A Phase III, randomised, double blind, placebo controlled, parallel group study, to evaluate the safety and efficacy of subcutaneous implants of afamelanotide (16 mg) in patients suffering from polymorphic light eruption (PLE) – Results

Sponsor	**CLINUVEL PHARMACEUTICALS LIMITED**
Finished product	**Test product:** afamelanotide (16 mg implant)
Active substance	Afamelanotide
Name of the trial	A Phase III, randomised, double blind, placebo controlled, parallel group study, to evaluate the safety and efficacy of subcutaneous implants of afamelanotide (16 mg) in patients suffering from polymorphic light eruption (PLE).
Protocol No	CUV032
Countries	Germany, The Netherlands, Belgium
Development phase	Phase 3
Study period	7 months
Objectives	**Primary objectives** -To determine if afamelanotide can reduce the severity of PLE related pruritis **Secondary objectives** -To determine if afamelanotide can reduce the frequency and duration of PLE episodes -To evaluate the effect of afamelanotide on the quality of life of PLE patients -To evaluate the safety and tolerability of afamelanotide by measuring treatment-emergent adverse events
Methodology	This was a phase III, multicentre, randomised, double-blind, placebo-controlled, parallel group study to evaluate the safety and efficacy of subcutaneous implants of afamelanotide (16 mg) in patients suffering from polymorphic light eruption (PLE). To determine eligibility for study inclusion, patients underwent a screening evaluation 7 days prior to the administration of the first dose. Eligible patients were randomised to receive either active (afamelanotide 16 mg) treatment or placebo in a ratio of 1:1 and were treated for a total period of 4 months. Implants (active or placebo) were administered on Day 0 and Day 60. Patients returned to the clinic on Day 120 for the final visit.
Number of patients (planned and analysed)	Approximately 120 eligible patients were planned to be enrolled in total, across all sites. The number of subjects actually enrolled was 31.
Diagnosis and Main Criteria for Inclusion	a) Aged greater than 18 years. b) Male or female patients with a documented history of PLE diagnosed or confirmed by a photodermatologist or photobiologist, with a history of PLE related pruritus symptoms. c) Recurrent PLE episodes that occur at least once a year (as evidenced by PLE related pruritus symptoms) developing in their own country (to exclude patients affected only when traveling to sunnier climates).
Study Treatment	Active: Afamelanotide (16 mg implant) contained in a poly(D,L-lactide-co-glycolide) implant core Placebo: Poly(D,L-lactide-co-glycolide) implant Formulation: subcutaneous resorbable implant formulation
Criteria for Evaluation	*Efficacy Endpoints:* Efficacy was assessed by: -Severity of PLE related pruritus using an 11-point Likert scale -Number of documented episodes of PLE -Duration of PLE episodes -Quality of life using the Dermatology Life Quality Index (DLQI) *Safety and Tolerability Endpoints:* -Type and incidence of treatment-emergent adverse events (TEAEs), including clinically significant changes in laboratory parameters following treatment

Statistical Methods	**<u>Efficacy Analysis</u>** *Primary Efficacy Endpoints* The mean pruritus score for Day 0 to Day 120 was compared between treatments using a non-parametric test. **H0:** there is no difference between patients treated with active and placebo. **H1:** there is more pruritus with patients treated with placebo than active. **<u>Safety and tolerability:</u>** The number of patients with TEAEs (including any clinically significant changes in laboratory parameters) was summarised by MedDRA System Organ Class and Preferred Term for each treatment group. TEAEs were further summarised by severity, seriousness, outcome and relationship to study drug.
Results	**Primary Efficacy Analyses** -The mean and median values of the mean pruritus score were numerically lower in the afamelanotide group. **Secondary Efficacy Analyses** -The mean frequency of PLE episodes was lower in the afamelanotide group. -The median values for the mean duration of PLE episodes were numerically lower in the afamelanotide group. - The mean DLQI score decreased in both treatment groups during the study period. There were no statistically significant differences between the groups at any visit. <u>Safety and tolerability:</u> No deaths, serious adverse events, or adverse events leading to discontinuation of the study were reported during this study.