Amphotericin Remains Initial Treatment for Talaromycosis

Amphotericin induction dosing is more effective than itraconazole for HIV-associated talaromycosis in open-label study.

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July 18, 2017 – For patients with HIV-related talaromycosis, initial dosing with the antifungal amphotericin improved symptoms more than itraconazole, according to a recent open-label trial.

Thuy Le, MD, DPhil, from the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam, and colleagues published their research in the June 15, 2017 issue of *The New England Journal of Medicine*.

"Talaromycosis (previously penicilliosis) is a major cause of human immunodeficiency virus (HIV)–related death," noted the authors. Standard talaromycosis treatment is initial (induction) dosing with amphotericin followed by the antifungal itraconazole.

According to researchers, amphotericin is efficacious but has prohibitive cost and substantial side effects. This open-label study examined the noninferiority of itraconazole induction dosing compared to amphotericin for talaromycosis treatment.

A total of 440 HIV-infected patients with talaromycosis were randomly assigned in a 1:1 ratio either amphotericin for 14 days (0.7-1.0 mg/kg once daily) or itraconazole (300 mg twice daily) for 3 days followed by 200 mg twice daily for 11 days. Both arms were then treated with 200 mg itraconazole twice daily for 10 weeks. Itraconazole dosing (100 mg twice daily) was maintained until CD4+ cell counts reached stable levels for at least 6 months while on antiretroviral therapy.

The primary outcome was all-cause mortality in the first 2 weeks after patient randomization. The risk of death was slightly lower in the amphotericin induction group compared with the itraconazole group (6.5% vs. 7.4% patient mortality, $P < 0.001$ for noninferiority).

All-cause mortality after 24 weeks was much lower with amphotericin than itraconazole (11.3% vs. 21.0%, $P = 0.006$). Amphotericin had significantly greater fungicidal activity up to day 14 compared with itraconazole (a decrease of 0.95 $\log_{10}$ CFUs/ml/day vs. a decrease of 0.36 $\log_{10}$ CFUs/ml/day, $P < 0.001$).

Patients had significantly more laboratory adverse events with amphotericin vs. itraconazole: hemoglobin <7.4 g/dl (41.0% vs. 29.4%, $P = 0.01$), potassium <2.4 mmol/liter (11.5% vs. 3.2%, $P <0.001$), and magnesium <0.44 mmol/liter (4.6% vs. 0.9%, $P = 0.02$). Serious adverse events occurred in 100 itraconazole-treated patients (45.9%) and 58 amphotericin patients (26.7%).

"This trial was pragmatic, in that the formulations of the treatments assessed were affordable and the trial had few exclusion criteria; these factors may help to enhance the potential generalizability of the trial across Asia," noted Dr. Le.

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