Conclusions The proportion of patients analysed and the HBV sequence changes observed were similar between patients in the TAF and TDF arms. Most substitutions occurred at polymorphic positions and no substitutions associated with resistance to TAF were detected through 96 weeks of treatment.

IDDF2018-ABS-0107 EFFICACY AND SAFETY OF TENOFOVIR ALAFENAMIDE (TAF) AT 96 WEEKS IN CHRONIC HBV (CHB) PATIENTS WITH RISK FACTORS FOR USE OF TENOFOVIR DISOPROXIL FUMARATE (TDF)

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Background The recently updated EASL Guidelines for Management of HBV Infection (2017) recommend the use of TAF as an alternative to TDF in patients with risk factors unfavourable to TDF use. We, therefore, performed an evaluation of the efficacy and safety of TAF compared with TDF in patients considered to be at risk for adverse bone and/or renal effects from TDF.

Abstract IDDF2018-ABS-0107 Table 1 Bone and renal safety results at week 96 in chb patients with tdf risk factors

n/N (%)	TAF (n=151)	TDF (n=88)	P value
Bone parameters			
Hip BMD, mean (SD)% change ^a	-0.28 (2.50)	-2.16 (3.10)	<0.001
Spine BMD, mean (SD)% change	-1.35 (4.46)	-2.46 (3.73)	0.071
Serum bone biomarkers, median (Q1, Q3)% change			
C-type collagen sequence (CTX) [resorption]	-3.9 (-25.5, 24.1)	37.7 (9.1-92.9)	<0.001
Procollagen type 1 N-terminal propeptide (P1NP) [formation]	-18.3 (-34.0, 8.99)	8.7 (-14.4, 42.5)	<0.001
Osteocalcin (OC) [formation]	4.5 (-13.4, 20.8)	34.8 (7.5-54.2)	<0.001
Renal parameters			
eGFR _{CG} median(Q1, Q3) change (mL/min) ^b	-2.4 (-8.4, 6.2)	-6.7 (-15.0, 2.4)	0.008
Urine biomarkers, median(Q1, Q3)% change			
Protein/creatinine ratio, mg/g	-17.5 (-49.5, 38.7)	6.9 (-39.8, 53.3)	0.18
Albumin/creatinine ratio, mg/g	10.4 (-34.4, 87.4)	10.7 (-47.6, 73.0)	0.44
Retinol binding protein/creatinine ratio, µg/g	13.1 (-17.1, 79.1)	48.4 (-2.0, 127.8)	0.014
Beta-2 microglobulin/creatinine ratio, µg/g	6.2 (-28.3, 62.9)	55.2 (0.3-248.0)	<0.001

^aBMD is bone mineral density by DXA scan; ^beGFR_{CG} is creatinine clearance (Cockcroft-Gault method)

Methods In two Phase 3 studies, patients (HBeAg-positive [n=873] and HBeAg-negative [n=425]) were randomised 2:1 to TAF or TDF. Antiviral efficacy (HBV DNA <29 IU/mL) and ALT normalisation (by central laboratory and AASLD criteria) were assessed by study and safety results were pooled for bone (serial DXA scans at hip/spine and serum bone biomarkers) and renal parameters (eGFR by Cockcroft-Gault [eGFR_{CG}] and urine biomarkers of tubular function) and assessed over 96 weeks in the subset with baseline risk factors for TDF use: Age>60 years, osteoporosis of hip or spine by t-score, eGFR_{CG} <60 mL/min, urine albumin to creatinine ratio >30 mg/g, or serum phosphorus <2.5 mg/dL.

Results Of 1298 patients randomised and treated in the 2 studies, 239 (18%; 151 TAF and 88 TDF) patients had at least 1 risk factor for TDF use. Baseline demographics were similar between groups. At Week 96, similar antiviral efficacy (HBV DNA <29 IU/mL), and higher rates of ALT normalisation were seen in the TAF compared with the TDF group which were comparable to the overall results in these studies. Significant differences in favour of TAF were observed in key bone and renal safety parameters (table 1). Patients receiving TAF had smaller declines in BMD, particularly at the hip, and smaller changes in markers of bone resorption and formation. TAF-treated patients also showed smaller declines in eGFR_{CG} with significantly smaller increases in markers of tubular function.

Conclusions In CHB patients considered to be at risk for TDF toxicity, TAF showed significantly less impact on bone and renal parameters while efficacy was maintained in this subgroup through 96 weeks.

IDDF2018-ABS-0108 IMPROVED BONE AND RENAL SAFETY AT 1 YEAR AFTER SWITCHING FROM TENOFOVIR DISOPROXIL FUMARATE (TDF) TO TENOFOVIR ALAFENAMIDE (TAF): RESULTS FROM 2 PHASE 3 STUDIES IN HBEAG-POSITIVE AND HBEAG-NEGATIVE PATIENTS WITH CHRONIC HEPATITIS B (CHB)

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Background TAF has shown less bone and renal effects with similar efficacy rates compared to TDF in Phase 3 studies after 96 weeks of double-blind (DB) treatment. We evaluated patients who completed 96 weeks of DB treatment with TAF or TDF and switched to open label (OL) treatment with TAF, including those with 1 year of data (through Week 144) to

determine changes in bone mineral density (BMD), creatinine clearance (CrCL), and the maintenance of viral suppression.

Methods 1298 CHB patients who were HBeAg-negative or HBeAg-positive were randomised and treated with TAF or TDF. At Week 96, 541 (42%; TAF 361; TDF 180) patients had completed DB treatment with TAF or TDF and switched to OL TAF. Analyses included subjects with values at Week 96 and at Week 144 for creatinine clearance (n=401), spine BMD (n=288) or hip BMD (n=287), HBV DNA (n=394) and ALT normalisation by AASLD criteria (n=398).

Abstract IDDF2018-ABS-0108 Figure 1 BMD also showed improvements at Week 144 from Week 96 (hip: n=88, mean (SD)% change=+0.94% (1.825), $p<0.001$; spine: n=88, mean (SD)% change=+1.54% (2.680), $p<0.001$)

Abstract IDDF2018-ABS-0108 Figure 2 Compared to Week 96, high rates of virologic control

Results CrCL improved in patients who switched from DB TDF to OL TAF at Week 144 compared to Week 96 (n=122, median (Q1, Q3) change=+3.6 (-4.2, +8.4) mL/min, $p<0.001$); (figure 1 and 2b). (HBV DNA <29 IU/mL) were maintained in both treatment groups at Week 144 (TDF 87% vs 88% and TAF 91% vs 89%). One year after switching the rate of ALT normalisation increased in the TDF group relative to Week 96 (n=122; 65% vs 47%; $p<0.001$) and did not differ from the TAF group (65% vs 66%; $p=0.83$) at Week 144.

Conclusions Patients who switched from TDF to TAF demonstrated continued improvements in BMD and CrCL over 48 weeks of treatment, virologic control was maintained, and rates of ALT normalisation increased.

IDDF2018-ABS-0109

SOFOSBUVIR/VELPATASVIR FOR 12 WEEKS IN GENOTYPE 1-4 HCV-INFECTED LIVER TRANSPLANT RECIPIENTS

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Background Treatment with SOF/VEL for 12 weeks results in high sustained virologic response rates 12 weeks after treatment (SVR12) in genotype 1-6 HCV infected patients in clinical trials and real-world settings. The current study evaluated the safety and efficacy of SOF/VEL in adult patients with recurrent chronic genotype (GT) 1-6 HCV infection post-liver transplant.

Methods This Phase 2, single-arm, open-label study evaluated 12 weeks of SOF/VEL 400/100 mg daily for 12 weeks in HCV-infected liver transplant recipients. Patients could be treatment experienced or treatment naive with no cirrhosis or compensated cirrhosis and had to be ≥ 3 months post-transplant with no signs of rejection at screening and history of pre-transplant chronic HCV. The primary endpoint was SVR12.

Results A total of 79 patients were enrolled and treated. Of these, 81% were male, 82% were white, 9% had compensated cirrhosis, 59% were treatment-experienced, 47% had GT1, 4% GT2, 44% GT3, and 5% GT4 HCV infections. For immunosuppression, 71% of patients used tacrolimus, 24% mycophenolic acid, 14% cyclosporine, 11% azathioprine, 10% sirolimus, 6% everolimus, and 1% prednisolone. Median (range) time from liver transplantation was 7.5 (0.3-23.9) years. Rates of SVR4 for available patients are presented in the Table (IDDF2018-ABS-0109 Table 1). There was one virologic failure (relapse; GT1a, non-cirrhotic, treatment naive) and one non-virologic failure (GT1b, cirrhotic, treatment naive). All 34 GT3 HCV-infected patients including 2 with cirrhosis achieved SVR4. Complete SVR12 and viral sequencing data will be presented. There were 61 (77%) patients with adverse events (AEs). Common (>10%) AEs were headache (24%), fatigue (20%), and cough (10%). One patient discontinued SOF/VEL on Day 7 due to an AE of grade 1 hyperglycemia. No serious or severe AEs were assessed by the investigator as related to SOF/VEL, there were no episodes of liver transplant rejection, and there were no deaths.

Abstract IDDF2018-ABS-0109 Table 1 SVR4 by Genotype After 12 Weeks of SOF/VEL

N(%)	Total n=75 ^a	GT1a n=15	GT1b n=19	GT1 (total) n=34	GT2 n=3	GT3 n=34	GT4 n=4
SVR4	73/75 (97)	14/15 (93)	18/19 (95)	32/34 (94)	3/3 (100)	34/34 (100)	4/4 (100)

a. SVR4 pending for three GT1b patients and one GT3 patient