LBA30 ERA 223: A phase III trial of radium-223 (Ra-223) in combination with abiraterone acetate and prednisone/prednisolone for the treatment of asymptomatic or mildly symptomatic chemotherapy-naïve patients (pts) with bone-predominant metastatic castration-resistant prostate cancer (mCRPC)

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Background: Abiraterone acetate and prednisone/prednisolone (AAP) improves progression-free survival and overall survival (OS) in men with mCRPC. Ra-223 increases OS and decreases symptomatic skeletal events (SSEs) in men with mCRPC and bone metastases. We evaluated concurrent treatment with AAP and Ra-223.

Methods: This phase 3, double-blind, placebo (PBO)-controlled trial randomised asymptomatic/mildly symptomatic men with chemotherapy-naïve mCRPC and bone metastases in a 1:1 ratio of AAP + Ra-223 or AAP + PBO. Bone health agents (BHAs [bisphosphonates or denosumab]) were only allowed in pts receiving them at baseline. The primary endpoint was SSE-free survival (SSE-FS).

Results: 806 pts were randomised (401 to AAP + Ra-223; 405 to AAP + PBO); 39% and 42% of pts were receiving BHAs at baseline in the AAP + Ra-223 and AAP + PBO arms, respectively. The trial was unblinded early after more fractures and deaths were observed in the AAP + Ra-223 arm. All pts had completed study-specified Ra-223/PBO treatment prior to unblinding. At the primary analysis, median SSE-FS was 22.3 mo (95% CI 20.4 – 24.8) with AAP + Ra-223 and 26.0 mo (95% CI 21.8 – 28.3) with AAP + PBO (HR 1.122, 95% CI 0.917 – 1.374; p = 0.2636). Median OS was 30.7 mo (95% CI 25.8–not estimable) with AAP + Ra-223 and 33.3 mo (95% CI 30.2 – 41.1) with AAP + PBO (HR 1.195, 95% CI 0.950 – 1.505; p = 0.1280). Other secondary/exploratory endpoints are shown in the Table. Fractures occurred in 29% and 11% of pts in the AAP + Ra-223 and AAP + PBO arms, respectively. In pts receiving BHAs, 15% and 7% experienced a fracture in the AAP + Ra-223 and AAP + PBO arms, respectively, vs 37% and 15% without BHAs.

Conclusions: Concurrent AAP + Ra-223 treatment did not improve SSE-FS or OS and led to a higher fracture rate. Based on these results, we do not recommend Ra-223 in combination with AAP.

Clinical trial identification: NCT02043678.

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Table: LBA30

	AAP + Ra-223 N = 401	AAP + PBO N = 405	HR (95% CI)
Additional secondary endpoints			
rPFS (central review), median (95% CI), months	11.2 (9.1–11.8)	12.4 (10.8–14.5)	1.152 (0.960–1.383)
Time to cytotoxic chemotherapy, median (95% CI), months	29.5 (26.5–35.7)	28.5 (23.7–NE)	1.033 (0.816–1.308)
Time to opiate use for cancer pain, median (95% CI), months	19.0 (14.4–23.2)	22.6 (18.0–25.7)	1.126 (0.921–1.378)
Exploratory endpoints			
Overall confirmed PSA response, n/N (%)	287/396 (72)	267/401 (67)	–
Time to PSA progression, median (95% CI), months	9.6 (8.2–10.8)	9.0 (7.9–10.1)	0.937 (0.792–1.108)
Overall confirmed ALP response, n/N (%)	218/398 (55)	104/402 (26)	–
Time to ALP progression, median (95% CI), months	7.4 (7.1–7.9)	6.8 (5.3–8.4)	1.083 (0.918–1.276)
Time to deterioration in health-related quality of life*, median (95% CI), months	9.5 (6.9–12.0)	10.5 (8.3–13.0)	1.079 (0.865–1.345)

*As reported in the safety population (AAP + Ra-223 N = 392, AAP + PBO N = 394) using the NCCN-FACT FPSI-17 physical disease-related symptoms subscale score measured during the treatment period. ALP: alkaline phosphatase; NE: not estimable; PSA: prostate-specific antigen; rPFS: radiological progression-free survival.