A Phase II, Randomised, Open Label Pilot Study to Evaluate the Efficacy and Safety of Two Dosage Regimens of Subcutaneous Bioresorbable Afamelanotide Implants in Patients with Mild to Moderate Acne Vulgaris – Results

Sponsor	CLINUVEL PHARMACEUTICALS LIMITED
Finished product	**Test product:** afamelanotide (16 mg implant)
Active substance	Afamelanotide
Name of the trial	A Phase II, Randomised, Open Label Pilot Study to Evaluate the Efficacy and Safety of Two Dosage Regimens of Subcutaneous Bioresorbable Afamelanotide Implants in Patients with Mild to Moderate Acne Vulgaris
Protocol No	CUV100
Countries	Germany
Development phase	Phase 2
Study period	The first subject visit was in August 2010 and the last subject completed the study on 08 March 2011. The study participation period was approximately 84 days for each subject.
Objectives	**Primary:** - To determine the effect of afamelanotide on the facial inflammatory acne-related lesions in patients with mild to moderate acne vulgaris. **Secondary:** - To determine the effect of afamelanotide on the facial total and non-inflammatory acne-related lesions in patients with mild to moderate acne vulgaris; - To determine whether afamelanotide can improve the quality of life of patients with mild to moderate acne vulgaris; - To compare the effect of two dosage regimens of afamelanotide in patients with mild to moderate acne vulgaris; - To determine the safety and tolerability of afamelanotide in patients with mild to moderate acne vulgaris.
Methodology	This was an open label pilot study in patients with mild to moderate acne vulgaris. Patients were allocated to receive afamelanotide (16 mg implant) according to the following regimen: -Group A - afamelanotide implant on Days 0, 21 and 42; -Group B - afamelanotide implant on Days 0 and 28. Clinical evaluations included an acne-related lesions count (total, inflammatory and non-inflammatory lesions). Routine laboratory assessments (haematology, serum chemistry, urinalysis) were performed at Screening and on Days 0, 21 (Group A only), 28 (Group B only), 42 (Group A only) and 56 or Premature Termination (if applicable). The quality of life, using the Dermatology Life Quality Index (DLQI) was measured at Days 0, 7, 14, 21, 28, 35, 42, 49 and 56 or Premature Termination (if applicable). Adverse events and concomitant medication were reviewed at each visit.
Number of patients (planned and analysed)	Approximately 10 eligible patients were planned to be enrolled in total. The number of subjects actually enrolled was 3, of whom 3 completed the study.
Diagnosis and Main	Main inclusion criteria:

Criteria for Inclusion	- Male subjects with a diagnosis of mild to moderate acne vulgaris defined as an Investigator's global assessment (IGA) score of 2-3; - Chronic course of acne vulgaris; - Acne-related lesions both on the face, chest and back; - Indication for treatment of acne vulgaris; - Aged 18-30 years (inclusive); - Fitzpatrick skin types I-III; - Providing written Informed Consent prior to the performance of any study-specific procedure. Main exclusion criteria: - Female subjects; - Diagnosis of severe acne vulgaris; - Allergy to afamelanotide or the polymer contained in the implant or to lidocaine or other local anaesthetic to be used during the administration of the implant; - Use of topical acne medication such as retinoids, benzoyl peroxide or topical antibiotics within 2 weeks prior to the first dose; - Use of oral antibiotics for acne within 4 weeks prior to the first dose; - Use of topical corticosteroids on the face, chest and back or systemic corticosteroids within the past 4 weeks prior to the first dose; - Use of systemic retinoids within 6 months prior to the first dose; - Use of anti-androgenic agents such as finasteride within 4 weeks prior to the first dose; - Use of phototherapy devices for acne such as ClearLight™ or Zenozapper within 1 week prior to the first dose; - Use of tanning booths or lamps within 1 week prior to the first dose; - Active skin disease that may interfere with evaluation; - Other forms of acne such as acne rosacea, acne excoriée, chloracne, acne conglobata, acne fulminans, acne inversa or drug-induced acne; - Participation in a clinical trial for an investigational agent within 30 days prior to the screening visit.
Study Treatment	Active: Afamelanotide (16 mg implant) contained in a poly(D,L-lactide-co-glycolide) implant core Formulation: subcutaneous resorbable implant formulation
Criteria for Evaluation	*Efficacy Endpoints:* Efficacy was assessed by: - The change from baseline to Day 56 in number of facial inflammatory acne-related lesions; - The change from baseline to Day 56 in total number of acne-related lesions; - The change in quality of life as measured by the DLQI. *Safety and Tolerability Endpoints:* Treatment-emergent adverse events (TEAEs) including clinically significant changes in haematology, serum chemistry and urinalysis measurements.
Statistical Methods	**<u>Efficacy Analysis</u>** *Primary Efficacy Endpoints* The percent change in the facial inflammatory acne-related lesions count from baseline to Day 56. This will be done on pooled data from Groups A and B. H_0: there will be no percent change in the facial inflammatory acne-related lesions count following afamelanotide treatment **<u>Safety and tolerability:</u>**

	TEAEs including clinically significant changes in laboratory parameters were to be summarised by MedDRA preferred term and body system for each treatment group. TEAEs were to be further summarised by intensity, seriousness, outcome and relationship to study drug.
Results	Efficacy Analyses Three patients with mild to moderate acne on the face and trunk were recruited. These patients were randomised to treatment arms A or B. Two patients received three injections at 3-week intervals, one patient two injections at 4-week intervals. The number of inflammatory acne lesions in the face declined from day 0 to day 56 (46 ± 30.3 versus 23.7 ± 15.6; means ± SEM) in all patients treated with afamelanotide. The total number of facial acne lesions (inflammatory and non-inflammatory lesions) dropped in all patients from day 0 to day 56 (68 ± 27.6 versus 30 ± 19.7; means ± SEM). Quality of life as measured by DLQI improved in all patients from day 0 to day 56 (7.7 ± 4.7 versus 4.3 ± 2.8; means ± SEM). Safety and tolerability: There were no adverse effects related to afamelanotide except for mild and short-term fatigue in one patient. The other two patients did not report any adverse events related to afamelanotide. There were no clinically important abnormalities in laboratory data.