PHASE IIIb, MULTICENTRE, OPEN-LABEL, SINGLE-ARM, STUDY TO ASSESS THE EFFICACY AND SAFETY OF LANREOTIDE AUTOGEL 120 mg ADMINISTERED EVERY 28 DAYS AS PRIMARY MEDICAL TREATMENT IN ACROMEGALIC PATIENTS WITH MACROADENOMA.

Published: 26-02-2008
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To evaluate the efficacy of Lanreotide Autogel 120 mg when used as primary medical treatment in untreated de novo acromegalic patients with macroadenoma

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Interventional

Summary

ID

NL-OMON35454

Source
ToetsingOnline

Brief title
207

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Acromegaly, Gigantism

Research involving
Human

Sponsors and support

Primary sponsor: Ipsen Pharmaceuticals
Source(s) of monetary or material Support: Ipsen

Intervention

Keyword: de novo acromegalic patients, Lanreotide Autogel, Primary medical treatment

Outcome measures

Primary outcome

To evaluate the efficacy of Lanreotide Autogel 120 mg when used as primary

medical treatment in untreated de novo acromegalic patients with macroadenoma,

as assessed by evaluating the change in pituitary tumor volume at Week 48

(after 12 injection - V5) compared to baseline (V2).

A 20% reduction from the baseline volume will be considered to be clinically

significant.

Secondary outcome

1) To assess the change in tumor volume after 3 injections (V3) and 6

injections (V4) compared to baseline,

2) To assess the change in GH, IGF-1 and prolactin levels* at all assessment

time-points in comparison to the baseline visit,

3) To assess the therapeutic activity of Lanreotide Autogel 120 mg as primary

medical treatment on:

- Acromegaly symptoms,

- Quality of life (using AcroQOL),

4) To assess safety based on:

- Adverse events, clinical examination, vital signs,

- Glucose tolerance,

- Standard haematology and biochemistry,

- Gallbladder ultrasound.

* Prolactin only for patients with initial increased prolactin level (Prolactin

> 20 ng/mL).

Study description

Background summary

Recent surgical advances have contributed to improved outcomes and in experienced hands, surgery is generally effective. However up to 10% of tumors recur, most probably due to persistent growth of residual nonresectable tumor tissue: for those patients with persistent GH hypersecretion and visible tumor on MRI, reoperation by an experienced pituitary surgeon after initial surgery by an inexperienced surgeon is recommended [7].
In one study, pituitary damage leading to transient or permanent hypopituitarism was reported in up to 30% of patients who underwent surgery [11], and overall rates of complications have been correlated with the number of pituitary operations performed by the individual neurosurgeon.
Because the majority of patients with macroadenomas, especially those with tumors extending into the cavernous sinus, will not be cured surgically, postoperative therapy is required in most patients [7]. Thus, somatostatin analogues were originally approved for use after noncurative pituitary surgery, however reports of slow release formulations of somatostatin analogues, being effective in more than 60% of patients regardless of tumor dimensions has led to their primary use in selected patients newly diagnosed with acromegaly [10].
The primary objective of initial medical treatment is GH and IGF1 level control. A benefit on the tumoral component of the disease is also desirable to recommend long term medical treatment.
Previous studies demonstrated that for patients who experience significant shrinkage, an approximately 50% decrease in pituitary mass is achieved when a somatostatin analogue is used exclusively or before surgery or radiotherapy. In other studies, where a definition of significant tumor shrinkage has been provided, the results showed that 36.6% (weighted mean percentage) of patients, receiving primary somatostatin receptor ligands therapy for acromegaly, experienced a significant reduction in tumor size. The weighted mean percent reduction in tumor size was 19.4% for those studies in which all patients

received somatostatin receptor ligands and showed tumor shrinkage [8, 9]. Beside their role in controlling GH and IGF1 level and elevated GH and IGF1 associated symptoms, there is a clinical indication of somatostatin analogue-inducing tumor volume reduction. This tumor shrinkage is associated with vital structure impingement relief, patient reassurance that the mass is shrinking, and possibly a lowered risk of intratumoral hemorrhage.
Overall, available information on the effect of somatostatin analogues on tumor size remains, however, limited to octreotide and needs to be demonstrated and confirmed for Lanreotide.

Study objective

To evaluate the efficacy of Lanreotide Autogel 120 mg when used as primary medical treatment in untreated de novo acromegalic patients with macroadenoma

Study design

Phase IIIb, multicentre, open-label, single-arm, study

Intervention

NA

Study burden and risks

Patients will not undergo more burden or risks under this protocol compared with their normal standard care for the disease.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria:
1) The patient has given written informed consent prior to any study related procedures,
2) The patient is male or female and is aged between 18 and 75 years, inclusive,
3) Diagnosis of acromegaly defined by i) GH nadir > 1 ng/mL as assessed by an oral glucose tolerance test for non diabetic patients (central laboratory results) or a mean GH level > 1 ng/mL based on 5 samples taken every 10 to 15 minutes for diabetic patients (central laboratory results) AND ii) IGF-1 concentrations elevated above the age- and sex-matched normal range for diabetic and non diabetic patients (central laboratory results),
4) The patient has a pituitary adenoma with a diameter * 10 mm based on Magnetic Resonance Imaging (MRI) central reading,
5) The patient has no visual field defect identified at the visual evaluation, performed by Goldman Visual Fields Analyser and Automated visual field static perimeter, except visual field abnormality at the time of screening and that is in the investigator*s opinion:
• Not related to the pituitary adenoma
• Clinically stable condition not presumed to change during the study period
• Not modifying the ability to evaluate visual field changes related to the macroadenoma.

Exclusion criteria

Exclusion criteria:
Patients will not be included in the study if:
1) The patient has a history of hypersensitivity to Lanreotide or drugs with a similar chemical structure,
2) The patient has received any unlicensed drug within the 30 days prior to the screening visit or is scheduled to receive an unlicensed drug other than Lanreotide Autogel during the course of the study,
3) The patient is likely to require treatment during the study with somatostatin analogues

other than Lanreotide Autogel 120 mg, dopamine agonist, GH receptor antagonist (pegvisomant), and Cyclosporine or drugs that are not permitted by the study protocol,
4) The patient is a female at risk of pregnancy during the study and is not using acceptable contraceptive method. Females of childbearing potential must provide a negative pregnancy test at start of study and must be using oral, double barrier (condom with spermicidal jelly, foam suppository, or film; diaphragm with spermicide; or male condom and diaphragm with spermicide) or injectable contraception or an intra uterine device. Non childbearing potential is defined as post-menopause for at least 1 year, surgical sterilisation or hysterectomy at least three months before the start of the study,
5) The patient is pregnant or lactating,
6) The patient has a history of, or known current, problems with alcohol abuse,
7) The patient has any mental condition rendering the patient unable to understand the nature, scope and possible consequences of the study, and/or evidence of an uncooperative attitude.
8) The patient has abnormal baseline findings, any other medical condition(s) or laboratory findings that, in the opinion of the Investigator, might jeopardise the patient*s safety or decrease the chance of obtaining satisfactory data needed to achieve the objective(s) of the study,
9) The patient has undergone pituitary surgery or pituitary radiotherapy prior to study entry,
10) The patient has previously been treated with a somatostatin analogue,
11) The patient has received a dopamine agonist or a GH receptor antagonist (pegvisomant) prior to study entry,
12) The patient is expected to require pituitary surgery (adenomectomy) or to receive radiotherapy during the study period,
13) Patients with suspected associated prolactinoma: prolactin level > 100 ng/mL (central laboratory results),
14) Patient known by Investigator, to have congenital or acquired optic nerve disease or any visual abnormality with risk of worsening during the course of the study (e.g glaucoma), influencing ability to evaluate Visual Field changes related to the macroadenoma .
Under no circumstances will patients be enrolled more than once.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-06-2008
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Somatuline Autogel 120mg
Generic name:	Lanreotide (as acetaat)
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	26-02-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-06-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-11-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-08-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	28-09-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-12-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-08-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-08-2010
Application type:	Amendment
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	EUCTR2007-000155-34-NL
ClinicalTrials.gov	NCT00690898
CCMO	NL20286.078.08