A Multicentre, Long-term Safety, Efficacy and Pharmacokinetics Study of Lubiprostone in Paediatric Subjects Aged *6 to <18 years with Functional Constipation

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To assess the long-term safety, efficacy, and pharmacokinetics of oral lubiprostone 12 or 24 mcg capsules dosed twice daily (BID) when administered orally for 36 weeks in paediatric subjects with functional constipation. Evaluation of lubiprostone...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Interventional

Summary

ID

NL-OMON41677

Source
ToetsingOnline

Brief title
Lubiprostone for the treatment of paediatric functional constipation

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
constipation in children and adolescents, functional constipation

Research involving
Human

Sponsors and support

Primary sponsor: Sucampo AG
Source(s) of monetary or material Support: industry

Intervention

Keyword: functional constipation, lubiprostone, paediatrics

Outcome measures

Primary outcome

The safety endpoints are as follows:

* Incidence of adverse events (AEs) grouped by MedDRA System Organ Class (SOC) and Preferred Term

* Changes from baseline in clinical laboratory parameters (haematology, serum chemistry, urinalysis)

* Changes from baseline in physical examination

* Changes from baseline in vital sign measurements, including height and weight

o Height will be measured using a wall-mounted stadiometer, if available

* For those subjects who were aged 6 to 9 or 14 to 17 at the time of enrolment into the SAG/0211PFC-1131 study, and who were qualified to participate and enrolled in the dual-energy X-ray absorptiometry (DXA) substudy:

o Per cent changes from baseline in bone mineral density (BMD) and bone mineral content (BMC)

o Changes from baseline in BMD Z-scores and in height-adjusted Z-scores, as assessed by DXA for DXA Subgroup

o Changes from baseline in height and weight Z-scores for DXA Subgroup

o Incidence of clinical fractures

A Data Safety Monitoring Board (DSMB) will monitor safety data on a regular basis throughout the study. Specifics, including meeting frequency and stoppage criteria, are provided in the DSMB Charter.

The efficacy endpoints are as follows:

* Overall and monthly changes from baseline in BM and SBM frequency rate
* Overall and monthly assessments of the average degree of, and changes from baseline in:
o Stool consistency of SBMs
o Straining associated with SBMs
o Abdominal pain associated with SBMs
o Constipation severity
* Monthly SBM Response
o A monthly responder is defined as a subject who is a weekly responder for 3 of 4 weeks per month.
o A weekly responder is defined as a subject who has a frequency rate of * 3 SBMs/week and an increase from baseline of * 1 SBM/week for that week.
* Overall and monthly assessment of average treatment effectiveness rating
* Overall Health-related quality of life (PedsQL*)
* Overall and monthly change from baseline in incontinence episodes frequency (analysis performed for subset of subjects presenting with incontinence at baseline)
* Overall and monthly change from baseline in the production of large diameter stool (a stool that clogs the toilet) frequency

* Overall and monthly change from baseline in frequency of faecal impaction

* Overall and monthly change from baseline in proportion of BMs and SBMs in toilet overall

* Overall and monthly change from baseline in frequency of posturing or excessive volitional stool retention

Plasma samples will be collected for population pharmacokinetic (PK) modelling at Visit 9 as follows:

* Pre-dose and 1 sample between 30 and 90 minutes after dose administration (2 samples total)

A population PK analysis will be performed using the concentration-time data from the sparse PK samples in this study. The analysis may include data from other studies with lubiprostone in adults, paediatric subjects, or healthy volunteers. A separate analysis plan for the population PK analysis will be prepared prior to database lock.

Secondary outcome

Not Applicable

Study description

Background summary

Study of the new IMP lubiprostone in the paediatric population suffering on functional constipation. This study is one of the studies proposed in the PIP. The study will be conducted in 9 EU member states, USA and Canada.

Study objective

To assess the long-term safety, efficacy, and pharmacokinetics of oral lubiprostone 12 or 24 mcg capsules dosed twice daily (BID) when administered orally for 36 weeks in paediatric subjects with functional constipation. Evaluation of lubiprostone safety is the primary objective of this study.

Study design

Multicentre, open, double-blind for 36 weeks.

Intervention

Treatment with 12 or 24 mcg of lubiprostone 2 times daily for 36 weeks.

Study burden and risks

RISKS:
no favorable clinical effects, occurence of adverse events (most likely nausea)

BURDEN:
donation of blood samples for PK analysis and serum biochemistry, undergoing physical examinations, undergoing DXA scans

BENEFITS:
Relief from signs and symptoms of functional constipation (increase of SBMs, decrease of bloating and straining, improvement
of stool consistency, increase of quality of life)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Written informed consent obtained from subject and/or parent/legal guardian (and assent from subject where applicable).
2. Subject must have completed the entire 12-week treatment period from the preceding study (SAG/0211PFC-1131) prior to enrolment.
3. Subject must continue to abstain from taking concomitant medication (prescribed or over-the-counter) that affects gastrointestinal motility; these medications include:
a. Cholinesterase inhibitors; anti-spasmodic, anti-diarrheal, anti-constipation, or prokinetic agents; laxative agents (e.g., PEG 3350), including homeopathic remedies;
b. Tricyclic antidepressants; or
c. Any medication, at the discretion of the Investigator, known to cause constipation or constipation-related symptoms.
Exceptions: Treatment with anticholinergic agents, SSRIs, SNRIs, or MAO inhibitors is allowed if a stable dose has been used for at least 30 days prior to the Baseline Visit (of the preceding study SAG/0211PFC-1131) and not likely to change during the study.
4. Subject (and if necessary, parent/legal guardian) must be willing and able to use or administer recommended (rectal and/or oral) rescue medications if needed.
5. If subject is taking a fibre supplement (e.g., Metamucil®, PerDiem®, Fybogel), usage must have been at a stable dose not likely to change during the study.
6. Subject and his/her parent/legal guardian must be willing and able to fill out his/her own diary.

Exclusion criteria

1. Subject has current evidence of untreated faecal impaction.
2. Subject has experienced an adverse event during the SAG/0211PFC-1131 study which the Investigator considers to be clinically significant and would limit the subject*s ability to

participate in the trial.
3. Subject has had a significant change in their medical status, newly diagnosed and uncontrolled cardiovascular, liver or lung disease, neurologic or psychiatric disorder, or other systemic disease, which the Investigator considers to be clinically significant and would limit the subject*s ability to participate in the trial.
4. Subject has developed abnormal laboratory test (haematology, urinalysis, or blood chemistry), which in the Investigator*s opinion is clinically significant, unexplained, and would limit the subject*s ability to participate in the trial.
5. Subject (female of childbearing potential) has a positive pregnancy test, refuses/unwilling to undergo pregnancy testing, and/or does not agree to use protocol-specified contraceptive measures for the duration of the study.
6. Subject demonstrated non-compliance with study protocol (i.e., dosing schedule, visit schedule, diary completion, or study procedures) during the SAG/0211PFC-1131 study.

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):	04-03-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	Lubiprostone

Ethics review

Approved WMO Date:	02-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2013-004384-31-NL
CCMO	NL47314.018.14