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Low Dose Tenofovir Disoproxil Fumarate Improves Kidney Function and Sustains Virologic Suppression in Renally Compromised Chronic Hepatitis B Patients

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Abstract Text

Background: Tenofovir disoproxil fumarate (TDF) therapy effectively inhibits viral replication in patients with chronic hepatitis B (CHB), but renal impairment can occur. Viral breakthrough and renal function were studied in renally impaired patients on reduced dose TDF and in patients on full dose TDF.

Methods: CHB patients with full and reduced dose TDF (due to GFR [Cockcroft-Gault] <50mL/min/1.73m^2 ± serum phosphate <0.8mmol/L) from a North-American hospital were evaluated. Viral breakthrough (confirmed HBV DNA>1 log IU/mL above nadir on-therapy [AASLD]) and biochemical breakthrough (confirmed ALT>1.5x ULN) were assessed from 1 month after starting (reduced) TDF dose (baseline) till end of follow-up (EOF). Renal function was calculated by Chronic Kidney Disease (CKD)-EPI and grouped as CKD stage 1-5. Outcome was compared between full and reduced dose TDF, and between before and after dose reduction among patients who started on full dose TDF.

Results: Of 739 patients on TDF, 67 (9%) had reduced dose vs. 672 (91%) full dose. At baseline the mean (SD) age was 68 (11) vs. 45 (13) years, 63% vs.70% was male, mean duration on TDF was 3 (2) vs. 5 (3) years for reduced vs. full dose of TDF. Low dose patients had a baseline HBV DNA of 1.4 log (71% undetectable), 75% received TDF 300mg Q48hr (range 75mg - 300mg Q48hr), mean CKD-EPI was 50 (20) mL, 22% had hypophosphatemia, 46% had CKD stage G3b or worse and 14% had decompensated cirrhosis. During a mean follow-up of 3 (2) years, all patients continued to have viral suppression except for 1 dialysis patient on TDF 300mg/week who had a viral breakthrough (HBV DNA peak 3.6 log) that resolved 4 months after dose increase to Q72hr without decompensation and 1 patient on full dose TDF (resolved naturally). Another reduced dose patient had a transient ALT increase (peak 2x ULN) without rise in HBV DNA. The CKD-EPI decline observed during full dose TDF reversed in the first year of lower dosing and remained stable thereafter (+2.0 (13) mL at EOF vs. baseline; p=0.28), with 50 (75%) patients reaching CKD-EPI>50mL and 11/15 (73%) patients normalizing serum phosphate. None developed Fanconi syndrome or lactic acidosis. TDF was further dose reduced or switched to ETV/LAM in 11% of patients and dose increased due to improved GFR in 14%.

Conclusion: Low dose TDF could preserve renal function and sustain viral suppression in most renally impaired CHB patients, even with advanced liver disease. This useful, yet simple strategy could be especially feasible in resource limited settings.

Disclosures

Kin Seng Liem – Merck: Speaking and Teaching

Scott K. Fung – Gilead Sciences: Speaking and Teaching; Gilead Sciences: Advisory Committee or Review Panel

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