Materials and Methods

This was an open-label, non-randomized, parallel-group study conducted at 2 centers in the United States during 2013. The study was conducted in accordance with Good Clinical Practice guidelines and conformed to the ethical principles of the Declaration of Helsinki. All subjects signed written informed consent and completed all required study procedures. Male and female subjects with mild, moderate, and severe hepatic impairment (Child-Pugh Class A, moderate; Child-Pugh Class B, severe; Child-Pugh Class C) and healthy matched control subjects with normal hepatic function. All subjects received a once-daily dose of 800 mg on Day 1 followed by 400 mg on Days 2 through 5.

Results

Solithromycin was well tolerated by both healthy subjects and hepatically impaired subjects. No deaths or serious AEs were reported on this study. There were no clinically significant changes in laboratory values, vital signs, or ECGs. 5 subjects discontinued the protocol: 1 subject (a healthy control) was discharged due to adverse effects (AEs) on Day 9, 2 (1 with moderate hepatic impairment and 1 with severe hepatic impairment) on Day 10, and 2 (1 with moderate hepatic impairment and 1 with severe hepatic impairment) on Day 5. The most common AE was mild diarrhea, reported a total of 7 times by 7 (21%) subjects, including 1 mild hepatic impairment subject, 4 moderately hepatically impaired subjects, and 2 severely hepatic-impaired subjects. No clinically important ECG shifts from normal at baseline to abnormal postdose were observed. There were no clinically significant shifts in chemistry, hematology, or coagulation parameters in this study.

Conclusions

Solithromycin, given orally as an 800 mg loading dose on Day 1 followed by 400 mg on Days 2 to 5, was safe and well tolerated by the hepatic-impaired and healthy matched subjects in this study.

The AE profiles of hepatic-impaired subjects did not differ significantly from the age-, weight-, and gender-matched control subjects.

Mean changes from baseline in liver function tests were also similar between hepatic impaired and healthy subjects.

There was no evidence of accumulation in hepatic impaired subjects.

These data suggest that no dosage adjustment is needed for solithromycin administration in patients with chronic liver disease, regardless of the degree of hepatic impairment.

References