Poster 181

Safety and Efficacy at 4 Years in Post-liver Transplant Patients with Chronic Kidney Disease Receiving Tenofovir Alafenamide (TAF) For HBV Prophylaxis

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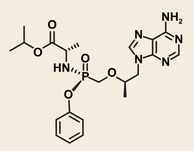
Introduction

- Chronic HBV remains an important indication for orthotopic liver transplantation (OLT) and leads to numerous complications postoperatively, including nephrotoxicity from use of calcineurin inhibitors, and osteoporosis secondary to preoperative malnutrition and postoperative corticosteroids[1]
  - Tenofovir disoproxil fumarate (TDF) given alone or with otherantivirals is frequently used to prevent viral relapse post-OLT[2]

Tenofovir Alafenamide (TAF)

- Novel tenofovir prodrug; greater plasma stability, with enhanced hepatic delivery of active drug and lower circulating levels of tenofovirrelative to TDF[3-6]
- Noninferior efficacy was demonstrated vs TDF at Weeks 48 and 96 in virally suppressed chronic HBV patients with/without compensated cirrhosis and creatinine clearance (estimated glomerular filtration rate by Cockcroft-Gault method [eGFRCG]) ≥50 mL/min when switched to TAF, with improved bone and renal safety[7-9]
- Week 48 results from the present study demonstrated that in patients with chronic HBV who were status post-OLT and had chronic kidney disease, switching to TAF maintained suppression of HBV, while bone and renal safety were improved compared with patients who continued to receive TDF[10]

TAF
Nucleotide reverse transcriptase inhibitor

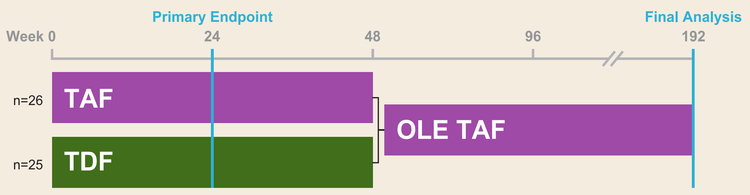


Objective

- To evaluate the long-term safety and efficacy of TAF vs TDF antiviral prophylaxis following OLT in patients with a pretransplant diagnosis of HBV through 192 wk

Methods

Study Design



OLE, open-label extension.

- Open-label, Phase 2 study (GS-US-320-3912 [NCT02862548])
  - Randomized phase: TAF 25 mg qd or continued TDF-containing treatment for 48 wk
  - OLE phase: all patients received TAF 25 mg qd through Week 192 (ie, TAF vs TDF→TAF)
- Key inclusion criteria:
  - Chronic HBV including patients with compensated cirrhosis maintained on TDF-containing regimen
  - OLT ≥12 wk prior to screening
  - HBV DNA <lower limit of quantitation; alanine aminotransferase (ALT) ≤10x upper limit of normal at screening
  - eGFR by Chronic Kidney Disease Epidemiology Collaboration ($eGFR_{CKD-EPI}$) <90 mL/min/1.73 m^2
- 1:1 randomization
  - Stratified by renal function ($eGFR_{CKD-EPI}$ < or ≥50 mL/min/1.73 m^2) at screening
  - COBAS® AmpliPrep/COBAS® TaqMan® HBV Test, v2.0 (Roche Diagnostics, Florham Park, NJ; lower limit of quantitation 20 IU/mL)

Study Endpoints (at Week 192)

- Efficacy endpoint: HBV DNA <20 IU/mL
- Secondary safety endpoints:
  - Serious adverse events (AEs)
  - Changes in $eGFR_{CKD-EPI}$
  - Changes in bone mineral density (BMD) at spine and hip by dual-energy x-ray absorptiometry

Results

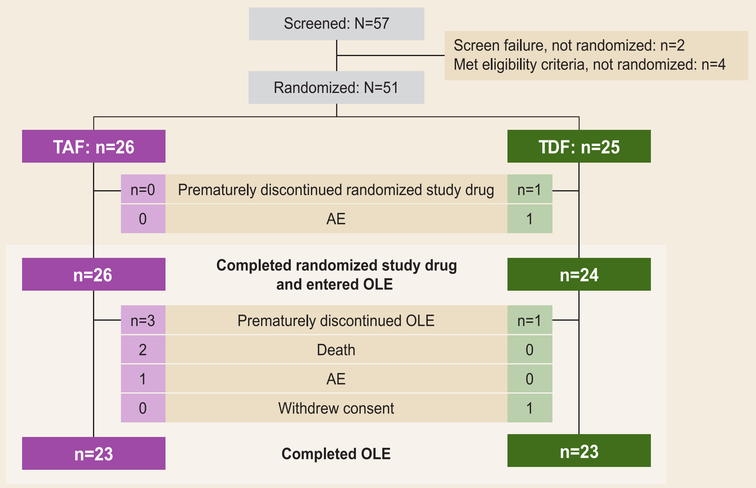
Demographics and Disease Characteristics

	TAF n=26	TDF n=25
Mean age, y (range)	58 (26–76)	62 (45–77)
Men, n (%)	16 (62)	22 (88)
Asian, n (%)	7 (27)	10 (40)
Pacific Islander, n (%)	15 (58)	12 (48)
Mean BMI, kg/m^2 (range)	27.7 (20.5–35.8)	28.3 (16.7–39.3)
HBV DNA <20 IU/mL, n (%)	26 (100)	25 (100)
Mean ALT, U/L (SD)	28 (12.6)	38 (43.7)
Median $eGFR_{CKD-EPI}$, mL/min/1.73 m^2 (Q1, Q3)	48.8 (44.8, 59.2)	52.2 (45, 60.3)
<50 mL/min/1.73 m^2, n (%)	15 (58)	12 (48)
Current calcineurin inhibitor use, n (%)	21 (81)	19 (76)
Median y since transplant (Q1, Q3)	9 (3, 14)	9 (4, 12)
History of rejection, n (%)	0	2 (8)
Multiple organ transplant, n (%)	1 (4)*	0
HBeAg-positive, n (%)	1 (4)	0
HBsAg-positive, n (%)	2 (8)	1 (4)

*Renal transplant. BMI, body mass index; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; Q, quartile; SD, standard deviation.

Results, cont'd

Patient Disposition



Efficacy at Week 192

	TAF n=26	TDF n=25
HBV DNA <20 IU/mL, n (%)*	20 (100)	20 (100)
HBV DNA DNA <20 IU/mL and TND, n (%)	20 (100)	20 (100)
HBeAg loss/seroconversion, n/N	1/1	0/0
HBsAg loss/seroconversion, n/N	0/2	0/1

*Missing=excluded analysis. TND, target not detected (lower limit of detection 20 IU/mL).

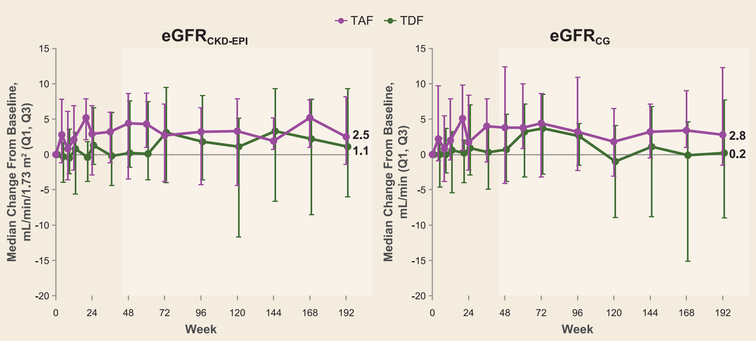
- All patients had sustained viral suppression through Week 192

Safety Summary

	Randomized Phase		OLE	
n (%)	TAF n=26	TDF n=25	TAF n=26	TDF→TAF n=24
Any AE	**24 (92)**	**24 (96)**	**25 (96)**	**24 (100)**
Grade 3–4 AE	2 (8)	6 (24)	6 (23)	8 (33)
Grade 3–4 AE related to study drug	0	0	0	0
Serious AE	3 (12)	7 (28)	8 (31)	8 (33)
Serious AE related to study drug	0	0	0	0
Discontinued study drug due to AE	0	1 (4)*	1 (4)†	0
Death	0	1 (4)‡	2 (8)§	0

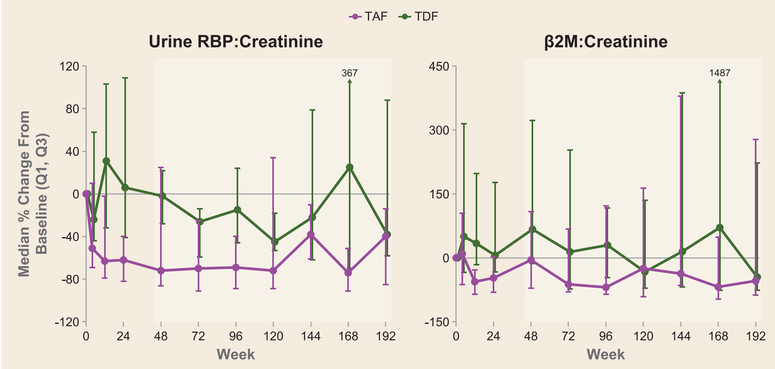
*Disseminated tuberculosis.
†Acute kidney injury not related to study drug.
‡Diagnosed with diffuse large B-cell lymphoma during treatment.
§Liver failure and cardiac arrest.

Changes in eGFR



- In the randomized phase, TAF patients had improved eGFR, which remained stable through Week 192
- In patients on TDF→TAF, eGFR remained stable through Week 192

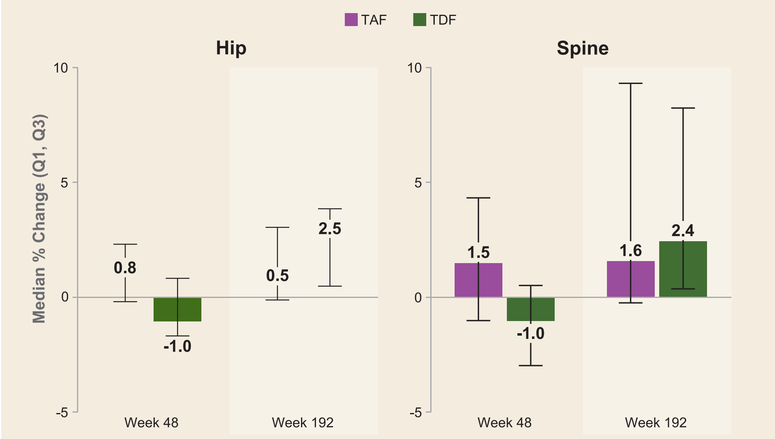
Changes in Renal Proximal Tubular Markers



RBP, retinol-binding protein; β2M, β2-microglobulin.

- At Week 192, changes in both markers were similar for the TAF and TDF→TAF groups

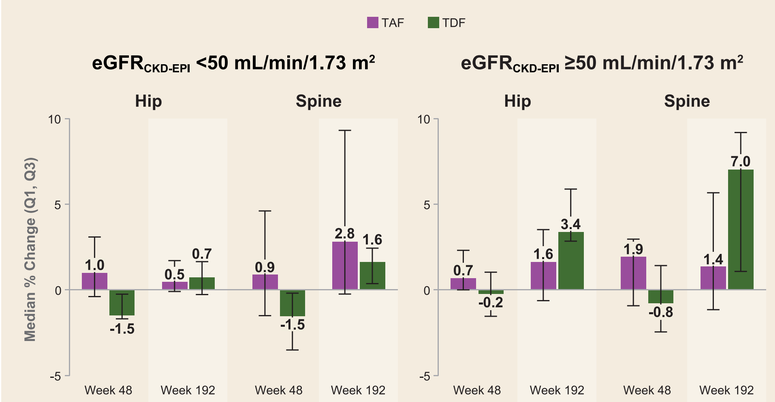
Bone Mineral Density Changes at Weeks 48 and 192



- TAF treatment resulted in greater improvements in hip and spine BMD compared with continued treatment with TDF-containing regimens in the randomized phase
- In the TDF→TAF group, BMD improvements were observed after switching to TAF through Week 192

Bone Mineral Density Changes at Weeks 48 and 192

Baseline $eGFR_{CKD-EPI}$ < and ≥50 mL/min/1.73 m^2



- In the randomized phase, TDF patients with baseline $eGFR_{CKD-EPI}$ <50 mL/min/1.73 m^2 had greater declines in BMD compared with those with baseline $eGFR_{CKD-EPI}$ ≥50 mL/min/1.73 m^2
- In contrast, during the randomized phase, similar increases were seen in TAF patients regardless of baseline $eGFR_{CKD-EPI}$
- At Week 192, patients treated with TAF showed BMD improvement regardless of baseline renal function and TDF→TAF patients had improved BMD in the OLE

Conclusions

- Long-term results in OLT recipients with chronic kidney disease switching from TDF-containing regimens to TAF monotherapy demonstrated that prevention of viral relapse was maintained
- Overall during the OLE, safety results were similar across both treatment groups
- Sustained improvements in key bone and renal parameters were observed in this high-risk patient population after switching to TAF
- The favorable effects of TAF in maintaining viral suppression and improved bone and renal safety profile relative to TDF lend support for the use of TAF in patients with chronic HBV who are post-OLT

References

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