Efficacy and Safety of Topical Efinaconazole 10% for Onychomycosis: Pooled Phase 3 Trials by Race

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SYNOPSIS

- Onychomycosis—a chronic fungal infection of the nail plate or bed—can cause toenail deformity, discomfort, and pain and interfere with daily activities of living[1,2]
- Although it is a common infection, data from clinical trials for treatment of onychomycosis in patients with skin of color (SoC) are lacking[3]
- It has been suggested that topical efinaconazole 10% solution could be beneficial as a first-line therapy for most patients with onychomycosis, alone or in combination with an oral antifungal[1]
  - Two phase 3, randomized, controlled trials have shown that once-daily efinaconazole is safe and efficacious in participants with mild to moderate toenail onychomycosis[4]
  - Post hoc analyses of these studies demonstrate the efficacy and safety of efinaconazole in diverse patient subgroups based on age, sex, ethnicity, disease severity, and concurrent tinea pedis or diabetes[5-10]

OBJECTIVE

- To evaluate the efficacy and safety of topical efinaconazole in adults self-reporting as White, Asian, or Black/African American with mild to moderate toenail onychomycosis

METHODS

- Data were pooled from 2 multicenter, randomized, double-blind, vehicle-controlled, phase 3 studies (NCT01008033, NCT01007708) of participants aged 18–70 years with mild to moderate distal lateral subungual onychomycosis affecting ≥1 great toenail
  - Participants were randomized (3:1) to once-daily application of efinaconazole 10% solution or vehicle treatment for 48 weeks, with a follow-up visit at week 52
- Efficacy endpoints included complete cure (primary endpoint), complete/almost complete cure, unaffected new toenail growth, mycologic cure, and clinical efficacy (all secondary endpoints) at week 52
- To adjust for multiplicity, sequential interpretation (statistical significance of efinaconazole vs vehicle) was performed on 3 secondary endpoints
  - If complete/almost complete cure rate was significant, then unaffected new toenail growth was tested for significance
  - If unaffected new toenail growth was significant, then mycologic cure was tested for significance
- Treatment-emergent adverse events (TEAEs) were also evaluated
- Pooled participants were categorized by self-reported race: White, Asian, or Black/African American (hereafter referred to as Black) for these post hoc analyses
- These studies were not statistically powered for subgroup analyses

RESULTS

Participants

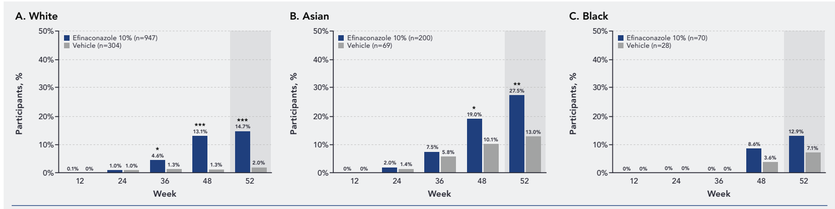
- From the 1,618 pooled participants in the intent-to-treat population, 77.3% were White, 16.6% were Asian, and 6.1% were Black
  - Most participants were male (range, 62%–82%) and not Hispanic (78%–100%)
  - Mean age was approximately 50 years
- Baseline clinical characteristics were generally similar across the 3 race subgroups and treatment groups, including percent affected toenail (mean range, 32%–37%) and number of affected nontarget toenails (mean range, 2.4–3.3)
- Treatment compliance with efinaconazole was >90% in all subgroups

Efficacy

Complete Cure

- At week 52, complete cure rates with efinaconazole were significantly greater vs vehicle in White and Asian participants ($P<0.01$, both; **Figures 1A and 1B**) and numerically greater in Black participants (**Figure 1C**)
  - Significant improvements were seen as early as weeks 36 and 48 for the White and Asian subgroups ($P<0.05$, both), respectively

FIGURE 1. Complete Cure[a] by Participant Race (ITT Population, Pooled)

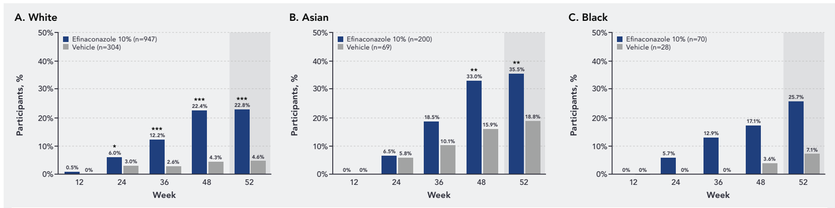


*P<0.05, **P<0.01, ***P<0.001 vs vehicle.
[a]No clinical involvement of the target nail (completely clear nail) + mycologic cure (negative potassium hydroxide examination + negative fungal culture).
Complete cure rates at week 52 with efinaconazole in the overall phase 3 populations were 17.8% and 15.2%.*
ITT, intent to treat.

Complete or Almost Complete Cure

- More efinaconazole- vs vehicle-treated participants achieved complete or almost complete cure at week 52 (**Figure 2**)
  - Significant improvements occurred as early as weeks 24 and 48 for the White and Asian subgroups ($P<0.05$, both), respectively (**Figures 2A and 2B**)
  - Numerically more efinaconazole-treated Black participants achieved complete or almost complete cure vs vehicle at weeks 24–52 (**Figure 2C**)

FIGURE 2. Complete or Almost Complete Cure[a] by Participant Race (ITT Population, Pooled)



*P<0.05, **P<0.01, ***P<0.001 vs vehicle.
[a]Affected target nail area ≤5% + mycologic cure (negative potassium hydroxide examination + negative fungal culture).
Complete/almost complete cure rates at week 52 with efinaconazole in the overall phase 3 populations were 26.4% and 23.4%.[4]
ITT, intent to treat.

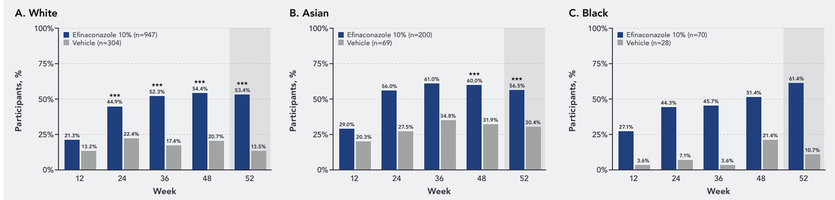
Unaffected New Nail Growth

- White and Asian efinaconazole-treated participants had significantly greater unaffected new nail growth versus vehicle at week 52 (White, 4.0 vs 0.7 mm; Asian, 5.0 vs 1.8 mm; $P<0.001$, both); significance occurred starting at week 24 for White and week 48 for Asian participants ($P<0.001$, both)
- Improvements in unaffected new nail growth with efinaconazole were numerically greater in Black participants at week 52 (3.9 vs 2.1 mm), with numeric differences starting at week 24

Mycologic Cure

- At week 52, over half of all efinaconazole-treated participants achieved mycologic cure vs less than one-third with vehicle (**Figure 3**)
  - Significance occurred as early as week 24 for White and week 48 for Asian participants ($P<0.001$, both)

FIGURE 3. Mycologic Cure[a] by Participant Race (ITT Population, Pooled)



***P<0.001 vs vehicle.
[a]Negative potassium hydroxide examination and negative fungal culture of the target nail specimen.
Interpretation of results was performed in a sequential manner to adjust for multiplicity. Mycologic cure rate was tested for statistical significance (active vs vehicle) only if both the complete or almost complete cure rate (see **Figure 2**) and unaffected new toenail growth (see **Methods**) were statistically significant.
Mycologic cure rates at week 52 with efinaconazole in the overall phase 3 populations were 55.2% and 53.4%.[4]
ITT, intent to treat.

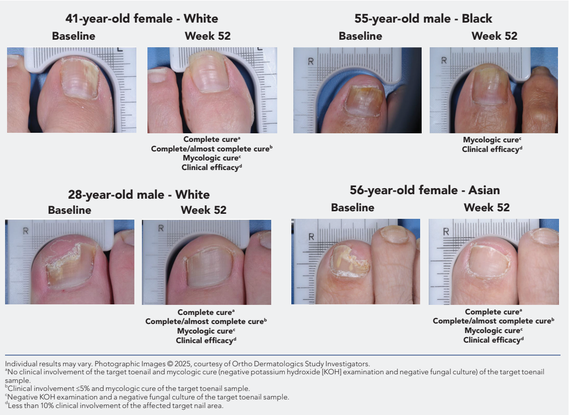
Clinical Efficacy

- At week 52, clinical efficacy (<10% of affected target nail area) with efinaconazole was significantly greater vs vehicle in White (31.2% vs 8.6%; $P<0.001$) and Asian (46.0% vs 23.2%; $P<0.001$) subgroups; improvements were numerically greater in Black efinaconazole-treated participants (31.4% vs 21.4%)

Participant Photographs

- Representative photographs of improvements in affected toenails treated with efinaconazole are shown in **Figure 4**

FIGURE 4. Representative Photographs From Participants Treated With Efinaconazole 10% for 48 Weeks



Individual results may vary. Photographic Images © 2025, courtesy of Ortho Dermatologics Study Investigators.
[a]No clinical involvement of the target toenail and mycologic cure (negative potassium hydroxide [KOH] examination and negative fungal culture) of the target toenail sample.
[b]Clinical involvement ≤5% and mycologic cure of the target toenail sample.
[c]Negative KOH examination and a negative fungal culture of the target toenail sample.
[d]Less than 10% clinical involvement of the affected target nail area.

Safety

- Treatment-related TEAE rates with efinaconazole were relatively low and similar across subgroups (**Table 1**)
  - Most TEAEs were mild to moderate in severity, and discontinuations due to adverse events were <6% across subgroups
  - The safety profile in the racial subgroups is generally in line with the overall phase 3 populations[4]

TABLE 1. Treatment-Emergent Adverse Events Through Week 52 by Participant Race (Safety Population, Pooled)

	White		Asian		Black	
	Efinaconazole 10% (n=939)	Vehicle (n=302)	Efinaconazole 10% (n=200)	Vehicle (n=69)	Efinaconazole 10% (n=70)	Vehicle (n=28)
Reporting any TEAE, n (%)	617 (65.7)	177 (58.6)	131 (65.5)	48 (69.6)	38 (54.3)	13 (46.4)
Treatment-related TEAEs, n (%)	52 (5.5)	12 (4.0)	17 (8.5)	1 (1.4)	6 (8.6)	0
Discontinued drug or study due to AE, n (%)	20 (2.1)	1 (0.3)	11 (5.5)	0	0	0
Number of AEs	1700	504	313	99	76	20
Mild, n (%)	986 (58.0)	289 (57.3)	59 (18.8)	18 (18.2)	50 (65.8)	13 (65.0)
Moderate, n (%)	639 (37.6)	204 (40.5)	247 (78.9)	81 (81.8)	19 (25.0)	6 (30.0)
Severe, n (%)	75 (4.4)	11 (2.2)	7 (2.2)	0	7 (9.2)	1 (5.0)
Most common treatment-related TEAEs,[a] n (%)						
AS dermatitis	10 (1.1)	0	15 (7.5)	0	1 (1.4)	0

[a]Reported in ≥3% of participants in any treatment group.
AE, adverse event; AS, application site; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Topical efinaconazole 10% solution is efficacious, safe, and generally well tolerated among White, Asian, and Black participants with onychomycosis, and results were generally in line with those of the overall phase 3 populations[4]
  - Generalizability may be limited owing to the small number of self-identified Black participants
- Overall, these results add to previous post hoc analyses, demonstrating that efinaconazole can be used in a variety of patient populations with onychomycosis, including racially and ethnically diverse patients[5-10]

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AUTHOR DISCLOSURES

Shari R. Lipner has served as a consultant for Moberg Pharmaceuticals and BelleTorus Corporation. **Aditya K. Gupta** has served as a consultant, speaker, and investigator for Ortho Dermatologics. **Tracey C. Vlahovic** has served as an investigator and speaker for Ortho Dermatologics. **Ted Rosen** has nothing to disclose. **Boni Elewski** has provided clinical research support (research funding to University) for AbbVie, Anaptys-Bio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Incyte, LEO Pharma, Lilly, Merck, Menlo, Novartis, Pfizer, Regeneron, Sun Pharma, Ortho Dermatologics, and Vanda and has served as a consultant (received honorarium) from Boehringer Ingelheim, Bristol Myers Squibb, Celgene, LEO Pharma, Lilly, Menlo, Novartis, Pfizer, Sun Pharma, Ortho Dermatologics, and Verrica. **Su Yong Choi** is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company. **Linda Stein Gold** has served as an investigator/consultant or speaker for AbbVie, Arcutis, Dermavant, Incyte, Lilly, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Sun Pharma, and UCB.

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