A Randomized, Multicenter, Phase II study to Investigate Efficacy and Safety of ITF2984 in Acromegalic patients.

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- To investigate the biochemical response of ITF2984, defined as a reduction in (random) GH < 1.0 mcg/l and/or normalization of IGF-1.- To investigate the biochemical response of ITF2984, defined as a reduction of GH to no more than 2.5 mcg/l and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON40166

Source
ToetsingOnline

Brief title
Acromegaly

Condition

- Other condition
- Glucose metabolism disorders (incl diabetes mellitus)
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Acromegaly, effect on GH and IGF-1 concentrations

Health condition

Growth Hormone

Research involving

Human

Sponsors and support

Primary sponsor: ITALFARMACO, S.p.A
Source(s) of monetary or material Support: ITALFARMACO S.p.A.

Intervention

Keyword: Acromegaly

Outcome measures

Primary outcome

- *Change of GH and/or IGF-1 levels at the end of each month of treatment.

Secondary outcome

- Number and percentage of patients with reduction of GH < 1.0 mcg/l and/or normalization of IGF-1 at the end of each month of treatment.

- Number and percentage of patients with reduction in GH <2.5 mcg/l and/or normalization of IGF-1 at the end of each month of treatment.

- Number and percentage of patients with improvement of signs and symptoms of acromegaly at the end of each month of treatment.

- Evaluation of pharmacokinetic parameters for ITF2984 and octreotide plasma concentration

Study description

Background summary

This study represents the proof of concept study in patients with active acromegaly, de novo or not adequately controlled with currently available somatostatin analogs.
The objectives of this study are to investigate in acromegalic patients the effect of different doses of ITF2984 on GH and IGF-1 concentrations and to

investigate safety and tolerability of three different doses of ITF2984.
In light of the potential therapeutic advancement represented by somatostatin receptors multiligands in acromegalic patients, Italfarmaco S.p.A has identified a series of cyclic peptides able to bind with high affinity to multiple somatostatin receptors, SSTR subtypes 1, 2, 3, and 5.
ITF2984 diacetate is a proprietary cyclic hexapeptide with broad somatostatin receptor agonist activity.
The results of phase I studies showed that ITF2984 (500, 1000 and 2000 mcg b.i.d) suppressed the GH and IGF-1 levels in a dose dependent manner in health volunteers stimulated by an exogenous stimulus and the reduction was stronger than those observed with octreotide administration (50 mcg t.i.d.). These results suggest the potential of ITF2984 to treat patients with acromegaly by achieving biochemical control.
At the proposed doses, ITF2984 administered for up to 14 consecutive days in the phase I studies, was safe and well tolerated. Moreover, to date the pre-clinical and clinical safety available data suggest that the safety profile of ITF2984 is largely similar to that seen with other somatostatin analogues with a predominance of gastrointestinal adverse events which can be clinically monitored.
The duration of the treatment, 4 periods lasting 28 consecutive days, followed by 2 weeks off-treatment period, chosen in this study was defined on the basis of exposure and of the GH, IGF-1 reduction data obtained in previous clinical studies with octreotide and pasireotide suggesting that 28 consecutive days of administration will be enough to evaluate the reduction of the GH and to detect a signal of biochemical response in acromegaly patients. In addition, in order to assess the intrapatient dose-response of ITF2984 and octreotide, two weeks of washout between two treatment periods is considered enough to bring back GH and IGF-1 values to a basal condition.
Octreotide was chosen as the active comparator because it is a Standard Of Care (SOC) therapy in patients with acromegaly. In this study, the immediate-release formulation was chosen with the recommended dose of 100 µg t.i.d as detailed in the SmPC

Study objective

- To investigate the biochemical response of ITF2984, defined as a reduction in (random) GH < 1.0 mcg/l and/or normalization of IGF-1.
- To investigate the biochemical response of ITF2984, defined as a reduction of GH to no more than 2.5 mcg/l and/or normalization of IGF-1.
- To evaluate variation of signs and symptoms of acromegaly at the end of each month of treatment in comparison with basal status.
- To investigate the pharmacokinetic (PK) profile of ITF2984 and Octreotide
- To compare the effects on GH and IGF1 circulating levels of different doses of ITF2984
- To compare the effects on GH and IGF1 circulating levels of ITF2984 and Octreotide

Study design

Open label, randomized, multicenter, multiple dose, cross-over study

Intervention

Not applicable

Study burden and risks

Not applicable

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

- Signed written informed consent.;- Patients with active acromegaly due to a pituitary adenoma. Active acromegaly should be confirmed by 2h five point mean GH level higher than 5 mcg/liter, lack of suppression of GH nadir to less than 1 mcg/liter after oral glucose tolerance test, and elevated IGF-1 for age and sex-matched controls.;- Patients aged between 18 to 80 years old inclusive.;- Patients treated with previous surgery and/or medical therapy or previously untreated (de novo). For patients who had previously received medical therapy for acromegaly a washout periods before study entry of 3 months for long-acting formulation of somatostatin analogs and 2 weeks for octreotide sc must be foreseen. Partial responder means a significant decrease (>50%), without achievement of control of GH and/or IGF-1 levels and/or >20 % tumor shrinkage after at least 6 months of SRL therapy.
- Patients with GH level and IGF-1 level for age and sex-matched controls out of range at baseline (GH at baseline > 2.5mcg/l).

Exclusion criteria

- Patients undergone pituitary surgery within the prior 6 months. ;- Patients who have received pituitary radiotherapy (within last 10 years).;- Patients with additional active malignant disease within the last five years (with the exception of basal cell carcinoma or carcinoma in situ of the cervix);- Patients with compression of the optic chiasm causing any visual field defect. ;- Patients who require a surgical intervention for relief of any sign or symptom associated with tumor compression. ;- Patients with uncontrolled diabetes defined as having a fasting glucose > 150 mg/dL (8.3 mmol/L) or HbA1c ? 8% (Patients can be rescreened after diabetes is brought under adequate control). ;- patients who have had a significant cardiovascular disease in the three months prior to inclusion such as congestive heart failure (NYHA [New York Heart Association] class III or IV), unstable angina, sustained ventricular tachycardia, ventricular fibrillation, sustained clinically significant bradycardia, advanced heart block, or with a history of acute myocardial infarction.;- A marked baseline prolongation of QT/QTc interval i.e. a mean QT/QTc >450ms after 3 consecutive measurements at least 5 minutes apart.;* Patients with abnormal coaugulation, Prothrombin time (PT), activated partial thromboplastin time (PTT) elevated by 30% above normal limits.;- Symptomatic cholelithiasis, gallstone or chronic liver disease.;- Patients who have an history or presence at the moment of the screening visit of pancreatitis.;- Clinically significant GI, renal or hepatic disease (in the opinion of investigator).;- AST and/or ALT>2ULN.;- Severely reduced renal function (serum creatinine >2.0 mg/dl or 176µmol/L).;- Active HBV and/or active HCV infection.;- Patients who have a history of alcohol or drug abuse in the six-month period prior to the enrollment visit. ;- Known hypothyroidism or hypocortisolism not adequately treated with a stable dose of thyroid or steroid hormone replacement therapy for at least the previous 3 months. ;- Known hypersensitivity to any of the study medications, or components thereof or a history of drug or other allergy that in the opinion of the Investigator contraindicates their participation. ;- Female patients who are pregnant or lactating, and female patient who are of childbearing potential or male patient with female partners of childbearing potential who do not accept the contraception requirements reported in the

protocol.;- Patients who have participated in any clinical investigation with an Investigational drug within 3 months before study entry.;- Current or recent (< 2 months) therapy with pegvisomant or cabergoline.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-02-2015
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ITF2984 diacetate
Generic name:	ITF2984 diacetate
Product type:	Medicine
Brand name:	Octreotide
Generic name:	Octreotide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-12-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-04-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2016
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	EUCTR2013-003183-31-NL
CCMO	NL46953.078.13