A Phase III, Multicentre, Randomised, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Subcutaneous Bioresorbable CUV1647 Implants in Patients with Erythropoietic Protoporphyria (EPP)

Published: 06-05-2008
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The objectives of the study are to evaluate the following in patients with a documented history of EPP:•determine whether CUV1647 can reduce the number of phototoxic reactions in patients with EPP•determine whether CUV1647 can reduce the severity of...

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

Summary

ID

NL-OMON31710

Source
ToetsingOnline

Brief title
Multicentre Phase III EPP Study

Condition

- Metabolic and nutritional disorders congenital

Synonym
EPP, Protoporphyria

Research involving

Human

Sponsors and support

Primary sponsor: Clinuvel Pharmaceuticals Limited
Source(s) of monetary or material Support: Clinuvel Pharmaceuticals Limited

Intervention

Keyword: CUV1647, EPP, Erythropoietic Protoporphyria

Outcome measures

Primary outcome

•Number and severity of phototoxic reactions

Secondary outcome

•Melanin density (measured by spectrophotometry)

•Duration of sunlight exposure, as recorded in patient diary

•Quality of life measured with SF36 questionnaire

•*Time taken to develop provoked symptoms* following phototesting (in a subset of patients only)

•Treatment-emergent adverse events (coded as MedDRA Preferred Terms)

•Changes in hematology, serum chemistry and urinalysis measurements from Screening to Study Days 1, 61, 121, 181, 241 and 301.

Study description

Background summary

The investigational product is a small solid implant containing a mixture of the active ingredient, CUV1647 [(Nle4, D-Phe7)-α-MSH] and polylactic acid. CUV1647 is a synthetic analogue of the naturally occurring melanotropin, α-MSH, an agonist for melanogenesis. The CUV1647 16 mg sustained release implant is administered into the suprailiac crest.

Study objective

The objectives of the study are to evaluate the following in patients with a documented history of EPP:

•determine whether CUV1647 can reduce the number of phototoxic reactions in patients with EPP
•determine whether CUV1647 can reduce the severity of phototoxic reactions in patients with EPP
•determine whether CUV1647 can increase the duration of sunlight tolerated by EPP patients
•determine whether CUV1647 increases melanin density in the skin at several specified body sites
•evaluate the safety and tolerability of CUV1647 by measuring treatment-emergent adverse events (AEs)
•determine whether CUV1647 can improve the quality of life of EPP patients
•in a subset of patients, determine whether CUV1647 implants can reduce the susceptibility to provocation with a standardized light source (time to appearance of provoked symptoms) - this part of the study will not be performed in the Netherlands

Study design

This is a randomized placebo-controlled study to be conducted in two parallel study arms with crossover between treatments every 60 days. Approximately 10 eligible patients per centre will be enrolled and will receive CUV1647 (16 mg implants) or placebo according to the following dosing regime:

- Group A will be administered active implants on Days 0, 120, 240 and placebo implants on Days 60, 180, 300
- Group B will be administered placebo implants on Days 0, 120, 240 and active implants on Days 60, 180, 300

To determine eligibility for study inclusion, patients will undergo a screening evaluation 7 days prior to the administration of the first dose. The number and severity of phototoxic reactions, skin melanin density (measured by spectrophotometry) will be determined at all clinic visits while the duration of sun exposure, treatment-emergent adverse events and the use of rescue medication will be recorded in patient diaries. Quality of life will be measured on Day 0 and again at the end of each treatment period. Participants will visit the clinic on Days 0, 14, 30, 60, 74, 90, 120, 150, 180, 210, 240, 270, 300, 330 and 360 for assessments of adverse events. In addition, follow up home/clinic visits will be scheduled for 24 hours after administration of each implant to collect blood samples for safety and to obtain specimens for urinalysis.
In two of the centers abroad, a subset of the included patients will be

phototested, and a *time taken to develop provoked symptoms* determined on the dorsal surface of one hand. Patients, which will be treated in the Netherlands, will not participate in this additional part of the study.

An Interim Efficacy Analysis will be undertaken after all participants have completed all Day 120 (Part I) requirements and the results of this analysis reviewed by a Data and Safety Monitoring Board or Independent Data Review Committee.

Intervention

Patients will receive CUV1647 (16 mg implants) or placebo according to the following dosing regime:

- Group A will be administered active implants on Days 0, 120, 240 and placebo implants on Days 60, 180, 300
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In two of the centers abroad, a subset of the included patients will be phototested, and a *time taken to develop provoked symptoms* determined on the dorsal surface of one hand. Patients, which will be treated in the Netherlands, will not participate in this additional part of the study.

An Interim Efficacy Analysis will be undertaken after all participants have completed all Day 120 (Part I) requirements and the results of this analysis reviewed by a Data and Safety Monitoring Board or Independent Data Review Committee.

Study burden and risks

Not Applicable

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Male or female subjects with a diagnosis of EPP (confirmed by elevated free protoporphyrin in peripheral erythrocytes)

Exclusion criteria

-Allergy to CUV1647 or the polymer contained in the implant or to lignocaine or other local anaesthetic to be used during the administration of the study medication
-EPP patients with significant hepatic involvement
-Personal history of melanoma or dysplastic nevus syndrome.
-Current Bowen*s disease, basal cell carcinoma, squamous cell carcinoma, or other malignant or premalignant skin lesions.

-Any other photodermatosis such as PLE, DLE or solar urticaria.
-Diagnosed with HIV/AIDS or hepatitis.
-Any evidence of clinically significant organ dysfunction or any clinically significant deviation from normal in the clinical or laboratory determinations.
-Acute history of drug or alcohol abuse (in the last 12 months).
-History of disorders of the gastrointestinal, hepatic, renal, cardiovascular, respiratory, endocrine (including diabetes, Cushing*s syndrome, Addison*s disease, Peutz-Jaegher syndrome), neurological (including seizures), haematological (especially anaemia of less than 10 g/100 mL) or systemic disease judged to be clinically significant by the Investigator.
-Major medical or psychiatric illness.
-Patient assessed as not suitable for the study in the opinion of the investigator (e.g. noncompliance history, allergic to local anaesthetics, faints when given injections or giving blood).
-Female who is pregnant (confirmed by positive serum β-HCG pregnancy test prior to baseline) or lactating.
-Females of child-bearing potential (pre-menopausal, not surgically sterile) not using adequate contraceptive measures (i.e. oral contraceptives, diaphragm plus spermicide, intrauterine device).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-11-2008
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CUV1647
Generic name:	[NLE4-D-Phe7]-&alfa;-melanocyte stimulating hormone

Ethics review

Approved WMO Date:	06-05-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-11-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-01-2010
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
Other	ACTRN012607000261415
EudraCT	EUCTR2007-000636-13-NL
CCMO	NL18784.078.08