A Phase II trial to assess the efficacy and safety of pasireotide s.c. alone or in combination with cabergoline in patients with Cushing*s disease

Published: 17-12-2014
Last updated: 21-04-2024

The purpose of this study, is to evaluate the efficacy and safety of pasireotide alone or in combination with cabergoline in patients with Cushing*s disease as measured by the proportion of patients achieving normal UFC at the end of the study...

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

Summary

ID

NL-OMON42150

Source
ToetsingOnline

Brief title
CSOM230B2411

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Cushing's disease

Research involving
Human

Sponsors and support

Primary sponsor: Novartis

Source(s) of monetary or material Support: Novartis

Intervention

Keyword: cabergoline, Cushing's disease, pasireotide, somatostatin analogue

Outcome measures

Primary outcome

Proportion of patients who attain mUFC <1.0xULN at week 35 with pasireotide alone or in combination with cabergoline

Secondary outcome

1. Actual and percentage change in mUFC from baseline to study end at each scheduled visit when UFC is measured

2. Proportion of patients that attain mUFC * 1.0xULN as assessed at each scheduled visit when UFC is measured

3. Proportion of patients who attain mUFC * 1.0xULN or have at least 50% reduction from baseline in mUFC as assessed at each scheduled visit when UFC is measured

4. Duration of controlled or partially controlled response

5. Change from baseline in plasma ACTH and serum cortisol over time

6. Actual and percentage change from baseline in clinical symptoms over time: blood pressure, body mass index, waist circumference, fasting serum lipid profile, and weight

7. Shift from baseline in clinical signs over time: facial rubor, fat pads, hirsutism, striae (via photographs) and muscle strength

8. Change from baseline in standardized scores, as measured by the Cushing*s QOL and SF-12v2 over time

9. Ctrough and Cmax at baseline, week 8 and week 17

10. Toxicity will be assessed using the National Cancer Institute-Common Toxicology Criteria Adverse Events version 4.0 (NCI-CTCAE v.4) and for laboratory assessments that include biochemistry, hematology, urinalysis; special safety assessments that include the regular monitoring and recording of blood glucose, insulin, HbA1c, GH and IGF-1, thyroid and liver function tests, gallbladder examinations and ECGs. Concomitant medications/Significant nondrug therapies will be assessed from study enrollment until the safety follow-up visit.

Study description

Background summary

For patients with Cushing's disease (CD), surgical removal of the pituitary adenoma is the first line therapy. Irradiation of the pituitary is another treatment option but it may take many years to be effective and it is curative in only 15 to 45% of the cases. When surgery and/or irradiation fail, or for those patients for whom such therapies are not an option, the remaining alternatives are pharmacological treatment or bilateral adrenalectomy. Pasireotide is currently approved for the treatment of Cushing*s disease, but does not optimally benefit all CD patients.
The non-approved treatments which physicians have available for use are fraught with suboptimal results and significant side effects (and the majority are limited to inhibit steroidogenesis at the adrenals, not targeting the pituitary adenoma). Bilateral adrenalectomy is a definite cure of Cushing*s disease but results in irreversible primary adrenal insufficiency and patients need lifelong replacement therapy with glucocorticoids and mineralocotricoids and have a higher likelihood to develop Nelson*s syndrome.
There is an unmet medical need for the treatment of CD for patients where pasireotide alone does not provide optimally benefit.

Study objective

The purpose of this study, is to evaluate the efficacy and safety of pasireotide alone or in combination with cabergoline in patients with Cushing*s

disease as measured by the proportion of patients achieving normal UFC at the end of the study period.

Study design

This is an open-label, two group, multi-center international non-comparative study.

Intervention

Treatment with pasireotide alone or in combination with cabergoline.

Study burden and risks

Toxicity of pasireotide and cabergoline therapy.
Frequent visits and blood sampling.

An overview of all procedures during the visits are given in the patient information. The side effects can be found in the patient information as well.
It is not certain that participation in the trial will provide direct benefit, the data can be usefull for future patients.
The burden on the patients is as expected for a phase II trial.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria for Group 1:
1. Adult patients with confirmed diagnosis of ACTH-dependent Cushing*s disease
2. Patients with de novo Cushing*s disease can be included only if they are not considered candidates for pituitary surgery
3. Male or female patients aged 18 years or greater
4. Karnofsky performance status * 60 (i.e. requires occasional assistance, but is able to care for most of their personal
needs)
5.Patients on medical treatment for Cushing*s disease the following washout periods must be completed before
screening assessments are performed
6.Patients have been on pasireotide in the past but discontinued
because of lack of efficacy are also allowed to enter Group 1. Patients treated with pasireotide subcutaneously must have been discontinued from the treatment for at least 4 weeks before
screening. Patients treated with pasireotide LAR must have been
discontinued from the treatment for at least 12 weeks before screening.
7. Patients who meet the any one of the following critieria:
* They are naive to pasireotide
* They have recieved pasireatide in the past and have been discontinued bcause of lack of efficacy (2 weeks for pasireotide subcutaneously and 12 weeks of washout prior to screening for patients treated with pasireotide LAR)
8.Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, if they are using
highly effective methods of contraception during dosing and for 30 days after stopping study medication.

Exclusion criteria

1. Patients with compression of the optic chiasm causing any visual field defect that requires surgical intervention

2. Diabetic patients with poor glycemic control as evidenced by HbA1c>8%
3. Patients with risk factors for torsade de pointes, i.e. patients with a baseline QTcF>450 ms in males, and >460 ms in females, hypokalemia, hypomagnesaemia, uncontrolled hypothyroidism, family history of long QT syndrome, or concomitant medications known to prolong QT interval.
4. Patients with clinically significant valvular disease.
5. Patients with Cushing*s syndrome due to ectopic ACTH secretion
6. Patients with hypercortisolism secondary to adrenal tumors or nodular (primary) bilateral adrenal hyperplasia
7. Patients who have congestive heart failure (NYHA Class III or IV), unstable angina, sustained ventricular tachycardia, clinically significant bradycardia, advanced heart block, history of acute MI less than one year prior to study entry or clinically significant impairment in cardiovascular function
8. Patients with liver disease such as cirrhosis, chronic active hepatitis, or chronic persistent hepatitis, or patients with ALT/AST > 2 X ULN, serum bilirubin > 2.0 X ULN
9. Patients with serum creatinine >2.0 X ULN
10. Patients with WBC <3 X 10e9/L; Hb 90% < LLN; PLT <100 X 10e9/L
11. Patients who have a known inherited syndrome as the cause for hormone over-secretion (i.e. Carney Complex, McCune-Albright syndrome, MEN-1)
12. Patients who are hypothyroid and not on adequate replacement therapy
13. Patients with symptomatic cholelithiasis

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-05-2015
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dostinex
Generic name:	cabergoline
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Signifor
Generic name:	pasireotide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-12-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-03-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-12-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	21-12-2015
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	EUCTR2013-002170-49-NL
ClinicalTrials.gov	NCT01915303
CCMO	NL49601.078.14