Pharmacokinetics and Safety of Lefamulin After Single Intravenous Dose Administration in Subjects With Impaired Hepatic Function

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INTRODUCTION & PURPOSE

• Lefamulin (LEF), the first pharmacokinetic (PK) and clinical trial, was recently approved for use in adults with community-acquired bacterial pneumonia (CABP) [1].
• Although LEF is being developed for the treatment of CABP, little is known about its PK and safety in subjects with hepatic impairment.
• The objective of this study was to determine the PK and safety of LEF and its major metabolite, BC-8041, in subjects with impaired hepatic function.

METHODS

• Subjects were enrolled in 1 of 3 groups based on hepatic function status:
  - Normal: Child-Pugh score 10–7
  - Moderate: Child-Pugh score 8–12
  - Severe: Child-Pugh score ≥13

• Patients with chronic liver disease (CLD) are at substantially increased risk of bacterial resistance and risks associated with current CABP treatments [2].

• Plasma LEF concentrations were comparable across hepatic function groups (Table 1).

• All groups were well balanced in terms of sex, age, and weight (Table 1).

• Differences in LEF PK across the hepatic function groups were small relative to the overall variability, and changes in PK parameters were not associated with increases in CL, and decreases in PBF [3].

• The clinical significance of these changes with respect to efficacy is low, as LEF efficacy has been shown to correlate with AUC [4], which was consistent across the hepatic function groups.

• Dosage adjustment is required for LEF when treating subjects with severe hepatic impairment but not mild or moderate hepatic impairment.

• Oral LEF has not been studied in subjects with hepatic impairment and, based on available data, is not recommended for subjects with moderate or severe hepatic impairment.

RESULTS

STUDY SUBJECTS

• 21 subjects enrolled and completed the study (Table 2).

• All subjects received the intended LEF dose.

• All groups were well balanced in terms of sex, age, and weight (Table 1).

• Differences in LEF PK across the hepatic function groups were small relative to the overall variability, and changes in PK parameters were not associated with increases in CL, and decreases in PBF [3].

• The clinical significance of these changes with respect to efficacy is low, as LEF efficacy has been shown to correlate with AUC [4], which was consistent across the hepatic function groups.

• Dosage adjustment is required for LEF when treating subjects with severe hepatic impairment but not mild or moderate hepatic impairment.

• Oral LEF has not been studied in subjects with hepatic impairment and, based on available data, is not recommended for subjects with moderate or severe hepatic impairment.

CONCLUSIONS

• LEF was generally well tolerated in all subjects regardless of hepatic function status.

• Differences in LEF PK across the hepatic function groups were small relative to the overall variability, and changes in PK parameters were not associated with increases in CL, and decreases in PBF [3].

• The clinical significance of these changes with respect to efficacy is low, as LEF efficacy has been shown to correlate with AUC [4], which was consistent across the hepatic function groups.

• Dosage adjustment is required for LEF when treating subjects with severe hepatic impairment but not mild or moderate hepatic impairment.

• Oral LEF has not been studied in subjects with hepatic impairment and, based on available data, is not recommended for subjects with moderate or severe hepatic impairment.

REFERENCES


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