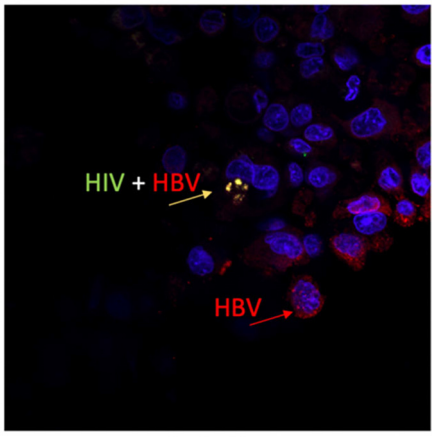
increase levels of HBV DNA or cccDNA. TAF or ETV inhibited HIV-1 RNA replication in co-cultured and coinfected cells. TAF, ETV or GLP-26 similarly inhibited HBV DNA replication in HepAD38 cells mono- or -cocultured with $CD4^+$T cells, with or without HIV-1. GLP-26 in the presence or absence of HIV-1 inhibited HBV DNA replication more potently than TAF or ETV, with EC_{90} values 3- to 7-fold lower for GLP-26 *versus* TAF or ETV.



DAPI = blue
Red arrow = HBV+
Yellow arrow = mix of green (HIV-1) + red (HBV)

Figure 1: Immunofluorescence image of 3D co-cultured HepAD38 plus $CD4^+$T cells co-infected with HIV-1.

Conclusions: Organoids contained HBV (HepAD38 or HepG2-NTCP) and HIV-1 ($CD4^+$T) permissive cells supported productive HBV and/or HIV-1 replication. This novel model was reproducible and provided multiple and simultaneous modalities to quantify HIV-1 and HBV replication; this system can be used to measure key cellular events that drive pathogenesis of HIV-1/HBV in co-infected individuals, and can also be used to identify novel agents that block these events in the context of a relevant cellular system of co-infection. More importantly, we validated this novel organoid system of co-infection as a model for HBV infection and antiviral evaluation.

SAT442

Safety and efficacy of switching to tenofovir alafenamide (TAF) in virally suppressed chronic hepatitis B (CHB) patients with hepatic impairment: week 48 results from a phase 2 open label study

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Background and Aims: Switching to TAF, a novel tenofovir prodrug, has shown maintenance of viral suppression with stable or improved bone and renal safety at Wk 24 in CHB patients with impaired hepatic function. Here we evaluated the efficacy and safety 48 weeks after CHB patients with hepatic decompensation were switched to TAF.
Method: In this Phase 2 study (NCT03180619) patients with CHB having a Child–Turcotte–Pugh (CTP) score ≥7 and ≤12 at screening, or by documented history, receiving TDF and/or other OAVs for ≥48 weeks, with HBV DNA <LLOQ for ≥24 weeks and <20 IU/mL at screening were eligible to participate. All patients were switched to TAF 25 mg QD and were to be treated for 96 weeks. Safety assessments including changes in bone (hip and spine BMD) and renal (CrCl by Cockcroft-Gault [$eGFR_{CG}$], serum creatinine) parameters, viral suppression, and biochemical responses were assessed at Week 48.
Results: 31 patients were enrolled at 18 sites in 7 countries and 90% completed 48 weeks of treatment. At baseline, 74% were ≥50 y, 68% male, 81% Asian, 90% HBeAg-negative, with median fibrotest (FT) score 0.81, median CTP and MELD scores of 6 and 10, respectively, median $eGFR_{CG}$ 98 mL/min, and 19% and had osteoporosis by T score at spine. Prior use of TDF and entecavir was reported by 68% and 45%, respectively. Key efficacy/safety results at Week 48 are summarized in the Table. By missing equals failure analysis, 31 patients (100%) had HBV DNA <20 IU/mL, 81% had normal ALT and CTP/MELD scores were stable. After switching to TAF in this population with liver impairment, CTP, MELD, and FT scores were unchanged while bone and renal parameters were stable. TAF was well tolerated with few having Grade 3 or 4 AEs (4 patients); no serious AEs related to study drug, and 1 patient who discontinued for worsening renal function unrelated to TAF.
Conclusion: CHB patients with hepatic impairment who were switched to TAF from TDF or other OAV showed high rates of viral suppression, normal ALT and bone and renal safety were stable at Week 48.

SAT443

Prospective evaluation of qHBsAg decline in patients affected by chronic hepatitis B, E genotype, treated with entecavir or tenofovir

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Background and Aims: European clinical practice guidelines (EASL) on chronic hepatitis B recently recognized the importance of migration flows in changing the prevalence and incidence of hepatitis B infection in low endemic European countries such as Italy and Germany. Phylogenetic analyses have shown that genotype E, which is mainly diffused in West Africa, is relatively recent. No data were available about a different serological or virological response in naïve patients affected by chronic hepatitis B (CHB), E genotype treated with tenofovir (TDF) or ETV. The aim of this study was the prospective evaluation of serological and virological response in a cohort of CHB patients with E genotype treated with TDF or ETV and followed for at least 5 years.
Method: we prospectively evaluated qHBsAg decline in chronic hepatitis B, HBeAg-negative, E genotype, treated with tenofovir 245 mg (TDF) or ETV 0.5 mg from 2008 to 2014. Inclusion criteria were: naïve patients with active chronic hepatitis B (CHB) without other viral co-infection. qHBsAg test was performed with ARCHITECT HBsAg (Abbott Diagnostics, Ireland). Serum HBV-DNA levels were quantified by the Real Time PCR COBAS AmpliPrep/COBAS TaqMan HBV Test 2.0 (Roche Molecular Systems, NJ, USA).
Results: sixty-five patients (89.2% males) were enrolled. Median age was 29 years [IQR 22–36] and the most prevalent route of transmission was familiar (25; 38.5%). Median liver stiffness was 7.4 kPa [IQR 4.5–9.3], ALT 65 U/L [IQR 31–122], HBV-DNA 3.4Log IU/ml [IQR 2.8–4.5], qHBsAg3.4Log UI/ml [IQR 2.8–4.5]. According to clinical evaluation, 40 patients (61.5%) started ETV whereas 25

Table. Efficacy and Safety Results at Week 48

n/N (%), or median (Q1, Q3)	TAF (N=31)
Efficacy	
HBV DNA <20 IU/mL[a]	31 (100)
ALT normal (2018 AASLD criteria)[a,b,c]	25 (81)
ALT normalization (2018 AASLD criteria)[a,d]	6/10 (60)
HBeAg loss[a,e]	0/3
HBsAg loss[a]	1/30 (3)
qHBsAg, log_{10} change (IU/mL)	-0.07 (-0.11, -0.02)
CTP score change	0 (-1, 0)
MELD score change	0 (-1.1, 1.1)
Bone safety	
Hip BMD, % change	-0.19 (-1.515, 1.635)
Spine BMD, % change	+0.95 (-1.461, 1.933)
CTX, % change (ng/mL)[f]	-8.9 (-21.4, 5.3)
P1NP, % change (ng/mL)[g]	3.11 (-23.25, 26.50)
Renal safety	
sCr, change mg/dL	0.01 (-0.07, 0.13)
$eGFR_{CG}$, mL/min	-0.2 (-14.4, 4.2)
RBP/Cr, % change[h]	-20.7 (-50.5, 4.2)
β2MG/Cr, % change[i]	-22.7 (-65.3, 11.4)

[a]Results are by missing=failure analysis and reported as median (Q1, Q3) unless otherwise stated.
[b]ALT normal is the proportion with ALT ≤ULN at Week 48, regardless of ALT level at baseline;
[c]ULN 35 U/L males, 25 U/L females; [d]Patients with ALT >ULN at baseline;
[e]HBeAg-positive at baseline. [f]Serum C-type collagen sequence (bone resorption marker); [g]Serum procollagen type 1 N-terminal propeptide (bone formation marker); [h]Urine retinol binding protein/creatinine (tubular marker); [i]Urine beta-2 microglobulin/creatinine (tubular marker). BMD, bone mineral density by DXA scan; sCr, serum creatinine; $eGFR_{CG}$, estimated creatinine clearance (Cockcroft-Gault method).

Figure: (abstract: SAT442)

patients (38.5%) TDF. The qHBsAg decline was significantly higher in patients treated with TDF at any time-points and after 5 years the median decline with ETV was 0.31 LogIU/mL and 0.68 LogIU/mL with TDF. At the same time-points higher response rate in HBV-DNA suppression were observed in patients receiving TDF. In the absence of resistance-associated mutations, in 20% of ETV-patients HBV-DNA persisted detectable at 5 years. In univariate analysis for qHBsAg decline the following factors were considered: age, sex, qHBsAg and HBV-DNA at baseline, liver stiffness, type of therapy. In the multivariate analysis the only predictive factor for qHBsAg decline is the treatment with TDF ($\beta = -0.119$; DS = 0.025; $p < 0.001$).
Figure: qHBsAg decline after 5 years of therapy in patients affected by CHB and treated with ETV or TDF.
Conclusion: in E genotype the patients treated with TDF showed greater qHBsAg decrease after 5 years than ETV; virological response was higher in TDF than ETV groups. The reason of this finding was unknown and further studies are required to explain this aspect. According to our results, however, TDF could represent the optimal choice in this setting of patients.

SAT444

Low HBcrAg and HBsAg levels identify patients most likely to achieve sustained response after nucleos(t)ide analogue cessation: results from a global individual patient data meta-analysis (create study)

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Background and Aims: Sustained response is observed in a limited number of patients after cessation of nucleo(s)tide analogue (NA) therapy. We aimed to study the relationship between serum levels of hepatitis B core related antigen (HBcrAg) and HBsAg at treatment