Real-world clinical outcomes study of sequential novel antihormonal therapy (NAH) or radium-223 (Ra-223) treatment of metastatic castration-resistant prostate cancer (mCRPC) that progressed after first-line NAH.

Authors: Oliver Sartor, Daniel George, Bertrand Tomball, Celestia S Higano, Cora N. Sternberg, Kurt Miller, XiaoLong Jiao, Helen Guo, Per Sandström, Frank Verholen, Fred Saad, Neal Shore

Background: We assessed real-life clinical outcomes in patients with mCRPC treated in the USA who received sequential first-line (1L)/second-line (2L) NAH (abiraterone/enzalutamide or enzalutamide/abiraterone) or switched to a different mechanism of action (alpha-emitter Ra-223) after progression on 1L NAH.

Methods: This was a retrospective study (PHENIX, NCT03896984) of the Flatiron electronic health record database in patients with mCRPC that progressed on 1L NAH and started 2L monotherapy with Ra-223 (n=120) or NAH (n=226) between Jan 2013 and Dec 2018. Patient characteristics, overall survival (OS) from 2L start, and symptomatic skeletal events (SSEs) were analyzed descriptively.

Results: The two cohorts were generally similar at 2L start, including similar rates of bone-health agent use, but the Ra-223 cohort had a higher incidence of bone-only metastases, shorter duration of 1L NAH, and higher rate of prior SSEs than the 2L NAH cohort (Table). Median treatment duration was 5.6 mo (median 4.5 doses) for Ra-223 and 4.7 mo for 2L NAH. Median OS from 2L start was 10.8 mo for Ra-223 and 11.2 mo for 2L NAH, with 49% and 39%, respectively, receiving subsequent therapy. Among those who received subsequent therapy, the proportion who received subsequent taxane was lower in the Ra-223 cohort (47%) than in the 2L NAH cohort (76%). SSEs were observed after 2L start in 32 patients (27%) on Ra-223 and 49 (22%) on 2L NAH.

Conclusions: OS from start of 2L mCRPC treatment was similar for patients who received Ra-223 or alternative NAH in 2L. Slightly more patients received subsequent therapy in the Ra-223 cohort than in the 2L NAH cohort. Patients who received subsequent therapy were more likely to receive chemotherapy in the 2L NAH cohort, which is unsurprising as 2L NAH after 1L NAH is not highly active. Although the SSE rate before 2L was higher in the Ra-223 cohort than in the 2L NAH cohort and the two cohorts had similar rates of bone-health agent use at start of 2L, the rate of SSEs after 2L start was similar in both cohorts.

Table. PHENIX patient characteristics and clinical outcomes

	2L Ra-223 (n=120)	2L NAH (n=226)
Patient characteristics		
At diagnosis		
Gleason score >7, %*	63	65
Metastatic, %*	52	54
At start of 2L		
Median age, y	75	79
ECOG 0/1, %*	78	72
Median time from mCRPC diagnosis, mo	9.7	9.9
Bone metastases only, %*	77	57
Median laboratory values		
ALP, U/L	105	106

Hb, g/dL	12	12
PSA, µg/L	48	34
Median 1L NAH therapy duration, mo	6.0	7.5
Prior SSEs, %	51	33
BHA use, %	57	58
Clinical outcomes from start of 2L		
Median OS (95% CI), mo	10.8 (9.3, 12.9)	11.2 (10.0 13.2)
Subsequent therapy use, % (n/N)	49 (59/120)	39 (88/226)
Subsequent taxane use, % (n/N†)	47 (28/59)	76 (67/88)
SSEs/person-years		
At 6 mo	0.35	0.31
At 12 mo	0.31	0.30

*Denominator excludes patients with missing/unknown data.
†Denominator is patients with subsequent therapy