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.

The purpose of this study was to evaluate the activity of IBX in a murine therapeutic model of PCP.

METHODS

Balb/c mice (10/group) were infected with *P. murina* pneumonia through exposure to mice with a fulminant *P. murina* infection (seed mice). These mice were immune suppressed by the addition of dexamethasone at 4 mg/liter to the drinking water. The seed mice were rotated within the cages for 2 weeks and then removed. After the mice developed a moderate infection level (approximately 5 weeks), the mice were divided into 4 treatment groups:

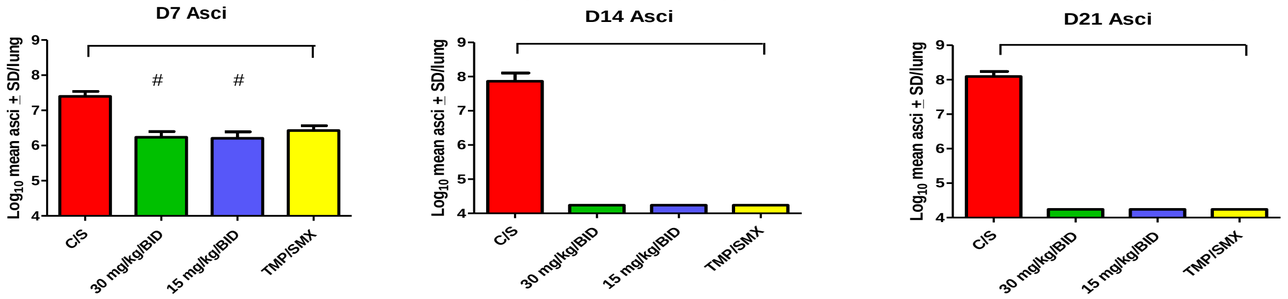
- Negative control group
- Positive control group - TMP/SMX 50/250 mg/kg/day
- IBX 15 mg/kg BID
- IBX 30 mg/kg BID

Drugs were administered by oral gavage (PO) for up to 3 weeks. Efficacy analysis was based on the reduction of organism burden between the treatment groups and the vehicle control group as determined by microscopic evaluation (total nuclei and asci counts) in lung tissue.

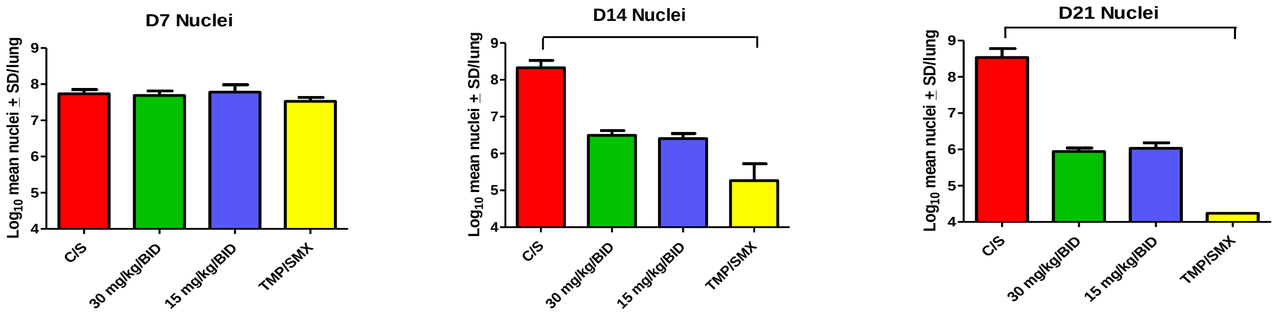
Statistical significance was determined by the analysis of variance (ANOVA); individual groups were compared by the Student-Newman-Keuls t test for multiple comparisons using GraphPad Prism. Survival curves are based on the 7, 14 and 21-day treatment period and compared using GraphPad Prism v5. Statistical significance is accepted at a p value < 0.05.

RESULTS

Both dose levels of IBX worked significantly better than the gold standard for treating PCP (TMP/SMX) at reducing asci burden at day 7; significant reductions in asci burden vs. the negative control group were observed in all treatment groups at day 14 and day 21 .



Significant reductions in nuclei vs. the negative control group were observed in all treatment groups at day 14 and day 21



C/S, vehicle treated negative control. TMP/SMX, trimethoprim/sulfamethoxazole. Bracket denotes statistical significant difference between treatment groups and C/S group. # denotes statistical significant difference between treatment group and TMP/SMX

There was no statistical difference in survival between groups at any time point

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 could potentially be a viable option for managing PCP in immunocompromised patients.