Methods Virally suppressed patients (HBV DNA <20 IU/mL at screening) on TDF were randomized (1:1) to switch to TAF or continue TDF for 48 weeks in a double-blind fashion. Viral suppression and changes in bone (BMD by DXA) and renal (creatinine clearance [$eGFR_{CG}$]) parameters were assessed over 48 weeks.

Results Among the 400 Asian patients enrolled, 288 (72%) had at least 1 TDF RF. At Week 48, similar proportions with ≥1 RF had HBV-DNA <20IU/mL (TAF 97%; TDF 97%) and normal ALT by 2018 AASLD criteria (TAF 76%; TDF 73%). TAF subjects with ≥1 RF had increases in $eGFR_{CG}$compared to decreases on TDF [median (Q1, Q3) change; TAF: +2.6 (-2.01, 7.34); TDF: -2.7 (-7.56, +15.79); p<0.0001)]. Among patients with ≥1 RF, improvements were seen in BMD for TAF vs. continued declines in TDF patients at both spine (p<0.0001) and hip (p<0.0001).

Conclusions Virally suppressed Asian patients with CHB and risk factors for TDF who switched to TAF showed improved bone and renal safety while efficacy was well-maintained.

IDDF2020-ABS-0059 SAFETY AND EFFICACY OF SOFOSBUVIR/VELPATASVIR (SOF/VEL) IN PEDIATRIC PATIENTS 6 TO < 18 YEARS OLD WITH CHRONIC HEPATITIS C (CHC) INFECTION

[1]Maureen Jonas*, [2]Rene Romero, [3]Etienne Sokal, [4]Philip Rosenthal, [5]Gabriella Verucchi, [6]Chuan-Hao Lin, [7]Jessica Wen, [8]Michael Narkewicz, [9]Sanjay Bansal, [10]Jiang Shao, [10]Sean Hsueh, [10]Anuj Gaggar, [10]Kathryn Kersey, [10]Carol Yee Kwan Chan, [11]Regino Gonzalez-Peralta, [12]Daniel Leung, [13]William Balistreri, [14]Karen Murray, [15]Kathleen Schwarz. *[1]Boston Children's Hospital, Boston, MA, USA; [2]Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, USA; [3]Cliniques Universitaires Saint-Luc, UC Louvain, Brussels, Belgium; [4]University of California San Francisco, San Francisco, USA; [5]University of Bologna, Bologna, Italy; [6]Children's Hospital Los Angeles, Los Angeles, USA; [7]University of Pennsylvania and The Children's Hospital of Philadelphia, Pennsylvania, USA; [8]University of Colorado School of Medicine and Children's Hospital of Colorado, Aurora, USA; [9]Kings College Hospital, UK; [10]Gilead Sciences, Inc, Foster City, USA; [11]Pediatric Gastroenterology, Hepatology and Liver Transplant, AdventHealth for Children, Orlando, USA; [12]Baylor College of Medicine and Texas Children's Hospital, Houston, USA; [13]Cincinnati Children's Hospital Medical Center, Cincinnati, USA; [14]University of Washington School of Medicine and Seattle Children's Hospital, Seattle, USA; [15]Johns Hopkins University School of Medicine, Baltimore, USA*

10.1136/gutjnl-2020-IDDF.142

Background DAA regimens have been approved for CHC treatment in 12 to <18 years, but for younger children, the standard of care is still pegylated-interferon plus ribavirin for ≤48 weeks. We evaluated the safety and efficacy of the pangenotypic regimen of SOF/VEL in children 6 to <18 years.

Methods Patients 6 to <18 years with CHC of any genotype (GT) were enrolled in this open-label, ongoing study. Patients 6 to <12 years received SOF/VEL 200 mg/50 mg and 12 to <18 years SOF/VEL 400 mg/100 mg QD for 12 weeks. Key efficacy endpoint was SVR12. Safety was assessed by adverse events (AEs) and clinical/laboratory data. Intensive pharmacokinetic sampling on Day 7 in a subgroup of patients of each age group was done to confirm the appropriateness of the chosen dose.

Results 102 patients 12 to <18 years and 73 patients 6 to <12 years were enrolled. GT distribution was 75% GT1, 5% GT2, 13% GT3, 3% GT4, 3% GT6; 51% female, 80% white, 85% treatment naïve, and 91% vertically infected. Intensive pharmacokinetics confirmed that the doses selected were appropriate. SVR12 rate was 95% (97/102) and 92% (67/73) among patients 12 to <18 years and 6 to 12 years respectively; 1 patient in each age group had virologic failure, the remaining patients did not achieve SVR for non-virologic reasons. Most AEs were mild or moderate. 5 subjects had serious AE none of which was attributed to treatment, 2 patients discontinued treatment due to AEs and considered treatment unrelated. The most common AEs (>15%) were headache, fatigue, and nausea in adolescents and vomiting, cough and headache in 6 to <12 years.

Conclusions In patients 6 to <18 years with GT1, 2, 3, 4 or 6 CHC infection, treatment with SOF/VEL for 12 weeks resulted in ≥ 92% SVR12 rate. SOF/VEL was well tolerated, supporting its potential as a treatment option for children 6 to 17 years of age. The study is ongoing in children aged 3 to <6 years old.

IDDF2020-ABS-0060 IMPACT OF PRIOR TENOFOVIR DISOPROXIL FUMARATE (TDF) TREATMENT DURATION ON TENOFOVIR ALAFENAMIDE (TAF) SAFETY PROFILE IN VIRALLY SUPPRESSED CHRONIC HBV PATIENTS SWITCHED FROM TDF TO TAF

[1]Henry Lik Yuen Chan*, [2]Pietro Lampertico, [3]Sang Hoon Ahn, [4]Scott Fung, [5]Ho Bae, [6]Alnoor Ramji, [7]Jung Sung Lee, [8]Stephen Shafran, [9]Stuart Gordon, [10]Charles Phan, [11]Susanna Tan, [11]John Flaherty, [11]Anuj Gaggar, [11]George Wu, [11]Vithika Suri, [12]Daryl Lau, [13]Kwan Soo Byun, [14]Kosh Agarwal, [15]Young-Suk Lim, [16]Maria Buti. *[1]Institute of Digestive Disease, Department of Medicine and Therapeutics, and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano, Italy; [3]Yonsei University College of Medicine, Korea, South; [4]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Canada; [5]Asian Pacific Liver Center, St. Vincent Medical Center, USA; [6]The University of British Columbia, Canada; [7]Inje University College of Medicine, Korea, South; [8]University of Alberta, Edmonton, Canada; [9]Henry Ford Health System, USA; [10]Greater Houston Gastroenterology, Sugar Land, USA; [11]Gilead Sciences, Inc., USA; [12]Beth Israel Deaconess Medical Center, Harvard Medical School, USA; [13]Korea University Guro Hospital, Korea, South; [14]Institute of Liver Studies, King's College Hospital, UK; [15]Asan Medical Center, University of Ulsan College of Medicine, Korea, South; [16]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Hospital Universitari Valle Hebron, Spain*

10.1136/gutjnl-2020-IDDF.143

Background TAF demonstrated noninferior efficacy to TDF with a superior bone and renal safety profile, in viremic chronic HBV (CHB) patients through week 96, and in virally suppressed patients switched from TDF to TAF at 48 weeks. The duration of prior TDF therapy may influence the degree and rate of recovery of bone and renal function following switch to TAF. Here, we evaluate the impact of prior TDF treatment duration on the safety profile of TAF in virally suppressed patients.

Methods In a double-blind, randomized, multicenter, active-controlled, Phase 3 study, 488 CHB patients who were virologically suppressed on TDF for 1 year, and on TDF monotherapy for 6 months were randomized 1:1 to switch to TAF or continue TDF for 48 weeks. In patients originally randomized to receive TAF, renal, bone, and lipid parameters were categorically evaluated by the duration of prior TDF treatment:

Results Of the 243 patients switched to TAF from TDF, 105 (43%) and 138 (57%) had received TDF for 50 years, 74% male, 80% Asian, median $eGFR_{CG}$91 mL/min, 4% and 12% had osteoporosis at hip and spine, respectively. Similar changes in renal, bone, and lipid parameters following 48 weeks of TAF treatment were observed by TDF treatment duration. A comparable increase in median $eGFR_{CG}$, decreases in tubular biomarkers (beta-2 microglobulin/creatinine ratio, retinol binding protein/creatinine ratio), increases in mean percent change in hip and spine BMD, and decreases in bone turnover markers (C-type collagen sequence, procollagen type 1 N-terminal propeptide) were observed among patients previously treated with <4 and ≥4 years of TDF, respectively (table 1). Changes in fasting lipid parameters were not influenced by treatment duration.

Conclusions In virally suppressed patients on TDF a median of 4 years who switched to TAF treatment, improvements in bone and renal parameters and changes in fasting lipids were not impacted by prior duration of TDF use.

Abstract IDDF2020-ABS-0060 Table 1 Renal, bone and fasting lipid parameters in patients previously treated with <4 or ≥4 years of TDF before switching to TAF

	<4 years	≥4 years	p-value
	n=105	n=138	
Renal parameters			
Serum creatinine, median (Q1, Q3) change, mg/dL	0 (-0.04, 0.05)	0 (-0.06, 0.05)	0.78
$eGFR_{CG}$, median (Q1, Q3) change, mL/min[3]	+0.87 (-3.96,6.01)	+1.03 (-4.64, 7.21)	0.95
≥1 stage improvement in CKD stage, n (%)	11/46 (23.9)	17/66 (25.8)	0.26
≥1 stage worsening in CKD stage, n (%)	3/99 (3.0)	12/135 (8.9)	
Urine biomarkers, median (Q1, Q3)% change			
Protein/creatinine ratio, mg/g	-14.6 (-44.0, 37.4)	-9.9 (-45.5, 32.6)	0.97
Albumin/creatinine ratio, mg/g	+5.5 (-24.1, 41.5	-5.8 (-37.0, 29.7)	0.08
Retinol binding protein/ creatinine ratio, µg/g	-15.8 (-39.1, 15.2)	-17.8 (-43.0, 18.4)	0.67
Beta-2 microglobulin/creatinine ratio, µg/g	-36.0 (59.4, 2.2)	-36.1 (-64.4, -2.8)	0.75
Bone parameters			
Hip BMD[b], mean (SD)% change	+0.69 (1.828)	+0.64 (2.263)	0.84
Spine BMD, mean (SD)% change	+1.84 (3.04)	+1.67 (3.76)	0.71
Serum bone biomarkers, median (Q1, Q3)% change			
C-type collagen sequence (CTX), ng/mL [resorption]	-29.8 (-45.8, -14.0)	-28.8 (-42.8, -15.3)	0.57
Procollagen type 1 N-terminal propeptide (P1NP), ng/mL [formation]	-20.4 (-37.5, -7.4)	-17.7 (-29.6, -8.5)	0.16
Parathyroid hormone, pg/mL (PTH) [metabolism]	-9.4 (-27.6, 16.4)	-13.4 (-32.5, 6.8)	0.07
Fasting Lipid parameters			
Total cholesterol, median (Q1, Q3) change, mg/dL	20 (6, 31)	19 (5, 33)	0.93
Total cholesterol/HDL, median (Q1, Q3) change, mg/dL	0.1 (-0.2, 0.4)	0.3 (-0.1, 0.5)	0.08
HDL, median (Q1, Q3) change, mg/dL	4 (0, 8)	3 (-2, 7)	0.13
LDL, median (Q1, Q3) change, mg/dL	17 (5, 27)	15 (5,27)	0.54
Triglycerides, median (Q1, Q3) change, mg/dL	13 (-5, 41)	17 (-1,46)	0.22

[a]eGFR in creatinine clearance (Cockcroft-Gault method); [b]BMD is bone mineral density by DXA scan

IDDF2020-ABS-0061

IMPACT OF TREATMENT WITH TENOFOVIR ALAFENAMIDE (TAF) OR TENOFOVIR DISOPROXIL FUMARATE (TDF) ON HEPATOCELLULAR CARCINOMA (HCC) INCIDENCE IN PATIENTS WITH CHRONIC HEPATITIS B (CHB)

[1]Henry Lik Yuen Chan*, [2]Young-Suk Lim, [3]Wai Kay Seto, [4]Qin Ning, [5]Kosh Agarwal, [6]Harry LA Janssen, [7]Calvin O Pan, [8]Wan Long Chuang, [9]Namiki Izumi, [10]Scott Fung, [11]Shalimar, [12]Maurizia Brunetto, [13]John Flaherty, [13]Shuyuan Mo, [13]Cong Cheng, [13]Lanjia Lin, [13]Anuj Gaggar, [13]Mani Subramanian, [14]Patrick Marcellin, [15]Edward Gane, [16]Jinlin Hou, [17]Maria Buti. *[1]Institute of Digestive Disease, Department of Medicine and Therapeutics, and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong; [2]Asan Medical Center, University of Ulsan College of Medicine, Korea, South; [3]University of Hong Kong, Hong Kong; [4]Tongji Hospital, Tongji Medical College, China; [5]Kings College Hospital, UK; [6]Toronto Western Hospital, Canada; [7]NYU Langone Medical Center, NYU School of Medicine, New York, USA; [8]Kaohsiung Medical University Hospital, Kaohsiung Medical University, Taiwan; [9]Musashino Red Cross Hospital, Japan; [10]Toronto General Hospital, Canada; [11]All India Institute of Medical Sciences, India; [12]University of Pisa, Pisa, Italy; [13]Gilead Sciences, Foster City, USA; [14]Hôpital Beaujon, France; [15]Auckland Clinical Studies, Auckland, New Zealand; [16]Nanfang Hospital of Southern Medical University, China; [17]Hospital Universitario Valle Hebron, Spain*

10.1136/gutjnl-2020-IDDF.144

Background Potent antivirals can reduce HCC incidence in CHB. TDF and TAF are first-line treatments, and in Phase 3 studies through 3 years, TAF has shown antiviral efficacy similar to TDF, higher rates of ALT normalization, and no resistance. We evaluated HCC incidence in patients participating in these ongoing studies.

Methods HBeAg-positive (n=1039) and -negative (n=593) patients with HBV DNA 20,000 IU/mL and ALT >60 U/L (males) or >38 U/L (females) were randomized (2:1) to TAF 25 mg QD or TDF 300 mg QD for up to 3 years, followed

Abstract IDDF2020-ABS-0061 Table 1 Observed vs predicted incidence of HCC in CHB patients treated with TAF or TDF through week 192 in 2 Phase 3 trials

Time Interval (Day)	Observed Cases	Predicted Cases	Standard Incidence Ratio (SIR)	95% CI	
				Lower bound	Upper bound
(0, 105]	1	2.6	0.38	0.053	2.695
(0, 174]	2	4.4	0.46	0.115	1.836
(0, 180]	3	4.5	0.67	0.215	2.065
(0, 253]	4	6.3	0.63	0.238	1.690
(0, 378]	5	9.5	0.53	0.220	1.267
(0, 392]	6	9.9	0.60	0.271	1.343
(0, 401]	7	10.2	0.68	0.326	1.434
(0, 460]	8	12.1	0.66	0.329	1.317
(0, 675]	9	19.0	0.47	0.246	0.908
(0, 729]	10	20.8	0.48	0.259	0.895
(0, 747]	11	21.0	0.52	0.290	0.946
(0, 854]	12	22.3	0.54	0.305	0.947
(0, 855]	13	22.3	0.58	0.338	1.003
(0, 1209]	14	28.7	0.49	0.289	0.825
(0, 1370]	15	32.9	0.46	0.275	0.756
(0, 1534]	16	34.9	0.46	0.281	0.749
(0, Max observed time at Week 192][†]	16	35.3	0.45	0.278	0.740

*SIR is Standardized Incidence Ratio for observed cases vs predicted cases based on the REACH-B model.
[†]The maximum observed time at Week 192 for each subject included in the analysis.