discriminate advanced (F3-F4) fibrosis was evaluated using AUROCs with 5-fold cross-validation repeated 100x. Optimal thresholds for F3-F4 fibrosis were selected based on the literature. Data presented are from an interim analysis on 1 May 2018.

Results A total of 4467 patients (median age 58 years, 55% women, 72% Caucasian, 59% with diabetes) were screened. In the 3220 with evaluable histology, median biopsy length was 2.0 cm, 8% F0, 9% F1, 13% F2, 31% F3, 40% F4, 59% with NAS ≥5. Median values of NFS, FIB-4, ELF, and LS by TE increased with worsening fibrosis (-0.962/1.19/9.21/8.8 kPa in F0-F2 vs 0.342/2.20/10.39/16.5 kPa in F3-F4 respectively). AUROCs ranged from 0.75 to 0.80 to discriminate advanced fibrosis (table 1). When tests were combined, performance characteristics improved and PPVs ≥98% were possible.

Conclusions In these large, global phase 3 trials of SEL, routinely available NITs demonstrated acceptable diagnostic performance for the discrimination of advanced fibrosis due to NASH.

IDDF2019-ABS-0134 SOFOSBUVIR/VELPATASVIR IS EFFECTIVE AND SAFE IN PATIENTS WITH CONCOMITANT PROTON PUMP INHIBITOR USE IN CLINICAL STUDIES

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Background Prior to the availability of Phase 1 drug interaction data, concomitant proton pump inhibitor (PPI) use was prohibited in clinical trials of sofosbuvir/velpatasvir (SOF/VEL). Later clinical studies allowed for the use of up to 20 mg omeprazole or equivalent dosing. This analysis evaluated the efficacy and safety of patients with and without compensated cirrhosis who received SOF/VEL for 12 weeks and reported concomitant use of a PPI.

Methods This was a retrospective analysis from 12 Phase 2 and Phase 3 clinical studies in which patients of all genotypes with and without compensated cirrhosis received 12 weeks of SOF/VEL and reported concomitant use of a PPI. Efficacy was assessed by SVR12 and relapse rates and safety was assessed by treatment-emergent adverse events (AEs).

Results 87 patients reported concomitant use of a PPI. The mean age (range) was 57 years (26–78), 79% were male and 75% white; 56% of patients were infected with genotype 3 and 29% with genotype 1; 37% of patients had compensated cirrhosis and 39% were treatment experienced. The most common PPI was omeprazole reported by 68% of patients. The SVR12 rate was 97% (84 of 87 patients). Of the 3 patients who did not achieve SVR12, 2 patients relapsed (relapse rate 2%) and one patient with a history of diabetes discontinued SOF/VEL after 7 days of dosing due to hyperglycemia. No other patient had an AE which led to discontinuation or interruption of SOF/VEL. 78% of patients had an AE, most of which were mild, and 11% had a serious AE. These efficacy and safety are comparable to patients enrolled in the same studies who received SOF/VEL for 12 weeks without concomitant use of a PPI (SVR12 rate 97% [2445 of 2517 patients]; relapse rate 2% [40 of 2488 patients]).

Conclusions In Phase 2 and Phase 3 clinical studies, the single-tablet regimen of SOF/VEL for 12 weeks was effective and safe in patients with concomitant PPI use. These data support the use of SOF/VEL according to labeled recommendations with respect to co-administration of PPIs and other acid reducing agents.

IDDF2019-ABS-0135 PHARMACOKINETICS OF ONCE-DAILY SOFOSBUVIR OR LEDIPASVIR/SOFOSBUVIR IN HCV-INFECTED PEDIATRICS AGED 3 TO

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Background SOF 400 mg and LDV/SOF 90/400 mg are approved HCV treatment in adults and adolescents. Pharmacokinetic (PK) data indicates that SOF 200 mg and LDV/SOF 45/200 mg are appropriate doses in children 6 to <12 years old (y). SOF and LDV/SOF oral granules were developed; PK was assessed in children 3 to < 6 y.

Methods HCV-infected children (3 to <6 y) received SOF or LDV/SOF with doses selected to target exposures similar to adults: subjects ≥17 kg received SOF 200 mg or LDV/SOF 45/200 mg; subjects <17 kg received SOF 150 mg or LDV/SOF 33.75/150 mg, QD. Subjects received SOF+RBV 12 or 24 weeks (GT2 or GT3, respectively) or LDV/SOF 12 weeks (GT1, 4). Intensive PK sampling (IPK lead-in) was performed on Day 7 (SOF; N=11) or 10 (LDV/SOF; N=15). Exposures (AUCtau and Cmax) from subjects were compared to exposures in Phase 2/3 adult clinical programs. The primary endpoint was AUCtau of GS-331007 and LDV with predefined PK equivalence bounds of 50–200%.

Results All but 1subject completed IPK assessments. At baseline, median age and weight for subjects was 5 y and 17 kg in SOF+RBV PK lead-in (N=11) and 5 y and 20 kg in LDV/SOF subjects (N=14). The predefined PK criteria were met as GS-331007 and LDV AUCtau were within the 50–200% boundaries as compared with the adult Phase 2/3 population (table 1). The GS-331007 Cmax (SOF+RBV) was modestly higher; these increases are not considered clinically relevant based on established exposure-safety analyses. SOF concentrations were within the range of those observed in the SOF and LDV/SOF adult Phase 2/3 population (data not shown).