Methods: Three hundred HCV patients and 860 family members were studied. All family members were screened for HCV antibodies by ELISA. Positive cases were examined using Real-Time PCR to confirm the presence of HCV-RNA. Seventy five patients of 300 were treated using SOC treatment. Molecular study of IL-28B gene was done to all patients and their families using PCR and restriction enzyme analysis.

Results: IL-28B gene (rs12979860) polymorphism in patients was 27.43%, 55.43% and 17.14% for C/C, C/T and T/T genotypes respectively, in non infected family members was 37.38%, 44.05% and 18.57% for C/C, C/T and T/T respectively. There was significant increase as regard CC genotype in non-infected family members than patients. Of the treated 75 patients, 36 achieved SVR (48%). Better response to treatment was found in CC genotype (75%) than CT (48%) and TT (28%).

Conclusions: CC genotype for IL-28B gene has better response to treatment and may have a protective role against HCV infection as it detected significantly in non infected family members of HCV patients.

Acknowledgement: Project was funded by Science, Technology Development Fund (STDF), Egypt, Grant No. 1687.

P1220
MODELING PREDICTS CLINICALLY MEANINGFUL SVR RATES IN GENOTYPE 1 TREATMENT-EXPERIENCED PATIENTS BASED ON RESULTS IN GENOTYPE 1 TREATMENT-NAIVE PATIENTS TREATED WITH SOFOSBUVIR + PEGINTERFERON + RIBAVIRIN FOR 12 WEEKS
A. Muir1, D.R. Nelson2, S.C. Gordon1, J.J. Feld3, K. Patel1, E. Lawitz2, A.M. Sheikh4, D.M. Brainard2, W.T. Symonds2, J.G. McHutchison2, B.N. Bekele2, A. Mangia5, E.J. Gane6. 1Duke University, Durham, NC, 2University of Florida, Gainesville, FL, 3Henry Ford Health Systems, Detroit, MI, United States; 4University of Toronto, Toronto, ON, Canada; 5Texas Liver Institute, University of Texas Health Science Center, San Antonio, TX, 6Gl Specialists of Georgia, Marietta, GA.

Background and Aims: In NEUTRINO, 89% of the treatment-naive (TN) patients with HCV genotype (GT) 1 receiving sofosbuvir (SOF)+peginterferon (PEG)+ribavirin (RBV) for 12 weeks achieved an SVR. Treatment-experienced (TE) patients with HCV GT1 were not evaluated. Given this high response rate, exploratory methods were used to predict a potential response rate for TE patients with HCV GT1.

Methods: Three exploratory methods were used to predict the SVR12 rate in GT1 TE patients. Method 1 assumes that in TN patients, approximately 50% will fail PEG+RBV. With SOF+PEG+RBV, 89% responded implying that 39% of the 50% who would have failed PEG+RBV would respond to SOF+PEG+RBV, resulting in a 78% SVR rate (39/50) for SOF+PEG+RBV in GT1 TE patients. Methods 2 and 3 assume that differences in response rates between TN and TE patients receiving telaprevir+ PEG+RBV are similar to relative differences in response rates between TN and TE patients receiving SOF+PEG+RBV. Method 2 uses a difference in response rates to define the relative difference. Method 3 uses a log odds difference.

Method | Projected SVR Rate (95% CI)
---|---
Method 1 (Additional Benefit) | 78% (71, 86)
Method 2 (Response Rate Difference) | 79% (71, 87)
Method 3 (Log Odds Difference) | 84% (76, 90)

Results: All 3 methods predicted that TE patients with HCV GT1 receiving 12 weeks of SOF+PEG+RBV would achieve an SVR12 rate ranging from 78% to 84%. Our analysis also predicted that within the subset of prior null/partial responders receiving 12 weeks of SOF+PEG+RBV, SVR rates would range from 56% to 67%.

Conclusions: These analyses suggest that SOF+PEG+RBV may provide a potential treatment option in TE GT1 patients. Studies are ongoing to evaluate SOF+PEG+RBV in patients who have failed PEG+RBV +/- protease inhibitors.

P1221
PHARMACOKINETIC (PK) DRUG–DRUG INTERACTION BETWEEN SAMATASVIR (IDX719), A PAN-GENOTYPIC NSSA INHIBITOR, AND SIMEPREVIR IN HEALTHY VOLUNTEERS AND HCV-INFECTED SUBJECTS
X.J. Zhou1, E. Donovan1, J. Chen2, R. van Heeswijk3, J.Z. Sullivan-Bolyai4, D. Meyers3. 1Idenix Pharmaceuticals, Inc., 2Janssen Infectious Diseases BVBA, Cambridge, MA, United States E-mail: dahlan.teresa@idenix.com

Background and Aims: PK drug-drug interaction (DDI) between samatasvir, a pan-genotypic NSSA inhibitor, and simeprevir, an NS3/4A protease inhibitor, was assessed in healthy volunteers and HCV-infected subjects.

Methods: Healthy volunteers (N=32) were randomized equally to receive one of two study drugs for 14 days (150 mg QD for both drugs), with the other drug added on Day 8 and continued for 7 days. PK of the study drugs alone and in combination was evaluated on Days 8 and 14, respectively. Treatment-naive HCV genotype 1b- or 4-infected subjects (N=60) were randomized equally to receive samatasvir (50, 100 or 150 mg QD) in combination with simeprevir 150 mg QD and ribavirin for 12 weeks as part of the HELIX-1 study. Intensive PK was performed at Day 14 with troughs obtained weekly.

Results: The study drugs were well tolerated in both populations. In healthy subjects, steady-state plasma exposures of samatasvir approximated doubled (mean ratios 1.87 and 2.22 for Cmax and AUC) in the presence of simeprevir. Plasma exposures of simeprevir were increased by 40–50% (mean ratios 1.47 and 1.49 for Cmax and AUC) in the presence of samatasvir. Elimination half-lives of both drugs remained unaffected. Exposures of samatasvir and simeprevir in combination were comparable to previous data. A positive correlation between the plasma PK parameters of samatasvir and simeprevir was observed.

Conclusions: The combination of samatasvir and simeprevir was well tolerated and resulted in increased plasma concentrations for both drugs. The observed safety and PK data support investigating all-oral regimens involving samatasvir and simeprevir.

P1222
A PHASE II STUDY OF SAMATASVIR (IDX719) IN COMBINATION WITH SMEPREVIR AND RIBAVIRIN IN TREATMENT-NAIVE HCV-INFECTED SUBJECTS WITH GENOTYPES 1B AND 4 (HELIX-1 STUDY)
E. Lawitz1, M. Rodriguez-Torres2, T. Nguyen1, A. Sheikh4, H. Tobias3, J. Galati4, J. Hill5, A. Lok6, D. Nelson7, G. Dubuc Patrick8, J. Chen10, D. Frank10, X.J. Zhou10, Z. Sullivan-Bolyai10, D. Meyers10. 1Duke University, Durham, NC, 2Texas Liver Institute, San Antonio, TX, United States; 3Fundacion De Investigacion De Diego, Santurce, Puerto Rico, 4San Diego, San Diego, CA, 5Gastrointestinal Specialists of Georgia, Marietta, GA, 6Concorde Medical Group PLCC, New York, NY, 7Research Specialists of Texas, Houston, TX, 8Avail Clinical Research, Deland, FL, 9University of Michigan Health System, Ann Arbor, MI, 10Idenix Pharmaceuticals, Inc., Cambridge, MA, United States E-mail: dahlan.teresa@idenix.com

Background and Aims: Samatasvir is a potent HCV NSSA inhibitor with pan-genotypic antiviral activity. Simeprevir (SMV) is an oral NS3/4A protease inhibitor approved for the treatment of GT 1 HCV infection.