Effectiveness and safety of radium-223 in patients with bone-metastatic castration-resistant prostate cancer: the prospective, observational KYUCOG-1901 study

Masaki Shiota[1], Hideki Enokida[2], Tomomi Kamba[3], Toshiyuki Kamoto[4], Tsukasa Igawa[5], Naoya Masumori[6], Hirotsugu Uemura[7], Kensuke Mitsunari[8], Takayuki Sumiyoshi[9], Hiroji Uemura[10], Katsuyoshi Higashijima[11], Shoji Tokunaga[12], Masatoshi Eto[1]

[1]Department of Urology, Kyushu University, [2]Department of Urology, Kagoshima University, [3]Department of Urology, Kumamoto University, [4]Department of Urology, University of Miyazaki, [5]Department of Urology, Kurume University, [6]Department of Urology, Sapporo Medical University, [7]Department of Urology, Kindai University, [8]Department of Urology, Nagasaki University, [9]Department of Urology, Kyoto University, [10]Department of Urology and Renal Transplantation, Yokohama City University Medical Center, [11]Department of Urology, University of Occupational and Environmental Health, [12]Clinical Research Support Center, Ehime University Hospital

BACKGROUND

- Radium-223 dichloride (Ra-223) improves survival in bone-metastatic castration-resistant prostate cancer (mCRPC).
- However, prospective real-world data are limited, particularly regarding treatment outcomes, predictors of continuation, and integration with subsequent therapies.
- The objective was to evaluate the real-world effectiveness and safety of Ra-223.

METHODS

Endpoints:

Effectiveness
- PSA response
- ALP response
- PSA-progression-free survival (PFS)
- ALP-PFS
- Radiographic PFS (rPFS)
- Overall survival (OS)

Safety
- Adverse events evaluated using CTCAE v5.0

KYUCOG-1901 (UMIN000040358)

Study design: The KYUCOG-1901 study was a prospective multicenter observational study at 19 Japanese institutions

Patients: mCRPC and ≥2 bone metastases received up to six cycles of Ra-223.

Key inclusion criteria
(1) Histologically confirmed prostatic adenocarcinoma
(2) Evidence of castration-resistant progression while receiving castration or continuous ADT
(3) ≥ 2 bone metastases
(4) Eastern Cooperative Oncology Group (ECOG) performance status of 0–2
(5) Adequate organ function
(6) An expected survival of ≥ 6 months.

Major exclusion criteria
(1) Prior radioisotope therapy (e.g., strontium-89)within 6 months
(2) Prior Ra-223 treatment
(3) Active malignancy other than prostate cancer
(4) Current or prior visceral or brain metastases
(5) Lymph node metastases ≥ 1.5 cm (short axis)
(6) Spinal cord compression

Study period: Enrollment began in May 2020 and ended in April 2023. Data were cut off on April 30, 2025.

Patients characteristics

Characteristics	n=93
Median age at baseline, years (IQR)	73 (68–77)
ECOG performance status at baseline, n (%)	
0	69 (74.2%)
1	22 (23.7%)
2	1 (1.1%)
Not available	1 (1.1%)
Pain at baseline, n (%)	
Asymptomatic/mild symptomatic	62 (66.7%)
Symptomatic	28 (30.1%)
Not available	3 (3.2%)
Median PSA level at baseline, ng/ml (IQR)	7.5 (2.0–38.2)
Median PSA doubling time at baseline, months (IQR)	2.3 (1.3–4.2)
Median hemoglobin level at baseline, g/dl (IQR)	12.8 (11.9–13.7)
Median ALP level at baseline, IU/ml (IQR)	90 (64–134)
Not available	1
Median LDH level at baseline, IU/ml (IQR)	197 (174–233)
Not available	3
ISUP grade group, n (%)	
≤3	13 (14.0%)
4	22 (23.7%)
5	58 (62.4%)
Prior local treatment, n (%)	
Absence	57 (61.3%)
Curative local treatment	36 (38.7%)
T-stage at diagnosis, n (%)	
Tx	1 (1.1%)
T1/2	34 (36.6%)
T3	40 (43.0%)
T4	18 (19.4%)
N-stage at diagnosis, n (%)	
N0	46 (49.5%)
N1	47 (50.5%)
M-stage at diagnosis, n (%)	
M0	32 (34.4%)
M1a	2 (2.2%)
M1b	59 (63.4%)
Lymph node metastasis at baseline, n (%)	
Absence	88 (94.6%)
Presence	5 (5.4%)
EOD score at baseline, n (%)	
1	36 (38.7%)
2	36 (38.7%)
3	14 (15.1%)
4	7 (7.5%)
Prior ARSI treatment, n (%)	
Absence	16 (17.2%)
Presence	77 (82.8%)
Prior taxane treatment, n (%)	
Absence	63 (67.7%)
Presence	30 (32.3%)

Ra-223 treatment

Treatment	n=93
Concomitant treatment, n (%)	
ADT monotherapy	43 (46.2%)
ADT plus bicalutamide	7 (7.5%)
ADT plus flutamide	6 (6.5%)
ADT plus abiraterone	3 (3.2%)
ADT plus enzalutamide	16 (17.2%)
ADT plus others	18 (19.4%)
Bone modifying agent, n (%)	
None	48 (51.6%)
Denosumab	43 (46.2%)
Zoledronate acid	2 (2.2%)
Number of Ra-223 cycles, n (%)	
1	3 (3.2%)
2	6 (6.5%)
3	4 (4.3%)
4	7 (7.5%)
5	4 (4.3%)
6	69 (74.2%)
Reason for Ra-223 early discontinuation, n (%)	
Disease progression	12 (12.9%)
New visceral metastasis	5 (5.4%)
Adverse event	4 (4.3%)
Physician decision for other reasons	3 (3.2%)

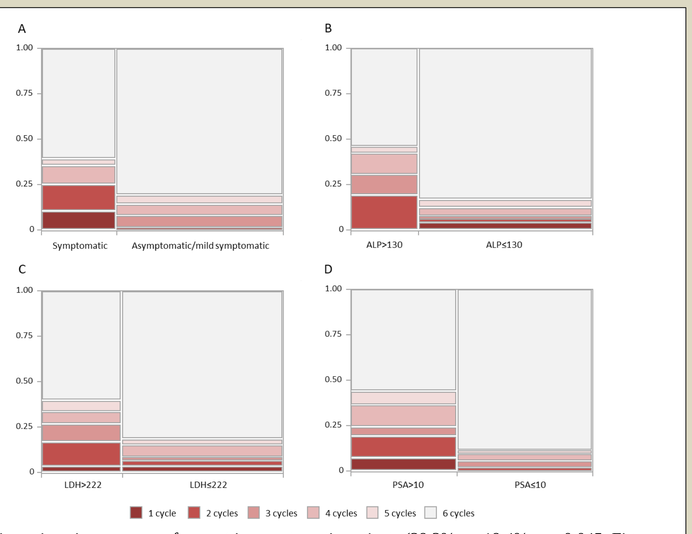
Subsequent therapies

Treatment	n=93
First line, n (%)	
Docetaxel	24 (25.8%)
Enzalutamide	19 (20.4%)
Cabazitaxel	11 (11.8%)
Abiraterone	9 (9.7%)
Others	3 (3.2%)
Second line, n (%)	
Cabazitaxel	13 (14.0%)
Docetaxel	8 (8.6%)
Abiraterone	5 (5.4%)
Enzalutamide	2 (2.2%)
Other	1 (1.1%)
Third line, n (%)	
Cabazitaxel	6 (6.5%)
Docetaxel	2 (2.2%)
Enzalutamide	1 (1.1%)
Others	2 (2.2%)
Fourth line, n (%)	
Abiraterone	1 (1.1%)
Enzalutamide	1 (1.1%)

Safety

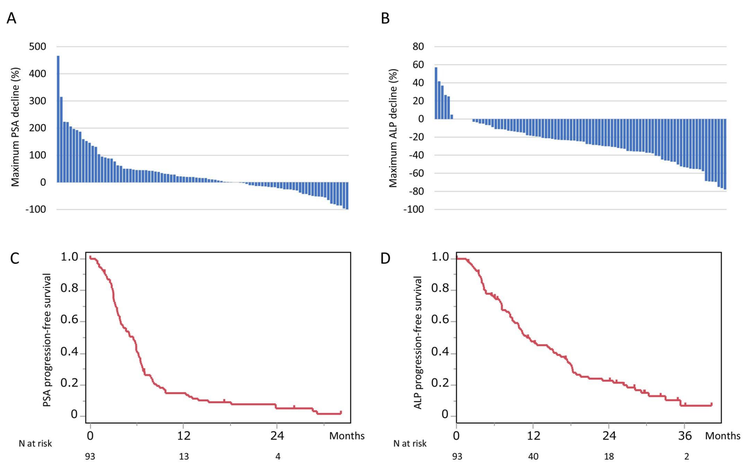
Adverse events	Any grade	≥Grade 3
Clinical events		
Fever	2 (2.2%)	0
Constipation	1 (1.1%)	0
Diarrhea	6 (6.5%)	1 (1.1%)
Nausea	6 (6.5%)	1 (1.1%)
Vomiting	2 (2.2%)	0
Anorexia	12 (12.9%)	2 (2.2%)
Dehydration	2 (2.2%)	1 (1.1%)
Dyspnea	2 (2.2%)	0
Hypoxia	1 (1.1%)	0
Pneumonitis	2 (2.2%)	1 (1.1%)
Lower gastrointestinal hemorrhage	1 (1.1%)	1 (1.1%)
Aortic injury	1 (1.1%)	1 (1.1%)
Arterial thromboembolism	1 (1.1%)	1 (1.1%)
Osteonecrosis of jaw	1 (1.1%)	1 (1.1%)
Laboratory abnormalities		
White blood cell decreased	20 (23.7%)	2 (2.2%)
Neutrophil count decreased	25 (26.9%)	3 (3.2%)
Platelet count decreased	40 (43.0%)	2 (2.2%)
Anemia	93 (100%)	6 (6.5%)
Hypoalbuminemia	74 (79.6%)	0
Aspartate aminotransferase increased	26 (28.0%)	2 (2.2%)
Alanine aminotransferase increased	13 (14.0%)	0
Alkaline phosphatase increased	10 (10.8%)	1 (1.1%)
Lactate dehydrogenase increased	58 (62.4%)	0
Hypercalcemia	17 (18.3%)	1 (1.1%)
Hypocalcemia	21 (22.6%)	2 (2.2%)
Creatinine increased	27 (29.0%)	1 (1.1%)
Chronic kidney disease	64 (68.8%)	4 (4.3%)

Early discontinuation of Ra-223 treatment



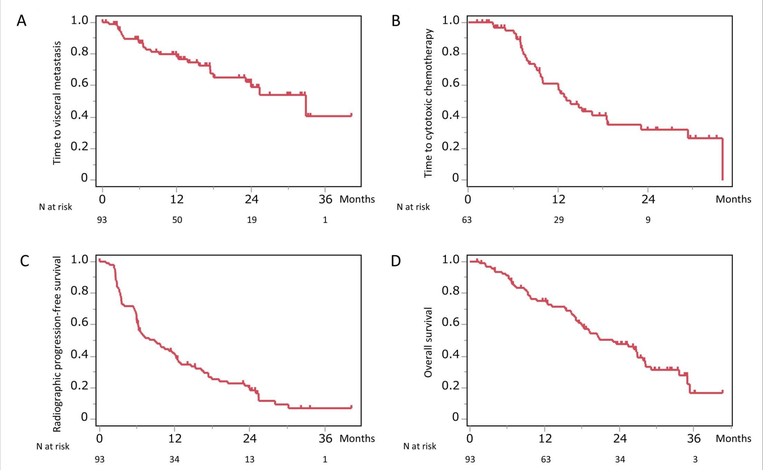
Early discontinuation was more frequent in symptomatic patients (39.3% vs. 19.4%, p = 0.045; Figure A), those with elevated baseline ALP (> 130 IU/mL, 39.3% vs. 16.7%, p = 0.0033; Figure B), elevated LDH (> 222 IU/mL, 40.0% vs. 18.3%, p = 0.026; Figure C), and elevated PSA (> 10 ng/mL, 43.9% vs. 11.5%, p = 0.0004; Figure D).

Short-term effectiveness



A maximum PSA decline of ≥ 30% and ≥ 50% was achieved in 16 (17.2%) and 12 (12.9%) patients, respectively (Figure A). A maximum ALP decline of ≥ 30% and ≥ 50% occurred in 39 (41.9%) and 16 (17.2%) patients, respectively (Figure B). Median PSA-PFS was 5.5 months (95% CI, 3.8–6.2; Figure C), while median ALP-PFS was 11.5 months (95% CI: 8.8–15.8; Figure D).

Long-term effectiveness



The median time to visceral metastasis was 32.9 months (95% CI: 23.2–not reached; Figure A). Among 63 chemotherapy-naïve patients, a median time to chemotherapy was 13.7 months (95% CI: 9.9–18.6; Figure B). Median rPFS was 8.8 months (95% CI: 6.1–12.2; Figure C). Median OS was 23.0 months (95% CI: 17.4–27.9; Figure D).

Comparison with ALSYMPCA study

Endpoints	ALSYMPCA study	This study
Complete rate	63%	74.2%
PSA-PFS	3.6 mo	5.5 mo
ALP-PFS	7.4 mo	11.5 mo
Time to SSE	15.6 mo	33.1 mo
rPFS	Not available	8.8 mo
OS	14.9 mo	23.0 mo
≥Grade 3 AE	56%	36.5%

Parker C, et al. N Engl J Med. 2013;369(3):213-23.
Sartor O, et al. Lancet Oncol. 2014;15(7):738-46.

CONCLUSION

- Ra-223 was effective and well tolerated in Japanese mCRPC patients.
- Early initiation in less symptomatic patients with lower disease burden may maximize benefit, and integration with subsequent therapies appears feasible.

Acknowledgements

We sincerely thank all the patients and their families for their participation in this study, as well as the investigators and site staff of the KYUCOG-1901 study for their dedicated efforts. We also acknowledge the Clinical Research Support Center Kyushu (CReS Kyushu, Fukuoka, Japan) for their invaluable support in research coordination and data management.

Funding

This work was conducted with financial support to CReS Kyushu from Bayer Yakuhin. The funder had no role in the study design and was not involved in its conduct, data analysis, interpretation, or the decision to submit the results for publication.