Safety and Efficacy at 48 Weeks After Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in Chronic HBV Patients With Risk Factors for TDF Use

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Introduction

- Tenofovir alafenamide (TAF), a novel tenofovir produg, has shown noninferior efficacy to tenofovir disoproxil fumarate (TDF), with a superior bone and renal safety profile through 96 weeks in viremic chronic hepatitis B (CHB) patients, and 48 weeks in virally suppressed patients switched from TDF to TAF.2,3
- TAF is a preferred treatment in the current European Association for the Study of the Liver (EASL) and AASLD hepatitis B virus (HBV) guidelines,4 particularly for patients with risk factors for TDF-associated renal and bone effects.

Objectives

- To assess safety and efficacy at Week 48 in virally suppressed CHB patients with TDF risk factors who were switched from TDF to TAF.

Methods

Study Design

Study 4018

- Randomized, double-blind, active controlled, Phase 3 study (NCT02979613)
- Key inclusion criteria: hepatitis B e antigen (HBeAg)-negative and -positive patients with/without compensated cirrhosis, and having estimated glomerular filtration rate by Cockcroft-Gault equation (eGFRCG) ≥50 mL/min.

Population: Patients With ≥1 Baseline Risk Factor for TDF Use

<table>
<thead>
<tr>
<th>Baseline Condition</th>
<th>Analysis</th>
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<tbody>
<tr>
<td>Advanced age ≥60</td>
<td>§80</td>
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</table>
| Bone diseases | Osteoarthritis by hip or spine *x3 scans
| Renal impairment | CKD stage ≥2 (baseline eGFRCG <60 mL/min)
| Albuminuria | UACR >300 mg/g
| Hypertension | Serum potassium >5.0 mmol/L
| Obesity | BMI ≥30 kg/m²
| Comorbidities | CVD, DM, HL, or HTN

Risk factor for TDF use in EASL HBV guidelines 2017: 50% >GFR <80 mL/min; 73% used in EASL HBV guidelines; BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; HL, hyperlipidemia; HTN, hypertension; urate, uric acid baseline creatinine ratio.

Safety assessments:
- Renal: serum creatinine, eGFR, and urine biomarkers of tubular function
- Bone: serial dual energy X-ray absorptiometry scans at hip/spine and serum bone biomarkers

Efficacy assessments:
- Viral suppression: HBV DNA <20 IU/mL
- Normal alanine aminotransferase (ALT) by 2018 AASLD criteria (≤25 and ≤35 UL for females and males, respectively) by central laboratory criteria (≤43 and ≤43 UL for females and males, respectively, aged <69 y; ≤32 and ≤35 UL aged ≥69 y)

Results

Patient Disposition

- At baseline, the majority of patients (73%) had ≥1 risk factor, while ~25% had ≥3 risk factors

Baseline Demographics and Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No TDF Risk Factors</th>
<th>TDF Risk Factors</th>
<th>TAF Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>55.1 (43.5, 63.6)</td>
<td>52.0 (40.8, 62.1)</td>
<td>49.1 (40.0, 58.2)</td>
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<td>Male sex (%)</td>
<td>50.6 (33.5, 67.6)</td>
<td>47.8 (32.3, 63.3)</td>
<td>54.4 (39.3, 69.5)</td>
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<td>Baseline ALT (U/L)</td>
<td>66.4 (38.9, 112.0)</td>
<td>67.2 (36.8, 119.0)</td>
<td>50.8 (30.1, 85.0)</td>
</tr>
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Efficacy assessments:
- Viral suppression was well maintained in CHB patients with TDF risk factors who switched from TDF to TAF
- Viral suppression was also maintained in CHB patients without TDF risk factors who switched from TDF to TAF (TAF 95% and TDF 96%)

Bone Biomarkers at Week 48

- Changes in hip bone mineral density (Hip BMD) and spine bone mineral density (Spine BMD) were minimal on switching to TAF from TDF

Conclusions

- Switching from TDF to TAF for 48 weeks demonstrated significant improvements in both bone and renal parameters in CHB patients with ≥1 TDF risk factor at baseline for bone or renal toxicity
- In patients with no risk factors at baseline, switching to TAF for 48 weeks also demonstrated a significant improvement in bone parameters, with a trend towards improvement in renal parameters
- In all patients, high rates of antiviral efficacy were maintained with TAF and were similar to those in patients treated with TDF.