Itraconazole is an Effective Oral Treatment for Onychomycosis: Results from a Phase 3 Randomized, Multicenter, Placebo-Controlled Study

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BACKGROUND

Onychomycosis (ailment of the nail) is considered a common fungal infection affecting the nails of 10% or more of adults worldwide.1 This condition is caused by dermatophytes or yeasts, which can affect the nails on any part of the body.2 Nail involvement is more common in toenails and less common in fingernails.2 The most common fungi associated with onychomycosis are Microsporum audouinii, Trichophyton rubrum, and Candida albicans.2

The prevalence of onychomycosis is estimated to be higher in colder climates and in regions with a humid climate.2 Moreover, onychomycosis is more common in individuals with diabetes mellitus due to the increased risk of skin infections and poor circulation.2 The disease also has a significant impact on quality of life due to the appearance of the toenails and interference with wearing shoes, walking, and participating in various sports activities.3

Tertiary onychomycosis may involve topical and/or systemic antifungal agents. Overall, treatment failure has been observed in 20% to 40% of cases.4-7 Topical antifungal agents are effective in superficial infections (ie, onycholysis) and superficial mycotic nails but less effective in deep-seated infections.8

Onychomycosis, also known as toenail fungus, has a long treatment period.5-7 Efforts to develop an oral, single-tablet-per-day dosing regimen aim to simplify the treatment of this chronic condition.5-7

In the mid-1990s, Itraconazole, a synthetic triazole antifungal agent that has been available in the US since 1996,5 was one of the most commonly used systemic antifungals for onychomycosis.5-6 Specifically, 200 mg itraconazole capsules were available only for oral dosage at 1 tablet per day.5,6 For example, the presence of the fungal spores in the nail plates has been associated with bacterial cellulitis of the lower extremities, ulcera cruris (chronic leg ulcers), and diabetes.9

METHODS

OBJECTIVES

1. To demonstrate the non-inferiority of itraconazole 200-mg oral tablets once daily (QD) to 2 itraconazole 100-mg capsules dosed QD in patients with onychomycosis of the toenail (less than 25% nail involvement) with nails of different lengths.

2. To compare the safety and efficacy of itraconazole 200-mg tablet compared with a placebo in patients with onychomycosis of the toenail and fingernail due to dermatophytes.

METHODS (CONTINUED)

Randomization

Eligible patients were randomized in a 3:3:1 ratio to receive a daily dose of either 1 itraconazole 200-mg capsule once daily, 2 itraconazole 100-mg capsules once daily, or placebo tablets once daily.

Study design

This was a randomized, double-blind, multicenter study conducted in 13 countries.10

Patients

Men and women aged 16 to 75 years who had a clinical diagnosis of distal and/or lateral subungual onychomycosis affecting ≥1 great toenail were eligible for the study. Subjects were instructed to self-administer the whole (e.g., not crushed or split) study drug QD. See Table 1 for a complete listing of inclusion and exclusion criteria.

Efficacy Assessments

Prior to screening, and those with onychomycosis due to subungual onychomycosis affecting ≥1 great toenail were eligible for the study. Furthermore, the difference in clinical improvement rates for itraconazole 200-mg tablets and placebo was 23.7% (p<0.001) and 23.8% (p<0.001) in the per-protocol population. In the ITT population, the difference in clinical improvement rates between active treatment groups was 29.3% (p<0.001) and 18.5% (p<0.001), respectively.

RESULTS

Figure 2. Primary and Secondary Efficacy: Proportion of patients achieving complete cure or clinical improvement at Week 52 (ITT population)

Safety

The most common adverse events during the study were mild to moderate in severity. There were not deaths reported during the trial.

DISCUSSION

Onychomycosis is a common fungal infection of the nails that is responsible for approximately 1% of primary care visits in the US.11

The oral route of administration of antifungals offers the advantage of systemic treatment of the disease.12

REFERENCES AND SUPPORT

REFERENCES


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