Clinical Outcomes of Patients with Metastatic Castration-Resistant Prostate Cancer (mCRPC) Receiving Radium-223 (Ra-223) Early Versus Late in the Treatment Sequence.

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Background: Ra-223 is the only targeted alpha therapy shown to prolong overall survival (OS) in men with mCRPC. The purpose of this real-world study is to evaluate clinical outcomes of patients (pts) when Ra-223 is used early(2nd line) or late (3rd or later lines) for mCRPC.

Methods: We used administrative databases in Ontario (2012-2017) to estimate OS from start of 2nd line life prolonging therapy (LPT), event free survival (EFS; time from start of 2 line LPT to start of 4th line or death) using counting process models, comparing 2 cohorts of patients: Early Ra-223 (2nd line) vs Late Ra-223 (3rd or later line). All models are adjusted for relevant fixed and time-varying covariates, including age, prostate specific antigen, hemoglobin, Charlson Comorbidity Index (CCI), use of bone health agents, prior systemic treatments, Gleason score, TNM score, Androgen Deprivation Therapy (ADT) and standardized pain score.

Results: Data from 598 men in Ontario with mCRPC who received at least 2 lines of LPT, including Ra-223 in second line or later were analyzed (Early Ra-223 = 253; 42.3%; Late Ra-223 = 345; 57.7%). The mean age (standard deviation) at the start of 1 line LPT was 72.2 years (8.8). Patients in the early Ra-223 cohort had a longer time from diagnosis of prostate cancer to receiving 1st line LPT, a longer time from start of 1st line to start of 2nd line LPT, and were less likely to receive docetaxel. The median number of Ra-223 cycles was 5 (range 3-6) and 4 (range 3-6) and the mean number lines of total LPT was 2.7 ± 0.9 (2.0 - 7.0) and 3.8 ± 0.9 (3.0 - 7.0) in the early and late Ra-223 cohorts, respectively.

OS was better in the Early Ra-223 cohort compared to the Late Ra-223 cohort (Hazard Ratio [HR] 0.79; 95% Confidence Interval [CI] 0.66-0.95). EFS was better in the Early Ra-223 cohort compared to the Late Ra-223 cohort (HR 0.71; 95% CI 0.58-0.86). Time to first hospitalization and time to first emergency department visit was longer in the early Ra-223 cohort.

Conclusions: Real-world data from Ontario, suggests that patients who received Ra-223 in 2nd line versus 3rd line or later had better outcomes. Patients who received Ra-223 early received less chemotherapy, but had better survival. The selection of patients who may benefit the most from Ra-223, and the optimal timing of the Ra-223 in the sequence of treatments, are being evaluated in a larger Canadian study including data from four Canadian provinces (REACTIVATE NCT04281147).