

# Efinaconazole in the Age of Antifungal Resistance

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## BACKGROUND

- The global rise and spread of antifungal resistance is complicating the treatment of onychomycosis, a fungal infection of the toenail bed or plate
- Causative dermatophyte species resistant to oral antifungals like terbinafine are being increasingly detected<sup>1,2</sup>
- Further, resistant yeast and mold species are now categorized by the World Health Organization as fungal pathogens that represent a great threat to public health<sup>3</sup>
- Accordingly, patients in the US are presenting with onychomycosis resistant to terbinafine or second-line systemic therapies like oral fluconazole or itraconazole<sup>4</sup>
- It is crucial to find alternative approaches to combat this clinical resistance, including implementing antifungal stewardships programs and identifying antifungals that are effective against both susceptible and resistant fungal strains

## OBJECTIVE

- The goal of this study was to evaluate the activity of oral and topical antifungals against susceptible and resistant clinical isolates of dermatophytes, yeasts, and molds

## METHODS

- Antifungal activity of efinaconazole was compared with terbinafine, itraconazole, and fluconazole using in vitro assays evaluating minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) against susceptible and resistant strains
- MIC is the lowest concentration of an antifungal that inhibits fungal growth (threshold for inhibition varies depending upon fungus being tested); MIC<sub>50</sub> is the lowest concentration that inhibits growth in 50% of the fungal isolates tested
  - MIC testing was performed according to the Clinical and Laboratory Standard Institute (CLSI) microdilution methods for yeasts<sup>5</sup> and for dermatophytes and non-dermatophyte molds<sup>6</sup>
- MFC determines if a test compound is fungicidal (≥99.9% reduction of the fungus) or fungistatic
- Lower MIC and MFC values are more favorable, as less drug is required for antifungal activity
- Clinical isolates tested due to suspicion of antifungal resistance included:
  - Dermatophytes (*Trichophyton mentagrophytes* [n=16], *T. rubrum* [n=43], *T. tonsurans* [n=18], and *T. violaceum* [n=4])
  - Yeasts (*Candida albicans* [n=55] and *C. auris* [n=30])
  - Molds (*Fusarium sp.*, *Scedosporium sp.*, and *Scopulariopsis sp.* [n=15 each])

## RESULTS

- Efinaconazole showed superior potent activity against a broad panel of susceptible and resistant dermatophyte, *Candida*, and mold isolates (Figures 1–3)
- Although none of the tested compounds showed fungicidal activity against all tested isolates, efinaconazole demonstrated more fungicidal activity against *T. rubrum* isolates compared to other antifungals (data not shown)

FIGURE 1. Antifungal Activity Against Dermatophytes

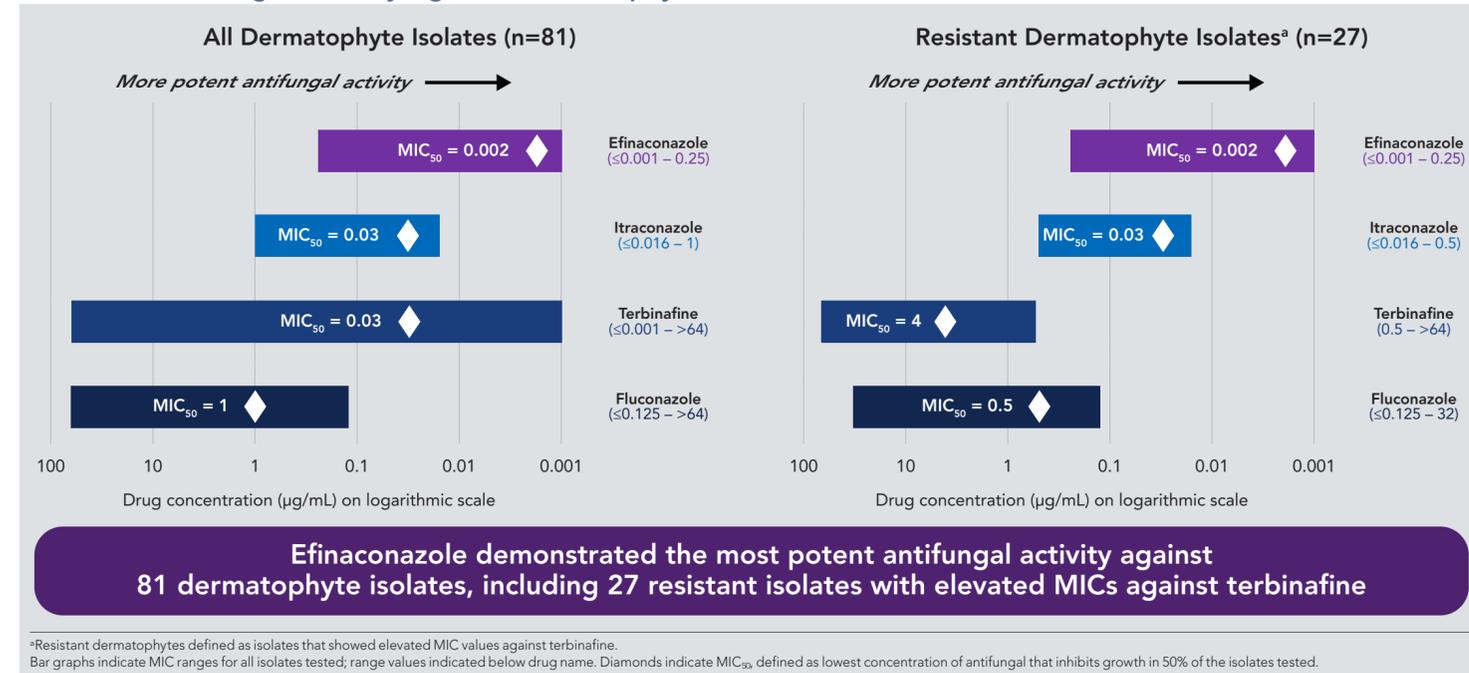


FIGURE 2. Antifungal Activity Against *Candida*

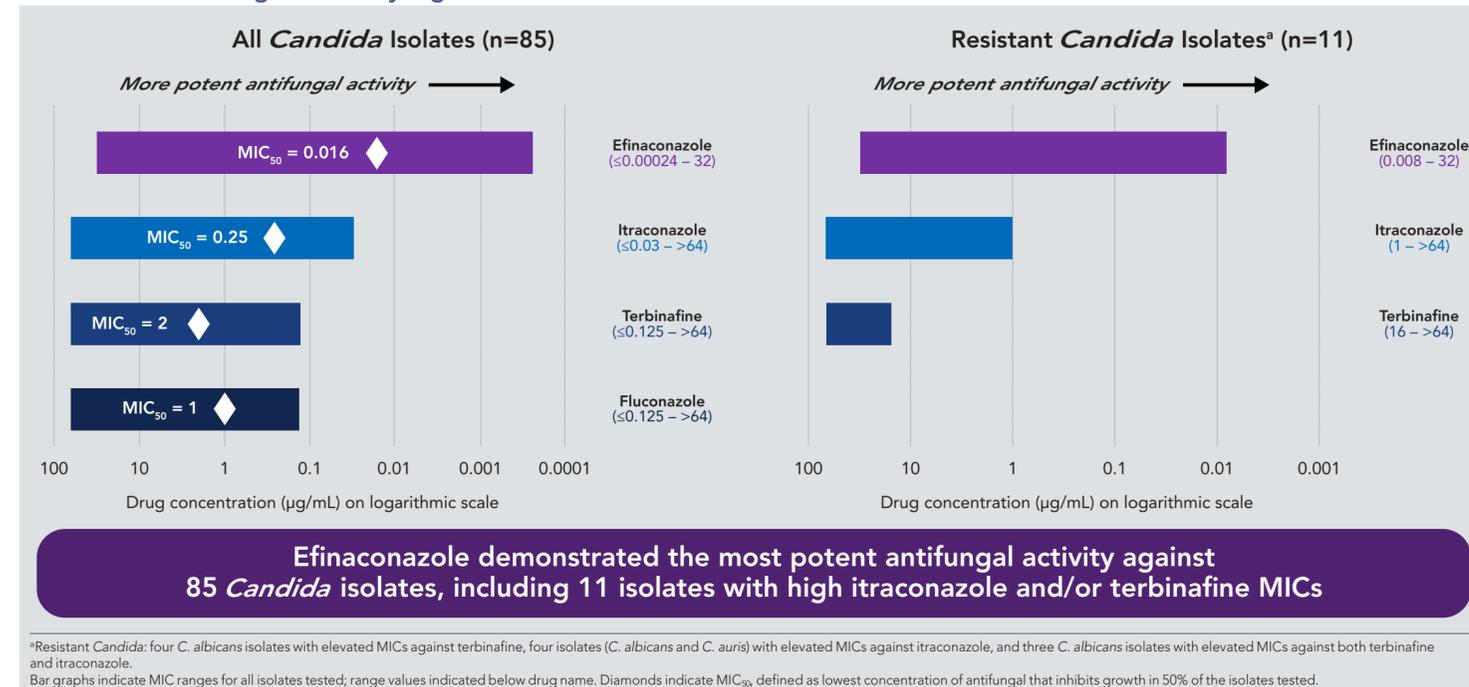
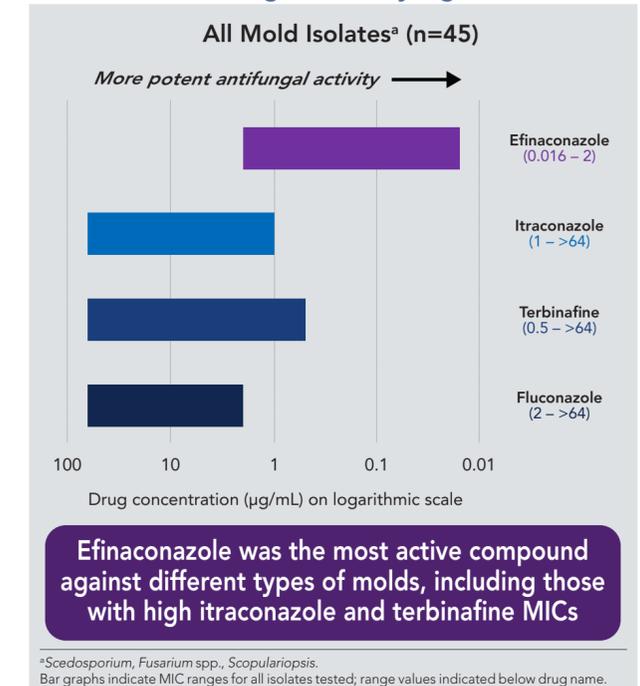


FIGURE 3. Antifungal Activity Against Molds



## CONCLUSIONS

- Efinaconazole demonstrated superior in vitro activity compared to fluconazole, itraconazole, and terbinafine against a broad range of dermatophytes and non-dermatophytes commonly implicated in onychomycosis
- Efinaconazole also demonstrated potent antifungal activity against isolates resistant to terbinafine and/or itraconazole, suggesting efinaconazole may be an efficacious treatment for resistant organisms

## REFERENCES

- Hiruma J, et al. *J Dermatol*. 2021;49(4):564-567.
- Noguchi H, et al. *J Dermatol*. 2019;46(12):e446-e447.
- World Health Organization. WHO releases first-ever list of health-threatening fungi. Accessed November 29, 2022. <https://www.who.int/news/item/25-10-2022-who-releases-first-ever-list-of-health-threatening-fungi>.
- Gu D, et al. *JAAD Case Rep*. 2020;6(11):1153-1155.
- Clinical and Laboratory Standards Institute. 2017. Document M27Ed4E.
- Clinical and Laboratory Standards Institute. 2017. Document M38Ed3E.

## AUTHOR DISCLOSURES

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