Conclusions Treatment with the single tablet regimen of SOF/VEL for 12 weeks was highly effective and well tolerated in genotype 1–4 HCV-infected liver transplant recipients with and without cirrhosis.

**Abstract DDF2018-ABS-0110**

Efficacy and Safety of Sofosbuvir/VELPatasvir Plus Ribavirin for 12 or 24 Weeks in Genotype 1 or 2 HCV-Infected Japanese Patients with Prior Treatment Failure to DAA-Based Regimens

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Background There is a growing number of Japanese patients with HCV infection who have failed direct acting antiviral (DAA)-based regimens and currently have no salvage therapies available. This Phase 3 study evaluates the efficacy and safety of sofosbuvir/velpatasvir (SOF/VEL) plus ribavirin (RBV) for 12 or 24 weeks in Japanese patients with genotype (GT) 1 or 2 HCV infection who have been previously treated with DAA.

Methods Approximately 110 subjects were randomised 1:1 to receive SOF/VEL+RBV for 12 or 24 weeks. Randomization was stratified by GT and presence of cirrhosis. All subjects must have been previously treated with a DAA for at least 4 weeks. Subjects with GT1 HCV infection must have previously been treated with an NS5A inhibitor. The primary efficacy analysis is a comparison of the SVR12 rates for GT1 patients in each of the two treatment groups to a historical control.

Results Of 117 patients enrolled, 45% were male, 81% had GT1 HCV infection, and 33% had cirrhosis. 84% had previously been treated with at least 2 different DAs. 66% of GT1 patients had previously been treated with daclatasvir plus asunaprevir and 91% of GT2 patients with SOF. Virologic outcomes at post-treatment week 4 are presented in the table below. There were no on-treatment virologic failures. Complete SVR12 and virology data will be presented. Three (3%) patients discontinued study drugs due to adverse events (AEs). One patient in the 12 week arm discontinued study drugs on Day 4 due to rash (related to study drugs). Two patients in the 24 week arm discontinued study drugs; one on Day 85 due to hepatic angiosarcoma (not related) and one on Day 57 due to depression (related). The two latter patients achieved SVR12. No Grade 3 or 4 AEs were considered related to study drugs (table 1).

Conclusions SOF/VEL+RBV has the potential to be a safe, well-tolerated, and effective treatment for Japanese patients with and without cirrhosis who have previously failed DAA-based regimens, a group without currently approved retreatment options. Baseline NS5A RASs did not affect treatment outcome.

**Abstract DDF2018-ABS-0111**

Safety and Efficacy of Treatment with Once-Daily Ledipasvir/ Sofosbuvir (90/400 mg) for 12 Weeks in Genotype 1 HCV-Infected Patients with Severe Renal Impairment

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Background Despite higher concentrations of the primary circulating sofosbuvir (SOF) metabolite, GS-331007, in patients with severe renal impairment (RI), retrospective case series and claims database analyses have suggested substantial use of ledipasvir (LDV)/SOF in this population with no untoward effects described. The current study evaluated the safety, efficacy, and pharmacokinetics (PK) of LDV/SOF (90/400 mg) once-daily for 12 weeks in patients with genotype (GT) 1 HCV-infection and severe RI.

Methods Treatment naive or experienced patients with or without compensated cirrhosis and creatinine clearance (CLcr) < 30 ml/min. In terms of liver disease characteristics, all 18 had GT1 HCV infection (14 GT1a and 4 GT1b), 14 (78%) were treatment naïve, and 2 (11%) had cirrhosis. All patients completed 12 weeks of LDV/SOF treatment. There were no early discontinuations nor any on-treatment virologic failures. The SVR12 rate is 100% (18/18). Plasma concentrations of the terminal
SOF metabolite GS-3310007 were approximately 6 fold higher than in the LDV/SOF Phase 3 trials. SOF and LDV concentrations were similar to those with normal, mild or moderate RI. The most common adverse events (AEs) were fatigue (22%), headache (22%), and hyperkalemia (22%). Six serious AEs were reported among 4 patients (22%), including 2 renal events; no SAEs related to study drugs. There were no treatment-related cardiac AEs, including bradycardia, and no meaningful changes in QTc intervals or other parameters.

Conclusions Treatment with LDV/SOF (90/400 mg) for 12 weeks in genotype 1 patients with and without cirrhosis and severe renal impairment resulted in 100% SVR12 rate. The regimen was safe and well-tolerated with no treatment discontinuations and no treatment-related SAEs. (no table selected) (No Image Selected) Co-Author Disclosure Status.

IDDF2018-ABS-0112 SAFETY AND EFFICACY OF SOFOSBUVIR/VELPATASVIR IN A GENOTYPE 1–6 HCV INFECTED POPULATION FROM SINGAPORE, MALAYSIA, THAILAND, AND VIETNAM: RESULTS FROM A PHASE 3, CLINICAL TRIAL

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Background The prevalence of hepatitis C virus (HCV) in Singapore, Malaysia, Thailand, and Vietnam, ranges from 1%–3%. Because of the heterogeneity of genotypes (GTs) in these countries (primarily GT1, 2, 3, and 6), there is a critical need for a pan-genotypic, all oral regimen to address the burden of HCV infection. This study evaluated the efficacy and safety of SOF/VEL for 12 weeks in patients with chronic GT1–6 HCV infection.

Methods Treatment experienced and treatment naive patients with chronic GT1–6 HCV infection with or without cirrhosis were enrolled in a single-arm, open-label trial of different doses of SOF/VEL 400/100 mg daily for 12 weeks. Patients were recruited from 13 sites in Singapore, Malaysia, Thailand, and Vietnam. The primary efficacy endpoint was SVR12 using the CAP/CTM HCV 2.0 assay (LLOQ=15 IU/mL), and the primary safety endpoint was adverse events (AEs) leading to SOF/VEL discontinuation.

Results A total of 111 patients were enrolled and treated. Of these, 51% were male, 14% had compensated cirrhosis, 18% were treatment-experienced, 82% had IL28B CC genotype, 20% had GT1a, 23% GT1b, 3% GT2, 23% GT3, and 31% GT6 HCV infection. The overall SVR12 rate was 97% (108/111) GT specific SVR12 rates are presented in the Table (IDDF2018-ABS-0112 Table 1). All 3 patients who did not achieve SVR experienced a virologic relapse. All 15 cirrhotic patients, including 8 with GT3 HCV infection achieved SVR12. Virology data will be presented. There were no discontinuations due to AEs. There were 50 patients (45%) who experienced any adverse events (AEs), with no AEs occurring in >10% of patients. No serious or severe AEs were assessed by the investigator as related to study drug and there were no deaths.

Abstract IDDF2018-ABS-0112 Table 1 SVR12 for GT1–6 HCV Infected Patients

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Total</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT2</th>
<th>GT3</th>
<th>GT6</th>
<th>Indeterminate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=111</td>
<td>n=22</td>
<td>n=25</td>
<td>n=3</td>
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<td>n=34</td>
<td>n=2</td>
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<tr>
<td>SVR12</td>
<td>108/111</td>
<td>22/22</td>
<td>23/25</td>
<td>47/47</td>
<td>3/3</td>
<td>33/34</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td></td>
<td>(97)</td>
<td>(100)</td>
<td>(100)</td>
<td>(100)</td>
<td>(100)</td>
<td>(92)</td>
<td>(97)</td>
</tr>
</tbody>
</table>

a. Sequence analysis to determine genotype pending

Conclusions Treatment with the single tablet, pan-genotypic regimen of SOF/VEL for 12 weeks was highly effective and well tolerated in a GT 1,2,3, and 6 HCV infected population with and without cirrhosis from Singapore, Malaysia, Thailand, and Vietnam. Seng Gee Lim is the presenter of the abstract.

IDDF2018-ABS-0114 SOF/VEL/VOX RESULTS IN HIGH SVR12 RATES WHEN ADMINISTERED FOR 12 WEEKS IN DAA-EXPERIENCED PATIENTS OR FOR 8 WEEKS IN DAA-NAIVE PATIENTS: AN INTEGRATED ANALYSIS OF THE POLARIS-1, POLARIS-2, POLARIS-3 AND POLARIS-4 STUDIES

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Background The once-daily fixed-dose combination tablet of sofosbuvir/velpatasvir/voxilaprevir(SOF/VEL/VOX) was evaluated for the treatment of genotype 1–6 HCV infection in four Phase 3 studies in direct-acting antiviral (DAI)-experienced (POLARIS-1 and POLARIS-4) and DAA-naive...