P2412

Uncertainty in onychomycosis assessment

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There are several issues in onychomycosis assessment that provide uncertainty in trials. Determination of efficacy typically relies on clinical observation of infected area, and mycologic assessment of the presence or absence of fungal organisms. To provide consistent and comparable data when determining efficacy, clinical evaluations need to be accurate and replicable between observers, while laboratory testing for organisms needs to provide conclusive infection status. Without replicable conclusive assessment, the accuracy of efficacy must also remain in question. There will always remain some subjectivity between individuals where clinical evaluation is done by visual methods, but trials can improve standardization by providing investigators with photos of infection limits/presentations acceptable for enrollment and to be considered "effective cure." Trial design should involve onychomycosis experts when deciding upon entry and cure criteria standards. To further improve clinical assessment, objective evaluation is obtained using computerized nail planimetry. Digital photography is now widespread. Digital photographs can be sent anywhere in the world for assessment; widespread experts could provide secondary visual evaluation to ensure enrollment/cure criteria is met. Computerized planimetry also provides an exact measure of proportion of affected area, which may be under- or overestimated by subjective visual assessment. Review of efficacy based on visual assessment compared to planimetry in a recent large-scale study showed that where effective cure was declared by visual assessment, more than 20% of subjects at week 84 and over 50% of subjects at week 48 would not be considered to have EC using planimetry data. New technology is also aiding mycologic assessment. Fungal organisms are being found at significantly higher rates with molecular biology compared to the standard microscopy/culture methods. It has long been known that mycologic detection of dermatophytes has a high rate of false negatives. The impact of this detection problem is currently unassessed. Only with the development of improved clinical and mycological methods will we be able to determine treatment efficacy rates with better reliability, and better modify treatment to improve cure rates.

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P2413

Disseminated cutaneous cryptococcus infection with neurocryptococcus presenting as cellulitis in a liver transplant patient

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Cryptococcosis is the infection caused by the encapsulated yeast *Cryptococcus neoformans*, a dimorphic fungus. Although the primary site of infection is most often the lungs, the disease frequently manifests with signs of extrapulmonary dissemination, involving the skin in approximately 10% to 15% of cases. We report a 55-year-old man with hepatitis C and multifocal hepatocellular carcinoma who underwent an orthotopic liver transplantation and was admitted to the hospital because of worsening encephalopathy. He was also found to have a new-onset left facial droop, recurrent fevers, and an erythema on his left medial thigh. The initial physical examination showed a 4- × 6-cm erythematous patch on the left inner thigh with surrounding mottled and reticulated diffuse erythema descending down the right leg with fine scale that was tender to palpation and slightly warm to touch. A 6-mm punch biopsy was performed within the erythematous patch on the left thigh, which revealed psuedoepitheliomatous hyperplasia of the epidermis and granulomatous infiltrates in the dermis, within which aggregates of spores was revealed. Mucicarmine, colloidal iron, Fontana–Masson, GMS, and PAS stains were consistant with cryptococcus infection. Laboratory studies revealed a serum cryptococcal antigen titer of 1:256 and a CSF cryptococcal antigen titer of 1:512. Despite treatment with multiple antifungal agents for disseminated cryptococcal infection, the patient developed sepsis with multiorgan failure and died. Cellulitis is the rarest skin finding associated with cryptococcosis; it is most commonly encountered in transplantation patients. The characteristic clinical presentation, differential diagnosis, and treatment reviewed in this case is helpful in promoting early recognition and appropriate management of this potentially life threatening disease.

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P2414

A novel itraconazole tablet for the treatment of onychomycosis

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Objectives: Itraconazole is approved for the treatment of onychomycosis as a 12-week, once-daily (QD) regimen of two 100-mg itraconazole capsules. In order to provide a more convenient, one tablet per day dosing regimen, a novel 200-mg itraconazole tablet has been developed using the proprietary Meltrex technology. This phase III study evaluates this new dosage form for treating onychomycosis.

Methods: This randomized, multicenter, parallel group, placebo-controlled, evaluator-blinded study was designed to compare the efficacy of itraconazole given as one 200-mg tablet QD with itraconazole given in two 100-mg capsules QD for 12 weeks of treatment and 40 weeks of follow-up. In addition, this study evaluated the superiority of 1 itraconazole 200-mg tablet to 1 placebo tablet. Noninferiority and superiority were evaluated using the proportion of subjects with complete cure of the great toenail at week 52. Complete cure was defined as clinical cure (an Investigator's Global Assessment score of 0) plus mycologic cure (a negative potassium hydroxide [KOH] examination and a negative culture for dermatophytes).

Results: A total of 1381 subjects were randomized (3:3:1) to treatment and received study drug. The proportions of subjects (intent to treat population) with complete cure at week 52 were greater in the active treatment groups (22.3% in the itraconazole 200-mg tablet group and 21.7% in the itraconazole 100-mg capsule group) compared with the placebo group (1.0%). In addition to demonstrating superiority to QD dosing with 1 placebo tablet ($P < .001$), QD dosing with one itraconazole 200-mg tablet demonstrated noninferiority to QD dosing with two itraconazole 100-mg capsules (lower limits of the 97.5% CI, -4.3%). Overall, no safety signals or trends associated with abnormal changes in clinical laboratory findings, ECG outcomes, or audiology evaluations were observed following intake of itraconazole 200-mg tablets. Furthermore, the AE profile of subjects treated with one itraconazole 200-mg tablet was comparable to that of subjects treated with two itraconazole 100-mg capsules or placebo tablet.

Conclusions: This novel itraconazole 200-mg tablet is well tolerated and effective in the treatment of onychomycosis. The convenience of a one tablet per day dosing regimen may improve patient compliance.

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P2415

An open-label study of the safety and efficacy of sertaconazole nitrate in the treatment of seborrheic dermatitis

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Introduction: Seborrheic dermatitis is a common recurrent dermatosis characterized by redness and scaling, with occasional papule and plaque formation and variable pruritus. Diagnosis is based chiefly on clinical findings, with dermatopathology helpful only occasionally. *Malassezia globosa* and *M restricta* are believed to play a role in its pathogenesis, although their presence is not definitive of disease because both yeasts are among the normal flora found in large numbers in the sebaceous regions. Treatment usually involves antifungal agents such as ketoconazole, alone or in combination therapy, topical corticosteroids, or other topical agents including shampoos, many of which are available over the counter. Corticosteroid therapy has been associated with frequent recurrence of disease and adverse events, however, and the need for safe, effective nonsteroidal therapy for seborrheic dermatitis has long been established. Sertaconazole nitrate has a long history of successful use in Europe in seborrheic dermatitis, which indicates that it may well be a useful agent in the United States as well.

Objective: To demonstrate the efficacy and evaluate the safety of sertaconazole nitrate 2% cream in the treatment of seborrheic dermatitis.

Methods: A single-center, open-label study of 30 male and female patients 19 years of age or older with seborrheic dermatitis of the face was conducted. Subjects applied sertaconazole cream twice daily for 4 weeks and were clinically evaluated at baseline and at the end of weeks 1, 2, and 4. Efficacy measures included the 5-point Investigator's Static Global Assessment (ISGA) as well as clinical assessment of target symptoms including pruritus, erythema, and scaling. Primary endpoint is the proportion of subjects who achieved ISGA scores of 0 or 1 by week 4. Secondary endpoints included percent change in sum of individual scores of signs of disease at target lesion by end of treatment. Safety assessment is by vital signs and reports of adverse events.

Conclusion: Sertaconazole nitrate cream, 2% proved to be effective for the treatment of seborrheic dermatitis, although some patients experienced minor irritation.

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