Sponsor–Novartis	**Web Page/Link to Prescribing/Label Information**– http://www.pharma.us.novartis.com/product/pi.jsp
Generic Drug Name–Pimecrolimus	
Therapeutic Area of Trial– Atopic dermatitis	
Approved Indication–Atopic dermatitis	
Study Number–ASM981 C2322	
Title– A 4-week, randomized, multicenter, double-blind, vehicle-controlled, parallel-group clinical trial to evaluate the efficacy and safety of pimecrolimus cream 1% in the short-term treatment of patients with mild to moderate Atopic Dermatitis (Eczema)	
Phase of Development–III	
Study Start/End dates– 18-Jan-2004 through 30-Aug-2004	
Study Design/Methodology– This was a multicenter, randomized, double-blind, parallel controlled clinical study in children and adults with mild to moderate atopic dermatitis (AD), affecting at least 5% total body surface area (TBSA), to investigate efficacy and safety of pimecrolimus cream 1% compared to its vehicle when used b.i.d for 4 weeks. **Centres**– This study was performed at 7 sites in one country (China).	
Publication– Ongoing	
Objectives– *Primary outcome/efficacy objective(s)*– • To investigate the efficacy of pimecrolimus cream 1% in the reduction of the IGA to 0 or 1 compared to vehicle after 4 weeks of double-blind treatment in both adult and pediatric patients with mild to moderate Atopic Dermatitis (Eczema) in China. *Secondary outcome/efficacy objective(s)*– • To explore the efficacy of pimecrolimus cream 1% in the overall EASI score, the IGA (head/neck), and the pruritus assessments, after 4 weeks of treatment compared to its vehicle. • To investigate the safety and tolerability of pimecrolimus cream 1% by testing the hypothesis of comparable rates of adverse events during 4 weeks of treatments with pimecrolimus cream 1% and its vehicle.	
Test Product, Dose, and Mode of Administration– Pimecrolimus cream 1% was supplied in 50g tubes and applied as a thin film b.i.d. on the affected areas as needed for the entire duration of the treatment phase of the study. The interval between two administrations was 12 hours. **Reference Product(s), Dose(s), and Mode(s) of Administration**– Vehicle cream was supplied in 50g tubes and applied as a thin film b.i.d. on the affected areas as needed for the entire duration of the treatment phase of the study. The interval between two administrations was 12 hours.	
Criteria for Evaluation– *Primary efficacy:* Overall Investigator's Global Assessment (IGA) *Secondary efficacy:* Head and neck IGA score; Eczema Area and Severity Index (EASI) score; Pruritus severity assessment; Subjective score of the subject/attendant; Assessment of other signs and symptoms of atopic dermatitis (eczema) *Safety/tolerability:* Safety evaluation comprised observation and recording of all adverse events, severe adverse events (and the relationship between severity and the trial drug) and pregnancy. Hematology, blood biochemistry and urinalysis were regularly monitored in the central laboratory. Vital symptoms, physical exam results and body weight were also evaluated. *Other:* not applicable *Pharmacology:* not applicable	

Statistical Methods– The primary objective of the study was to compare the efficacy and safety of pimecrolimus cream 1% and vehicle in the treatment of patients with atopic dermatitis (eczema). The null hypothesis was that there was no difference in the proportions of treatment success (IGA=0 or 1) between pimecrolimus cream 1% and vehicle group. If greater efficacy of pimecrolimus cream 1% could be proven with two-sided a=5% as statistical significance test level, the null hypothesis was rejected. In addition, the secondary objective of the trial also required assessing short-term safety and tolerance of pimecrolimus cream 1%.

Study Population: Inclusion/Exclusion Criteria and Demographics–Patients aged 2 to 17 years with mild to moderate AD affecting at least 5% of total body surface area (TBSA) were enrolled. Excluded were females of childbearing potential using inadequate contraception or who were pregnant or breastfeeding; treatment with topical therapy having an effect on AD applied within 7 days prior to first study drug application; treatment with any systemic corticosteroid or leukotriene antagonist during one month preceding first study drug application; treatment with phototherapy or immunosuppressants or cell growth inhibitors during one month preceding first study drug application; HIV positive subjects; immunocompromised subjects; skin conditions that interfere with study evaluation; any investigational therapy; hypersensitivity to ingredients of study medication.

Number of Subjects	Pimecrolimus cream 1%	Vehicle
Planned N	150	150
Randomised n	168	168
Completed n (%)	160 (94.24)	142 (84.52)
Withdrawn n (%)	8 (4.76)	26 (15.48)
Included in the primary analysis n (%)	168	168
Withdrawn due to adverse events n (%)	1 (0.6)	4 (2.38)
Withdrawn due to lack of efficacy n (%)	4 (2.38)	16 (9.52)
Withdrawn for other reasons n (%)	3 (1.8)	6 (3.58)
Demographic and Background Characteristics		
N (ITT)	168	168
Females:males	57:111	70:98
Mean age, years (SD)	21.05 (13.94)	19.07 (13.33)
Mean weight, kg (SD)	53.22 (20.04)	49.10 (20.57)
Race White n (%) Black n (%) Asian n (%) Other n (%)	 0 0 168 (100) 0	 0 0 168 (100) 0
Body height, cm (SD)	169.08 (8.17)	168.12 (7.87)

Primary Efficacy Result(s)–intent to treat population

Change of IGA in comparison with baseline n (%)	Pimecrolimus cream 1%	Vehicle
Baseline, p=1.0000	2.61 (0.49)	2.61 (0.49)
Week 1-baseline, p<0.0001	-0.38 (0.55)	-0.06 (0.46)
Week 2-baseline, p=0.0001	-0.52 (0.67)	-0.21 (0.57)
Week 4-baseline, p<0.0001	-0.82 (0.87)	-0.39 (0.86)

Secondary efficacy result(s)–intent to treat population		
IGA success rate n (%)	Pimecrolimus cream 1%	Vehicle
Week 1, p=0.0152	26 (22.03)	13 (10.83)
Week 2, p=0.0207	38 (32.20)	24 (20.00)
Week 4, p=0.0233	54 (45.76)	38 (31.67)
Change of IGA (head/neck)in comparison with baseline, Mean (SD)		
Baseline stage, p=0.7244	1.68 (1.20)	1.66 (1.17)
Week 1-baseline, p=0.0259	-0.27 (0.64)	0.04 (0.63)
Week 2-baseline, p=0.0201	-0.44 (0.77)	-0.11 (0.69)
Week 4-baseline, p=0.0330	-0.64 (0.95)	-0.29 (0.90)
Change of EASI score compared to baseline, Mean (SD)		
Baseline stage, p=0.9450	20.05 (9.47)	20.12 (8.69)
Week 1-baseline, p=0.0096	-4.26 (4.84)	-1.73 (5.12)
Week 2-baseline, p=0.0435	-6.91 (6.84)	-4.90 (6.92)
Week 4-baseline, p=0.0014	-9.31 (8.57)	-5.84 (8.45)
Change of pruritus compared to baseline, Mean (SD)		
Baseline stage, p=0.5193	2.22 (0.60)	2.27 (0.56)
Week 1-baseline, p<0.0001	0.71 (0.77)	-0.33 (0.73)
Week 2-baseline, p=0.0001	-0.88 (0.79)	-0.61 (0.78)
Week 4-baseline, p<0.0001	-0.99 (0.93)	-0.64 (0.91)

Safety Results		
Patients with Adverse Events and Adverse Events by System Organ Class		
No. of patients studied	168	168
No. (%) of patients with AEs	47 (28.0)	55 (32.7)
AEs suspected related to study drug	33 (19.6)	41 (24.4)
AEs leading to termination of trial	1 (0.60)	5 (2.98)
AEs of various systems		
Digestive system damage	1 (0.60)	0 (0.00)
Respiratory system damage	1 (0.60)	0 (0.00)
Urinary system damage	0 (0.00)	1 (0.60)
Metabolism and nutritional disturbance	1 (0.60)	0 (0.00)
Dysfunction of nervous system	1 (0.60)	0 (0.00)
Skin and appendant damage	31 (18.45)	40 (23.81)

10 Most Frequently Reported AEs Overall by Preferred Term Skin-related AEs during the trial period	Pimecrolimus cream 1%	Vehicle
Erythema/swelling	15 (8.93)	19 (11.3)
Tenderness at the application site	7 (4.17)	4 (2.38)
Pruritus/aggravation of pruritus	7 (4.17)	9 (5.36)
Burning sensation	6 (3.57)	4 (2.38)
Folliculitis	4 (2.38)	0 (0.00)
Rubeosis	1 (0.60)	0 (0.00)

Infection	1 (0.60)	0 (0.00)
Asteatosis cutis	1 (0.60)	4 (2.38)
Aggravation of rash	1 (0.60)	4 (2.38)
Desquamation	1 (0.60)	3 (1.79)
Serious Adverse Events and Deaths		
No. of patients studied	168	168
SAEs	0 (0.00)	1 (0.60)
Deaths	0 (0.00)	0 (0.00)
Other Relevant Findings–		
Date of Clinical Trial Report–	Dec 2004	
Date Inclusion on Registry– **Date of Latest Update–**	Aug 2005 Aug 2005	