Biafungin (CD101), a Novel Echinocandin, Displays Excellent Stability in Plasma, Aqueous Solution, and at Elevated Temperature

R. Krishnan1, K. James1, S. Smith2, C. Laudeman2, A. Vaidya2, B. Bryant2, K. Polowy2

1 Cidara Therapeutics, San Diego, CA, USA; 2Seachead Pharmaceuticals, Durham, NC, USA

ABSTRACT

Stability of biafungin in plasma, aqueous solution, and at elevated temperature was examined. In the absence of stabilization agents, biafungin was shown to be highly stable in both conditions. The presence of excipients, such as dextrose, lactate, and lyophilized preparations, also did not affect the stability of biafungin. However, when stored at room temperature, biafungin showed a slight decrease in purity.

BACKGROUND

Since their introduction in 2001, the echinocandins have become an increasingly important class of antifungal agents. They have a very low drug interactions, a low incidence of resistance, and no dose adjustments based on renal function.

METHODS

Stability of biafungin in Plasma: Blank plasma (n=10), dog, monkey, and human plasma were evaluated with or without the addition of 5% dextrose. Phosphate buffered saline (PBS, pH 7.4) was used in the place of plasma. Each sample was incubated at 37 °C. At 0, 1, 2, 4, and 6 hours, samples were collected and analyzed. Aqueous stability was similarly assessed by placing biafungin solutions in either 50 mM acetate buffer at pH 4.5 or 5.0.

RESULTS

Stability of Biafungin: Stability of biafungin in plasma, aqueous solution, and at elevated temperature was evaluated. In the absence of stabilization agents, biafungin was shown to be highly stable in both conditions. The presence of excipients, such as dextrose, lactate, and lyophilized preparations, also did not affect the stability of biafungin. Stability data are presented in Figure 1. In the presence of 5% dextrose, biafungin was found to be stable for at least 48 hours.

CONCLUSIONS

• Biafungin was more stable than anidulafungin in plasma (rat, dog, monkey, and human) and in PBS buffer.

REFERENCES

2. ICADD 2014 Poster A-802.

ACKNOWLEDGEMENTS

We wish to thank David Song of PBS, for work on the plasma stability studies.

F-1592

Ken Bartizal, PhD
Cidara Therapeutics
6130 Nancy Ridge Drive, Suite 101
San Diego, CA 92121
kbartizal@cidara.com

RESULTS cont.

RESULTS cont.

Conclusions

Stability of Biafungin in IV Infusion Solutions: The results from stability studies indicate that biafungin solution in 5% dextrose was stable for at least 48 hours. After storage at RT and exposure to light in the absence of stabilizers or other excipients, biafungin solution was found to be stable for at least 15 months and in 0.9% saline solution after 12 months. No epimerization of the hemimelanic ether was observed.

Biafungin was more stable than anidulafungin in plasma (rat, dog, monkey, and human) and in PBS buffer.

The stability of biafungin in plasma suggests that (unlike the other echinocandins) chemical degradation may not be the primary mechanism for clearance.

Biafungin acetate, free of fructose or stabilizers, exhibited less than 3% degradation over 9 months at 40 °C.

Biafungin acetate, free of stabilizers or other excipients, exhibited negligible degradation at room temperature in the presence of light at sterile pH (pH 4.5) for 15 months, and 0.9% saline (12 months) solutions.

Biafungin acetate, free of stabilizers or other excipients, exhibited acceptable stability (6 - 9 months) in acetate and lactate buffers (pH 4.5 - 5.5) at 40 °C accelerated conditions.

Biafungin dosing solutions may not be required to be discarded within 24 hours, but perhaps could be stored at room temperature under light for much longer periods.

Precautions such as refrigeration, controlled room temperature protection, from light, and the use of stabilizers and solubilizers may not be required for dosage preparations and storage at 40 °C.

Further work needs to be done to determine if the stability of biafungin could enable subcutaneous or topical dosage forms.