POSTERS

Results: A total of 527 HIV/HCV-coinfected patients were identified, of whom 344 had F0–F2 at baseline. Peginterferon-ribavirin therapy was given to 205 patients with null-mild fibrosis, of whom 92 (44.9%) achieved sustained virological response (SVR). After a mean follow-up of 53 months, LFP occurred in 5.4% SVR, 25.7% non-SVR and 18% untreated patients (p = 0.005). In multivariate analysis, only achievement of SVR prevented LFP (adjusted hazard ratio 2.1; 95% confidence interval 1.1–4.1; p = 0.01).

In 139 untreated patients, only greater baseline elastometry values predicted LFP in multivariate analysis (adjusted hazard ratio 1.84; 95% CI: 1.03–3.3; p = 0.03). The area under the receiver operating characteristic (AUROC) curve was 79%. A discriminant threshold of 7.1 kPa gave 68% sensitivity and 82% specificity.

Conclusions: In the absence of successful treatment, more than 20% of HIV/HCV-coinfected patients with null-mild liver fibrosis progress to advanced fibrosis within 5 years. Patients with >7.1 kPa (Metavir F2) display the highest risk. Therefore, all coinfected patients with any significant liver fibrosis should be considered as candidates for new DAA-based therapies.

P0839 EVALUATION OF DRUG–DRUG INTERACTIONS BETWEEN THE FIXED-DOSE COMBINATION OF DACLATAVIR/ASUNAPREVIR/BECLABUVIR AND METHADONE OR BUPRENORPHINE/NALOXONE

X. Tao1, K. Sims1, M. Hesney1, S. Lubin1, M. Stonier1, M. Wind-Rotolo1, L. Reynolds2, D. Liang3, J. Pursley1, M. AbuTarif1.

1Bristol-Myers Squibb Research and Development, Princeton, 2ICON Development Solutions, Hannover, United States

E-mail: neslihan.oz@articulatescience.com

Background and Aims: Daclatasvir (DCV; NSSA inhibitor), asunaprevir (ASV; NS3 inhibitor) and beclabuvir (BCV [BMS-791325]; nonnucleoside NS5B inhibitor) are in phase 3 evaluation for hepatitis C virus (HCV) infection as a twice-daily (BID) fixed-dose combination (DCV/ASV/BCV; 30/200/75 mg). HCV is common among injection drug users, and often medically managed with the opioids methadone (MET), or buprenorphine (BUP) + naloxone (NAL). The effect of DCV/ASV/BCV on the pharmacokinetics (PK) of MET or BUP/NAL was assessed.

Methods: An open-label study of the effect of steady-state DCV/ASV/BCV BID on the PK of MET (Part 1; N = 16) or BUP/NAL (Part 2; N = 16) was conducted in HCV-infected subjects on stable opioid maintenance. Subjects received daily oral MET (40–120 mg) or BUP/NAL (8/2–24/6 mg), plus DCV/ASV/BCV BID on Days 2–12 plus additional BCV (75 mg BID) to adjust for higher systemic BCV exposure in HCV patients. Serial PK sampling was on Days 1 (opioid alone) and 12. Dose-normalized PK parameters for R-, S-, and total-MET, BUP and its metabolite norBUP were derived. Geometric mean ratios (GMR; Day12:Day 1) and 90% confidence intervals (90%CI) for Cmax and AUCinf of each analyte were derived from linear mixed-effect models. No clinically relevant interaction was to be inferred if Cmax and AUCinf 90%CI were within literature-derived boundaries (R-MET: 0.7–1.43; BUP/norBUP: 0.5–2.0). Safety and opioid pharmacodynamics (PD, withdrawal scales and overdose assessment) were assessed.

Results: Opioid PK parameters are shown. Steady-state DCV/ASV/BCV (+ BCV) BID resulted in a ~30% reduction in dose-normalized R-, S- and total-MET systemic exposures with 90%CI outside prespecified boundaries. However, no loss of MET maintenance efficacy was observed by investigator or PD assessment throughout dosing. No relevant effects were observed on BUP or norBUP PK. All-cause adverse events (AEs, mild/moderate) occurred in: Part 1, 10 subjects (63%); Part 2, 6 subjects (38%). There were no deaths, serious AEs, withdrawal/overdose AEs or discontinuations for AEs. All AEs resolved without sequelae.

Conclusions: Steady-state DCV/ASV/BCV (+ BCV 75 mg) BID was generally well tolerated and had no clinically meaningful effect on the PK of BUP/NAL. A reduction in MET systemic exposure was observed but was not associated with loss of clinical maintenance. No a priori dose adjustments appear warranted when DCV/ASV/BCV is administered to HCV patients on MET or BUP/NAL maintenance.

P0840 SAFETY AND EFFECTIVENESS OF SOFOSBUVIR-BASED REGIMENS FOR THE TREATMENT OF HEPATITIS C GENOTYPE 3 AND 4 INFECTIONS: INTERIM ANALYSIS OF A PROSPECTIVE, OBSERVATIONAL STUDY


1Johns Hopkins University, Baltimore, United States; 2Goethe University Hospital, Frankfurt, 3Hannover Medical School, Hanover, Germany; 4University of California, San Diego, San Diego; 5Saint Louis University School of Medicine, St. Louis; 6University of Pennsylvania, Philadelphia; 7University of Nebraska Medical Ctr, Omaha; 8Baylor University Medical Center, Dallas; 9Scripps Clinical Research Center, La Jolla; 10Indiana University, Indianapolis; 11Yale University School of Medicine, New Haven; 12Mayo Clinic, Phoenix; 13University of North Carolina, Chapel Hill; 14University of Florida, Gainesville, United States

E-mail: salqaht1@jhmi.edu

Background and Aims: HCV genotype (GT) 3 and 4 are common in many regions of the world and optimal treatment regimens continue to evolve. The real-world safety and efficacy of available antiviral options in clinical practice has not been reported. The aim of this study is to evaluate the safety and efficacy of sofosbuvir (SOF) containing regimens for the treatment of patients with GT 3 and 4 in HCV-TARGET (HCVT), a multicentre, prospective, observational cohort study.

Methods: Patients who initiated HCV treatment in clinical practice were enrolled and treated according to the regional standards of care at academic (n = 43) and community medical centres (n = 13) in North America (n = 51) and in Europe (n = 5). Information was collected from the medical records and abstracted into a unique centralized data core. Independent data monitors systematically review data entries for completeness and accuracy. Demographic, clinical, adverse events (AEs) and virological data were collected throughout treatment and post-treatment follow-up.

Results: Of 202 patients with GT 3 and 47 with GT4, 110 (54%) GT 3 and 4 (106 GT 3 and 26 GT 4) patients experienced at least one AE, although most were mild. Among patients with GT 3, five discontinued due to AEs (anemia, flu-like symptoms, nausea, vision loss and intolerance) and 4 for lack of efficacy; 1 was lost to follow-up and 1 underwent liver transplant. One patient with GT 4 stopped due to worsening encephalopathy. As of most recent follow-up, 144/162 GT3 and 34/37 GT 4 had HCV RNA below level of quantitation. Among patients for whom post-treatment data is
学霸图书馆
www.xuebalib.com

本文献由“学霸图书馆-文献云下载”收集自网络，仅供学习交流使用。

学霸图书馆（www.xuebalib.com）是一个“整合众多图书馆数据库资源，
提供一站式文献检索和下载服务”的24小时在线不限IP图书馆。
图书馆致力于便利、促进学习与科研，提供最强文献下载服务。

图书馆导航：
图书馆首页  文献云下载  图书馆入口  外文数据库大全  疑难文献辅助工具