

Efinaconazole Solution 10% for Treatment of Toenail Onychomycosis in Latino Patients

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PRACTICE POINTS

- Onychomycosis is a common disease of importance in the increasing Latino population of the United States, especially due to predisposing factors such as obesity and diabetes mellitus. Specific data on the treatment of this patient population are lacking.
- Two large phase 3 studies with topical efinaconazole treatment included a notable number of Latino patients.
- Complete cure rates with efinaconazole in Latino participants were notably greater than those observed in the non-Latino population, and treatment was well tolerated in both groups.
- Treatment of onychomycosis is important to possibly prevent a more serious infectious disease involving the lower extremities, especially in those with comorbidities such as obesity, diabetes, and peripheral vascular disease.

Onychomycosis is a common progressive fungal infection of the nail bed, matrix, or plate leading to destruction and deformity of the toenails and fingernails. The prevalence of onychomycosis is increasing in the United States, particularly in the growing population of Latino patients. In this study, we evaluated the efficacy and safety of efinaconazole solution 10% in Latino patients with onychomycosis. Once-daily application of efinaconazole solution 10% may be an effective topical option for treatment of onychomycosis in this patient population.

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Onychomycosis is a common progressive fungal infection of the nail bed, matrix, or plate leading to destruction and deformity of the toenails and fingernails.^{1,2} It represents up to 50% of all nail disorders^{1,3} with a notable increasing prevalence in the United States.⁴⁻⁶

Latinos represent the largest ethnic minority group in the United States,⁷ which is growing rapidly through immigration, particularly in the southern United States. Prevalence data are limited. An incidence of 9.3% secondary to dermatophytes was recorded in a dermatology clinic setting (N=2000).⁸ Onychomycosis was reported in 31.9% of a group of Latino immigrants in North Carolina (N=518), with higher prevalence in poultry workers, possibly due to the work environment.⁹

Efinaconazole solution 10% was shown to be well tolerated and more effective than a vehicle in a phase 2 study in Mexico.¹⁰ Two identical phase 3 studies of 1655 participants assessed the safety and efficacy of efinaconazole solution 10% in the treatment of onychomycosis.¹¹ This post hoc analysis compares the data for Latino versus non-Latino populations.

Methods

We evaluated the results of 2 multicenter, randomized, double-blind, vehicle-controlled studies that included

a total of 1655 participants with mild to moderate toenail onychomycosis (20%–50% clinical involvement). Participants were randomized to efinaconazole solution 10% or vehicle once daily (3:1) for 48 weeks with a 4-week posttreatment follow-up period.¹¹

Our post hoc analysis included 270 Latino patients, defined as an individual of Cuban, Mexican, Puerto Rican, or South or Central American origin or other Latino culture, regardless of race. In addition, data were compared to the 1380 non-Latino patients in the 2 studies. Patients who were randomized in error and never received treatment were excluded from the intention-to-treat analysis.

Efficacy Evaluation—The primary efficacy end point was complete cure rate (0% clinical involvement of target toenail, and both negative potassium hydroxide examination and fungal culture) at week 52. Secondary end points included mycologic cure, complete/almost complete cure ($\leq 5\%$ clinical involvement of target toenail, mycologic cure), and treatment success ($\leq 10\%$ clinical involvement of target toenail) at week 52.

Safety Evaluation—Safety assessments included monitoring and recording of adverse events (AEs) at every postbaseline study visit through week 52. All AEs were classified using the Medical Dictionary for Regulatory Activities (version 12.1). Treatment-emergent AEs (ie, events that began after the first application of study drug) that occurred during the study were summarized for each treatment group by the number of patients reporting each event, as well as by system organ class, preferred term, severity, seriousness, and relationship to the study drug.

Results

A total of 270 Latino participants with toenail onychomycosis (efinaconazole solution 10%, $n=193$; vehicle, $n=77$) were included in our study. The mean age of participants at baseline was 45.9 years. They were predominantly male (69.6%) and white Latinos

(91.1%). The mean area of target toenail involvement was 36.6%, and the mean number of affected nontarget toenails was 2.5. Latino participants tended to be younger than non-Latino participants (45.9 vs 52.6 years), with a higher proportion of females (30.4% vs 21.3%). Disease severity was similar in both populations. Diabetes was reported in 7.0% and 6.7% of Latino and non-Latino participants, respectively, and mean weight was 83.6 and 86.6 kg, respectively.

Primary Efficacy End Points (Observed Case [OC])—At week 52, 25.6% of Latino participants in the efinaconazole group achieved complete cure versus 0% in the vehicle group ($P<.001$) (Figure 1). The efficacy of efinaconazole was statistically superior in Latino participants versus non-Latino participants (17.2% [$P=.012$]). The net effect (calculated by active treatment minus vehicle) for Latino participants also was superior to non-Latino participants (25.6% vs 11.6%).

Secondary Efficacy End Points (OC)—At week 52, 61.5% of Latino participants in the efinaconazole group achieved mycologic cure versus 15.3% in the vehicle group ($P<.001$) (Figure 2). The net effect for Latino participants was superior to non-Latino participants (46.2% vs 38.5%). More Latino participants in the efinaconazole group compared to vehicle group achieved complete/almost complete cure (32.7% vs 1.7%) or treatment success (49.4% vs 5.1%) (all $P<.001$) (Figure 3). Although there was no significant difference between the 2 groups for secondary efficacy end points, the net effect of efinaconazole was greater for all end points.

Safety—Adverse event rates were higher in the efinaconazole group than the vehicle group (65.3% vs 54.4%) and were similar in both populations; they were generally mild (61.8% vs 54.5%) or moderate (35.3% vs 45.5%) in severity, not related to study medication (96.8% vs 98.0%), and resolved without sequelae. Only 3 Latino participants (1.6%) discontinued efinaconazole treatment compared to 29 (2.8%) in the non-Latino population.

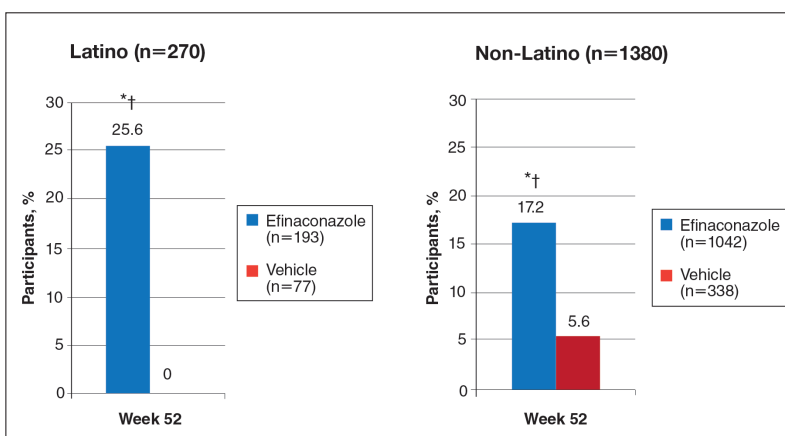


Figure 1. Primary efficacy end point of complete cure at week 52 (intention-to-treat pooled data) for Latino and non-Latino subpopulations. Asterisk indicates $P<.001$ vs vehicle; dagger, $P=.012$ between the 2 efinaconazole groups.

Figure 2. Secondary efficacy end point of mycologic cure at week 52 (intention-to-treat pooled data) for Latino and non-Latino subpopulations. Asterisk indicates $P < .001$ vs vehicle; dagger, $P = .154$ between the 2 efinaconazole groups.

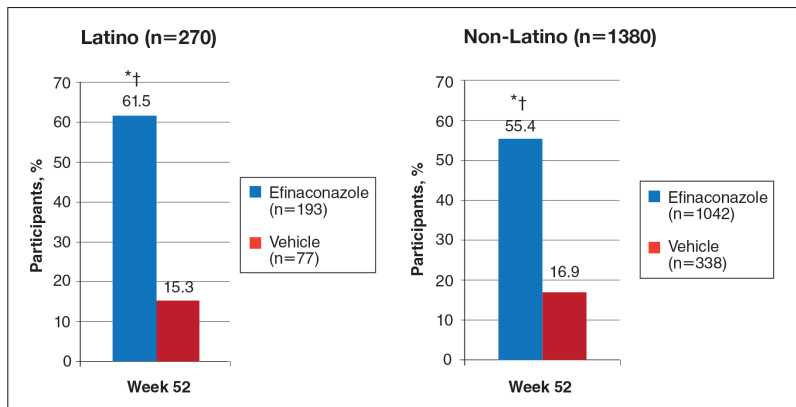
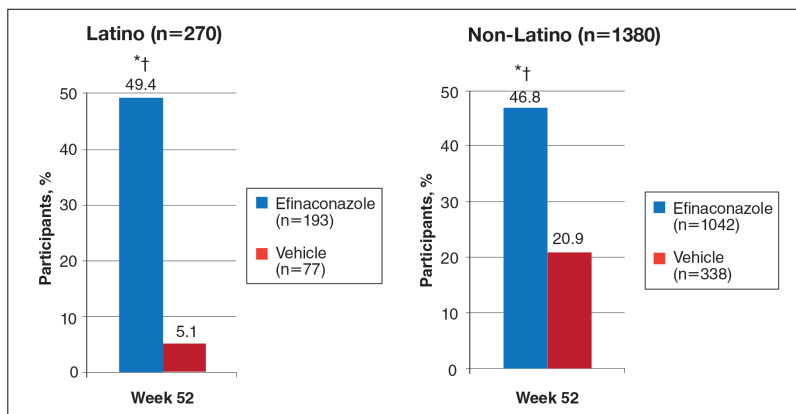


Figure 3. Secondary efficacy end point of treatment success ($\leq 10\%$ clinical involvement of target toenail) at week 52 (intention-to-treat pooled data) for Latino and non-Latino subpopulations. Asterisk indicates $P < .001$ vs vehicle; dagger, $P = .559$ between the 2 efinaconazole groups.



Comment

With the continued growth of the Latino population in the United States and likely higher prevalence of onychomycosis,⁹ this post hoc analysis provides important insights into treatment of onychomycosis in this patient population.

Efinaconazole solution 10% was significantly more effective than vehicle in the Latino population ($P < .001$) and also appeared significantly more effective than the non-Latino population across the 2 phase 3 studies ($P = .012$). Interestingly, complete cure rates (25.6%) were identical to those reported in the phase 2 study of Mexican patients treated with efinaconazole for 36 weeks.¹⁰ Specific data with other topical therapies, such as tavaborole, in Latino patients are not available. One phase 3 study of tavaborole for onychomycosis included 89 Mexican patients (15% of the total study population), but complete cure rates for the overall active treatment group were higher in a second phase 3 study (6.5% vs 9.1%) that did not include participants outside the United States or Canada.¹²

It is not clear why phase 3 efficacy results with efinaconazole appear better in the Latino population. There are a number of predisposing factors for onychomycosis that are important treatment considerations in Latinos. Obesity is an important factor in the development of onychomycosis,¹³ with more than 42% of Latino adults

in the United States reportedly obese compared to 32.6% of non-Latino adults.¹⁴ Obese patients reportedly have shown a poorer response to efinaconazole treatment¹⁵; however, in our analysis, the mean weight of the 2 subpopulations was similar at baseline. Diabetes also is associated with an increased risk for onychomycosis^{16,17} and may be a more important issue in Latinos perhaps due to differences in health care access, social and cultural factors, and/or genetics, as well as the greater incidence of obesity. Prior reports suggest the efficacy of efinaconazole is not substantially influenced by the presence of diabetes,¹⁸ and in our 2 subpopulations, baseline incidence of coexisting diabetes was similar. These factors are unlikely to account for the better treatment success seen in our analysis. Efinaconazole has been reported to be more effective in females,¹⁹ though the reasons are less clear. The higher proportion of female Latinos (30.4% vs 21.3%) in our study may have had an impact on the results reported, though this baseline characteristic cannot be considered in isolation.

When considering the net effect (active minus vehicle), the apparent benefits of efinaconazole in Latino patients with onychomycosis were more marked. Vehicle complete cure rates at week 52 were 0% compared with 5.6% of non-Latino participants. Vehicle cure rates in randomized controlled trials of toenail onychomycosis are relatively low and appear to be independent of the

study characteristics.²⁰ Vehicle cure rates of 2 topical treatments—efinaconazole and tavaborole—reported in their 2 respective phase 3 studies were 3.3% and 5.5% for efinaconazole¹¹ and 0.5% and 1.5% for tavaborole.¹² It has been suggested that the higher results seen with the efinaconazole vehicle relate to the formulation, though there is no reason to expect it to perform differently in a Latino population. It also has been suggested that baseline disease severity might impact vehicle treatment outcome.²⁰ In our analysis, the percentage affected nail at baseline was higher in the Latino participants treated with vehicle (38.9% vs 36.2%).

Although the overall level of AEs was similar in Latino versus non-Latino participants treated with efinaconazole, events were generally milder in the Latino subpopulation and fewer participants discontinued because of AEs.

Our study had a number of limitations. A study period of 52 weeks may be too brief to evaluate clinical cure in onychomycosis, as continued improvement could occur with either longer treatment or follow-up. Also, the pivotal studies were not set up to specifically study Latino participants; the demographics and study disposition may not be representative of the general Latino population.

Conclusion

Once-daily treatment with efinaconazole solution 10% may provide a useful topical option in the treatment of Latino patients with toenail onychomycosis.

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