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 Chronic hand dermititis
Approved Indication Investigational
Study Number CASM981M2301
Title A 6-week randomized, multicenter, double-blind, placebo-controlled, parallel group study to investigate the efficacy and safety of pimecrolimus cream 1% in patients with mild to moderate chronic hand dermatitis, followed by a 6-week open-label phase to assess the safety of pimecrolimus cream 1%
Phase of Development Phase III
Study Start/End Dates 02 Jul 2004 to 02 May 2005
Study Design/Methodology This was a randomized, multicenter, placebo controlled, parallel group study to investigate the safety and efficacy of pimecrolimus cream 1%. The 6-week double-blind phase of the study was followed by a 6-week open label phase.
Centres 57 centers in 7 countries: Austria (4), Canada (5), Denmark(7), Hungary (5), Italy (8), Norway (4), United States (24).
Publication Ongoing
Objectives **Primary outcome/efficacy objective(s)** To compare the efficacy of pimecrolimus cream 1% to that of placebo after 6 weeks of treatment in patients with mild to moderate chronic hand dermatitis (CHD) of the entire hand. **Secondary outcome/efficacy objective(s)** 1. to determine the safety and tolerability of pimecrolimus cream 1% in patients with mild to moderate chronic hand dermatitis when treated for up to 12 weeks; 2. to monitor the continued effects of pimecrolimus cream 1% in the management of CHD when used uncontrolled for up to an additional 6 weeks; 3. to measure work productivity loss of patients with mild to moderate chronic hand dermatitis.
Test Product (s), Dose(s), and Mode(s) of Administration Pimecrolimus cream 1% was supplied in 50 g tubes. Study medication was to be topically applied twice daily to all affected areas on both hands, at the same time each day and 12 hours apart. The evening application of study medication was to be immediately followed by occlusion with vinyl gloves for at least 6 hours.
Reference Product(s), Dose(s), and Mode(s) of Administration Placebo cream was supplied in 50 g tubes and applied in the same manner as

pimecrolimus cream 1%.

Criteria for Evaluation

Primary efficacy:

The primary efficacy variable was the Investigators Global Assessment (IGA) of the entire target hand at day 43 or at the time of early discontinuation. Treatment success was defined as achieving an IGA score of 0 or 1 (clear or almost clear of disease) of the entire target hand.

Secondary efficacy:

Secondary efficacy variables that were assessed at each study visit during the double-blind (DB) and open-label (OL) phases included: overall IGA of the non-target hand, pruritus/burning assessment for the target and non-target hands, and non-key signs of hand dermatitis (vesiculation, oozing/crusts, edema/papulation, lichenification).

Safety/tolerability:

Safety was assessed by monitoring and recording all adverse events, and monitoring vital signs, physical condition and local tolerability of the target and non-target hands.

Pharmacology:

No pharmacokinetic assessments were performed in this study.

Other:

Work Productivity and Activity Impairment questionnaire

Statistical Methods

The primary objective of this study was to compare the efficacy of pimecrolimus cream 1% to that of placebo after 6 weeks of treatment in patients with mild to moderate chronic hand dermatitis (CHD) of the entire hand. A null hypothesis of no difference between the proportion of patients achieving treatment success in the pimecrolimus cream 1% and placebo group was tested at the two-sided 5% significance level using the Cochran-Mantel-Haenszel test (stratified by baseline IGA score and pooled investigator center). Stratification of patients was required by baseline IGA score (mild or moderate) within each investigator center so that half of the randomized (mild or moderate) patients would receive pimecrolimus cream in the study. No interim analysis was planned or performed.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria

- Patients who are outpatients at baseline (Day 1).
- Patients must be 18 years of age or above.
- Patients must have chronic hand dermatitis based upon clinical diagnosis with mild to moderate dermatitis of the target hand at baseline, as defined by an Investigator's Global Assessment score of 2 (mild) or 3 (moderate). The target hand is defined as the more severely affected hand when both hands (mild to moderate CHD) are involved. If both hands are equally affected the "dominant" hand will be documented as the target hand.
- Patients must have been informed of the study procedures and medication and have given their written informed consent.

Exclusion criteria

A patient must not be enrolled in the study if any of the following apply:

- Women who are pregnant or who are breast-feeding. Women of child-bearing potential must follow a medically recognized form of contraception. "Medically recognized" contraception may, at the investigator's discretion, include abstinence.
- Patients who have received systemic corticosteroids (i.e., oral, intravenous, intra-articular, rectal, intramuscular) within one month prior to first application of study medication. Patients on a stable maintenance dose of inhaled or intranasal steroids for asthma or rhinitis may participate.
- Patients who have received phototherapy (e.g., UVB, PUVA) or systemic therapy (e.g., immunosuppressants, cytostatics) known or suspected to have an effect on hand dermatitis within at least one month prior to first application of study medication.
- Patients who have received pimecrolimus cream 1% or tacrolimus ointment 0.1% or 0.03% within 14 days prior to first application of study medication.
- Patients who were treated with topical therapy (e.g., tar, topical corticosteroids, Burrows solution soaks) known or suspected to have an effect on hand dermatitis within 7 days prior to first application of trial medication.
- Patients who have received systemic antibiotics for infections of the hand within one week prior to the first application of study medication.
- Patients who have had prior treatment with any medication (e.g. bexarotene, herbal medicines, etc.) or therapeutic modality known by the investigator to have a probable influence on the treatment outcome or the evaluations for efficacy and safety within 7 days of application of study medication.
- Patients who participated in study ASMB 009 or ASMB 306 (prior studies with pimecrolimus cream 1% in the treatment of chronic hand dermatitis).
- Patients who have received an investigational drug within eight weeks prior to the first application of trial medication or intend to use other investigational drugs during the course of this study.
- Patients who have dyshidrotic dermatitis of the hand with positive KOH and/or culture from clinically observed dermatitis of the feet.
- Patients who are immunocompromised (e.g., lymphoma, AIDS, Wiskott-Aldrich Syndrome) or have a history of malignant disease including skin cancer in the treatment areas.
- Patients who have psoriasis (exhibiting acute or chronic inflammatory signs) of the hands based on clinical assessment.
- Patients who have concurrent flaring of atopic dermatitis (exhibiting acute or chronic inflammatory signs) anywhere on the body outside the study areas since the hand dermatitis may be associated with this flare.
- Patients who have concurrent skin diseases in the study area that requires concomitant topical treatment (e.g., tinea manuum, scabies, infected eczema, paronychia) that could interfere with the evaluation of their dermatitis.
- Patients allergic to latex gloves and are unable to abstain from their use (due to profession or any other reason). Those patients allergic to latex and are unable to abstain from latex gloves and have had a positive latex RAST [radioallergosorbent test] within the past 2 years.
- Patients with known hypersensitivity to any of the ingredients in pimecrolimus cream or placebo.

- Patients with a history of drug and/or alcohol abuse, mental dysfunction or other factors limiting their ability to cooperate fully.
- Uncooperative patients, who are unlikely to follow medical instructions, be compliant with medical treatment or who are not willing to attend regular visits.
- Patients with any other condition that, in the opinion of the investigator, would render the patient ineligible for the trial.

Number of Subjects

Double-blind phase

	Pimecrolimus cream	**Placebo**
Planned N	296	296
Randomised n	325	327
Completed n (%)	277 (85.2)	278 (85.0)
Withdrawn n (%)	48 (14.8)	49 (15.0)
Withdrawn due to adverse events n (%)	10 (3.1)	14 (4.3)
Withdrawn due to unsatisfactory therapeutic effect (%)	14 (4.3)	23 (7.0)
Withdrawn for other reasons n (%)	24 (7.4)	12 (3.7)
Open-label phase		
Entered open-label phase n	269	275
Completed n (%)	248 (92.2)	264 (96.0)
Withdrawn n (%)	21 (7.8)	11 (4.0)
Withdrawn due to adverse events n (%)	4 (1.5)	0 (0.0)
Withdrawn due to unsatisfactory therapeutic effect (%)	11 (4.1)	3 (1.1)
Withdrawn for other reasons n (%)	6 (2.2)	8 (2.9)

Demographic and Background Characteristics

	Pimecrolimus cream	**Placebo**
N (Safety Population)	325	327
Females:males	1.50:1	1.81:1
Mean age, years (SD)	43.9 (14.4)	44.1 (15.1)
Mean weight, kg (SD)	77.2 (17.4)	76.4 (17.9)
Race White n (%) Black n (%) Asian n (%) Other n (%)	 293 (90.2) 6 (1.8) 7 (2.2) 19 (5.8)	 302 (92.4) 4 (1.2) 3 (0.9) 18 (5.5)

Primary Efficacy Result(s)

Treatment success based on target hand IGA by visit in double-blind phase (ITT population, Last Observation Carried Forward [LOCF])

CRF visit	**Pimecrolimus cream N=325**	**Placebo N=327**	**p-value [1]**
Day 8	12 (3.7)	12 (3.7)	0.9736
Day 15	29 (8.9)	29 (8.9)	0.8912
Day 22	48 (14.8)	50 (15.3)	0.7817

Day 29	64 (19.7)	50 (15.3)	0.1026
Day 36	72 (22.2)	62 (19.0)	0.3256
Day 43	97 (29.8)	76 (23.2)	0.0573

[1] Cochran-Mantel-Haenszel test of proportions using baseline IGA scores and center as stratification factors.

Secondary efficacy result(s)

Summary of dichotomized pruritus/burning by visit – target hand during double-blind phase (ITT population, LOCF)

Variable	Pimecrolimus Cream		Placebo		Treat-ment effect p-value (1)	Homo-geneity of odds p-value (2)	Odds ratio (3)	95% CI for odds ratio
CRF visit	Success (%)	N	Success (%)	N				
Pruritus								
Day 8	233 (71.7)	325	212 (64.8)	327	0.0259	0.9267	1.48	(1.05, 2.09)
Day 15	243 (74.8)	325	220 (67.3)	327	0.0210	0.9146	1.51	(1.06, 2.14)
Day 22	257 (79.1)	325	221 (67.6)	327	0.0005	0.9718	1.92	(1.33, 2.76)
Day 29	261 (80.3)	325	226 (69.1)	327	0.0005	0.7494	1.93	(1.33, 2.80)
Day 36	275 (84.6)	325	230 (70.3)	327	<.0001	0.8401	2.49	(1.67, 3.69)
Day 43	272 (83.7)	325	238 (72.8)	327	0.0004	0.9779	2.05	(1.38, 3.05)
Burning								
Day 8	279 (85.8)	325	267 (81.7)	327	0.0943	0.3859	1.43	(0.94, 2.19)
Day 15	281 (86.5)	325	273 (83.5)	327	0.2190	0.9640	1.33	(0.85, 2.08)
Day 22	295 (90.8)	325	281 (85.9)	327	0.0399	0.8682	1.67	(1.02, 2.72)
Day 29	292 (89.8)	325	279 (85.3)	327	0.0667	0.5045	1.56	(0.97, 2.52)
Day 36	294 (90.5)	325	281 (85.9)	327	0.0550	0.8135	1.62	(0.99, 2.65)
Day 43	295 (90.8)	325	283 (86.5)	327	0.0639	0.6330	1.60	(0.97, 2.63)

*Success defined as pruritus/burning assessment score of 0 or 1;(1) Effect of treatment from Cochran-Mantel-Haenszel general association test stratified by baseline IGA and pooled center;(2) Homogeneity of odds ratio assessed by Breslow-Day test;(3) Mantel-Haenszel estimator.

Summary of dichotomized pruritus/burning by visit – non-target hand during double-blind phase (ITT population, LOCF)

Variable	Pimecrolimus Cream		Placebo		Treat-ment effect p-value (1)	Homo-geneity of odds p-value (2)	Odds ratio (3)	95% CI for odds ratio
CRF visit	Success (%)	N	Success (%)	N				
Pruritus								
Day 8	254 (78.2)	325	237 (72.5)	327	0.0464	0.3665	1.46	(1.00, 2.11)
Day 15	267 (82.2)	325	249 (76.1)	327	0.0256	0.8645	1.57	(1.06, 2.33)
Day 22	277 (85.2)	325	246 (75.2)	327	0.0005	0.7474	2.05	(1.36, 3.08)

Day 29	273 (84.0)	325	251 (76.8)	327	0.0100	0.7174	1.69	(1.13, 2.53)
Day 36	281 (86.5)	325	255 (78.0)	327	0.0018	0.7273	1.95	(1.28, 2.97)
Day 43	280 (86.2)	325	264 (80.7)	327	0.0432	0.9851	1.57	(1.02 2.41)
Burning								
Day 8	289 (88.9)	325	279 (85.3)	327	0.0992	0.4572	1.48	(0.93, 2.35)
Day 15	291 (89.5)	325	288 (88.1)	327	0.4524	0.7629	1.21	(0.74, 2.00)
Day 22	302 (92.9)	325	291 (89.0)	327	0.0562	0.7492	1.71	(0.98, 2.97)
Day 29	302 (92.9)	325	291 (89.0)	327	0.0561	0.1722	1.69	(0.98, 2.91)
Day 36	300 (92.3)	325	291 (89.0)	327	0.1062	0.7827	1.57	(0.91, 2.69)
Day 43	299 (92.0)	325	292 (89.3)	327	0.1630	0.7665	1.47	(0.86, 2.52)

*Success defined as pruritus/burning assessment score of 0 or 1; (1) Effect of treatment from Cochran-Mantel-Haenszel general association test stratified by baseline IGA and pooled center; (2) Homogeneity of odds ratio assessed by Breslow-Day test; (3) Mantel-Haenszel estimator

Shift table of non-key signs from baseline to endpoint – target hand during double-blind phase (ITT population, LOCF)

Variable			Endpoint Assessment	
Treatment	**Baseline Assessment**	**Total**	**Not Present**	**Present**
Vesiculation				
Pimecrolimus Cream 1%	Not Present	226	206 (91.2)	20 (8.8)
	Present	99	54 (54.5)	45 (45.5)
	Total	325	260 (80.0)	65 (20.0)
Placebo	Not Present	240	213 (88.8)	27 (11.3)
	Present	87	40 (46.0)	47 (54.0)
	Total	327	253 (77.4)	74 (22.6)
Oozing/crusts				
Pimecrolimus Cream 1%	Not Present	200	177 (88.5)	23 (11.5)
	Present	125	64 (51.2)	61 (48.8)
	Total	325	241 (74.2)	84 (25.8)
Placebo	Not Present	215	195 (90.7)	20 (9.3)
	Present	112	41 (36.6)	71 (63.4)
	Total	327	236 (72.2)	91 (27.8)
Edema/population				
Pimecrolimus Cream 1%	Not Present	182	164 (90.1)	18 (9.9)
	Present	143	68 (47.6)	75 (52.4)
	Total	325	232 (71.4)	93 (28.6)
Placebo	Not Present	184	155 (84.2)	29 (15.8)
	Present	143	54 (37.8)	89 (62.2)
	Total	327	209 (63.9)	118 (36.1)
Lichenification				
Pimecrolimus Cream 1%	Not Present	136	115 (84.6)	21 (15.4)
	Present	189	62 (32.8)	127 (67.2)
	Total	325	177 (54.5)	148 (45.5)
Placebo	Not Present	141	119 (84.4)	22 (15.6)
	Present	186	49 (26.3)	137 (73.7)
	Total	327	168 (51.4)	159 (48.6)
Other				

Pimecrolimus Cream 1%	Not Present	284	278 (97.9)	6 (2.1)
	Present	41	16 (39.0)	25 (61.0)
	Total	325	294 (90.5)	31 (9.5)
Placebo	Not Present	293	287 (98.0)	6 (2.0)
	Present	34	12 (35.3)	22 (64.7)
	Total	327	299 (91.4)	28 (8.6)

Endpoint is the last non-missing post-baseline assessment in the double-blind phase, up to and including Day 43.

Shift table of non-key signs from baseline to endpoint – non-target hand during double-blind phase (ITT population, LOCF)

Variable			**Endpoint Assessment**	
Treatment	**Baseline Assessment**	**Total**	**Not Present**	**Present**
Vesiculation				
Pimecrolimus Cream 1%	Not Present	255	235 (92.2)	20 (7.8)
	Present	70	37 (52.9)	33 (47.1)
	Total	325	272 (83.7)	53 (16.3)
Placebo	Not Present	258	240 (93.0)	18 (7.0)
	Present	69	34 (49.3)	35 (50.7)
	Total	327	274 (83.8)	53 (16.2)
Oozing/crusts				
Pimecrolimus Cream 1%	Not Present	233	208 (89.3)	25 (10.7)
	Present	92	49 (53.3)	43 (46.7)
	Total	325	257 (79.1)	68 (20.9)
Placebo	Not Present	246	224 (91.1)	22 (8.9)
	Present	81	34 (42.0)	47 (58.0)
	Total	327	258 (78.9)	69 (21.1)
Edema/population				
Pimecrolimus Cream 1%	Not Present	215	191 (88.8)	24 (11.2)
	Present	110	51 (46.4)	59 (53.6)
	Total	325	242 (74.5)	83 (25.5)
Placebo	Not Present	220	186 (84.5)	34 (15.5)
	Present	107	47 (43.9)	60 (56.1)
	Total	327	233 (71.3)	94 (28.7)
Lichenification				
Pimecrolimus Cream 1%	Not Present	167	140 (83.8)	27 (16.2)
	Present	158	54 (34.2)	104 (65.8)
	Total	325	194 (59.7)	131 (40.3)
Placebo	Not Present	171	146 (85.4)	25 (14.6)
	Present	156	42 (26.9)	114 (73.1)
	Total	327	188 (57.5)	139 (42.5)
Other				
Pimecrolimus Cream 1%	Not Present	287	281 (97.9)	6 (2.1)
	Present	38	21 (55.3)	17 (44.7)
	Total	325	302 (92.9)	23 (7.1)
Placebo	Not Present	298	293 (98.3)	5 (1.7)
	Present	29	9 (31.0)	20 (69.0)

	Total	327	302 (92.4)	25 (7.6)
Endpoint is the last non-missing post-baseline assessment in the double-blind phase, up to and including Day 43.				

Treatment success based on non-target hand IGA by visit in double-blind phase (ITT population, LOCF)

CRF visit	Pimecrolimus Cream N=325	Placebo N=327	p-value [1]
Day 8	92 (28.3)	73 (22.3)	0.0570
Day 15	107 (32.9)	96 (29.4)	0.2476
Day 22	114 (35.1)	109 (33.3)	0.5990
Day 29	128 (39.4)	119 (36.4)	0.4094
Day 36	131 (40.3)	116 (35.5)	0.1726
Day 43	149 (45.8)	125 (38.2)	0.0368

[1] Cochran-Mantel-Haenszel test of proportions using baseline IGA scores and center as stratification factors.

Treatment success based on target and non-target hand IGA by visit in during open label phase (ITT population, observed)

	Pimecrolimus Cream/Pimecrolimus Cream			Placebo/Pimecrolimus Cream		
CRF Visit	N	Target Hand **Success (%)**	Non-Target Hand **Success (%)**	N	Target Hand **Success (%)**	Non-Target Hand **Success (%)**
Week 9	249	68 (27.3)	116 (46.6)	262	81 (30.9)	126 (48.1)
Week 12	267	116 (43.4)	151 (56.6)	273	122 (44.7)	152 (55.7)

WPAI (Work Productivity and activity impairment): Summary statistics and change from baseline during the double blind phase (ITT population)

Question: During the past seven days, how many hours did you miss from work because of problems associated with your Chronic Hand Dermatitis?

	Pimecrolimus Cream (N=325)		Placebo (N=327)	
CRF Visit	At each visit	Change from baseline	At each visit	Change from baseline
Baseline n	221		234	
Mean (SD)	0.9 (5.52)		0.7 (4.27)	
Max	44		40	
Day 22 n	164	156	178	173
Mean (SD)	0.6 (4.29)	-0.7	1.0 (6.05)	0.0 (3.70)

		(4.76)		
Max	40	4	48	35
End of DB phase n	206	198	231	225
Mean (SD)	0.5 (3.02)	-0.5 (5.46)	0.6 (4.41)	-0.2 (3.29)
Max	37	16	40	35

Safety Results

Overall summary of treatment emergent AEs (Safety population)

Parameter	Pimecrolimus cream/ Pimecrolimus cream n (%)	Placebo/ Pimecrolimus cream n (%)	Total n (%)
Double-blind Phase	325	327	652
At least 1 AE	209 (64.3)	218 (66.7)	427 (65.5)
At least 1 local AE	153 (47.1)	161 (49.2)	314 (48.2)
Any drug-related AE	128 (39.4)	123 (37.6)	251 (38.5)
Open label Phase	269	275	544
At least 1 AE	86 (32.0)	84 (30.5)	170 (31.3)
At least 1 local AE	86 (32.0)	84 (30.5)	170 (31.3)
Any drug-related AE	24 (8.9)	24 (8.7)	48 (8.8)

Denominator for each phase is the number of patients who entered that phase. Local adverse event for double-blind phase is any adverse event with site specified as right hand and left hand. Local adverse event for open label phase is any adverse event with site specified as right hand, left hand, head/neck, trunk, upper limbs, lower limbs, or whole body.

Incidence rates of the most common (>= 1% in any treatment group) overall treatment emergent AEs in double-blind phase by preferred term and treatment (Safety population)

	Pimecrolimus cream	Placebo
At least 1 AE	209 (64.3)	218 (66.7)
Application site pruritus	73 (22.5)	69 (21.1)
Application site irritation	69 (21.2)	72 (22.0)
Application site erythema	37 (11.4)	43 (13.1)
Headache	19 (5.8)	21 (6.4)
Application site pain	18 (5.5)	18 (5.5)
Application site warmth	16 (4.9)	11 (3.4)
Application site reaction	14 (4.3)	17 (5.2)
Pruritus	14 (4.3)	16 (4.9)
Nasopharyngitis	12 (3.7)	12 (3.7)
Upper respiratory tract infection	11 (3.4)	11 (3.4)
Influenza	9 (2.8)	8 (2.4)

Dermatitis contact	8 (2.5)	20 (6.1)
Application site perspiration	4 (1.2)	4 (1.2)
Eczema	4 (1.2)	5 (1.5)
Pharyngolaryngeal pain	4 (1.2)	3 (0.9)
Sinusitis	4 (1.2)	2 (0.6)
Skin burning sensation	4 (1.2)	8 (2.4)
Herpes simplex	3 (0.9)	5 (1.5)
Pharyngitis	2 (0.6)	4 (1.2)
Dermatitis	0 (0.0)	4 (1.2)

Serious Adverse Events and Deaths

Number (%) of patients with any serious or significant AEs (Safety population)

Significant AE	Pimecrolimus cream/ Pimecrolimus cream n (%)	Placebo/ Pimecrolimus cream n (%)	Total n (%)
Double-blind Phase	325	327	652
Deaths	0 (0.0)	0 (0.0)	0 (0.0)
At least 1 SAE	2 (0.6)	2 (0.6)	4 (0.6)
Discontinuations due to AE	15 (4.6)	30 (9.2)	45 (6.9)
Dose adjustment or temporary interruption due to AE	7 (2.2)	7 (2.1)	14 (2.1)
Open label Phase	269	275	544
Deaths	0 (0.0)	0 (0.0)	0 (0.0)
At least 1 SAE	1 (0.4)	2 (0.7)	3 (0.6)
Discontinuations due to AE	5 (1.9)	1 (0.4)	6 (1.1)
Dose adjustment or temporary interruption due to AE	2 (0.7)	2 (0.7)	4 (0.7)

Denominator for each phase is the number of patients who entered that phase.

Incidence rates of all treatment emergent serious adverse events during the double-blind phase (safety population)

Primary system organ class Preferred Term	Pimecrolimus Cream (N = 325) n (%)	Placebo (N = 327) n (%)	Total (N = 652) n (%)
Any primary system organ class	2 (0.6)	2 (0.6)	4 (0.6)
Ear and labyrinth disorders	1 (0.3)	0 (0.0)	1 (0.2)
Vertigo	1 (0.3)	0 (0.0)	1 (0.2)
Infections and infestations	0 (0.0)	1 (0.3)	1 (0.2)
Cellulitis	0 (0.0)	1 (0.3)	1 (0.2)

Injury, poisoning and procedural complications	0 (0.0)	1 (0.3)	1 (0.2)
Joint dislocation	0 (0.0)	1 (0.3)	1 (0.2)
Surgical and medical procedures	1 (0.3)	0 (0.0)	1 (0.2)
Triple vessel bypass graft	1 (0.3)	0 (0.0)	1 (0.2)

A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment. A patient with multiple adverse events within a primary system organ class is counted only once.

Incidence rates of all treatment emergent serious adverse events during the open-label phase (safety population)

Primary system organ class Preferred Term	Pimecrolimus Cream (N = 325) n (%)	Placebo (N = 327) n (%)	Total (N = 652) n (%)
Any primary system organ class	1 (0.4)	2 (0.7)	3 (0.6)
Injury, poisoning and procedural complications	1 (0.4)	0 (0.0)	1 (0.2)
Lower limb fracture	1 (0.4)	0 (0.0)	1 (0.2)
Metabolism and nutrition disorders	0 (0.0)	1 (0.4)	1 (0.2)
Dehydration	0 (0.0)	1 (0.4)	1 (0.2)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	0 (0.0)	1 (0.4)	1 (0.2)
Papillary thyroid cancer	0 (0.0)	1 (0.4)	1 (0.2)

A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment. A patient with multiple adverse events within a primary system organ class is counted only once.

Date of Clinical Trial Report

Ongoing.

Date Inclusion on Novartis Clinical Trial Results Database

18 October 2006

Date of Latest Update

18 October 2006