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MINIMAL CHANGES IN URINE MARKERS OF TUBULAR DYSFUNCTION IN CHB PATIENTS RECEIVING TAF COMPARED WITH TDF

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Background: The use of Tenofovir (TDF) for the treatment of CHB results in high rates of viral suppression with no described resistance, but has been associated with small declines in renal function over time. Tenofovir alafenamide (TAF), a novel prodrug of tenofovir (TFV), is more stable in plasma and more efficiently delivers TFV into lymphoid cells and hepatocytes. Phase 3 studies of TAF in CHB demonstrated less renal effects vs TDF with a mean reduction of eGFR from baseline of 0.6 ml/min after 48 wks TAF, and 4.7 ml/min after 48 wks TDF .
Aims: Here, we explore changes in urine renal biomarkers in patients treated with TAF versus TDF.
Methods: In two identically-designed Phase 3 studies of TAF (Study 110, HBeAg+ and Study 108, HBeAg-), patients were randomized 2:1 to TAF 25 mg QD or TDF 300 mg QD, with matching placebo, and treated for 96 wks. After wk 96, patients receive open label TAF for 48 wks. Biomarkers for renal glomerular dysfunction and tubular dysfunction and beta-2 microglobulin (B2M) were measured throughout the study and ratios to urine creatinine were calculated. Correlations between biomarkers were calculated using Spearman Correlation coefficients.
Results: Baseline correlations were highest for urine albumin/creatinine and protein/creatinine (correlation coefficient 0.57; $p<0.001$) as well as for RBP/creatinine and b2M/creatinine (correlation coefficient 0.44; $p<0.001$). Week 48 change in markers also showed similar correlation coefficients among tubular and glomerular markers. These correlations were strengthened when evaluating the TDF patients alone. At Week 48, changes in all 4 renal biomarkers were less in the TAF arm than in the TDF arm. Evaluating biomarker changes by baseline renal risk factors (older age, lower baseline GFR, pre-existing hypertension) demonstrated greater changes with TDF than with TAF which was accentuated in the high risk groups. The differences were greatest for RBP and B2M which are more sensitive markers for tubular dysfunction.
Conclusions: Baseline correlations were highest for urine albumin/creatinine and protein/creatinine (correlation coefficient 0.57; $p<0.001$) as well as for RBP/creatinine and b2M/creatinine (correlation coefficient 0.44; $p<0.001$). Week 48 change in markers also showed similar correlation coefficients among tubular and glomerular markers. These correlations were strengthened when evaluating the TDF patients alone. At Week 48, changes in all 4 renal

biomarkers were less in the TAF arm than in the TDF arm. Evaluating biomarker changes by baseline renal risk factors (older age, lower baseline GFR, pre-existing hypertension) demonstrated greater changes with TDF than with TAF which was accentuated in the high risk groups. The differences were greatest for RBP and B2M which are more sensitive markers for tubular dysfunction.

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