of participants
Planned Sample Size: 100; UK Sample Size: 34

Key exclusion criteria
1. Known or suspected allergy to growth hormone
2. Previous participation in growth hormone trial
3. Severe mental retardation as judged by the investigator

4. Previous or active malignancy
5. Benign intracranial hypertension (present or past)
6. Diabetes
7. Growth retardation due to chronic diseases, syndromes (like FAS) and chromosomal anomalies (except for Silver Russell syndrome)
8. Psychological problems likely to lead to significant non-compliance

Date of first enrolment
30/09/2004

Date of final enrolment
31/12/2008

Locations

Countries of recruitment
Ireland

Scotland

United Kingdom

Study participating centre
Department of Child Health
Glasgow
United Kingdom
G3 8SJ

Sponsor information

Organisation
Rigshospitalet (Denmark)

Sponsor details
Blegdamsvej 9
Copenhagen
Denmark
2100

Sponsor type
Hospital/treatment centre

Website
http://www.rigshospitalet.dk/RHenglish/Menu/

ROR
https://ror.org/03mchdq19

Funder(s)

Funder type
Research organisation

Funder Name
British Society of Paediatric Endocrinology and Diabetes (BSPED) (UK)

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	01/01/2013		Yes	No