Sponsor– Novartis	**Web Page/Link to Prescribing/Label Information**– http://www.pharma.us.novartis.com/product/pi.jsp
Generic Drug Name– Pimecrolimus cream 1%	
Therapeutic Area of Trial– Dermatology	
Approved Indication– Mild/moderate atopic dermatitis, >2 yr age	
Study Number– ASM981C2307	
Title– A single-center, open-label study to investigate the relationship between neuropeptide levels and application-site reactions in patients with atopic dermatitis treated twice daily with pimecrolimus cream 1% for a three week period	
Phase of Development–III	
Study Start/End dates– 10-Feb-2003 / 07-Jul-2003	
Study Design/Methodology– Single-center, open-label study. Patient groups were created post-hoc based on whether or not they have experienced skin burning over the course of the study. Neuropeptide levels were analyzed from suction blister fluid from suction blisters generated on treated atopic dermatitis lesional skin on all patients at Baseline, Day 2 and Day 22. All patients received pimecrolimus cream 1% treatment on all skin surfaces affected with atopic dermatitis.	
Centres– 1 (Germany)	
Publication–on-going	
Objectives– *Primary outcome/efficacy objective(s)*– • The primary objective was to investigate the etiology of skin burning in atopic dermatitis (AD) patients treated with pimecrolimus cream 1% by comparing substance P levels in patients reporting skin burning with substance P levels in patients not reporting skin burning at Day 2. *Secondary outcome/efficacy objective(s)*– • To investigate the etiology of pruritus and erythema as application site reactions (ASR) in atopic dermatitis (AD) patients treated with pimecrolimus cream 1% by looking at the relationship between neuropeptide levels (in particular that of substance P) and increase of respectively, pruritus and erythema, at application site after application of pimecrolimus cream 1% • To examine the profile of neuropeptides (in particular that of substance P) over the course of the study in patients reporting skin burning versus patients not reporting skin burning at Day 2 **Test Product, Dose, and Mode of Administration**– Pimecrolimus cream 1% was supplied in tubes and applied topically, twice daily to affected areas.	
Reference Product(s), Dose(s), and Mode(s) of Administration– None	
Criteria for Evaluation– *Primary efficacy:* Efficacy variables were the Investigator's Global Assessment (IGA) of atopic dermatitis and the total body surface area affected (TBSA) at baseline to determine eligibility, even though demonstrating efficacy of pimecrolimus was not an objective of this exploratory safety study. The primary objective was the hypothetical involvement of substance P in the etiology of skin burning, in AD patients treated with pimecrolimus cream. *Secondary efficacy:* The etiology of pruritus and erythema as well as the profile of neuropeptides	

over the course of the study were investigated as secondary objectives.

Safety/tolerability: Other safety variables were adverse events, serious adverse events and physical examination.

Other: N/A

Pharmacology: not applicable

Statistical Methods– Data was summarized with respect to demographic and baseline characteristics, efficacy observations and measurements, safety observations and measurements. All analyses were descriptive and no p-value was calculated. There were no interim analyses performed.

Study Population: Inclusion/Exclusion Criteria and Demographics– Outpatients of either gender or race, aged = 18 years with three or more major and three or more minor features of atopic dermatitis (AD), with a baseline Investigator's Global Assessment (IGA) score of "2, 3 or 4" corresponding to mild to severe atopic dermatitis, and with a minimum of 15% of Body Surface Area affected including trunk and upper extremities with at least three AD lesions of comparable severity with at least a minimum diameter of 10 cm either on the trunk or upper arms.
Patients treated with phototherapy affecting their dermatitis within 1 month prior to first use of study medication were excluded, as were patients who received topical therapy within 7 days, systemic corticosteroids within 1 month, or systemic antibiotics or antihistamines within 2 weeks, or radiation therapy, systemic cytostatics or immunosuppressives within 24 weeks prior to first use of study medication. Pregnant or breastfeeding females were excluded as were women of childbearing potential without a medically approved method of contraception.

Number of Subjects	Pimecrolimus cream 1%	
Planned N	25	
Randomised n	24	
Completed n (%)	24	
Withdrawn n (%)	0	
Included in the primary analysis n (%)	0	
Withdrawn due to adverse events n (%)	0	
Withdrawn due to lack of efficacy n (%)	0	
Withdrawn for other reasons n (%)	0	
Demographic and Background Characteristics		
N (ITT)	24	
Females:males	15:9	
Mean age, years (SD)	33.1 (12.3)	
Mean weight, kg (SD) Race White n (%) Black n (%) Asian n (%) Other n (%)	n.a. 24 0 0 0	

Primary Efficacy Result(s)–intent to treat population

Change and percent change from baseline in substance P level by visit	Pimecrolimus cream 1% Non-burner (N=14)	Pimecrolimus cream 1% Burner (N=10)

and burning classification as defined at	Mean (SD)	Mean (SD)
Day 2	41.7 (28.8)	62.7 (30.6)
Baseline (Visit 1)	38.5 (25.3)	47.0 (15.3)
Day 2	-0.8 (34.1)	-15.7 (25.2)
Change from Baseline	11.64 (95.505)	-1.12 (76.462)
% Change from Baseline	44.2 (26.67)	50.0 (26.44)
Day 22	2.9 (41.40)	-12.7 (40.81)
Change from Baseline	27.90 (107.10)	44.74 (234.87)
% Change from Baseline		
Secondary efficacy result(s)–intent to treat population		
Change and percent change from baseline in substance P level by visit and pruritus classification as defined at	Pimecrolimus cream 1% Non-pruritus (N=14)	Pimecrolimus cream 1% Pruritus (N=10)
	Mean (SD)	Mean (SD)
Day 2	51.1 (31.99)	49.5 (30.71)
Baseline (Visit 1)	45.6 (27.33)	37.8 (10.16)
Day 2	-3.9 (34.51)	-11.7 (26.60)
Change from Baseline	-6.78 (68.814)	19.14 (102.09)
% Change from Baseline	41.8 (25.05)	53.1 (27.42)
Day 22	-9.6 (42.25)	3.6 (40.19)
Change from Baseline	-17.38 (51.226)	94.55 (240.55)
% Change from Baseline		
Change and percent change from baseline in substance P level by visit and pruritus classification as defined at Day 2	No patients were classified with erythema at Day 2. The change and percent change from baseline in substance P level by visit for non-erythema patients is identical to the data presented in primary efficacy results for the total population.	
Safety Results		
Patients with Adverse Events and Adverse Events by System Organ Class		
Patients studied n (%)	**Pimecrolimus cream 1%**	
Total no. with AEs	10 (41.7)	
Significant events		
AEs leading to premature discontinuation	0	
AEs leading to interruption of study drug	0	
System organ class		
Eye disorders	1 (4.2)	
Gastrointestinal disorders	1 (4.2)	
Infections and infestations	2 (8.3)	
Injury, poisoning and procedural complications	1 (4.2)	
Nervous system disorders	2 (8.3)	
Respiratory, thoracic and mediastinal disorders	1 (4.2)	
Skin and subcutaneous tissue disorders	2 (8.3)	
Infections and infestations	1 (4.2)	
Skin and subcutaneous tissue disorders	2 (8.3)	

10 Most Frequently Reported AEs Overall by Preferred Term	Pimecrolimus cream 1%	
Headache	3 (12.5)	
Herpes simplex	3 (12.5)	
Conjunctivitis allergic	1 (4.2)	
Diarrhea NOS	1 (4.2)	
Dyspnea	1 (4.2)	
Photosensitivity reaction NOS	1 (4.2)	
Sunburn	1 (4.2)	
Urticaria NOS	1 (4.2)	
Serious Adverse Events and Deaths		
Patients studied Serious events Deaths	24 0 0	
Other Relevant Findings–		
Date of Clinical Trial Report–	12-Jan-2004	
Date Inclusion on Registry–	17 Dec 2004	
Date of Latest Update–	Aug 2005	