Review of the Clinical Efficacy and Safety of Efinaconazole 10% Topical Solution for Onychomycosis Across Subgroups

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SYNOPSIS

- Onychomycosis can be difficult to treat, and factors like age and disease severity can impact treatment response[1]
- Topical efinaconazole 10% solution was first approved in the US in 2014 for once-daily treatment of toenail onychomycosis[2]
- Efficacy and safety of efinaconazole have been demonstrated in 2 identical pivotal phase 3 trials,[3] and in several post hoc analyses (eg, patient age, sex, race, etc)[4-11]

OBJECTIVE

- To summarize the efficacy/safety data for efinaconazole in different subgroups from all phase 3 post hoc analyses published to date

METHODS

- A literature search was conducted to identify post hoc analyses of the 2 efinaconazole phase 3 trials (NCT01008033; NCT01007708) that provided data for ≥1 efficacy endpoints noted below
  - A poster presentation was also included as these data are currently unpublished
  - In these identically designed trials, participants aged 18-70 years with mild to moderate toenail onychomycosis (20%-50% clinical involvement; N=1655) were randomized (3:1) to once-daily topical efinaconazole 10% or vehicle for 48 weeks with 1 follow-up at week 52[3]
- Efficacy endpoints at week 52 included rates of:
  - Complete cure (primary; 0% clinical involvement + negative potassium hydroxide examination and fungal culture [mycologic cure])
  - Complete/almost complete cure (secondary; ≤5% clinical involvement + mycologic cure)
  - Mycologic cure (secondary)
- Safety data were also summarized

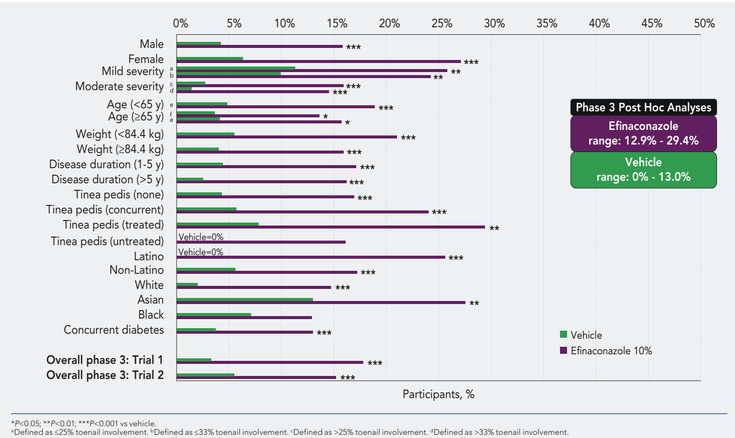
RESULTS

- A total of 9 post hoc analyses have been published/presented as a poster[4-12]
  - Twenty-five subgroups were examined (**Table 1**)
  - Note that the subgroups of sex, age, and severity were analyzed in more than 1 publication

Efficacy

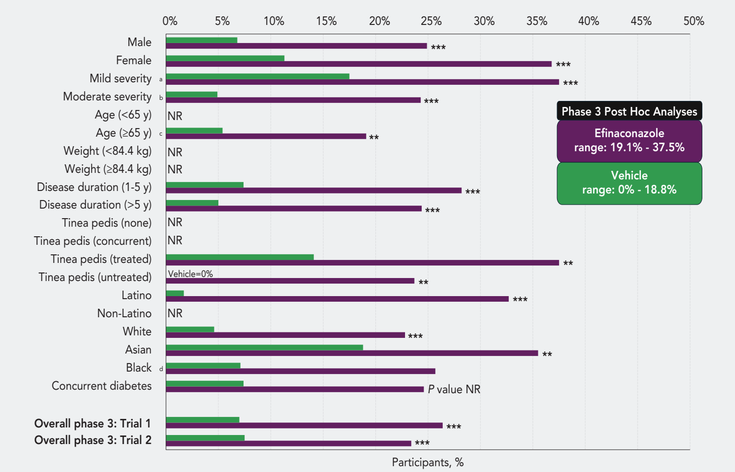
- All 9 analyses (25 subgroups) reported complete cure rates for efinaconazole vs vehicle, which were generally similar to the overall phase 3 populations[3] (**Figure 1**)
- Eight analyses reported complete/almost complete cure (14 subgroups; **Figure 2**)
  - These rates were generally similar to the overall populations[3]
- Mycologic cure rates were reported in 8 analyses (17 subgroups; **Figure 3**)
  - Similar to complete and complete/almost complete cure, mycologic cure rates were generally comparable to those of the overall populations[3]

FIGURE 1. **Complete Cure at Week 52 by Subgroup**



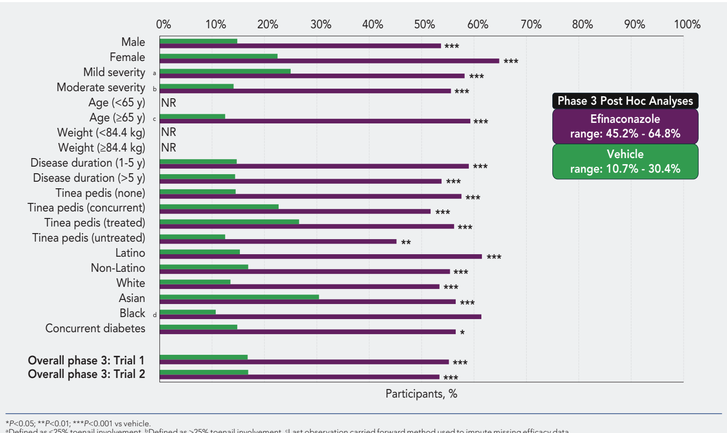
*P<0.05; **P<0.01; ***P<0.001 vs vehicle.
[a]Defined as ≤25% toenail involvement. [b]Defined as ≤33% toenail involvement. [c]Defined as >25% toenail involvement. [d]Defined as >33% toenail involvement.
[e]Observed cases (no imputation of missing efficacy data). [f]Last observation carried forward method used to impute missing efficacy data.

FIGURE 2. **Complete/Almost Complete Cure at Week 52 by Subgroup**



**P≤0.01; ***P<0.001 vs vehicle.
[a]Defined as ≤25% toenail involvement. [b]Defined as >25% toenail involvement. [c]Last observation carried forward method used to impute missing efficacy data.
[d]Owing to the sequential statistical analyses performed, significance was not tested for this population.
NR, not reported.

FIGURE 3. **Mycologic Cure at Week 52 by Subgroup**



*P<0.05; **P<0.01; ***P<0.001 vs vehicle.
[a]Defined as ≤25% toenail involvement. [b]Defined as >25% toenail involvement. [c]Last observation carried forward method used to impute missing efficacy data.
[d]Owing to the sequential statistical analyses performed, significance was not tested for this population.
NR, not reported.

TABLE 1. **Efinaconazole Phase 3 Post Hoc Efficacy Analysis Populations**

Subgroup	Efinaconazole 10%, n	Vehicle, n
Sex[a 5,6]		
Male	944	274
Female	314	85
Severity[a]		
Mild: ≤25% involvement[7]	311	103
Moderate: >25% involvement[7]	925	312
Mild: ≤33% involvement[5]	434	131
Moderate: >33% involvement[5]	628	212
Age		
<65 y[a 5]	922	294
≥65 y[5,11]	140[a] / 162[b]	49[a] / 56[b]
Weight[a 5]		
<84.4 kg	543	165
≥84.4 kg	517	176
Disease duration[a 8]		
1-5 y	512	170
>5 y	576	194
Tinea pedis[b 9]		
None	833	255
Concurrent	229	88
Treated	136	44
Untreated	93	24
Ethnicity (self-reported)[a 10]		
Latino	193	77
Non-Latino	1042	338
Race (self-reported)[b 12]		
White	947	304
Asian[c]	200	69
Black/African American	70	28
Concurrent diabetes[a 4]	82	30

[a]Observed cases (no imputation of missing efficacy data).
[b]Last observation carried forward method used to impute missing efficacy data.
[c]Includes participants enrolled in the US and Japan.

Safety

- Adverse event (AE) and discontinuation rates with efinaconazole were reported in 5 analyses (9 subgroups) and 6 analyses (11 subgroups), respectively (**Table 2**)
  - AE rates with efinaconazole ranged from 54.3%-71.3%, and discontinuations due to AEs were low (range: 0%-5.5%)
  - These rates were in line with those of the overall populations[3]

TABLE 2. **Adverse Events and Discontinuations Through Week 52 by Subgroup**

Subgroups	AEs/TEAEs, %		Discontinuations, %	
	Efinaconazole 10%	Vehicle	Efinaconazole 10%	Vehicle
Male[a]	63.5	NR	2.5	NR
Female[a]	71.3	NR	2.8	NR
Mild[a,b]	69.3	NR	1.0	NR
Moderate[a,c]	63.9	NR	3.2	NR
Age (≥65 y)[d]	67.9	75.0	4.3	1.8
Latino	NR	NR	1.6	NR
Non-Latino	NR	NR	2.8	NR
White[d]	65.7	58.6	2.1	0.3
Asian[d]	65.5	69.6	5.5	0
Black[d]	54.3	46.4	0	0
Concurrent diabetes[a]	64.2	66.7	2.5	NR
Overall phase 3 populations[a]	66.0	61.0	3.2	0.5
	64.5	58.5	1.9	0

[a]Reported as at least 1 AE or TEAE.
[b]Defined as ≤25% toenail involvement.
[c]Defined as >25% toenail involvement.
[d]Reported as any AE or TEAE.
AE, adverse event; NR, not reported; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Once-daily topical efinaconazole 10% solution demonstrated generally similar efficacy and safety to the overall phase 3 trials in multiple populations with onychomycosis, including those who may be more difficult to treat, such as older patients and those with greater disease severity[1]

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AUTHOR DISCLOSURES

Ted Rosen has served as consultant for Ortho Dermatologics. **Aditya K. Gupta** has served as consultant, speaker, and investigator for Ortho Dermatologics. **Linda Stein Gold** has served as investigator, consultant, or speaker for AbbVie, Arcutis, Dermavant, Incyte, LEO Pharma, Lilly, Novartis, Ortho Dermatologics, Pfizer, Sun Pharma, and UCB. **Leon H. Kircik** has served as consultant, speaker, advisor or investigator for Allergan, Almirall, EPI Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma. **Tracey C. Vlahovic** has served as investigator and speaker for Ortho Dermatologics. **Eric Guenin** is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company. **Shari R. Lipner** has served as a consultant for BelleTorus Corporation and Moberg Pharmaceuticals. **Fran E. Cook-Bolden** has served as advisor, served as investigator, and served on speakers' bureaus for AbbVie, Aclaris, Almirall, Cassiopea, Cutanea, Dermavant, Encore, Foamix, Galderma, Hovione, LEO Pharma, and Ortho Dermatologics. **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, Menlo, Merck, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sun Pharma, Vanda; and served as consultant for/received honorarium from Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, LEO Pharma, Lilly, Menlo, Novartis, Ortho Dermatologics, Pfizer, Sun Pharma, and Verrica.

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