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Assessment of the efficacy of Lanreotide Autogel® in the reversal of sleep apnoea, left ventricular hypertrophy and hypertension when used as primary medical therapy in acromegaly

Submission date
11/07/2011

Recruitment status
No longer recruiting

Registration date
28/09/2011

Overall study status
Completed

Last Edited
29/01/2018

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Acromegaly is a relatively rare disorder, affecting 4-6 people per million per year. In the majority of cases, a swelling on the pituitary gland releases an excess of growth hormone (GH), which can cause the hands, feet, nose and jaw to enlarge and the skin to become greasy. The condition itself has often been present for some time before the diagnosis is made, and is frequently complicated by high blood pressure, diabetes, enlargement of the heart and sleep disturbance (typically manifesting as snoring). Left untreated, people with acromegaly have a higher risk of developing diseases such as angina, heart attacks and stroke, as well as suffering from problems directly related to the pituitary swelling (e.g. headaches and visual disturbance). Surgery by an experienced neurosurgeon remains the mainstay of treatment, although complete removal of the pituitary swelling is often not possible because of the risk of damage to important surrounding structures, including the nerves to the eyes. Accordingly, further treatment (either in the form of radiotherapy, drugs or, on occasion, both) is often required to control the condition. In recent years it has become standard clinical practice to consider medical treatment prior to surgery with a class of drug commonly referred to as somatostatin receptor ligands (SRLs). These drugs can lower GH levels and improve symptoms and in some instances this is associated with shrinkage of the pituitary swelling, which may improve the surgical outcome. Many centres now routinely offer ‘pre-treatment’ to newly diagnosed cases of acromegaly. However, it remains unclear as to how effective these drugs are in terms of correcting the sleep disturbance, high blood pressure, metabolic upset, blood vessel changes and heart enlargement of acromegaly. This study aims to examine the effectiveness of a drug called ‘Lanreotide Autogel’ in reversing blood pressure, cardiac and breathing pattern changes seen in many acromegaly patients before they proceed to surgery.

Who can participate?
Newly diagnosed patients with acromegaly, aged over 18, who have not undergone any previous medical or surgical treatment or radiotherapy for their acromegaly.

What does the study involve?
Participants are asked to score various symptoms of acromegaly (e.g. headache, sweating, fatigue, arthralgia, carpal tunnel syndrome) using a 5-point scale. A full physical examination is performed. Clinical assessments include height, weight, waist and hip circumference, blood pressure measurement, ring size and neck size. At the first visit, blood tests are carried out to confirm the diagnosis of acromegaly. Participants in whom the diagnosis is confirmed are then invited for a second visit during which a more detailed assessment is undertaken with hourly blood sampling to estimate average GH levels. Liver function, fasting glucose and lipid profiles are also checked. Detailed studies of the heart and blood vessels are performed using ultrasound and a magnetic resonance imaging (MRI) scan is performed to determine the pituitary tumour volume. Ultrasound scans of the liver and gallbladder are performed to look for evidence of gall stones and gallbladder polyps. The former can sometimes develop in patients receiving treatment with SRLs and so it is helpful for us to know if these are already present before treatment begins. Participants also undergo overnight sleep studies (polysomnography) to determine the severity of their sleep disturbance. All participants will receive an injection of short-acting SRL octreotide to gauge their likely response to a longer course of SRL treatment. Participants are then treated with the longer acting Lanreotide Autogel, with the dose determined based on their response to octreotide. At each visit, patients are asked to re-score their acromegaly symptoms. At the end of the study, participants are assessed again, as outlined above.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
University of Cambridge (UK).

When is study starting and how long is it expected to run for?
March 2004 to March 2014.

Who is funding the study?
IPSEN Fund, National Institute for Health Research, and Cambridge Biomedical Research Centre.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
v.3 December 2009

Study information

Scientific Title
A comprehensive study of clinical, biochemical, radiological, cardiovascular and sleep parameters in an unselected cohort of patients with newly diagnosed ACROmegaly undergoing Pre-surgical somatostatin Analogue Therapy with Lanreotide Autogel® (ACROPAT)

Acronym
ACROPAT

Study objectives
Medical therapy with Lanreotide Autogel® may improve biochemical parameters like growth hormone (GH) and Insulin-like growth factor 1 (IGF-1) levels which may benefit a comprehensive improvement in radiological, sleep and cardiovascular sequelae of acromegaly in a newly diagnosed acromegaly cohort

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridgeshire 2 Research Ethics Committee, 09/12/2003, ref: 03/354

Study design
Prospective open-label cohort study

Primary study design
Interventional

Secondary study design
Non randomised study

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
Acromegaly and medical pre treatment with Lanreotide Autogel®

Interventions
Phase 1: Baseline assessments
1. Clinical
Subjects will be asked to score various symptoms of acromegaly (e.g. headache, sweating, fatigue, arthralgia, carpal tunnel syndrome) using a 5-point scale (ranging from 0 = not present to 4 = severe/incapacitating). A full physical examination will be performed. Clinical assessments include height, weight, waist and hip circumference, blood pressure measurement, ring size and neck size estimations.
2. Biochemical
At the first visit, the diagnosis of acromegaly will be confirmed with blood tests, including a glucose challenge test. Those subjects in whom the diagnosis is confirmed will then be invited for a second visit during which a more detailed characterisation of residual pituitary status will be undertaken together with a growth hormone (GH) day profile (1 hourly blood sampling from 09:00 hrs - 17:00 hrs) to permit an estimate of average GH levels pre-treatment. Liver function, fasting glucose and lipid profiles will also be checked.
3. Cardiovascular
Detailed studies of the heart and blood vessels using ultrasound will be performed in conjunction with the Clinical Pharmacology Unit at Addenbrooke's Hospital.
4. Radiological
During the second visit, magnetic resonance imaging (MRI) of the pituitary fossa will be performed to permit accurate determination of pituitary tumour volume.
Ultrasound of the liver and gallbladder will also be performed to look for evidence of gall stones and gallbladder polyps. The former can sometimes develop in patients receiving treatment with SRLs and so it is helpful for us to know if these are already present before treatment is commenced.
5. Sleep disturbance
All subjects will be invited to the internationally recognised Respiratory Support and Sleep Centre (RSSC), Papworth Hospital for evidence of sleep disturbance. Patients will undergo formal overnight sleep studies (so-called polysomnography) to determine the degree/severity of sleep-disordered breathing.

Phase 2: Somatostatin analogue administration and interim assessments
At completion of the baseline assessments, all subjects will be started on an injection of subcutaneous (sc) octreotide 100mcg to gauge their likely response to a longer course of SRL therapy - octreotide is a short-acting SRL. Following a repeat GH series and IGF-1 measurement patients will be commenced on the longer acting depot preparation Lanreotide Autogel®, with the dose (60, 90 or 120mg by deep subcutaneous injection every 4 weeks) determined on the basis of mean GH level and observed response to the octreotide test dose.
Repeat GH series and IGF-1 measurements will be performed at 12 weeks to determine whether further dose adjustments are necessary.
At each visit, patients will be asked to re-score their symptoms of acromegaly.

Phase 3: Post-treatment assessments
At the completion of the study (6 months post-transition to Lanreotide Autogel®), subjects will be invited to attend for clinical, biochemical, cardiovascular, radiological and sleep-apnoea status re-assessment, as outlined above

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lanreotide Autogel®

Primary outcome measure
To determine the extent to which pre-surgical medical treatment with the SRL Lanreotide Autogel® ameliorates/reverses the following in newly diagnosed previously untreated acromegaly subjects:
1. Sleep disordered breathing
2. Cardiac hypertrophy and dysfunction
3. Hypertension and arterial dysfunction

Secondary outcome measures
To determine the extent to which pre-surgical medical treatment with the SRL Lanreotide Autogel®:
1. Reduces GH and IGF1 levels
2. Reduces pituitary tumour volume
3. Corrects 'metabolic dysfunction'
4. Induces biliary 'sludge'/gallstone formation

Overall study start date
01/03/2004

Completion date
01/03/2014

Eligibility

Key inclusion criteria
1. Treatment naive newly diagnosed subjects with biochemically confirmed acromegaly
2. Males and females
3. More than 18 years of age

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
40

Key exclusion criteria
Subjects who had prior medical therapy, surgery or radiotherapy or sight-threatening tumours requiring urgent surgical decompression

Date of first enrolment
01/03/2004

Date of final enrolment
01/03/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Cambridge
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Sponsor information

Organisation
Addenbrooke's NHS Trust R&D

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Sponsor type
Not defined

ROR
https://ror.org/055vbxf86

Funder(s)

Funder type
Industry

Funder Name
IPSEN Fund (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
National Institute for Health Research (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Cambridge Biomedical Research Centre (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	01/03/2013		Yes	No