PHASE 1 STUDY TO ASSESS THE SAFETY, TOLERABILITY AND PHARMACOKINETIC PROFILE OF BOCEPREVIR AND SILDENAFIL WHEN DOSED SEPARATELY AND TOGETHER, IN HEALTHY MALE VOLUNTEERS

Background/introduction Boceprevir is a first generation direct-acting antiviral (DAA) licensed for the treatment of hepatitis C infection. Sildenafil is an oral therapy for erectile dysfunction. As boceprevir is a potent inhibitor of CYP3A4, potential pharmacokinetic interactions may occur when co-administered with sildenafil.

Aim(s)/objectives The aim of this study was to assess the pharmacokinetic profile of sildenafil and boceprevir when dosed separately and together in healthy volunteers.

Methods Thirteen male subjects completed the following study procedures: phase 1 (day 0), single dose sildenafil 25 mg was administered; phase 2 (days 1–9), washout period; phase 3 (days 10–15), boceprevir 800 mg three times a day was administered; phase 4 (day 16), boceprevir 800 mg and sildenafil 25 mg were administered. All drugs were administered in a fed-state.

Intensive pharmacokinetic sampling was undertaken on days 0, 15 and 16. Differences in pharmacokinetic parameters of sildenafil, N-desmethyl-sildenafil and boceprevir between phase 4 and earlier phases were evaluated by changes of geometric mean ratios (GMR).

Results All drugs were well tolerated with no safety concerns arising. In the presence of boceprevir (phase 4 versus phase 1), sildenafil GMR maximum plasma concentration (Cmax) and area-under-the-concentration-time-curve (AUC24) increased by 1.9 fold (95% CI: 1.5–2.4) and 2.7 fold (95% CI: 2.1–3.4), respectively whereas a reduction in N-desmethyl-sildenafil Cmax was observed (GMR 0.5, 95% CI: 0.4–0.7). No significant changes in boceprevir exposure were observed between phases 4 and 3.

Discussion/conclusion Sildenafil exposure is increased in the presence of boceprevir. Dose adjustment of sildenafil is necessary. An initial dose of 25 mg of sildenafil is suggested.