In Vitro Activity of Ibrexafungerp in pH 7.0 and pH 4.5 Testing Environments Against 187 Fluconazole-susceptible and -resistant *Candida* Species from Vulvovaginal Candidiasis Patients.

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Background: Recent studies report a rapidly growing incidence of resistance to the azole drug class in *Candida* species, notably *C. glabrata*, *C. parapsilosis*, and *C. krusei*. Among patients with vulvovaginal candidiasis (VVC), *C. albicans* is the most frequently observed *Candida* species. What is extremely worrisome is the increase in fluconazole (FLU) resistance observed in *C. albicans* vaginal isolates. Previous *in vitro* studies have shown that fluconazole in low pH testing environments, pH 4.5, has a negative effect on the activity of fluconazole. Ibrexafungerp is an oral anti-fungal agent belonging to a novel class of glucan synthase inhibitors, triterpenoids, and has shown activity against azole-resistant *Candida* species.

Materials/methods: Ibrexafungerp was evaluated *in vitro* against 187 vaginal *Candida* isolates: 52 FLU–resistant *C. albicans* (FLU MIC > 2 ug/mL), 30 FLU–sensitive *C. albicans* (FLU MIC < 2 ug/mL), 30 randomly selected *C. glabrata* isolates and 25 each randomly selected isolates of *C. krusei, C. parapsilosis*, and *C. tropicalis*. Susceptibility tests were performed according to CLSI M27-A4 guidelines with the media adjusted to pH 7.0 and pH 4.5; ibrexafungerp MIC readings were conducted at 24 and 48 hrs.

Results: Ibrexafungerp demonstrated *in vitro* activity against all the VVC clinical isolates tested. No differences were observed in ibrexafungerp's MIC90 values (24 hr endpoint at pH7) between the FLU-resistant and FLU-sensitive *C. albicans* isolates (MIC90 = 0.03 μg/mL). Against the *C. glabrata*, *C. krusei, C. parapsilosis*, and *C. tropicalis* isolates, ibrexafungerp MIC90 values were 0.125, 0.5, 0.25, and 0.125 μg/mL, respectively. Ibrexafungerp's MIC values were not adversely affected when tested at lower pH (4.5). These values are similar to those observed in earlier epidemiologic studies of ibrexafungerp.

Conclusions: Ibrexafungerp exhibited significant *in vitro* activity against FLU-resistant and FLU-sensitive, vaginal, *Candida* spp isolates. The potent *in vitro* activity of ibrexafungerp was retained at lower pH (4.5), relevant for the vaginal milieu. These results suggest that ibrexafungerp is a highly-promising, orally bioavailable antifungal agent for the treatment of VVC and prevention of recurrence