A Phase II, Multicentre, Double-blind, Placebo Controlled, Pilot Study to Evaluate the Safety and Efficacy of CUV1647 Administered as A Subcutaneous Bioresorbable 16mg Implant in Patients Undergoing Photodynamic Therapy (PDT) utilising Porfimer Sodium – Results

Sponsor	**CLINUVEL PHARMACEUTICALS LIMITED**
Finished product	**Test product:** afamelanotide (16mg implant)
Active substance	Afamelanotide
Name of the trial	A Phase II, Multicentre, Double-blind, Placebo Controlled, Pilot Study to Evaluate the Safety and Efficacy of CUV1647 Administered as A Subcutaneous Bioresorbable 16mg Implant in Patients Undergoing Photodynamic Therapy (PDT) utilising Porfimer Sodium
Protocol No	CUV025
Countries	France
Development phase	Phase 2
Study period	First Subject Recruited: 05 August 2008 Last Subject Completed: 28 May 2009
Objectives	**Main Objective** -To determine whether afamelanotide implants can reduce the period of phototoxicity experienced by patients who have undergone photodynamic therapy with porfimer sodium. **Secondary Objective** -To evaluate the effect of afamelanotide treatment on the quality of life. -To evaluate the safety and tolerability of afamelanotide by measuring treatment-emergent adverse events.
Methodology	This was a phase II, multicentre, double-blind, placebo-controlled, pilot study to evaluate the safety and efficacy of afamelanotide as adjunctive therapy in patients undergoing photodynamic therapy using porfimer sodium. To determine eligibility for entry into the study, patients underwent a screening evaluation prior to photodynamic therapy (PDT) treatment. The amount of time exposed to light and any phototoxicity experienced was recorded in patient diaries commencing at Day 0 (Screening and product administration). Evaluation of phototoxicity upon exposure to light commenced at Day 4, continued at Day 7 and then every 5 days thereafter. Subjects visited the clinic on Day 0 (administration of afamelanotide and porfimer sodium), Day 2 (photodynamic therapy), and Days 20 and 90 for assessments of adverse events, concomitant medication and the results of evaluation of phototoxicity.
Number of patients (planned and analysed)	Up to 30 eligible patients were planned to be enrolled, and to receive either a 16 mg afamelanotide or placebo implant, in this parallel study with test product and placebo assigned double-blind in proportions of 1:1. There were 16 patients who received study treatment (9 afamelanotide, 7 placebo), of whom 8 were eligible for assessment of quality of life (4 afamelanotide, 4 placebo), having completed all 4 questionnaires over the study period.
Diagnosis and Main Criteria for Inclusion	Patients undergoing photodynamic therapy for gastrointestinal cancer using porfimer sodium.

Study Treatment	Afamelanotide 16mg in a subcutaneous resorbable injectable implant formulation or placebo.
Criteria for Evaluation	**Primary Efficacy endpoint**: The first day on which patients are free from dermal symptoms following evaluation of phototoxicity. **Primary Safety Endpoint**: Type and incidence of treatment emergent adverse events.
Statistical Methods	**Efficacy Analysis** The primary efficacy analysis was to compare the mean number of days for patients to be free of phototoxic reactions between treatment groups. The secondary efficacy analysis was change in SF-36 scores over time. Comparisons between treatments of the overall Mental and Physical component scores at each assessment day and the changes from baseline were performed, using a 2-sided t-test, with supporting analyses using Wilcoxon Rank Sum test. **Safety and Tolerability**: Safety and tolerability measures of adverse events, vital signs, and clinical laboratory parameters, are summarised by treatment using descriptive statistics.
Results	**Efficacy and Safety:** -Exploratory analysis of quality of life suggested that the subjects receiving afamelanotide had more favourable post-dose levels of mental health and change in general health, and less bodily pain, than subjects receiving placebo, particularly between Day 20 and Day 60. -Differences were also noted post-dose for role emotional, physical functioning, and the mental component score. However, for these scales, the baseline values also differed similarly between the treatment groups. -Clinical observations from all physicians and reports from patients supported and encouraged further use of afamelanotide in PDT cancer trials. No significant drug-related adverse events were reported.