A POOLED ANALYSIS OF THE EFFECTS OF CONJUGATED ESTROGENS/BAZEDOXIFENE (CE/BZA) ON BONE LOSS FROM THE SELECTIVE ESTROGENS, MENOPAUSE, AND RESPONSE TO THERAPY (SMART) TRIALS

J. Gallagher, S. Palacios, K. Ryan, M. Messig, K. Pan, D. Kendler, B. Komm, S. Mirkin

Objective: We evaluated pooled bone mineral density (BMD) and bone marker (BM) data for CE/BZA from SMART-1 and -5.

Method: SMART-1 and -5 were randomized, double-blind, placebo (PBO)- and active-controlled, phase 3 studies in nonhysterectomized postmenopausal women. BMD and BM (osteocalcin [OC], C-telopeptide [CTx]) data were pooled for women (N=1433) given CE 0.45 and 0.625mg/BZA 20mg and PBO over 12 mos. BMD responders were defined as having an increase >=0% from baseline (BL). Sensitivity analyses used age, body mass index (BMI), race, and geographic region.

Result: Mean (SD) BL characteristics were age 55.2 (5.4) y; BMI 25.8 (3.5) kg/m2; and lumbar spine (LS) BMD T-score -1.3 (1.0). Women were at low BL fracture risk: 59.1, 34.3, and 6.4% had Fracture Risk Assessment Tool (FRAX) scores <5, 5-<10, and >=10%, respectively. At 12 mos, the CE/BZA doses significantly improved BMD vs PBO (mean % change from BL at LS, 2.3 and 2.5%, respectively; both P<.001) and also improved total hip (TH) BMD vs PBO (mean % change from BL 1.4 and 1.5%; both P<.001). LS BMD responders at 12 mos for the 2 CE/BZA doses were 69.0 and 65.2% vs 36.5% for PBO. CE/BZA had similar improvements in LS and TH BMD at 12 mos regardless of age, BMI, or geographic region. At 12 mos, the CE/BZA doses significantly reduced OC (median % change from BL, -28.0 and -34.8%) and CTx (-45.3 and -51.3%) vs PBO (-2.7% [OC] and -5.0% [CTx]; all P<.001).

Conclusion: CE/BZA significantly improved BMD and turnover in a large, low-fracture-risk population of nonhysterectomized postmenopausal women and may provide an effective alternative to hormone therapy to treat menopausal symptoms and prevent postmenopausal bone loss.