Phase 2a, Double-Blind, Placebo-Controlled, 2-Period, 2-Treatment, Crossover Study to Evaluate the Safety, Efficacy and Pharmacokinetics of Multiple Oral Doses of XPF-001 (400 mg bid) in Patients with Inherited Erythromelalgia

Published: 15-12-2009
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• To evaluate the safety and efficacy of multiple doses of XPF-001 (400 mg bid) for relief of pain in patients with IEM.• To evaluate the efficacy of multiple doses of XPF-001 (400 mg bid) for relief of vasomotor signs in patient with IEM.• To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac and vascular disorders congenital
Study type	Interventional

Summary

ID

NL-OMON34941

Source
ToetsingOnline

Brief title
XPF-001-202

Condition

- Cardiac and vascular disorders congenital
- Peripheral neuropathies
- Vascular disorders NEC

Synonym
acromelalgia, Mitchell's disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 2month trial, erythromelalgia (IEM), pain relief, sodium channel blocker

Outcome measures

Primary outcome

Efficacy:

Efficacy measures will include the PINRS, CRS and REL scales.

The PINRS is an 11-point scale to measure pain intensity (0 - 10: 0 = no pain;

10 = pain as bad as you can imagine).

The CRS is a 4-point scale to measure pain severity (none, mild, moderate,

severe)

The REL is a 5-point scale to measure pain relief (none, a little, some, a lot,

and complete).

If rescue measures/rescue medication is administered before any of the

scheduled observation time points, the PINRS, CRS, REL, and/or GE should be

completed immediately before administration of rescue measures or medication.

Onset of analgesia will be measured following each morning and evening dose

using 2 stopwatches (Stopwatches 1 and 2). Both stopwatches will be started at

the time of dose administration (Time 0). Stopwatch 1 will be stopped when any

pain relief is first perceived and Stopwatch 2 will be stopped when pain relief

becomes meaningful to the subject.

Safety:

Safety evaluations will include medical history, physical examination, vital signs, ECGs, laboratory tests, and AEs.

The Principal Investigator will discuss any questionable medical conditions, abnormal laboratory findings, and/or ECG findings with the Medical Monitor before a patient with such findings is enrolled.

AEs will be recorded when they occur.

Clinical Laboratory Evaluations (serum chemistry, haematology, and urinalysis) will be performed at specific timepoints (see protocol).

The GE is a 5-point scale to measure global evaluation of study drug (poor, fair, good, very good or excellent). The GE will be completed on Days 1 and 7at the completion of each Treatment Period.

Pharmacokinetic:

Blood samples (2 mL each) for PK assessment will be obtained at specific timepoints (see protocol).

Secondary outcome

NA (see primary parameters)

Study description

Background summary

The hypotheses is that the multiple doses of the IMP (400 mg bid) will provide an overall efficacy that is greater than placebo and that it will provide a longer period of pain relief than placebo.
It concerns a research study with an experimental drug called XPF 001, a drug

that blocks signals to the brain that control pain.
The trial patients concern patients with Inherited Primary Erythromelalgia (IEM). The purpose of this study is to find out:
• If XPF-001 relieves the pain from IEM
• If XPF-001 relieves other symptoms of IEM (e.g. skin temperature and colour changes/redness)
• The effects of XPF-001 on the body and the relationship between drug concentration and its effects.
Due to the small sample number of subject expected to complete the study, statistical methods will not be used to analyze or summarize collected data. Simple graphical presentation and/or descriptive statistics will be used to elucidate any within-subject drug effects, PK/PD relationship and/or overall findings of the study.
Exploratory Study parameters/endpoints:
Group A subjects
• TOTPAR-4 and SPID-4, TOTPAR-6 and SPID-6, TOTPAR-8 and SPID-8
• Time to first perceptible relief (confirmed)
• Time to meaningful relief
• Duration of relief
• Mean PID and REL scores at each observation time
Group B subjects
• Pain Intensity scores
• Duration of pain induction
• Maximum pain intensity scores following induction
• Duration of pain following induction
All subjects
• Time to rescue medication/rescue measures
• Amount of rescue medication/number of rescue measures per day/Treatment Period
• Amount of time rescue medication/measures take to have an effect per day/Treatment Period
• Average total daily dose of rescue medication
• Cumulative percentage of subjects taking rescue medication by each time point
• Percentage of subjects rescuing at 2, 4, 6, 8, 10 and 14 hours post dose (and/or post induction time for Group B subjects)
• Global Evaluation (GE) at the end of each Treatment Period
The pharmacokinetic parameters Cmax, Tmax,, AUC0-*, and other parameters of interest, will be evaluated.

Study objective

• To evaluate the safety and efficacy of multiple doses of XPF-001 (400 mg bid) for relief of pain in patients with IEM.
• To evaluate the efficacy of multiple doses of XPF-001 (400 mg bid) for relief of vasomotor signs in patient with IEM.
• To evaluate the PK profile of XPF-001 and correlate plasma levels of drug to the pharmacodynamic/efficacy endpoints.

Study design

Single-centre, double-blind, placebo-controlled, 2-period, crossover.

Intervention

Eligible subjects will receive multiple doses of Investigational Medicinal Product (IMP) XPF-001 400 mg bid and matching placebo in a randomized sequence under double blind conditions and while resident in the unit. Subjects will receive IMP each morning and evening for 2 consecutive days in each Treatment Period. The two Treatment Periods are separated by a 2 day Washout Period.
Dose and Mode of Administration: XPF-001 400 mg bid; orally administered 100 mg capsules (4 capsules per dose).

Study burden and risks

mentioned earlier

Contacts

Public
Xenon Pharmaceuticals Inc.

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Burnaby, British Columbia
CA
Scientific
Xenon Pharmaceuticals Inc.

Gilmore way, 3650
Burnaby, British Columbia
CA

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects will include males and females 18 - 75 years of age (inclusive), with a BMI between 19.5 and 34.0 kg/m2 (inclusive) who have a clinical diagnosis of Inherited Erythromelalgia (IEM)and an identified SCN9A gene mutation.
Subjects must (either spontaneously, or using one of the protocol-defined pain induction methods) achieve pain scores of
NRS greater or equal to 4, and/or moderate/severe on the CRS, or an intolerable level of pain irrespective of pain scores. Subjects with pain scores lower than 4/moderate will be included at the PI*s discretion, if he believes they will be able to distinguish a change in their level of pain following dosing.
Subjects must be willing to comply with all study procedures, including the stopping use of all medication, including those for pain management between Check-in and Discharge;
Subjects must be in general good health and have no contraindications to the study drug, its ingredients, or the permitted rescue medication.

Exclusion criteria

Subjects with a coexistent source of pain from other conditions that may interfere with the study interpretation;
History or evidence of any condition that, in the opinion of the PI, may pose undue risk to the subject;
Patients with active HIV, Hepatitis C or Hepatitis B, or currently taking medications for any of these conditions;
Use of any prescription or over the counter (OTC) medication or supplement from Check-in until Discharge (except for rescue medication);
Receiving professional psychological support specifically for coping with IEM;
Treatment for significant depression within the 6 months prior to Screening;
Females who are pregnant, lactating, or who test positive on a serum-based pregnancy test at Screening or Check-in;
Not currently undertaking adequate measures to prevent a pregnancy throughout the entire study;
Findings in laboratory data, ECG, vital signs or on physical examination at Screening or Check-in that in the opinion of the PI, may pose undue risk to the subject;
History or presence of alcoholism or alcohol or substance abuse (not including nicotine or caffeine);
Presence or history of major psychiatric disturbance and/or substance abuse, or a positive urine drug test at Check-in;

Ingestion of any caffeine-containing food or beverages (including chocolate) in excess of the permitted 1 cup of caffeine containing beverage per day, between Day -1 until Discharge;
Consumption of alcohol from Check-in until Discharge, or a positive alcohol breath test on Check-in;
Consumption of grapefruit or grapefruit containing products within 7 days of Day 1 until Discharge;
Smoking more than 3 cigarettes per day (or the equivalent in tobacco or nicotine substitutes) within the 1 week prior to ICheck-in, and the inability to refrain from all nicotine use between Check-in and Discharge;
Has taken an investigational drug within the 60 days prior to Day 1;
Donation or loss of whole blood or plasma (excluding the volume of blood that will be drawn during the Screening procedures of this study) prior to Day 1 as follows: 50 mL to 499 mL within 30 days, or more than 499 mL within 56 days prior to drug administration;
Has previously been enrolled into this study;
Study site or Sponsor employee or relative of an employee who is directly involved in the study;
Any other reason that would make the subject, in the opinion of the PI or Sponsor, unsuitable for the study.

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:	Recruitment stopped
Start date (anticipated):	11-03-2010
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Sodium channel blocker
Generic name:	NA

Ethics review

Approved WMO Date:	15-12-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-02-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2009-015619-42-NL

Register	ID
CCMO	NL30053.091.09