Efficacy of ibrexafungerp (formerly SCY-078) against Pneumocystis pneumonia in a murine therapeutic model

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Background: Pneumocystis pneumonia (PCP) is an opportunistic fungal infection that affects immunocompromised patients, including those infected with HIV, undergoing organ transplants or receiving chemo- or immune-therapy as a cancer treatment. Current drugs used to treat PCP are limited by problems with efficacy and toxicity. Ibrexafungerp (IBX), formerly SCY-078, is an oral and intravenous anti-fungal agent belonging to a novel class of glucan synthase inhibitors, triterpenoids, and has shown activity against Candida and Aspergillus spp. In this study, we evaluated the efficacy of IBX in a therapeutic model of murine PCP.

Materials/methods: Balb/c mice (10 mice/group) were infected by exposure to mice with fulminant PCP and immune suppressed with dexamethasone in drinking water. After 5 weeks, daily oral treatment with IBX (30 and 15 mg/kg BID), trimethoprim-sulfamethoxazole (TMP/SMX 50/250 mg/kg QD, as positive control) or vehicle treated negative control was initiated. Efficacy was determined after 7, 14 and 21 days based on the reduction of organism burden (both asci and nuclei) between treatment groups and negative control group as determined by microscopic evaluation (p < 0.05).

Results: IBX at both dose levels worked significantly better than the gold standard for treating PCP (positive control TMP/SMX) at reducing asci burden at day 7. IBX at both dose levels significantly reduced nuclei and asci levels and performed equally as well as the positive control against asci at days 14 and 21.

Conclusions: These results demonstrate that IBX shows significant activity against PCP in a murine therapy model. Previous work by our group has shown that IBX also shows significant activity in a murine prophylaxis model. Taken together, these results indicate that IBX potentially could be a viable option for managing PCP in immunocompromised patients.