Clinical Study Synopsis

This Clinical Study Synopsis is provided for patients and healthcare professionals to increase the transparency of Bayer's clinical research. This document is not intended to replace the advice of a healthcare professional and should not be considered as a recommendation. Patients should always seek medical advice before making any decisions on their treatment. Healthcare Professionals should always refer to the specific labelling information approved for the patient's country or region. Data in this document or on the related website should not be considered as prescribing advice.
The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

1. Abstract

Acronym/Title	PARABO - **P**ain evaluation in **Ra**dium-223 (Xofigo®) treated mCRPC patients with **bo**ne metastases – a non-interventional study in nuclear medicine centers
Report version and date Author	v1.0; 01 JUN 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®, Bone Metastases, Pain Control
Rationale and background	Phase III ALSYMPCA trial in metastatic castration-resistant prostate cancer (mCRPC) demonstrated that Radium-223 improves overall survival (OS), quality of life (QoL) and indicated a reduction of bone pain compared to placebo+best standard of care. However, the real-world data on effect of Radium-223 on pain reduction and bone pain-related QoL is scarce.
Research question and objectives	This study aimed to assess bone pain in mCRPC patients receiving Radium-223 in the real-world setting. The primary objective was evaluation of pain response (two points improvement from baseline in worst pain score on BPI-SF questionnaire) Secondary objectives included evaluation of change from baseline in pain related assessments, symptomatic skeletal event (SSE) including fractures, time to: next tumor treatment (TTNT) and first SSE (TSSE), overall survival, blood values and treatment-emergent adverse events (TEAE).
Study design	Prospective, non-interventional, multi-center, single arm

	cohort study.
Setting	Twenty-seven nuclear medicine clinics and practices 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 with symptomatic bone metastases and no known visceral metastases and initiating Radium-223 therapy.
Variables and data sources	Historic demographic and clinical data were obtained from medical records or through patient interview. Clinical, pain assessment and QoL data were collected during treatment and follow-up visits.
Results	Out of 358 patients were enrolled, 356 initiated Radium-223 therapy. 354 patients were included in the efficacy analysis. 73.4% had Eastern Cooperative Oncology Group performance status 0-1. 214 patients (60.1%) completed 6 Ra-223 cycles and 242 (68.4%) of the patients had at least one prior systemic anticancer therapy. 52.5% received concomitant bone-health agents. Primary objective analysis revealed that 59.3% of patients had at least one clinically meaningful pain response during the study. Patients with 5-6 Radium-223 injections more often achieved pain response than those with 1-4 injections (67.12% vs 42.86%). Mean BPI-SF component scores were maintained from baseline during the treatment with Radium-223. Pain control rate was 67.13% (95%CI 60.43-73.35 Mean FACT-BP score was 35.93 (SD=14.79) at baseline and 41.85 (SD=14.50) at visit 6. Median OS (time from the start of Radium-223 therapy to death due to any cause) was 17.15 months (95%CI 15.33-18.97) Median TSSE was not reached (95%CI 37.45-NR). Prior or concomitant therapy with abiraterone/prednisone or enzalutamide did not appear to increase fracture incidence. 56.2% of patients experienced at least one TEAE, most often Anaemia, Fatigue and Diarrhoea. Serious TEAE occurred in 26.97% of patients, most frequently Anaemia and Pancytopenia. 25.84% of patients experienced a drug-related TEAE, most often anaemia (9.3%), diarrhoea (4.8%), and

	fatigue (2.8%). 11.2% of patients experienced grade ≥3 drug-related TEAEs. 21.4% and 8.2% of patients discontinued Radium-223 due to TEAE or drug-related TEAE, respectively. The most common reasons for early termination were adverse events (12.1%) and disease progression (10.1%).
Discussion	In this real-world study 59.3 % of the patients had a clinically meaningful pain response. A higher number of patients with 5-6 Radium-223 injections achieved a pain response. The overall clinical outcomes with Radium-223, including pain response, safety and OS, were consistent with previous observations.
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).