Pasireotide and Pegvisomant (PAPE) study in Acromegaly

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26386

Source
NTR

Brief title
PAPE

Health condition

Acromegaly

Sponsors and support

Primary sponsor: Erasmus University Medical Center Rotterdam

Source(s) of monetary or material Support: Novartis Pharma

Intervention

Outcome measures

Primary outcome

The primary endpoint is the proportion of patients who achieve normalized IGF-I levels at 24 weeks in each treatment arm.

Secondary outcome

To assess the efficacy of pasireotide LAR (60 mg) alone in normalizing IGF-I levels, within the IGF-I age adjusted normal limits, after 48 weeks of treatment.

The efficacy of pasireotide LAR (60 mg) combined with PEGV in normalizing IGF-I levels, within the age adjusted normal limits, after 48 weeks of treatment.

The necessary dose of PEGV, during co-treatment of pasireotide LAR (60 mg) with PEGV in patients with an IGF-I level within the age adjusted normal limits.

Safety will be assessed based on: adverse events, clinical examination, vital signs, glucose tolerance, EKG, standard hematology, biochemistry, endocrine function tests, GH, PEGV levels and liver function tests.

Study description

Study objective

Pasireotide Long Acting Release (Signifor® LAR), a novel long-acting multi-receptor ligand somatostatin analogue, has been shown to be more effective for the treatment of GH-secreting pituitary adenomas than currently used long-acting somatostatin analogues (LA-SSAs). The long-term efficacy of acromegaly patients using the combination pegvisomant (PEG-V) and LA-SSAss was over 90% in terms of normalization of IGF-I. However, PEGV is an expensive drug. The combination pegvisomant with pasireotide LAR has not been studied yet. Combining PEGV with pasireotide LAR could result in a lower dose / less injections of pegvisomant needed and ultimately in a more cost-effective treatment.

Study design

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Intervention

After enrollment, patients on combination therapy with pegvisomant (PEGV) and long-acting somatostatin analogues (LA-SSA) will half their regular weekly dose of PEGV for 12 weeks (run-in period).

When IGF-I remains within the age adjusted normal limits after 12 weeks, PEGV and the LA-

SSA are discontinued and patients are switched to pasireotide LAR 60 mg for 12 weeks until week 24.

When IGF-I rises above the adjusted normal limits after 12 weeks, these subjects will switch their LA-SSA to pasireotide LAR 60 mg every 4 weeks and continue with the reduced PEGV dose of the run-in period, for the remaining 12 weeks. Between week 12 and 24 dose adaptations of PEGV are not permitted unless IGF-I drops below the age adjusted normal limits, then the dose of PEGV will be decreased stepwise with 20 mg weekly until IGF-I is within the age adjusted normal limits.

At week 24, efficacy will be assessed, as the number of patients with a normal IGF-I in the two different groups; the combination pasireotide LAR 60 mg with PEGV and pasireotide LAR 60 mg monotherapy.

From week 24 patients will continue with pasireotide LAR 60 mg monotherapy, or pasireotide will be combined with 50% of the original dose of PEGV, or with an increasing dose of PEGV every 8 weeks depending on the treatment arm.

If at any visit during pasireotide LAR treatment IGF-I drops below the age adjusted normal limits the dose of PEGV will be decreased stepwise with 20 mg weekly until IGF-I is within the age adjusted normal limits. If patients use pasireotide LAR 60 mg monotherapy and IGF-I is below the age adjusted normal limits, pasireotide LAR will be decreased to 40 mg every 4 weeks.

Contacts

Public
‘s Gravendijkwal 230

S.J.C.M.M Neggers
PO Box 2040

Rotterdam 3000CA
The Netherlands
Scientific
‘s Gravendijkwal 230

S.J.C.M.M Neggers
PO Box 2040

Rotterdam 3000CA
The Netherlands

Eligibility criteria

Inclusion criteria

- Written informed consent male or female aged ≥ 18 years

- Documentation supporting the diagnosis of acromegaly based on elevated GH and/or IGF-I levels due to a pituitary tumor

- The patient is treated with lanreotide Autogel or octreotide LAR and PEGV (twice) weekly for at least 6 months and has a serum IGF-I level within 120 % of the age adjusted normal limits. These patients were previously not controlled by somatostatin analogs alone.

- Female of no childbearing potential or male. No childbearing potential is defined as being postmenopausal for at least 1 year, or women with documented infertility (natural or acquired) or using two acceptable contraceptive measures, except for oral contraceptives.

- Male subjects must agree that, if their partner is at risk of becoming pregnant, they will use a medically accepted, effective method of contraception (i.e. use a condom) for the duration of the study

- Subjects must be willing and able to comply with study restrictions and to remain at the clinic for the required duration during the study period and willing to return to the clinic for the follow up evaluation as specified in the protocol.

Exclusion criteria

- Has undergone pituitary surgery or radiotherapy within 6 months prior to study entry.

- It is anticipated that the patient will receive pituitary surgery or radiotherapy during the study.

- Has a history of hypersensitivity to lanreotide, octreotide or pegvisomant or drugs with a similar chemical structure

- Has been treated with any unlicensed drug within the last 30 days before study entry.

- Has abnormal hepatic function at study entry (defined as AST, ALT, gGT, alkaline phosphatase, or total bilirubin above 3 ULN)

- Is at risk of pregnancy or is lactating. Females of childbearing potential must provide a negative pregnancy test within 5 days before the start of the study and must be using contraception. Non-childbearing potential is defined as post-menopause for at least one year, surgical sterilization or hysterectomy at least three months before the start of the study.

- Has a history of, or known current problems with alcohol or drug abuse.

- Has a mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study, and/or evidence of an uncooperative attitude.

- Has abnormal baseline findings, any other medical condition(s) or laboratory findings that, in the opinion of the investigator, might jeopardize the subject’s safety or decrease the chance of obtaining satisfactory data needed to achieve the objective(s) of the study.

- Renal insufficiency, clearance < 50ml/min

- Poorly controlled diabetes mellitus with an HbA1c > 9.0%

- Patients with a QTc > 500 ms on the EKG

- Participation in a clinical trial in the last 6 months

Study design

Design

Study type:	Interventional
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-07-2015
Enrollment:	60
Type:	Anticipated

Ethics review

Positive opinion

Date:	18-06-2015
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 41731
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL5142
NTR-old	NTR5282
CCMO	NL49517.078.14
OMON	NL-OMON41731

Study results