Pharmacokinetics of TMC435 in subjects with moderate hepatic impairment

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INTRODUCTION

TMC435 is an investigational potent and selective inhibitor of NS3/4A (SARS Institute Inc., Cary, NC, USA). Findings from Phase I and II studies have shown that TMC435 is well tolerated in all subjects, and routine clinical monitoring may be considered adequate.9 TMC435 treatment period.

Methods

Study Design and Treatment

The study was a Phase 1, open-label, study. Period A included 16 subjects: 8 with moderate hepatic impairment and 8 healthy matched controls. Subjects in Panel B are not yet fully recruited, so are not available for reporting.

Pharmacokinetic profile of TMC435 after 7 days of dosing is similar to that of healthy subjects infected with HCV who participated in the OPRA-01 trial.9

Results

Subject Disposition

Subjects were well balanced between treatment groups in terms of age, sex, BMI, and smoking status.

Safety

A summary of AEs reported during the TMC435 treatment period is shown in Table 3. The most common AE, reported by three subjects.

Conclusions

The study suggests that TMC435 dose accumulation is necessary for HCV-infected patients with moderate hepatic impairment, and without clinical monitoring may be considered adequate.

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References

4. Reesink H et al. Poster presented at the 60th Annual Meeting of the American Association for the Study of the Liver (AASLD), Boston, MA, USA.

Posters presented at the 46th Annual Meeting of the European Association for the Study of the Liver (EASL) 13 March – 17 April, 2011, Berlin, Germany

Graph 1: Time vs. plasma concentration of TMC435 in normal plasma samples compared with healthy matched controls.

Graph 2: Area under the concentration-time curve of TMC435 from time of administration up to 24 hours post-dosing (AUC24h).

Graph 3: The median (range) ratios for TMC435 exposure (AUC24h) and Cmax for TMC435 in HCV-infected patients with moderate hepatic impairment compared with healthy matched controls.