Clinical Experience of Oral Ibrexafungerp for Treatment of Four Patients with Invasive Candidiasis from the FURI Study

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Background:

Ibrexafungerp (formerly SYC-078) is a novel glucan synthesis inhibitor and the first member of a new class of Triterpenoid antifungals. Its mode of action is inhibition of 1,3-ß-D-glucan synthesis of the fungal cell wall, similar to echinocandins. However, ibrexafungerp is available orally and retains activity in *Candida* strains resistant to echinocandins. As part of the open-label FURI trial (NCT03059992), we report on four clinical invasive candidiasis cases treated with oral ibrexafungerp at the Medical University of Graz.

Methods:

FURI is an open-label Phase3 trial to determine the efficacy and safety of oral ibrexafungerp in patients with invasive fungal infections that are refractory to or intolerant of standard antifungal treatments or for whom long-term intravenous (IV) treatment is not feasible. Ibrexafungerp is administered orally b.i.d. with a dosage of 750mg for the first two days followed by 750mg once daily.

Results:

Twenty-five patients were screened for study inclusion between February 2018 and October 2019, and four patients were ultimately included. The main underlying diseases were malignancy in two patients, psoriatic arthritis and kidney/pancreas transplantation in one patient each. The types of invasive candidiasis were as follows: Femoro-tibial osteomyelitis due to *C. glabrata* and *C. albicans* (N=1), candidemia due to *C. parapsilosis* (N=1), intraabdominal abscess due to *C. krusei* (N=1) and oropharyngeal candidiasis due to *C. krusei* and *C. albicans* (N=1). Two patients received oral ibrexafungerp because long-term IV treatment with an echinocandin was not feasible, one due to azole toxicity and one because of refractory disease despite standard antifungal treatment. The treatment duration with ibrexafungerp ranged from seven to 75 days.

At the end of treatment, two patients (candidemia and abscess) had a complete response (defined as XXX), one patient (osteomyelitis) had a partial response (defined as XXX) and one (oropharyngeal candidiasis) had stable response (persisting thrush).

Most common adverse events possibly or probably related to ibrexafungerp were diarrhoea (n=3), nausea (N=1), rash (N=1) and tooth discoloration (N=1). Gastrointestinal adverse effects resolved in two out of three patients after a couple of days.

Discussion:

Oral ibrexafungerp was well tolerated, besides gastrointestinal side effects in the first days of loading dose. Ibrexafungerp was shown to be an effective treatment for invasive candidiasis infections. In addition, in-hospital stays could be significantly reduced in two patients as long-term IV treatment would be avoided with the use of oral ibrexafungerp, as a step-down agent.