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P0831 **HIGH SERUM ALKALINE PHOSPHATASE PREDICTS THE RISK OF CKD PROGRESSION: EFFECT NODIFICATION BY THE GFR**

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Background and Aims: In the post-hoc analyses of the SUSTAIN and ASSURE trials (Kidney Blood Press Res. 2018;43:449-457), Apabetalone, an epigenetic modulator which lowers serum alkaline phosphatase (AlkPhos), stabilized the GFR in patients with cardiovascular disease and a GFR <60/ml/min/1.73m2. Analyzing the relationship between AlkPhos and renal outcomes in patients with established CKD is useful to preliminarily explore the biological hypothesis that AlkPhos is implicated in CKD progression.

Method: We investigated the relationship between AlkPhos and the risk for a combined renal end-point (30% GFR loss or dialysis/renal transplantation) in a cohort of 609 stage 3-5 CKD patients with an average GFR of 34.8±12.1ml/min/1.73 m2.

Results: Median AlkPhos levels were 91 IU/L (Interquartile range 71-117 IU/L) and in the vast majority of patients had values below 147 IU/L (the upper limit of the normal range). Over a median follow up of 3 years, two-hundred patients had the combined renal end-point. In an unadjusted analysis 1 ln increase in AlkPhos entailed a 49% risk excess for the renal end-point (HR: 1.49, 95% CI 1.11-2.01, P=0.008). Adjusting for traditional (age, gender, smoking, diabetes, total cholesterol, BMI, systolic BP, CV comorbidities) and CKD specific risk factors (hemoglobin, albumin, phosphate, and hs-CRP) did not modify the strength of this association (HR:1.48, 95% CI 1.08-2.02, P=0.016). Furthermore, In a fully adjusted analysis testing the GFR as an effect modifier of the AlkPhos - combined renal end point relationship showed a strong GFR- AlkPhos interaction (Figure). Indeed the risk for the combined renal end-point was gradually more pronounced at progressively more severe degrees of renal dysfunction, the HR being 0.94 (CI95% 0.60-1.47) at a GFR of 40 ml/min/m2 and 2.71 (CI95% 1.49-4.93) at 10 ml/min/1.73m2.

Conclusion: In patients with stage 3-5 CKD alkaline phosphatase within the normal range is associated with the risk for progression to ESRD and the GFR is an effect modifier of this relationship. Findings in this study are compatible with the hypothesis that within the normal range of this biomarker, the risk for CKD progression by alkaline phosphatase is amplified by the severity of CKD. These data are in keeping with post-hoc analyses of the SUSTAIN and ASSURE trials and provide circumstantial support to the hypothesis that interventions lowering serum alkaline phosphatase may mitigate CKD progression.

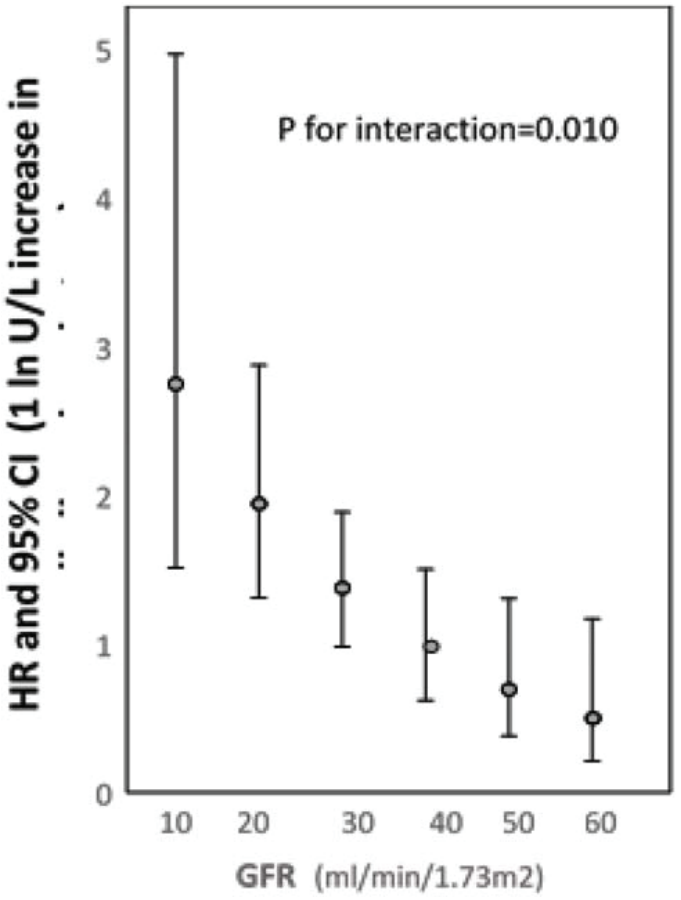

Figure: