Determination of Antifungal Activity of SCY-078, a Novel Glucan Synthase Inhibitor, against a Broad Panel of Rare Pathogenic Fungi

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Background: The aim of this study was to evaluate the *in vitro* efficacy of ibrexafungerp, a novel glucan synthase inhibitor with oral availability against a broad panel of rare pathogenic fungi.

Methods: Five strains each of the following genera were tested: *Absidia, Acremonium, Alternaria, Aspergillus, Candida, Cladosporium, Cryptococcus , Epidermophyton, Malassezia, Microsporum, Paecilomyces, Penicillium, Phialophora, Pichia, Scopulariopsis, Neoscytalidium, Scytalidium, Trichoderma, Trichophyton,* and *Trichosporon*. Susceptibility tests were performed according to CLSI M27-A4 and M38-A3 protocols. Incubation times at 35°C were 24-48 h (72 h for *Cryptococcus*) for yeasts, 48 h for moulds, and 96 h for dermatophytes. Endpoints for yeast were 50% and 100% growth inhibition, while dermatophytes and moulds were read at 80% inhibition and MEC, respectively.

Results: Moulds: Ibrexafungerp demonstrated modal MECs of ≤0.25 µg/mL against *Alternaria sp, Aspergillus (tamarii, calidoustus, and westerdijkiae), Cladosporium sp, Paecilomyces variotii, Penicillium citrinum and S. dimidiatium* isolates. Ibrexafungerp showed less activity against *Absidia coerulea, A. corymbifera, Acremonium sp., Cladosporium cladosporioides, Scopulariopsis, Trichoderma citrinoviride and Trichoderma longibrachiatum,* with modal MECs of 1->8 µg/mL. Dermatophytes: Ibrexafungerp demonstrated modal MIC values of ≤ 0.06 µg/mL against *M. canis* and *T. tonsurans*, and ≤0.125 µg/mL against *T. mentagrophytes* and *T. rubrum*. Ibrexafungerp showed a modal MIC of 0.25 µg/mL against *E. floccosum* with one outlier having an MIC of 4 µg/mL. Yeast: Ibrexafungerp demonstrated an MIC range of 0.03-4 µg/mL for *C. utilis*. Against *Cr. neoformans* ibrexafungerp showed MICs of 2 µg/mL. Against *Malassezia pachydermatis*, ibrexafungerp had MICs of 0.5 µg/mL and an MIC range of 0.5-1 µg/mL against *Pichia* strains. Finally, against *Trichosporon mucoides*, ibrexafungerp showed an MIC range of 0.125-2 µg/mL.

Conclusion: Ibrexafungerp has potent activity against *Alternaria alternata, A. tamarii, A. calidoustus, Cladosporium cladosporioides, Paecilomyces variotii, Penicillium citrinum, Phialophora verrucosa,* and *Neoscytalidium dimidiatum.* Additionally, ibrexafungerp also showed potent activity against *E. floccosum, M. canis, T. mentagrophytes, T. rubrum, and T. tonsurans.*
Finally, ibrexafungerp was effective against *C. utilis, Cr. neoformans, Malassezia pachydermatis, Pichia anomala, P. farinosa, P. manshurica,* and *Trichosporon mucoides.*