1. Abstract

Acronym/Title	URANIS – Data collection in **u**rological centers during treatment with **Ra**-223 dichloride (Xofigo) within the framework of a **n**on-**i**nterventional **s**tudy assessing overall survival (OS) and effectiveness predictors of Ra-223 dichloride treated mCRPC patients in a real life setting in Germany
Report version and date **Author**	V 1.0, 01 SEP 2021 PPD Bayer Vital GmbH Building K 56 51368 Leverkusen, Germany PPD Alcedis GmbH, CRO Winchesterstrasse 3 35394 Giessen, Germany
Keywords	Prostate Cancer, Oncology, Xofigo®, overall survival, quality of life
Rationale and background	Phase III ALSYMPCA trial in metastatic castration-resistant prostate cancer (mCRPC) demonstrated that Radium-223 improves overall survival (OS) compared to placebo plus best standard of care. However, the real-world data on effect of Radium-223 on OS is scarce.
Research question and objectives	This observational study sought to evaluate (OS) in mCRPC patients receiving Radium-223 in daily clinical practice. The primary objective was evaluation of OS. Secondary objectives included evaluation of symptomatic skeletal events (SSEs) and SSE-free survival (SSE-FS), estimation of pathological and non-pathological fractures and bone associated events, treatment-emergent adverse events (TEAE), type and time to next tumor treatment (TTNT), safety, quality of life (QoL, using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) questionnaire), activities of daily living (using the Katz-Index) and body function (using MOSES questionnaire).
Study design	Prospective, non-interventional, multi-center, single arm cohort study.
Setting	Thirty-six departments of urooncology throughout Germany. Patients were observed from start of Radium-223 therapy until

	death, withdrawal of consent, loss to follow-up or regular end of the study.
Subjects and study size, including dropouts	Included were men aged ≥18 years with mCRPC and symptomatic bone metastases and no known visceral metastases and initiating Radium-223 therapy. 82 patients were available for safety analysis (SAF set); and 73 patients were included in the full analysis set (FAS).
Variables and data sources	Historic demographic and clinical data were obtained from medical records. Clinical and patient-reported data were collected during treatment and follow-up visits.
Results	Median age at registration was PPD 82.2% had Eastern Cooperative Oncology Group performance status 0-1. Patients had a median number of 1 prior systemic anti-cancer therapy. Median number of Radium-223 injections was 6; 64.4% of patients received BHA prior to or overlapping with Radium-223. Overall, median OS was 16.72 months (95%CI 12.65-23.72) and it was longest in patients without prior/concomitant chemotherapy (20.47 months, 95%CI 13.67-26.09) and in patients with prior/concomitant abiraterone (23.52 months, 95%CI 9.76-not reached (NR)). Median SSE-FS was 14.98 months (95%CI 11.40-20.90). Seven patients (8.5%) had SSEs, including external radiotherapy for relief of skeletal symptoms (n=5, 6.1%) and new symptomatic pathological bone fracture (n=4, 4.5%). Median TTNT was 14.42 months (95%CI 10.12-NR); 28 patients (38.4%) received a mCRPC therapy after the first Radium-223 injection. Mean FACT-P total score remained stable form baseline (109.66, SD 19.94) until follow-up after 6 months (108.08, SD 25.83). Mean Katz index total score remained stable at a high level from baseline (5.6, SD 0.9) until follow-up after 1 month (5.3, SD 1.4). Scores for most of the domains in MOSES remained at the same level from baseline until follow up after 1 month. 61% and 25.6% of patients experienced at least one TEAE or drug-related TEAE, respectively, most often anemia, fatigue and diarrhea. Serious TEAE occurred in 29.3% of patients, most frequently anemia (in 3.7%).
Discussion	This real-world study confirmed an efficacy of Radium-223 to prolong OS, TTNT and SSE-FS in mCRPC patients. Occurrence of SSEs was similar as previously reported. QoL, functional status and ability to independently perform activities of daily living remained

	stable throughout the study. Finally, this study confirmed the favorable safety profile of Radium-223.
Marketing Authorization Holder(s)	Bayer Pharma AG, D-13342 Berlin, Germany Please note that, effective 1st January 2017, Bayer Pharma AG has transferred its assets to Bayer AG, an affiliated company within the Bayer Group. Thereby, Bayer AG assumed all rights and obligations of Bayer Pharma AG, including the role as initiator and funder of this study. No study procedures have changed.
Names and affiliations of principal investigators	Contact details of the principal and/or coordinating investigators for each country and site participating in the study are listed in a stand-alone document (see Annex 1: List of stand-alone documents) which is available upon request).