Efficacy of CD101, a Novel Echinocandin, in Prevention of Pneumocystis pneumonia (PCP): Thwarting the Biphasic Life Cycle of Pneumocystis

M.T. Cushion,1,2 A. Ashbaugh,1,2 K. Lynch,1,2 M. Linke,1,2 K. Bartizal2
1Cincinnati VAMC, Cincinnati, OH; 2Univ. of Cincinnati Coll. of Medicine, Cincinnati, OH; 3Cidara Therapeutics, San Diego, CA

INTRODUCTION

Current standard treatment is trimethoprim/sulfamethoxazole (TMP/SMX), which targets trophic acid and synthesis. However, there is evidence of emerging resistance to both TMP and SMX, and some patients suffer severe allergic reactions and hepatotoxicity with current standard treatment (TMP/SMX), with no organism microscopically detected (20 mg/kg given once or 3x per wk and 2 mg/kg given 3x/wk).

METHODS

The mice were divided into 8 groups (n=10/group) to receive either vehicle (untreated control), trimethoprim/sulfamethoxazole (TMP/SMX, 50/250 mg/kg 3x/wk) or CD101 (0.2, 0.5 or 2 mg/kg once or 3x per wk). The groups were stratified by the time mice were inoculated. After 6 weeks, mice were humanely euthanized and lungs were processed for analysis by homogenization. Extracted lungs were log transformed and analyzed by ANOVA. The nuclei counts for each lung were log transformed and analyzed by ANOVA. Individual groups were compared by Dunn’s test for multiple comparisons (GraphPad Prism 6).

RESULTS

The reduction in nuclei compared with the untreated controls was evaluated. The nuclei and asci counts for each lung group were compared by ANOVA. Individual groups were compared by Dunn’s test for multiple comparisons (GraphPad Prism 6).

DISCUSSION

In the current study, CD101 significantly reduced total counts of trophic and asci forms compared with untreated controls in all but the 0.2 mg/kg 1x/wk dose group.

REFERENCES


Mice were euthanized after 6 weeks, and lung homogenates were prepared for quantitation of trophic and asci forms by rapid Wright-Giemsa and cyscht violet staining, respectively.

The reduction in P. murina burden of trophic nuclei and asci in treated and untreated control groups was evaluated. The nuclei and asci counts for each lung group were compared by ANOVA. Individual groups were compared by Dunn’s test for multiple comparisons (GraphPad Prism 6).

- Trophic nuclei and asci counts compared with untreated controls were significantly different from the current standard treatment (TMP/SMX), with no organism microscopically detected (20 mg/kg given once or 3x per wk and 2 mg/kg given 3x/wk).

- CD101 blocked formation of both trophic and cystic forms, suggesting that CD101 offers a potential new means to PCP prophylaxis.

CONCLUSIONS

- CD101 efficacy in preventing infection in a mouse model of PCP (P < 0.05 vs control group).

- All but the 0.2 mg/kg CD101 dose given once per week significantly reduced total organ counts.

- Three of the CD101 groups were not significantly different from the current standard treatment (TMP/SMX), with no organism microscopically detected (20 mg/kg given once or 3x per wk and 2 mg/kg given 3x/wk).

ACKNOWLEDGMENTS / DISCLOSURES

Editorial assistance was provided by Theresa Chung, PhD, CMPNP (TMC Medical Communications) and was funded by Cidara Therapeutics. A.A., K.L., and M.J.L. have no relationships to disclose. M.C. is employed by and an equity owner of Cidara Therapeutics.