A Phase 2b/3 study to evaluate the safety, tolerability, and effects of livoletide (AZP-531), an unacylated ghrelin analog, on food-related behaviors in patients with Prader-Willi syndrome

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This Phase 2b/3 double-blind, placebo-controlled study will evaluate the safety, tolerability, and effects of livoletide on food-related behaviors in patients with Prader-Willi Syndrome (PWS).

Ethical review	Approved WMO
Status	Completed
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON48225

Source
ToetsingOnline

Brief title
Millendo AZP531PWS Study

Condition

- Metabolic and nutritional disorders congenital
- Appetite and general nutritional disorders
- Eating disorders and disturbances

Synonym
Prader-Willi syndrome, PWS

Research involving

Human

Sponsors and support

Primary sponsor: Millendo Therapeutics SAS
Source(s) of monetary or material Support: Millendo Therapeutics SAS

Intervention

Keyword: hyperphagia, obesity, Prader-Willi syndrome, PWS

Outcome measures

Primary outcome

Primary Outcome Measures :

Change in hyperphagia and food-related behaviors (Hyperphagia Questionnaire for Clinical Trials; HQ-CT) [Time Frame: Baseline to month 3]

Change from baseline to the end of the 3-month Core Period for HQ-CT total score. The HQ-CT score range is 0 to 36 where the higher score represents more severe abnormal food related behaviors.

Secondary outcome

Secondary Outcome Measures :

Change in fat mass [Time Frame: Baseline to month 3]

Percentage change from baseline to the end of the 3-month Core Period in total body fat mass in overweight/obese patients with PWS

Change in waist circumference [Time Frame: Baseline to month 3]

Change from baseline to the end of the 3-month Core Period in waist circumference in overweight/obese patients with PWS

Change in body weight [Time Frame: Baseline to month 3]

Percentage change from baseline to the end of the 3-month Core Period in body

weight in overweight/obese patients with PWS

Study description

Background summary

Prader-Willi syndrome (PWS) is genetic disorder, which is caused by the absence of some genes on chromosome 15. Genes are contributing to making you different this is why there so many different people with different hair and eye colours. Because of the absence of these genes in PWS, PWS patients will develop several disease specific features including short stature (growth hormone deficiency), dysmorphic features, hypogonadism, low calorie expenditure, and abnormal body composition with reduced fat free mass and increased fat mass. Patients with PWS also suffer from cognitive impairments, behavioural disturbances, and psychiatric disorders. These patients also suffer from hyperphagia (this is a feeling of insatiable hunger) and food-related behaviours, which is the worst salient and constant symptom of PWS. Hyperphagia leads to significant mortality and morbidity. Currently, there no approved prescription or over-the counter drugs for the treatment of hyperphagia and food-related behaviours in patients with PWS.

This study involves research and is being conducted to test if a drug called livoletide will have an effect on hyperphagia and food-related behaviors. The study will also test if livoletide is safe and well tolerated. Livoletide is an investigational drug. This means that livoletide is still being studied. Livoletide (AZP-531) is a synthetic molecule (chain of 8 amino acids), similar to physiological hormone unacylated Ghrelin. Livoletide might counteract the effect of another hormone in the body called Ghrelin (AG). Ghrelin (AG) stimulates appetite and has obesogenic and diabetiogenic properties

Study objective

This Phase 2b/3 double-blind, placebo-controlled study will evaluate the safety, tolerability, and effects of livoletide on food-related behaviors in patients with Prader-Willi Syndrome (PWS).

Study design

This is a double-blind, randomized, multi center placebo-controlled study with

livoletide in patients with Prader-Willi Syndrome.

Intervention

Experimental: Low-Dose Livoletide
Daily subcutaneous injection of ~ 60 mcg/kg for 3 month double-blind core period and 9 month open label extension period.

Experimental: High-Dose Livoletide
Daily subcutaneous injection of ~120 mcg/kg for 3 month double-blind core period and 9 month open label extension period.

Placebo Comparator: Placebo
Daily subcutaneous injection of 0.9% NaCl for the 3 month double-blind core period and then low-dose or high-dose livoletide for 9 month open label extension period.

Study burden and risks

Participation in this study will include approximately 14 Months. During this study the following study procedures will be performed:

Questions about health and medications, physical exam (including vital signs, height and weight, WC, BW and BMI), ECG, DXA-scan, pregnancy test, different blood tests, consumption of isocaloric breakfast, completing different questionnaires (Appetite-NRS, HQ-CT, Quality of Life: PedsQL* Parent-Proxy Report, Caregiver and Clinical Global Impression of Severity - Hyperphagia scales (CgGIS-H and CGIS-H), Caregiver and Clinical Global Impression of Change - Hyperphagia scales (CgGIC-H and CGIC-H), Clinical Global Impression of Improvement (CGI-I), Clinical Global Impression
of - Severity (CGI-S) scale; EQ-5D-5L, and Developmental Behavior Checklist 2-Parent/Carer (DBC2-P).

When taking blood samples the subject may feel pain or be light-headed. The subject may have the following reactions at the site of the needle stick when blood is drawn:
- Additional bleeding at the site of the blood draw
- Temporary discomfort
- Bruising
- Infection (rarely)

During the electrocardiogram, subjects may experience temporary discomfort (pulling on the skin/skin hair) during removal of the sensors. They may develop some minor skin irritation from the ECG patch adhesive.

Subject are asked to fast for 8 hours before each visit. This may cause:

- Dizziness,
- Headache
- Stomach discomfort
- Fainting

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- A confirmed gentic diganosis of PWS. Documentation of PWS subtype. If PWS subtype is not known, a sample for testing may be obtained
and the patient may continue on to be enrolled into the study if he/she meets

all the other inclusion criteria and non of the
exclusion criteria.

- Male and female patients 4 to 65 years of age.

- Evidence of increased appetite or hyperphagia, as jugded by the investigator and HQ-CT score.

- Patient must have a single primary caregiver who should be available for the duration of the study. On average,
approximately 4 (or more) waking hours per day with the patient.

- BMI * 65 kg/m2

- Growth hormone treatment permitted if doses are stable

Exclusion criteria

- History of chronic liver disease
- Type 1 diabetes mellitus
- HbA1c > 10%

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	05-08-2019

Enrollment:	23
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AZP-531
Generic name:	Livoletide - unacylated ghrelin analog

Ethics review

Approved WMO Date:	09-04-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2019
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	EUCTR2018-003062-13-NL
ClinicalTrials.gov	NCT03790865
CCMO	NL68543.078.19

Study results

Date completed: 30-04-2020

Results posted: 19-11-2020

Summary results
Trial ended prematurely

First publication
17-09-2020