A Randomized, Double-blind, Vehicle-controlled Trial of Luliconazole Cream 1% in the Treatment of Interdigital Tinea Pedis

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ABSTRACT

Objective: To evaluate the efficacy and safety of luliconazole cream 1% applied once daily for 14 days in patients with interdigital tinea pedis. **Design:** Multicenter, randomized, double-blind, parallel-group, vehicle-controlled study. **Setting:** Private dermatology clinics and clinical research centers in the United States and Central America. **Participants:** Three hundred twenty-two male and female patients ≥12 years of age diagnosed with interdigital tinea pedis. **Measurements:** Complete clearance (i.e., clinical and mycological cure), effective treatment, and fungal culture and susceptibility. **Results:** At study Day 42, complete clearance was obtained by a larger percentage (14.0% [15/107] vs. 2.8% [3/107]; $p<0.001$) of patients treated with luliconazole cream 1% compared with vehicle. Also at Day 42, more luliconazole-treated patients compared with vehicle-treated patients obtained effective treatment (32.7% vs. 15.0%), clinical cure (15.0% vs. 3.7%), and mycologic cure (56.1% vs. 27.1%). Erythema, scaling, and pruritus scores were lower for the luliconazole cream 1% group compared with vehicle on Day 14, Day 28, and Day 42. For all species and the same isolates, the MIC50/90 for luliconazole cream 1% was 6- to 12-fold lower than for other agents tested. No patients discontinued treatment because of a treatment-emergent adverse event. **Conclusion:** Luliconazole cream 1% was safe and well-tolerated and demonstrated significantly greater efficacy than vehicle cream in patients with interdigital tinea pedis. (*J Clin Aesthet Dermatol.* 2014;7(10):20–27.)

Interdigital tinea pedis is one of the most common infections reported in the United States and throughout the Americas.[1–3] The incidence of disease has increased progressively since the 1970s.[4] The most common causative agents for this condition include a number of pathogenic dermatophytes that are capable of establishing infections within interdigital skin folds; these include *Trichophyton rubrum* and, less frequently, *Trichophyton mentagrophytes* and *Epidermophyton floccosum*. *Candida* species account for a small fraction of the overall incidence of tinea pedis,[5] typically in patients with diabetes.[6]

Topical therapy is an accepted method for the treatment of tinea pedis, and effective treatment of this condition has been reported with topical application of an azole antifungal agent for 1 to 2 weeks or an allylamine medication for up to four weeks.[1] In patients with tinea pedis in the interdigital or plantar areas, relapse following topical therapy has been attributed to poor patient compliance, persistence of infectious dermatophytes on the skin, and disease recurrence.[7,8]

Some of the newer antifungal therapies for tinea infection require shorter duration of therapy and once-daily treatment.[1] Luliconazole cream 1% is a broad-spectrum, imidazole antimycotic agent that was approved in the United States in 2013 for the treatment of tinea pedis, tinea corporis, and tinea cruris[9]; it had previously been approved in Japan since 2005 for these indications as well as for candidiasis and tinea versicolor. Safety information has been gathered from exposure of more than 10 million patients to this antifungal product in Japan as of April 2011. The objective of this study, which was conducted in the United States and Central America, was to evaluate the efficacy and

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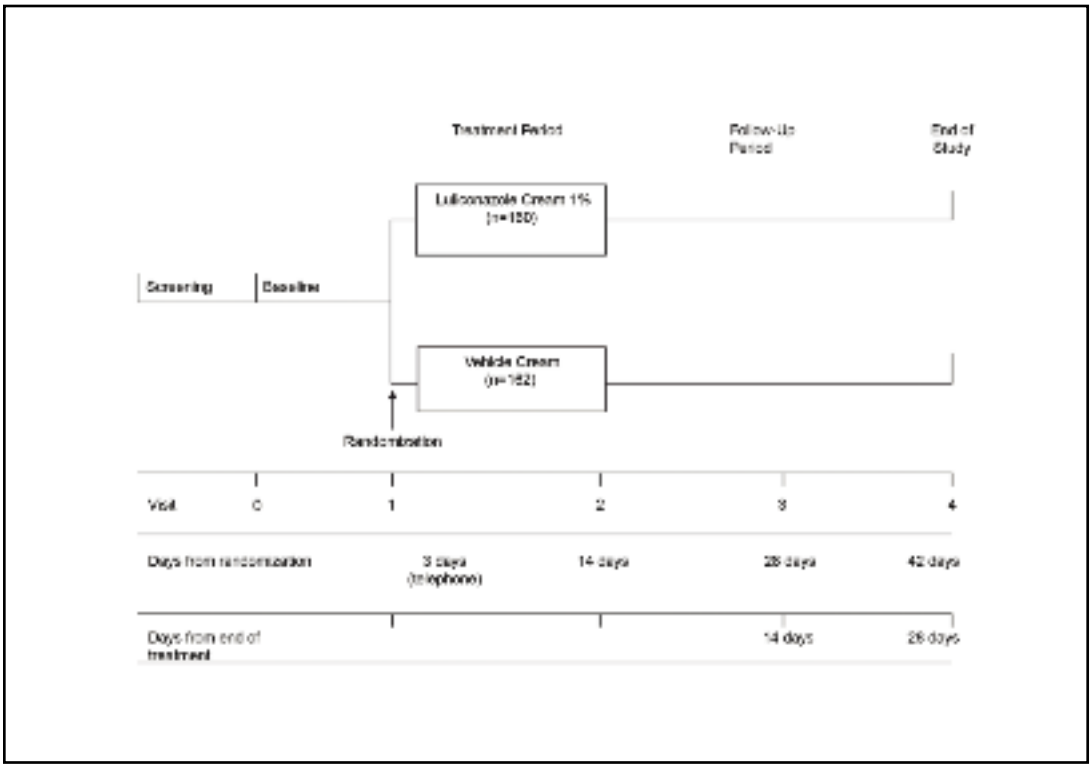

Figure 1. Study design

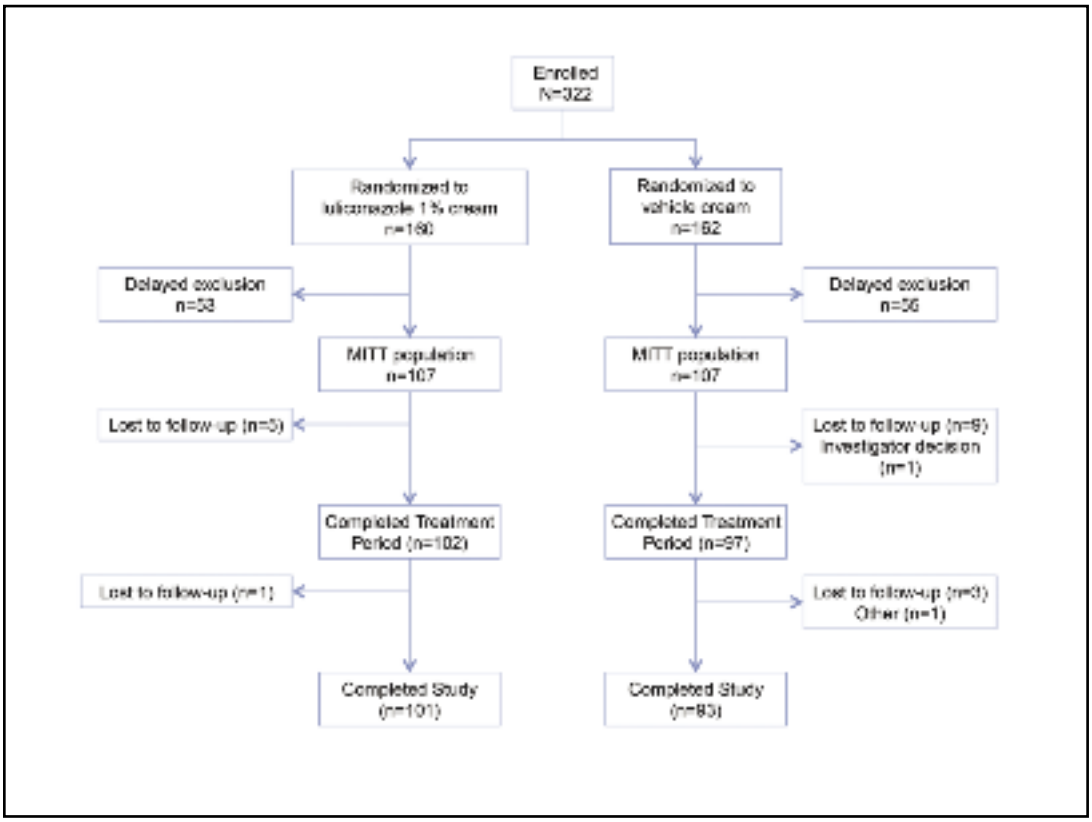

Figure 2. Disposition of patients in MITT population.
MITT=modified intent to treat.

TABLE 1. Patient demographic and baseline characteristics

VARIABLE	LULICONAZOLE CREAM 1%	VEHICLE CREAM	TOTAL
MITT population, n	107	107	214
Age, y			
Mean (SD)	43.7 (14.38)	40.6 (13.35)	42.2 (13.93)
Gender, n (%)			
Male	82 (76.6)	84 (78.5)	166 (77.6)
Female	25 (23.4)	23 (21.5)	48 (22.4)
Ethnicity, n (%)			
Hispanic or Latino	45 (42.1)	45 (42.1)	90 (42.1)
Not Hispanic or Latino	62 (57.9)	62 (57.9)	124 (57.9)
Race, n (%)			
Caucasian	61 (57.0)	50 (46.7)	111 (51.9)
Black or African American	46 (43.0)	56 (52.3)	102 (47.7)
Asian	0	1 (0.9)	1 (0.5)
Geographic location, n (%)			
United States	76 (71.0)	70 (65.4)	146 (68.2)
Central America	31 (29.0)	37 (34.6)	68 (31.8)

MITT=modified intent to treat

TABLE 2. Baseline clinical signs and symptoms and fungal culture characteristics

VARIABLE	LULICONAZOLE CREAM 1%	VEHICLE CREAM	TOTAL
MITT population, n	107	107	214
Fungal organism, n (%)*			
Trichophyton rubrum	84 (78.5)	85 (79.4)	169 (79.0)
Trichophyton mentagrophytes	18 (16.8)	14 (13.1)	32 (15.0)
Epidermophyton floccosum	9 (8.4)	13 (12.1)	22 (10.3)
Other dermatophyte	0	0	0
Erythema, n (%)			
Moderate	98 (91.6)	96 (89.7)	194 (90.7)
Severe	9 (8.4)	11 (10.3)	20 (9.3)
Scaling, n (%)			
Moderate	75 (70.1)	63 (58.9)	138 (64.5)
Severe	32 (29.9)	44 (41.1)	76 (35.5)
Pruritus, n (%)			
Mild	18 (16.8)	13 (12.1)	31 (14.5)
Moderate	66 (61.7)	62 (57.9)	128 (59.8)
Severe	23 (21.5)	32 (29.9)	55 (25.7)

MITT=modified intent to treat
*All patients in the MITT population had positive fungal cultures at baseline. Percentages across fungal types may sum to more than 100% because of the presence of multiple organisms in a given patient.

safety of luliconazole cream 1% applied once daily for 14 days in patients with interdigital tinea pedis.

METHODS

Study design. This was a multicenter, randomized, double-blind, parallel-group, vehicle-controlled study conducted at 12 sites in the United States and two sites in Central America. The protocol and study procedures were approved by an institutional review board at each study center and conducted according to the Declaration of Helsinki, the International Conference on Harmonisation Guidelines for Good Clinical Practice, and local regulations. Patients eligible for treatment were randomized 1:1 in blocks of four to treatment with luliconazole cream 1% or vehicle cream (Figure 1). All study participants provided written informed consent before the initiation of study procedures. This study was registered on ClinicalTrials.gov as NCT01396811 on July 15, 2011.

Study population. *Inclusion criteria.* Patients of both genders ≥12 years of age with a diagnosis of interdigital tinea pedis and signs and symptoms of tinea infection (i.e., at least moderate erythema, moderate scaling, and mild pruritus)

were eligible for enrollment. Women of childbearing potential must have used an effective method of contraception. Patients were required to be in good health and free of disease that in the investigator's opinion might have interfered with the study evaluation.

Exclusion criteria. Patients were excluded if they had moccasin (dry type) tinea pedis, concomitant onychomycosis of the fingernails, concomitant onychomycosis affecting more than three toenails and >3mm in thickness, severe dermatophytoses, or a concurrent tinea infection or bacterial skin infection on the target foot. Exclusion criteria also included use of a topical antifungal agent within 14 days of baseline (30 days for terbinafine, butenafine, and naftifine); use of systemic antifungals within eight weeks or five half-lives of the antifungal before the baseline visit; use of topical antibiotics within 30 days of baseline; use of systemic antibiotics within 30 days or five half-lives of the antibiotic before the baseline visit; use of antibacterial soaps on the affected area within seven days of baseline; or use of a topical corticosteroid within 14 days or systemic or intralesional corticosteroids within 30 days of baseline. Women who were pregnant or nursing or planned to become pregnant during the course of the study were excluded from enrollment in the study. Patients who were immunocompromised or had a history of abuse of drugs or alcohol or a history of intolerance or hypersensitivity to imidazole compounds or the inactive components of the cream were also excluded from enrollment in the study. In addition, patients whose mycologic diagnosis of interdigital tinea pedis was not confirmed by the detection of fungal hyphae on a microscopic potassium hydroxide (KOH) wet mount were excluded post randomization (i.e., delayed exclusions).

Intervention. Patients were randomly assigned to apply luliconazole cream 1% or vehicle cream to affected areas once daily for 14 days. The first application was applied by the patient at the investigational site under the supervision of site staff (Day 0); all subsequent applications were applied by the patient at home based on instructions provided by site staff. Patients were instructed to thoroughly clean and dry the skin and then apply an adequate amount of study medication to cover the entire surface of the forefeet, including all interdigital spaces and approximately 2.5cm of surrounding healthy skin, and to leave the treated area uncovered for five minutes after each application. Patients were permitted to use allowable concurrent medications if their use was kept constant during the study.

Assessments. *Efficacy.* The primary efficacy assessment (clinical and mycologic cure: "complete clearance") and secondary efficacy assessments based on clinical signs and symptoms and mycology were conducted on study Day 42; complete clearance was also assessed on Day 28. Investigators used a 4-point scale (0=none, 1=mild, 2=moderate, 3=severe) at screening, baseline, and on Days 14, 28, and 42 to evaluate erythema and scaling. Patients assessed pruritus as the average severity score during the 24 hours before the study visit using the same 4-point scale. Mycology assessments included microscopic KOH

TABLE 3. Analysis of primary and secondary efficacy endpoints for MITT and PP populations

CLINICAL OUTCOME	LULICONAZOLE CREAM 1%	VEHICLE CREAM	*P*-VALUE*
MITT population, n	**107**	**107**	
Primary efficacy endpoint, n (%)			
Complete clearance, Day 42†	15 (14.0)	3 (2.8)	<0.001
Secondary efficacy endpoints, n (%)			
Day 42			
Effective treatment§	35 (32.7)	16 (15.0)	<0.001
Clinical cure‖	16 (15.0)	4 (3.7)	<0.001
Mycologic cure††	60 (56.1)	29 (27.1)	<0.001
Day 28			
Complete clearance#	10 (9.3)	4 (3.7)	0.055
PP population, n	**66**	**60**	
Primary efficacy endpoint, n (%)			
Complete clearance, Day 42†	11 (16.7)	2 (3.3)	0.004
Secondary efficacy endpoints, n (%)			
Day 42			
Effective treatment§	22 (33.3)	6 (10.0)	<0.001
Clinical cure‖	12 (18.2)	3 (5.0)	0.008
Mycologic cure††	32 (48.5)	15 (25.0)	0.002
Day 28			
Complete clearance#	7 (10.6)	4 (6.7)	0.312

MITT=modified intent to treat; PP=per protocol.
*Cochran-Mantel-Haenszel general association test stratified by analysis center.
†Complete clearance: negative potassium hydroxide and fungal culture results and severity score of 0 (none) for erythema, scaling, and pruritus.
§Effective treatment: negative potassium hydroxide and fungal culture results and severity score of 0 (none) or 1 (mild) for erythema and scaling and 0 (none) for pruritus.
‖Clinical cure: severity score of 0 (none) for erythema, scaling, and pruritus.
††Mycologic cure: negative potassium hydroxide and fungal culture results.
#Complete clearance: negative potassium hydroxide and fungal culture results and "clinical cure."

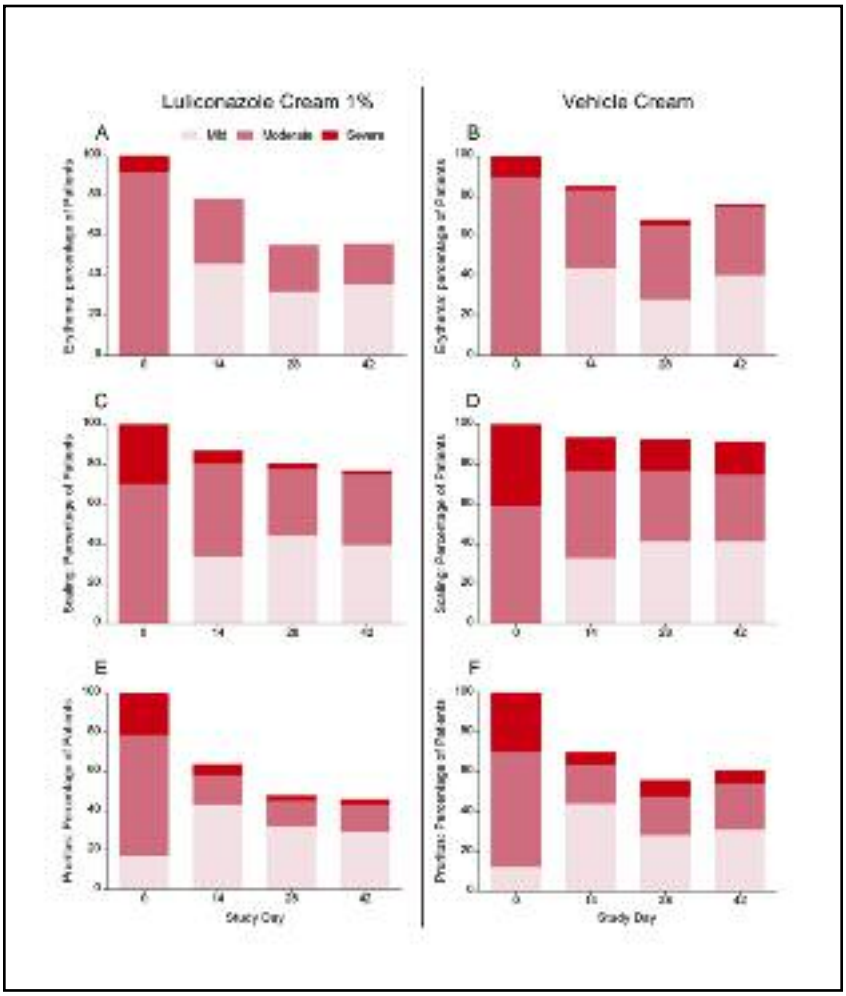

Figure 3. Severity of signs and symptoms of tinea pedis over time in patients in the modified intent-to-treat population treated with luliconazole cream 1% compared with vehicle cream: (A–B) erythema; (C–D) scaling; and (E–F) pruritus. Bar height represents the proportion of patients with the sign/ symptom, and color represents the severity of the sign/symptom.

examination and fungal cultures.

Fungal culture and susceptibility testing. Dermatophytes recovered in skin scrapings were used to compare the antifungal activity (minimum inhibitory concentration [MIC]) of luliconazole compared with terbinafine and itraconazole following standardized methods.[10]

Safety. All treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) occurring during the study, whether or not the event was considered related to treatment, were rated as mild, moderate, or severe; were classified as expected or unexpected; and were categorized according to Medical Dictionary for Regulatory Activities terminology, version 14.0. Safety assessments also included medical history, physical examination, and laboratory tests (i.e., hematology, urinalysis, kidney, and liver tests).

Statistical methods. *Efficacy.* Efficacy was evaluated in a modified intent-to-treat (MITT) population and a per-protocol (PP) population. The MITT population included all patients who were randomized, dispensed medication, and had positive baseline KOH and fungal culture results. The PP population was a subset of the MITT population and included patients who met all inclusion criteria, did not take excluded concomitant medications, completed the Day 28 end-of-treatment and Day 42 evaluations, were compliant with the dosing regimen (i.e., had applied 80–120% of expected dose), and attended the Day 42 evaluation within ±4 days of the visit window. Patients who prematurely discontinued from the treatment phase due to a TEAE or treatment failure were included in the PP population regardless of whether they were compliant with the dosing regimen at the time of discontinuation. The primary efficacy endpoint was the proportion of patients who achieved complete clearance on Day 42, defined as both clinical (i.e., absence of signs and symptoms of tinea pedis) and mycologic cure (i.e., negative KOH test and fungal culture) based on the MITT population. Secondary outcome measures included effective treatment (i.e., negative KOH test and fungal culture and, at most, mild erythema and/or scaling and no pruritus), clinical cure, mycologic cure, and complete clearance at Day 42.

Statistical analysis. Demographic data and baseline disease status were summarized by treatment group and overall using descriptive statistics. Primary and secondary endpoints were summarized using descriptive statistics and analyzed using the Cochran-Mantel-Haenszel general association test, stratified by treatment center. Continuous variables were analyzed using 2-way analysis of variance with factors of treatment and analysis center. Subgroup analyses were conducted on the MITT population stratified by age, gender, ethnicity, race, geographic location, and baseline clinical signs. These analyses were conducted on the MITT and PP populations using descriptive statistics and were restricted to the Day 42 evaluations. Secondary endpoints were analyzed using a step-down approach to account for multiplicity of comparisons. The sample size of the MITT population had 95 percent power to detect a complete clearance success rate of 35.9 percent for the luliconazole cream 1% and 13.2 percent for the vehicle cream using an alpha of 0.05. To accommodate an expected dropout rate of approximately 35 percent, 300 patients (150 per treatment group) were planned for enrollment. All statistical analyses were performed using SAS®, version 9.3 (SAS Institute, Inc., Cary, North Carolina).

Safety. Safety was assessed in all patients who applied at least one dose of study medication.

The extent of exposure to study medication and all TEAEs were summarized using descriptive statistics. TEAEs

that occurred at frequencies ≥1% within a treatment group were compared using the Fisher exact test.

RESULTS

Patient disposition and characteristics. A total of 322 male and female patients were randomized to luliconazole cream 1% (n=160) or vehicle cream (n=162). The first randomized patient was enrolled on July 18, 2011, and the last patient completed the study on January 30, 2012. Delayed exclusion of 53 patients in the luliconazole cream 1% group and 55 in the vehicle cream group resulted in an MITT population of 107 patients in each treatment group (Figure 2). The safety population consisted of 306 patients who met eligibility requirements (luliconazole cream 1%, n=153; vehicle cream, n=153). Patients in the MITT population had a mean age of 42.2 years and most were men (77.6%) and Caucasian (51.9%) (Table 1). The majority of patients (68.2%) were from investigational sites in the United States.

All patients in the MITT population had positive fungal cultures at baseline and the majority tested positive for *T. rubrum* fungal organisms (Table 2). The incidence of different fungal organisms was similar in the luliconazole cream 1% and vehicle cream groups. The majority of patients in the MITT population had moderate erythema (90.7%), scaling (64.5%), and pruritus (59.8%) at baseline (Table 2). No relevant differences were found between luliconazole cream 1% and vehicle cream, except for pruritus scores, which were higher for the latter. There were no relevant differences in demographic and baseline characteristics between patients randomized to luliconazole cream 1% or vehicle cream or between patients from investigational sites in the United States or Central America.

TABLE 4. Summary of primary and secondary endpoints by geographic location (MITT population)

	UNITED STATES		CENTRAL AMERICA	
VARIABLE	LULICONAZOLE CREAM 1% (N=76)	VEHICLE CREAM (N=70)	LULICONAZOLE CREAM 1% (N=31)	VEHICLE CREAM (N=37)
Primary endpoint				
Day 42				
Complete clearance,* n (%)	14 (18.4)	2 (2.9)	1 (3.2)	1 (2.7)
Secondary endpoints				
Day 42				
Effective treatment,† n (%)	25 (32.9)	5 (7.1)	10 (32.3)	11 (29.7)
Clinical cure,‡ n (%)	15 (19.7)	2 (2.9)	1 (3.2)	2 (5.4)
Mycologic cure,§ n (%)	40 (52.6)	12 (17.1)	20 (64.5)	17 (45.9)
Day 28				
Complete clearance,* n (%)	8 (10.5)	3 (4.3)	2 (6.5)	1 (2.7)

KOH=potassium hydroxide; MITT=modified intent to treat.
*Complete clearance: negative KOH and fungal culture results and a severity score of 0 (none) for erythema, scaling, and pruritus.
†Effective treatment: negative KOH and fungal culture results and severity scores of 0 (none) or 1 (mild) for erythema and scaling and 0 (none) for pruritus.
‡Clinical cure: severity score of 0 (none) for erythema, scaling, and pruritus.
§Mycologic cure: negative KOH and fungal culture results.

The PP population consisted of 126 patients (luliconazole cream 1%, n=66; vehicle cream, n=60) who had completed the end-of-treatment and 28 days post-treatment evaluations without remarkable study protocol violations.

Efficacy. *Overall.* Results for the primary efficacy endpoint are summarized in Table 3. Complete clearance on study Day 42 was achieved by a larger percentage (14.0% [15/107] vs. 2.8% [3/107]; $p<0.001$) of patients treated with luliconazole cream 1% compared with vehicle cream. The percentage of patients in the PP population who achieved complete clearance on study Day 42 was consistent with findings from the MITT population.

A significantly larger percentage of patients in the luliconazole cream 1% group compared with the vehicle cream group obtained effective treatment (32.7% vs. 15.0%), clinical cure (15.0% vs. 3.7%), and mycologic cure (56.1% vs. 27.1%) on study Day 42 (Table 3). Complete clearance on study Day 28 was higher for patients treated with luliconazole cream 1% (9.3% vs 3.7%; $p=0.055$) compared with vehicle cream. The percentage of patients in the PP population who achieved complete clearance at Day 42 supported findings from the MITT population (Table 3).

Erythema, scaling, and pruritus scores were lower for the luliconazole cream 1% group compared with the vehicle cream group at Day 14, Day 28, and Day 42, indicating improvements in signs and symptoms associated with tinea pedis infection favored luliconazole cream 1% (Figure 3). There were no substantive effects of gender, age, ethnicity, and race on primary and secondary efficacy endpoints.

Geographic location. Numerical differences were

TABLE 5. Summary of treatment-emergent adverse events occurring in >1% of patients (safety population)

VARIABLE	LULICONAZOLE CREAM 1% (n=153)	VEHICLE CREAM (n=153)
Patients reporting, n (%)		
≥1 AE	20 (13.1)	11 (7.2)
≥1 SAE	0	0
Death	0	0
Discontinued due to AE	0	0
Number of AEs reported	22	13
Maximum severity, n (%)		
Mild	17 (77.3)	9 (69.2)
Moderate	4 (18.2)	4 (30.8)
Severe	1 (4.5)	0
Relationship to study medication, n (%)		
Not related	21 (95.5)	13 (100)
Probably not related	1 (4.5)	0
Possibly related	0	0
Probably related	0	0
Related	0	0
System organ class,* n (%)		
Infections and infestations	6 (3.9)	4 (2.6)
Nervous system disorders	5 (3.3)	2 (1.3)
Gastrointestinal disorders	4 (2.6)	2 (1.3)
Musculoskeletal and connective tissue disorders	2 (1.3)	2 (1.3)
Injury, poisoning, and procedural complications	2 (1.3)	1 (0.7)
Preferred term,* n (%)		
Headache	5 (3.3)	2 (1.3)
Nasopharyngitis	4 (2.6)	3 (2.0)
Influenza	2 (1.3)	0
Toothache	1 (0.7)	2 (1.3)

AE=adverse event; SAE=serious adverse event
***Patients counted once for each system organ class and preferred term**

observed for primary and secondary efficacy endpoints between patients from investigational sites in the United States and Central America (Table 4). A larger percentage of patients from investigational sites in the United States achieved complete clearance (18.4% vs. 3.2%) and clinical cure (19.7% vs. 3.2%) at Day 42 in response to luliconazole cream 1% compared with patients from investigational sites in Central America.

Following treatment with luliconazole cream 1%, similar percentages of patients from investigational sites in the United States and Central America achieved no erythema (44.7% [34/76] vs. 41.9% [13/31]) and no pruritus (52.6% [40/76] vs. 58.1% [18/31]). A larger percentage of patients from investigational sites in the United States achieved no scaling at Day 42 (30.3% [23/76] vs. 6.5% [2/31]) in response to luliconazole cream 1% compared with patients in Central America. The effects of vehicle differed among patients from different geographic regions. When patients were administered vehicle cream, a higher percentage of patients from investigational sites in Central America achieved no erythema (37.8% [14/37] vs. 17.1% [12/70]), no scaling (16.2% [6/37] vs. 4.3% [3/70]), and no pruritus (48.6% [18/37] vs. 34.3% [24/70]) compared with patients in the United States.

Fungal culture and susceptibility testing. Clinical isolates included *T. rubrum, T. mentagrophytes, E. floccosum,* and *Microsporum canis* (n=381). For all species and for the same isolates, the MIC that inhibited 50 percent and 90 percent (MIC50/90) of fungal species was 0.001/0.001µg/mL for luliconazole cream 1%, 0.03/0.06µg/mL for itraconazole, and 0.008/0.015µg/mL for terbinafine.

Safety. The extent of exposure to study medication was similar for patients in the luliconazole cream 1% and vehicle cream groups. Overall, 31 of 306 patients (10.1%) who received at least one dose of study medication experienced at least one TEAE, including 20 of 153 patients (13.1%) randomized to luliconazole cream 1% and 11 of 153 patients (7.2%) randomized to vehicle cream (Table 5). Most TEAEs in the luliconazole cream 1% (77.3%) and vehicle cream groups (69.2%) were mild in severity. All TEAEs were considered not related or probably not related to treatment. The incidence of TEAEs by system organ class and preferred term was similar for patients in the luliconazole cream 1% and vehicle cream groups. No treatment-emergent application site AEs, deaths, or other SAEs were reported. In addition, no patients discontinued treatment because of a TEAE and no unexpected findings were reported for either treatment group.

DISCUSSION

This was a large randomized trial in patients ≥12 years of age in the United States and Central America with interdigital tinea pedis and signs and symptoms of tinea infection. In this study, luliconazole cream 1% demonstrated superior efficacy compared with vehicle cream on the primary efficacy outcome. A significantly higher percentage of patients in the MITT population treated with luliconazole

cream 1% once daily for 14 days achieved complete clearance at Day 42. Luliconazole cream 1% was also favored over vehicle cream in results obtained for the secondary outcomes, including effective treatment, clinical cure, and mycologic cure at Day 42, in addition to complete clearance at Day 28, thus supporting the clinical benefits of luliconazole over vehicle in patients with tinea pedis.

Luliconazole cream 1% was safe and well tolerated when administered once daily for 14 days. The safety profiles for luliconazole cream 1% and vehicle cream were similar, as evidenced by type and frequency of TEAEs. Importantly, no TEAEs were identified as treatment related, there were no deaths or other SAEs, the majority of TEAEs were mild in severity and self-limiting, and no safety signals were identified from clinical laboratory assessments.

The *in vitro* activity (i.e., MIC50/90) of luliconazole demonstrated in this trial is consistent with previous *in vitro* studies,[11,12] Although the *in vitro* activity of luliconazole was more potent than that for terbinafine and itraconazole, further studies may be required to confirm the clinical impact of this finding.

The availability of topical agents that achieve relatively rapid and effective relief may be important in obtaining optimal clinical outcomes in patients with interdigital tinea pedis. The results of this study demonstrate that effective treatment of interdigital tinea pedis with luliconazole cream 1% can be achieved with once-daily application for 14 days, which may enhance compliance and rapid resolution of disease symptoms. It is important to note that using this regimen, relief of signs and symptoms of tinea pedis, a hallmark of clinical benefit in this disease, continued to increase at 2 to 4 weeks post-treatment with luliconazole cream 1% compared with vehicle. Even so, follow-up studies would be needed to clarify the rates of recurrence of tinea pedis infection and the long-term need for retreatment in these patients.

The overall study population included male and female patients in the United States and Central America with active interdigital tinea pedis who would be expected to benefit from luliconazole cream 1%. Although the overall primary endpoint of the study was met, this effect was primarily driven by the larger number of patients enrolled at investigational sites in the United States and the numerically higher percentage of patients from this region who achieved complete clearance. The different response to luliconazole cream 1% by patients in Central America was not unexpected given the differences in humidity, footwear (e.g., barefoot vs. shoes), and overall environment that may make it more difficult to achieve complete clearance of tinea pedis.

The finding that patients in Central America did not fare as well in terms of clinical benefit is, in part, reflected in the greater response to vehicle (e.g., effective treatment, mycologic cure, others) compared with patients in the United States. Achieving clinical benefit among patients in Central America with tinea pedis may be aided by longer duration of treatment and better education on hygienic foot care. A limitation of this study is the relatively small patient population from investigational sites in Central America.

CONCLUSION

This study met the overall primary endpoint. Luliconazole cream 1% applied once daily for 14 days demonstrated significantly greater efficacy than vehicle cream in patients of both genders ≥12 years of age with a diagnosis of interdigital tinea pedis and signs and symptoms of tinea infection. Luliconazole cream 1% was safe and well tolerated with the same safety profile as vehicle cream.

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