ASSESSMENT OF SEQUENTIAL RADIUM-223 AND DOCETAXEL TREATMENT IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER: INSIGHTS FROM THE GLOBAL REASSURE STUDY

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BACKGROUND

- The alpha-particle emitting radionuclide Radium-223 (Ra-223) and the chemotherapeutic docetaxel are both approved for extending overall survival (OS) in patients with metastatic castration-resistant prostate cancer (mCRPC)[1,2]
- Data supporting the safety and ability to sequence Ra-223 and docetaxel in mCRPC are key to optimising patient treatment and outcomes
- REASSURE (NCT02141438) was a global, prospective, observational study that investigated the long-term safety and efficacy of Ra-223 in mCRPC in routine clinical practice[3]

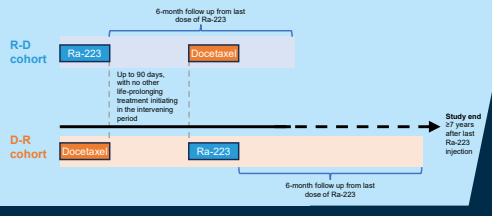
OBJECTIVE

To compare real-world safety and OS outcomes for patients with mCRPC who received radium-223 prior to or after docetaxel with no intervening therapy in between

PLAIN LANGUAGE SUMMARY

- Radium and docetaxel are anti-cancer drugs used for prolonging the lives of patients with advanced prostate cancer
- Data on the best order to give these treatments can help guide treatment decisions to plan for best outcomes
- The REASSURE study followed over 1,400 patients with prostate cancer who were treated with radium as a part of their normal treatment
- Some of the patients in the study also received docetaxel, either before or after radium. We compared patients who were treated with radium first with those who received docetaxel first to see which group had better outcomes
- The length of time that patients survived from the start of treatment was similar even though there were some differences in their characteristics at the start of radium treatment
- More patients treated with radium before docetaxel completed their radium treatment and had fewer severe side effects after they received radium compared with those patients treated with docetaxel first

METHODS



- The REASSURE study included 1,472 patients in 20 countries treated between 2014–2017
  - Data cutoff: Oct 24, 2024
- Patients were included in this analysis if they were treated with radium-223 prior to (R-D) or following (D-R) docetaxel, without initiation of life-prolonging treatment in between. Additionally, the second treatment had to start within 90 days of stopping the first
- Here we report:
  - Safety data from the start of Ra-223 treatment
  - OS data from the start of the first treatment in each sequence
- Statistics were descriptive in nature

Baseline characteristics at Ra-223 treatment start

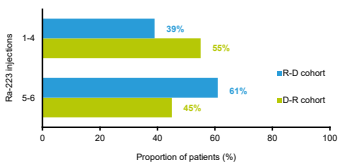
Patient and disease characteristics	R-D cohort (N = 72)	D-R cohort (N = 86)
Median age, years, (min, max)[a]	71 (57, 92)	69 (51, 90)
ECOG PS, %		
0	40	25
1	57	57
≥2	3	18
Sites of metastases, %		
Bone only	75	84
Bone and lymph nodes	17	9
Bone and other sites (excl. lymph nodes)	4	4
Bone and other sites (incl. lymph nodes)	4	4
Extent of metastatic disease, %[b]		
<6 metastases	24	9
6–20 metastases	43	43
>20 metastases but not Superscan	18	29
Superscan	4	9
Laboratory values, median (range)[c]		
PSA, ng/mL	66 (2–2,595)	130 (0–2,810)
ALP, U/L	118 (35–530)	173 (40–800)
LDH, U/L	242 (150–516)	309 (134–1,277)
Haematology[d]		
Haemoglobin		
Median (range), g/dL	13 (10–15)	11 (7–14)
≥10 g/dL, %	86	70
Platelets		
Median (range), 10^9/L	216 (8–486)	240 (76–509)
≥10 × 10^9/L, %	89	84
Neutrophils		
Median (range), 10^9/L	4 (0–9)	5 (0–12)
≥1.5 × 10^9/L, %	56	55

Note: percentages may not total 100 because of missing data and/or rounding. [a]Calculated at date of informed consent. [b]R-D cohort n=68, D-R cohort n=79. [c]PSA: R-D cohort n=51, D-R cohort n=60; ALP: R-D cohort n=51, D-R cohort n=60; LDH: R-D cohort n=25, D-R cohort n=34. [d]Haemoglobin (median): R-D cohort n=65, D-R cohort n=76; Platelets (median): R-D cohort n=65, D-R cohort n=74; Neutrophils (median): R-D cohort n=41, D-R cohort n=49.

Ra-223 treatment

- The median follow-up time (from the start of Ra-223) was 18.3 months (range 3.7–59.7) for the R-D cohort and 9.0 months (range 0.4–79.4) for the D-R cohort
- **61%** of patients in the R-D cohort received ≥5 doses of Ra-223 compared with 45% in the D-R cohort
- Patients in the R-D cohort received a **median of 6 doses** compared with 4 doses for patients in the D-R cohort

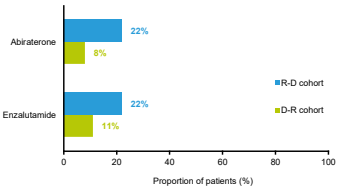
Doses of Ra-223 received per cohort



Concomitant life-prolonging therapies received with Ra-223

- Abiraterone and enzalutamide were the most common life-prolonging therapies received alongside Ra-223 in both cohorts
- More patients received concomitant abiraterone and enzalutamide in the R-D cohort than in the D-R cohort

Concomitant treatment received with Ra-223[a]



[a]Concomitant therapy is defined as therapy in addition to Ra-223

Safety events during Ra-223 treatment

Adverse events	R-D cohort (N = 72)	D-R cohort (N = 86)
Any adverse event, %	53	54
Treatment-emergent drug-related adverse events, %	43	28
Grade ≥3	11	13
Resulting in Ra-223 discontinuation	4	5
Related to blood and lymphatic systems	13	9
Grade ≥3	7	9
Treatment-emergent serious adverse events, %	11	34
Resulting in Ra-223 discontinuation	4	13
Drug-related serious adverse events, %	10	7
Resulting in Ra-223 discontinuation	1	1
Treatment-emergent drug-related adverse events[a]		
Most common treatment-emergent drug-related adverse events, %		
Diarrhoea	14	9
Fatigue	14	8
Nausea	11	9
Anaemia	7	9
Pain	6	4

[a]Shown are treatment-emergent drug-related adverse events occurring in >5% of patients in either cohort

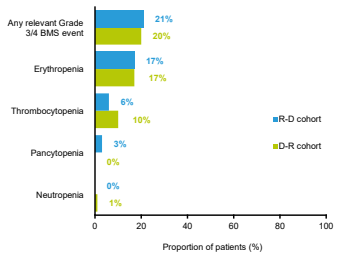
Second primary malignancies

- There were 2 SPMs (3%) in the R-D cohort and 1 (1%) in the D-R cohort
  - In the R-D cohort, the SPMs occurred 12–18 months and 18–24 months after the last Ra-223 injection
  - In the D-R cohort, the SPM occurred 18–24 months after the last Ra-223 injection

Bone marrow suppression post Ra-223

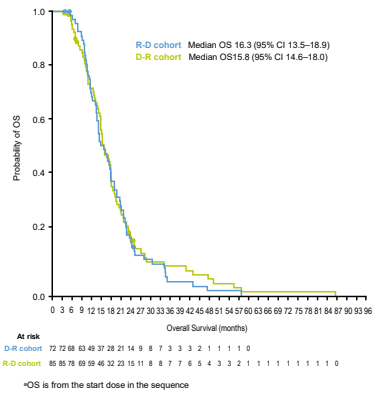
- Grade 3/4 bone marrow suppression (BMS) events post Ra-223 treatment were similar between cohorts

Grade 3/4 BMS events post Ra-223 treatment[a]



[a]Incidences of Grade 3/4 haematological adverse events based on bone marrow suppression from last dose of Ra-223 and up to 6 months (183 days) after

Overall survival[a]



[a]OS is from the start dose in the sequence

- Median OS from the first dose in the sequence was similar between the cohorts:
  - R-D cohort: **16.3 months** (95% CI: 13.5–18.9 months)
  - D-R cohort: **15.8 months** (95% CI: 14.6–18.0 months)

CONCLUSIONS

- Overall survival was similar between radium-docetaxel and docetaxel-radium sequences
- More patients in the radium-docetaxel group completed therapy (received ≥5 doses) of radium-223 and had fewer treatment-emergent serious adverse events during radium-223 treatment
- Overall, our findings support the treatment sequence of starting with radium-223

ABBREVIATIONS

ALP, alkaline phosphatase; BMS, bone marrow suppression; D-R, docetaxel – radium-223 sequence; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LDH, lactate dehydrogenase; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; PSA, prostate-specific antigen; Ra-223, radium-223; R-D, radium-223 – docetaxel sequence; SPM, second primary malignancy.

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EP-0809

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ACKNOWLEDGEMENTS

Statistical support was provided by Elizabeth Patel (Bayer) and Peter Hassenpflug of (Cerner Enviza). Dr Nick Davies and Stefan Courtney of Cancer Communications and Consultancy Ltd (part of Bioscript), Macclesfield, UK provided medical writing support. Study sponsored by Bayer.

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