Preclinical Evaluation Shows CD101, a Novel Echinocandin, is Highly Stable with No Hepatotoxicity in Rats

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INTRODUCTION

CD101 is a novel echinocandin antifungal under development as an IV formulation to treat serious fungal infections. It was designed to be highly stable* and exhibits a longer half-life and lower clearance compared with other echinocandins in multiple species. 1,2

RESULTS

Figure 3. CD101 was stable when incubated across different species' hepatocytes.

Table 1. Human plasma protein binding compared to anidulafungin. CD101 also shows same protein binding values across different animal species.

Table 2. CYP3A4 inhibition was slightly assessed at 10µM incubations of fluorogenic substrates with recombinant CYP3A4, 2C8, 2C9, 2C19, 2D6, 2D7, 3A4, and 3A4 as well as 3A4 substrates were further characterized using human liver microsomal membranes deficient in CYP3A4.

Figure 5. Evidence of reactive intermediate formation from ANID degradation using HRMS following 24 h incubation in PBMC.

RESULTS (cont’d)

Figure 6. CD101 showing excellent stability following 24 h incubation in PBS.

CONCLUSIONS

• CD101 is highly stable chemically and metabolically.
• No interaction with CYP enzymes – i.e., no biotransformation.
• No evidence of reactive intermediate formation.
• Low clearance in vivo – i.e., plasma half-life.
• No evidence of hepatotoxicity after repeated administration.

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REFERENCES

1. IAAC 2014, Poster F-1592.
2. IAAC 2014, Poster A-693.

*Since their introduction, the echinocandins have become increasingly important as antifungals. However, nonclinical toxicity studies for the previous echinocandins have reported hepatotoxicity. A major hypothesis for echinocandin-induced hepatotoxicity is chemical and/or metabolic instability which can generate potentially reactive intermediates. CD101, unlike previous echinocandins, is stable both chemically and metabolically and, therefore, does not generate any reactive intermediates.