Resazufungin Safety and Pharmacokinetics in Subjects with Moderate or Severe Hepatic Impairment

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INTRODUCTION

Resazufungin is a novel echinocandin antifungal being developed for treatment of candidemia/invasive candidiasis, and for prevention of invasive fungal disease caused by Candida and Aspergillus spp. and Pneumocystis jirovecii in immunosuppressed patients following BMT.

This study was designed to assess the safety and pharmacokinetics (PK) of resazufungin in subjects with normal hepatic function and subjects with moderate or severe hepatic impairment, as resazufungin clinical trials have been limited to enrolling patients with moderate hepatic impairment due to the comparator caspofungin’s product label.

METHODS

The safety, tolerability, and PK of resazufungin in subjects with moderate (Group 1a) and severe (Group 2a) hepatic impairment (Child-Pugh class B and C) and healthy subjects (Groups 1b, and 2b) was investigated in this open-label, single-dose study.

Each hepatic impairment group was matched to a separate healthy subject group (n=8 each, 32 total) by age, sex, and body mass index (BMI). Subjects with moderate or severe hepatic impairment were well matched to their respective healthy subject groups (Table 1).

RESULTS

• Subjects with moderate or severe hepatic impairment were well matched to their respective healthy subject groups (Table 1).

• There were 9 adverse events (AEs) in 7 subjects:
  - 3 occurred in the severe hepatic impairment group (bronchitis, worsening hepatic encephalopathy, hyponatremia), all of moderate severity and unrelated to RZF
  - 5 occurred in the moderate hepatic impairment group (nausea, headache, infusion site infiltration, body aches, productive cough), all of mild severity and unrelated to RZF
  - 1 AE occurred in the healthy group (headache) was considered related to RZF (headache)

• All AEs resolved or were resolving at the end of the study.

• Mean RZF exposure in subjects with moderate or severe hepatic impairment was up to ~30% lower than that in healthy subjects, with considerable overlap between individuals (Figure 1A, 1B). These differences were not considered to be clinically relevant. Mean half-life values were similar between groups and ranged from 110 to 124 hours.

CONCLUSIONS

• Resazufungin exposure was modestly reduced on average in subjects with moderate or severe hepatic impairment relative to matched healthy subjects, with considerable overlap between individuals.

• There were no significant safety findings associated with resazufungin in any group.

• More AEs were experienced by subjects with moderate or severe hepatic impairment than healthy subjects, as expected given their underlying liver disease.

• These results indicate that resazufungin can be administered to subjects with all levels of hepatic impairment without dose adjustment.

DISCLOSURES / ACKNOWLEDGEMENTS

This study was funded by Cidara Therapeutics and Mundipharma. Editorial assistance was provided by T. Chung (Cidara Therapeutics).