A Phase 3, Randomized, Placebo-controlled, Multicenter, Double-blind Study to Evaluate the Safety and Efficacy of Telotristat Etiprate (LX1606) in Patients with Carcinoid Syndrome

Published: 13-01-2014
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Primary Study Objective: To evaluate the effect of telotristat etiprate versus placebo over the double-blind portion of the study on the incidence of treatment-emergent adverse events (TEAEs)

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON41701

Source
ToetsingOnline

Brief title
LX1606-303 TELECAST

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
Carcinoid tumor; Carcinoid Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Lexicon Pharmaceuticals Inc.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: LX1606-303, Phase 3, TELECAST, Telotristat etiprate

Outcome measures

Primary outcome

The primary efficacy endpoint is the change from Baseline in the number of

daily BMs averaged over a 12-week treatment period.

Safety endpoints are as follows:

• Incidence of TEAEs, suspected adverse reaction, AEs leading to

discontinuation from the study, SAEs, and deaths

• Actual and change from Baseline in clinical laboratory results

• Actual and change from Baseline in vital signs results

• Actual and change from Baseline in physical examinations

• Actual and change from Baseline in ECG findings

Secondary outcome

Secondary efficacy endpoints include:

• Change from Baseline in the number of daily bowel movements (BMs) averaged

over a 12-week treatment period

• Change from Baseline in stool consistency, as measured by the Bristol Stool

Form Scale averaged across all time points

• Change from Baseline in the number of cutaneous flushing episodes

• Change from baseline in abdominal pain averaged across all time points

• Change from baseline in the frequency of rescue short-acting SSA is used to

treat CS symptoms

• Change from Baseline in the number of daily BMs averaged over the 12-week

treatment period and at each study week, among patients who are not on an SSA

background at Baseline

Study description

Background summary

Currently, no approved therapy exists for the treatment of symptoms driven by underlying serotonin pathophysiology of CS in patients whose disease is refractory to SSA therapy.

For patients with carcinoid syndrome who do not receive SSA therapy either because of its extensive side effects or requirement for frequent intramuscular injections. With protocol LX1606-303 it is for this group of patients appropiate to participate in research.

(See Protocol LX1606.303 section 3.4 Rationale for Study Design and Control Groups)

Study objective

Primary Study Objective: To evaluate the effect of telotristat etiprate versus placebo over the double-blind portion of the study on the incidence of treatment-emergent adverse events (TEAEs)

Study design

The study will be conducted as a Phase 3, randomized, placebo controlled,parallel-group, multicenter, double-blind study in patients with CS, to evaluate 2 oral dose levels of telotristat etiprate, 250 and 500 mg given 3 times daily (tid), versus placebo.

Patients will enter into a Screening/Run-in Period of at least 3 weeks to establish baseline symptoms. During the Run-in Period, no changes to SSA therapy may occur. Patients on SSA therapy will continue to receive stable-dose

SSA therapy; those not currently receiving SSA therapy will remain without SSA therapy in order to establish baseline characteristics and symptomatology. For the purposes of this study, stable-dose SSA therapy is defined as long acting release (LAR) Depot, or a continuous subcutaneous infusion via a pump at an fixed dosisregime for at least 3 months prior to the Run-in Period. Following the Screening/Run-in Period, eligible patients will be randomly assigned (1:1:1) to 1 of the 3 arms, see protocol LX1606.303 section 5. Investigational Plan Table 5.1-1 for a tabular study dosing overview.

No changes to SSA therapy will be permitted during the double-blind Treatment Period (12 weeks), with the exception of the use of rescue, short-acting SSA. All patients must remain on their baseline therapy during the Treatment Period. Upon completion of the Treatment Period, patients will enter the Extension Period of this study (36 weeks).

Intervention

Three arms are used and there will be 2 different doses of Telotristat etiprate :
- arm 1 (Placebo): 2 tablets, 2x Placebo, will be administered 3 times a day
- arm 2 (250 mg): 2 tablets, 1x 250 mg Telotristat etiprate and 1x Placebo, will be administered 3 times a day
- arm 3 (500 mg): 2 tablets, 2x 250 mg Telotristat etiprate, will be administered 3 times a day

In this way all patients will actually take 2 tablets 3 times a day.

Study burden and risks

Patients taking part in this study may have an improvement of response on their current Carcinoid Syndrome treatment, this can outweighs any potential risks or burden for patients participating. We hope LX1606 will be effective in treating carcinoid syndrome compared to the standard treatment; Information from this study will help us learn more about LX1606 as a treatment for carcinoid syndrome. Information from this study could help future carcinoid syndrome patients.

Contacts

Public
Lexicon Pharmaceuticals Inc.

Technology Forest Place 8800
The Woodlands TX 77381

US
Scientific
Lexicon Pharmaceuticals Inc.

Technology Forest Place 8800
The Woodlands TX 77381
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients >=18 years of age at the time of the Screening visit;2. Patients (males and females) of reproductive potential must agree to use an adequate method of contraception (defined as having a failure rate of less than 1% per year) during the study and for 12 weeks after the follow-up visit. Adequate methods of contraception for patient or partner include condoms with spermicidal gel, diaphragm with spermicidal gel, coil (intrauterine device), surgical sterilization, vasectomy, oral contraceptive pill, depot progesterone injections, progesterone implant, and abstinence during the study and for 12 weeks after the Follow-up visit. Note: For females, childbearing potential is defined as those who have not undergone surgical sterilization, or those who are not considered postmenopausal. Postmenopause is defined as absence of menstruation for at least 2 years. If necessary, folliclestimulating hormone (FSH) results >50 IU/L at Screening are confirmatory in the absence of a clear postmenopausal history.;3. Histopathologically-confirmed, well-differentiated metastatic neuroendocrine tumor (NET) confirmed by CT, MRI or radionuclide imaging;4. Documented history of CS and meeting 1 of the following 2 criteria:;• If currently receiving LAR/Depot/infusion SSA therapy for the treatment of CS, must be currently receiving a stable dose, averaging less than 4 Bowel movements (BMs) per day, and must have >=1 of the following sign/symptoms of CS:
a)Daily stool consistency of type>=5 on Bristol Stool Form Scale (Appendix D in Protocol) for equal or greater than 50% of the days during the Run-in, or
b) Average daily flushing frequency of >=2, or

c) Average daily rating of >=3 for abdominal pain, or
d) Nausea present >=20% of days, or
e) u5-HIAA > ULN;• If not currently receiving SSA therapy, must have >=1 of the following sign/symptoms of CS:
a) Daily stool consistency of type >=5 on Bristol Stool Form Scale (Appendix D of protocol) for equal or greater than 50% of the days during the Run-in, or
b) Average daily flushing frequency of >=2, or
c) Average daily rating of >=3 for abdominal pain, or
d) Nausea present >=20% of days, or
e) u5-HIAA > ULN, or
f) Currently averaging >=4 BMs per day;5. Patient is able and willing to provide written informed consent prior to participation in any study-related

Exclusion criteria

Patients who meet any of the following criteria will be excluded from participating in the study:
1. Presence of diarrhea attributed to any condition(s) other than CS including, but not limited to, fat malabsorption or bile acid malabsorption;2. Presence of >12 watery BMs per day associated with volume contraction, dehydration, or hypotension compatible with a "pancreatic cholera"-type clinical syndrome, as judged by the Investigator;3. Positive stool examination for enteric pathogens, pathogenic ova or parasites, or Clostridium difficile at Screening;4. Karnofsky Performance Status <=60% (see Appendix C);5. Clinical laboratory values for hematology (at Screening):
• Absolute neutrophil count (ANC) <=1500 cells/mm3; or
• Platelets <=75,000, cells/mm3; or
• Hemoglobin (Hgb) <=9 g/dL for males and <=8 g/dL for females;6. Hepatic laboratory values (at Screening) such that:
• Asparate transaminase (AST) or alanine aminotransferase (ALT):
a. >=5.5 x ULN if patient has documented history of hepatic metastases,or
b. >=2.5 x ULN if patient does not have documented history of hepatic metastases
• Total bilirubin >1.5 x ULN (unless patient has a ocumented history of Gilbert's Syndrome); or
• Alkaline phosphatase (ALP) >=5 x ULN, if total bilirubin is >ULN
a. No upper limit on the ALP value if the total bilirubin is <=ULN;7. Serum creatinine >=1.5 x ULN;8. Treatment with any tumor-directed therapy including, but not limited to: interferon, chemotherapy, mTOR inhibitors <4 weeks prior to Screening, or hepatic embolization, radiotherapy, radiolabelled SSA,and/or tumor debulking <12 weeks prior to Screening;9. Major surgery defined as procedures requiring general anesthesia or major regional anesthesia within 8 weeks prior to Screening;10. A history of short bowel syndrome (SBS);11. Current complaints of constipation or history of chronic or idiopathic constipation within 2 years prior to Screening;12. Positive pregnancy test or pregnant or nursing (lactating) (female patients only);13. Life expectancy <12 months from the Screening visit;14. Presence of any clinically significant findings at Screening medical history, or physical examination (relative to patient population) that, in the Investigator's or

Medical Monitor's opinion, would compromise patient safety or the outcome of the study;15. Any other clinically significant laboratory abnormality at Screening that would compromise patient safety or the outcome of the study;16. Clinically significant cardiac arrhythmia, bradycardia, or tachycardia that would compromise patient safety or the outcome of the study;17. A history of substance or alcohol abuse (DSM-IV Criteria for Substance-Related Disorders12) within 2 years prior to Screening;18. Administration of any investigational agent within 30 days of Screening or investigational therapeutic protein or antibody within 90 days prior to Screening;19. Patients who are currently committed to an institution by virtue of an order issued either by judicial or administrative authorities

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-02-2015
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Telotristat etiprate
Generic name:	Telotristat etiprate

Ethics review

Approved WMO Date:	13-01-2014
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	01-10-2014
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	12-03-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	13-07-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	16-12-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	17-12-2015

Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	EUCTR2013-001543-31-NL
ClinicalTrials.gov	NCT02063659
CCMO	NL47073.015.13