Abstract
Solithromycin was well tolerated by both healthy subjects and hepatically impaired subjects. No deaths or serious AE were reported in the study. Overall, 16 treatments were administered to 37 subjects, 13 reported by 13 subjects, with 9 of 24 (38%) hepatic impaired subjects and 4 of 9 (44%) healthy matched controls reporting AE. Thirty-two subjects completed the study in accordance with the protocol; 1 subject (a healthy control) was discontinued by the investigator after dosing on Day 2 due to the AE of rash. This subject was replaced with another healthy control.

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 designed and initiated with Glaxo Clinical Practice Guidelines and conform to the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all subjects prior to enrollment, and the study protocol was approved by an independent ethics committee. Male and female subjects with mild, moderate, and severe hepatic impairment (Child-Pugh Score ranging from 5 to 12), ages 18 to 75 years with a total body mass index (BMI) ≥20 kg/m² and ≤30 kg/m² were enrolled. A cohort of healthy matched control subjects with normal (functional) hepatic impairment and healthy matched controls with normal hepatic function. All subjects received a once-daily dose of 800 mg on Day 1 followed by 400 mg for Days 2 through 5.

Results
Solithromycin was well tolerated by both healthy subjects and hepatically impaired subjects. No deaths or serious AE were reported in the study. Overall, 16 treatments were administered to 37 subjects, 13 reported by 13 subjects, with 9 of 24 (38%) hepatic impaired subjects and 4 of 9 (44%) healthy matched controls reporting AE. Thirty-two subjects completed the study in accordance with the protocol; 1 subject (a healthy control) was discontinued by the investigator after dosing on Day 2 due to the AE of rash. This subject was replaced with another healthy control.

References

**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.
- The PK of plasma solithromycin in subjects with mild and moderate hepatic impairment were similar to that in subjects with normal liver function.
- 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.

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