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3

APABETALONE REDUCES CARDIOVASCULAR EVENTS IN PATIENTS WITH CHRONIC KIDNEY DISEASE, TYPE 2 DIABETES, AND RECENT ACUTE CORONARY SYNDROME: A BETONMACE TRIAL REPORT.:

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Chronic kidney disease (CKD) is highly prevalent in patients with type 2 diabetes (T2D) and associated with increased morbidity and mortality. Patients with T2D and acute coronary syndrome (ACS) are at high risk for recurrent cardiovascular (CV) events particularly in the presence of CKD. Maladaptive epigenetic responses in CKD may augment CV risk (Wasiak 2018). Apabetalone (APB) is a novel inhibitor of bromodomain and extraterminal (BET) proteins.

BETonMACE was a randomized, double-blind, comparison of effects of ABP or placebo (PBO) on major adverse CV events (MACE: CV-death, non-fatal myocardial infarct or stroke), in 2425 pts with T2D and recent ACS. MACE including hospitalization for CHF (expanded MACE) is reported according to presence or absence of CKD at baseline (eGFR 30-59 mL/min/1.73m^2).

Overall baseline characteristics: median age 62 years, 25.6% female, 87.6% white, 90% high intensity statin use, mean LDL-C 70.3 and HDL-C 33.3 mg/dl, median HbA1c 7.3%, and 11% with CKD. In patients with CKD, expanded MACE occurred in 12.9% on APB and 25% on PBO (HR 0.48, 95% CI 0.26-0.89 (p=0.02). In patients without CKD, expanded MACE occurred in 11.3% and 12.7% with APB or PBO, respectively (HR 0.89, 95% CI 0.70-1.14 (p=0.38). The interaction of CKD and treatment on expanded MACE was significant (P=0.03).

Patients with ACS and T2D have a very high risk of subsequent MACE or hospitalization for CHF. This risk is further augmented by CKD. APB may reduce CV events in high-risk patients with ACS, T2D, and CKD.