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

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COI Disclosure Information

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Matters requiring disclosure of COI with regard to our presentation are as follows;

Lecture fee: Janssen Pharmaceutical, AstraZeneca, Astellas Pharma, Sanofi, and Bayer

Research founding: Astellas Pharma

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

Study design This 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.

Endpoints

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

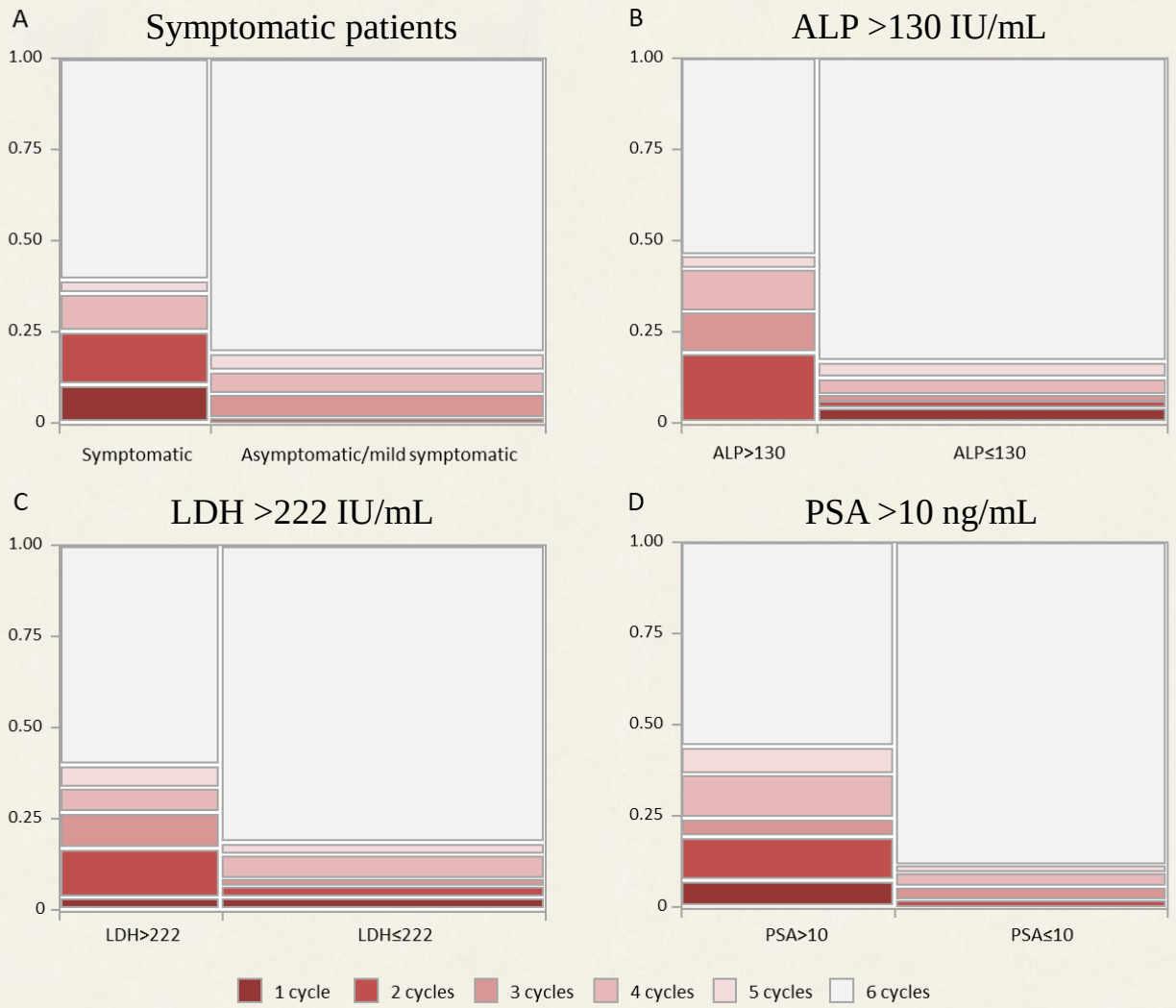
Safety
- Adverse events evaluated using CTCAE v5.0

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%)

Characteristics	n=93
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%)

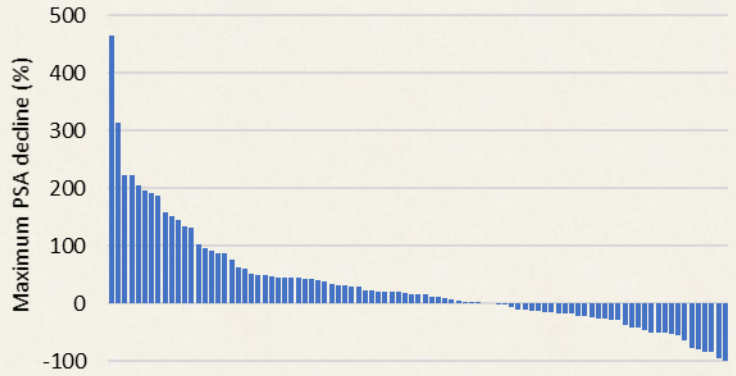
Early discontinuation of Ra-223 treatment



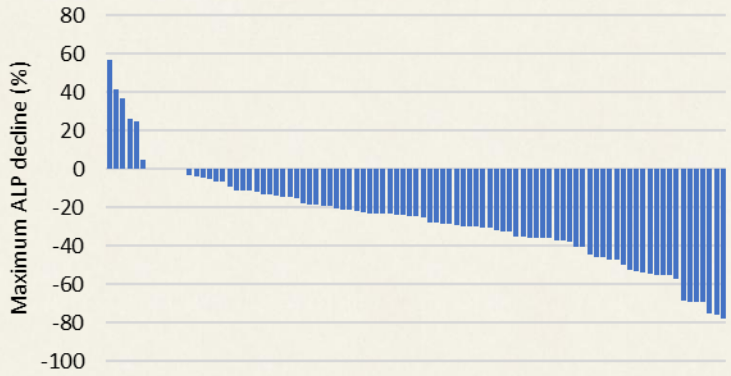
Early discontinuation was more frequent in symptomatic patients (39.3% vs. 19.4%, p = 0.045; Figure A), those with elevated baseline ALP (> 130 IU/mL, 39.3% vs. 16.7%, p = 0.0033; Figure B), elevated LDH (> 222 IU/mL, 40.0% vs. 18.3%, p = 0.026; Figure C), and elevated PSA (> 10 ng/mL, 43.9% vs. 11.5%,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

Effectiveness

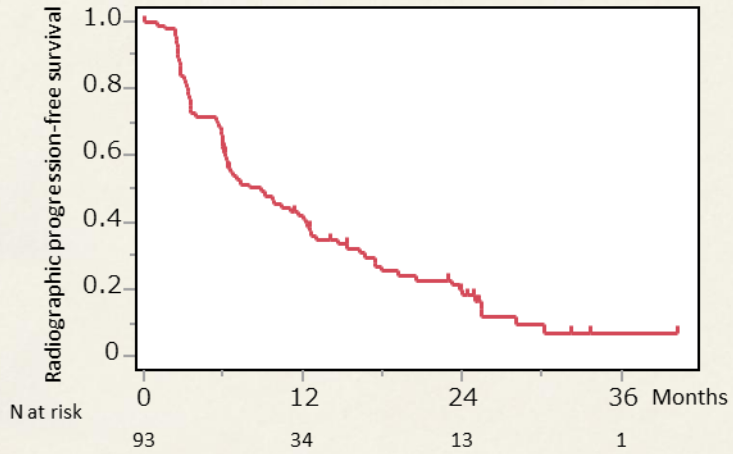
A ≥ 30% PSA decline in 16 (17.2%)



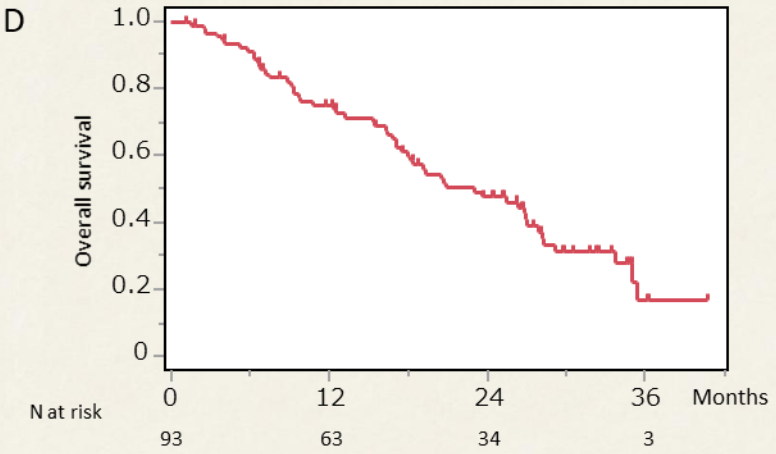
B ≥ 30% ALP decline in 39 (41.9%)



Median rPFS: 8.8 months



Median OS: 23.0 months



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 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).

Safety

Adverse events	≥Grade 3
Clinical events	
Diarrhea	1 (1.1%)
Nausea	1 (1.1%)
Anorexia	2 (2.2%)
Dehydration	1 (1.1%)
Pneumonitis	1 (1.1%)
Lower gastrointestinal hemorrhage	1 (1.1%)
Aortic injury	1 (1.1%)
Arterial thromboembolism	1 (1.1%)
Osteonecrosis of jaw	1 (1.1%)
Laboratory abnormalities	
White blood cell decreased	2 (2.2%)
Neutrophil count decreased	3 (3.2%)
Platelet count decreased	2 (2.2%)
Anemia	6 (6.5%)
Aspartate aminotransferase increased	2 (2.2%)
Alkaline phosphatase increased	1 (1.1%)
Hypercalcemia	1 (1.1%)
Hypocalcemia	2 (2.2%)
Creatinine increased	1 (1.1%)
Chronic kidney disease	4 (4.3%)

≥Grade 3 AEs in total were observed in 34 (36.5%)

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%

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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.

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