Treatment of toenail fungus with tavaborole topical antifungal solution

Fungal infection of the nails affects up to 14% of North Americans, particularly older people and those with cardiovascular disease and diabetes. Toenails are affected more often than fingernails, with symptoms that include separation of the nail from the bed, build-up of debris under the nail, and thickening, brittleness, and discoloration of the nail. These symptoms may result in pain and embarrassment, and interfere with the ability to walk.

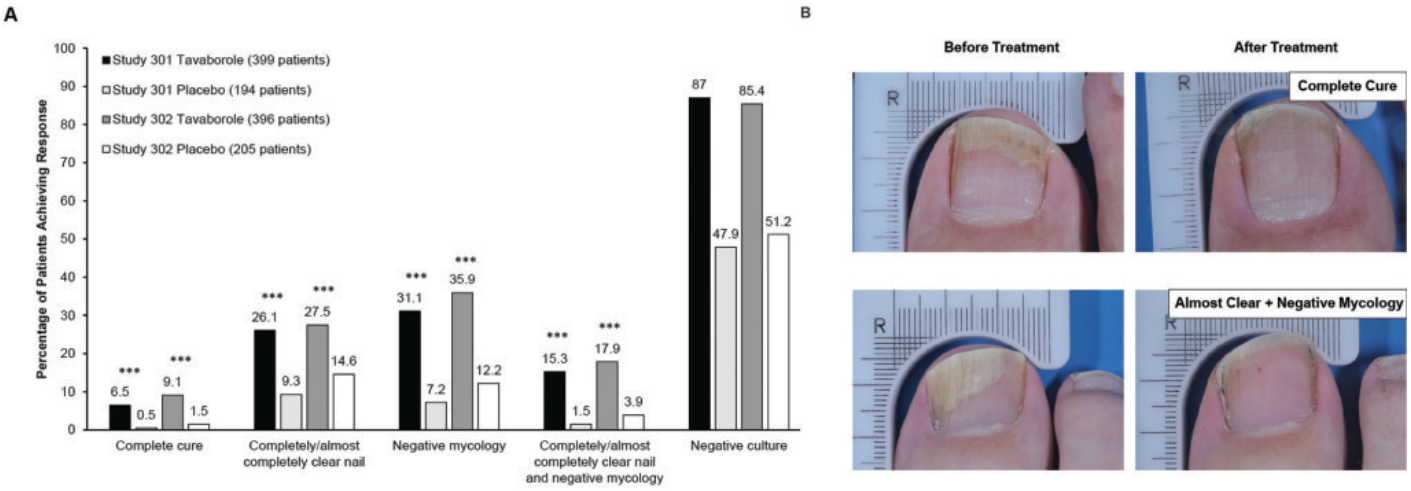

Fig. 1. Effect of treatment with tavaborole topical solution 5% once daily for 48 weeks in clinical trials showing (A) percentage of patients who achieved responses and (B) representative toenails from a single patient. ***Denotes that the difference between tavaborole and placebo was statistically significant. Complete cure defined as completely clear nail and negative mycology; negative mycology means that the nail sample tested negative for fungi using a potassium hydroxide or KOH test from nail scrapings or samples and had negative culture. Negative culture means that the sample did not grow fungi under laboratory culture conditions.

This type of fungal infection is mainly caused by two types of fungus (Trichophyton rubrum and T. mentagrophytes). Some patients may prefer to be treated with topical antifungal medication instead of oral medication because topical medication can be applied directly to the nail and may reduce the risk of unwanted side effects and interactions with other drugs that the patient may be taking. Ideally, a topical treatment for toenail fungus should provide broad-spectrum activity against the fungal species causing the infection and be able to penetrate the nail to reach the site of infection, while minimally absorbed in the bloodstream to reduce the risk of unwanted side effects and drug interactions. Topical antifungal medications that can be applied over nail polish may be preferred for cosmetic reasons.

Tavaborole topical solution, 5% (Kerydin®, Anacor Pharmaceuticals, Inc., Palo Alto, CA, USA) is a topical antifungal solution approved by the FDA in 2014 for the treatment of toenail fungus caused by T. rubrum or T. mentagrophytes. Initial laboratory studies demonstrated that tavaborole topical solution had broad-spectrum antifungal activity against 19 types of fungi, including T. rubrum and T. mentagrophytes. Tests on healthy fingernails showed that tavaborole topical solution was able to penetrate the nail through up to four layers of nail polish. Laboratory studies on human cells suggested a low potential for adverse interactions with other drugs that a patient may be taking. Studies of tavaborole in patients with toenail fungus showed that the drug was minimally absorbed into the bloodstream and that any absorbed medication was rapidly metabolized and excreted in the urine.

Two clinical trials were conducted in the United States, Mexico, and Canada in 1,198 patients who had 20%–60% of at least one toenail affected by fungal infection. Patients, male and female between 18-88 years old, were treated with tavaborole topical solution or a placebo solution that did not contain tavaborole. Both trials' primary endpoint was to determine the percentage of patients achieving a complete cure, defined as having a completely clear nail and negative mycology. (Negative mycology means that the nail sample tested negative for fungi using a potassium hydroxide or KOH test from nail scrapings or samples and had negative culture. Negative culture means that a sample did not grow fungi under laboratory conditions.) Secondary endpoints examined the percentage of patients who achieved an almost clear nail as well as the status of their mycology and fungal culture. After 48 weeks of treatment, more patients treated with tavaborole as compared with placebo achieved the primary and secondary endpoints (Fig. 1.). Discontinuations occurred at low rates in tavaborole-treated patients with only three out of 791 patients discontinuing tavaborole treatment because of side effects. (Three out of 395 patients discontinued placebo treatment.) The most common side effects reported with tavaborole treatment were skin exfoliation at the application site (2.7% of patients), ingrown toenail (2.5%), or redness (1.6%) or inflammation (1.3%) at the application site.

The FDA has approved tavaborole to be applied over the entire surface and under the tip of affected toenails once daily for 48 weeks. The tavaborole study program has shown the drug to be an effective topical treatment for toenail fungus.

Publication

Tavaborole topical solution, 5% for the treatment of toenail onychomycosis.
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