STUDY REPORT SYNOPSIS

REMPRO Registry

A Multi-country, Multi-centre, Non-interventional, REtrospective Study to Describe the Real-world Treatment Patterns and Associated Clinical Outcomes in Patients With Metastatic Castration-resistant PROstate Cancer

Milestones:	Final approved protocol (Version 2.0)	June 2021
	Start of data collection	September 2021
	End of data collection	September 2022
	Final database lock	January 2023
	Global level data analysis	July 2023
	Global CSR	August 2023

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This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.

Background/rationale: Metastatic castration-resistant prostate cancer (mCRPC) is a formidable disease with limited treatment modalities. Although clinical trials have extensively explored different therapeutic interventions, real-world evidence is indispensable for gaining a holistic understanding of the existing treatment landscape and identifying unaddressed needs.

Objectives: To describe the real-world treatment patterns in patients with mCRPC.

Methods: A retrospective, multicentre, non-interventional cohort study was conducted in 8 countries globally. Adults diagnosed with mCRPC between January 2016 and December 2018 were enrolled as the study subjects. Treatment patterns were thoroughly analyzed, including those pertaining to patients diagnosed with metastatic hormone-sensitive prostate cancer (mCSPC) and non-metastatic castration-resistant prostate cancer (nmCRPC).

Results: A total of 795 patients diagnosed with mCRPC between January 2016 and December 2018 were recruited, and most participants were from Asia (63% from Asia, 27% from the Middle East, and 10% from Latin America). The majority of patients across all regions were aged 65 years and older, and the average BMI lied within the normal to overweight range. Furthermore, although most patients were covered by public or governmental insurance, there was a noteworthy proportion of patients with unknown insurance status. Overall 10% had a positive family history of cancer. Among patients with a known family history of cancer, the majority reported a prostate cancer family history (43.2%), mostly in their brothers (48.6%). Notably, in South Asia, no such cases were reported, setting this region apart from others. In the initial diagnosis, most patients were diagnosed with adenocarcinoma (83.3%), a Gleason score of 8 and above (62.9%), stage IVB (de novo metastatic) (58.4%), being bone-only metastasis (82.3%) the most common pattern. The average period from the initial prostate cancer diagnosis to the evolution into mCRPC was 33.5 months. Among those with available ECOG information, 74.8% were classified within the ECOG 0-1 category at mCRPC diagnosis. Genetic testing was performed in very few patients (1.5%); notably, none received any testing in Latin America. The majority of patients (97.2%) underwent at least one line of

systemic therapy, while a minority of 22 (2.8%) patients received exclusive radiotherapy treatment for the mCRPC disease. Among the patients who received the first line of therapy (LOT), 49.5% proceeded to a second line, and of those, 44.9% underwent a third line of treatment. The most common first-line treatment strategy was the new hormone agents (NHA)-based treatment (46.5%), trailed closely by chemotherapy-based treatment (39.6%). Similar trends were mirrored in the second line of treatment, with over half of the patients receiving NHA-based therapy during the second line. However, there was a consistent decline in the proportion of patients receiving NHA-based treatment from the second line to treatment beyond the third line, whether with Abiraterone (decreasing from 32.3% to 8.7%) or Enzalutamide (reducing from 25.2% to 13%). Chemotherapy-based treatment primarily employing Docetaxel also witnessed a continuous decrease (falling from 38.2% in the first line to 10.9% in treatment beyond the third line). In contrast, chemotherapy-based treatment mainly utilizing Cabazitaxel demonstrated a consistent surge (rising from 0.4% in the first line to 17.4% in treatment beyond the third line). In the initial line (1L), Docetaxel was the predominant regimen, prescribed to 38.2% of patients, trailed by Enzalutamide and Abiraterone at 28.2% and 18.3%, respectively. In the second line of therapy, Abiraterone surfaced as the leading regimen, accounting for 32.3%, followed by Docetaxel at 29% and Enzalutamide at 25.2%. Moving to the third line, Docetaxel reemerged as the most common at 23%, with Abiraterone at 20% and Enzalutamide at 18.8%. In treatments beyond the third line (>3L), Cabazitaxel took the lead as the most common regimen, constituting 17.4% of the treatments, followed by Enzalutamide at 13%. Notably, radium-223 was utilized by none of the patients in 1L, only 0.3% in 2L, and 3.6% in 3L. A minor subset of patients received NHA plus chemotherapy (1.2%), Olaparib (1.2%), or 177luPSMA617-based therapies (0.2%) as first-line therapy. The employment of NHA plus chemotherapy, Radium 223, and 177luPSMA617-based treatments exhibited a steady increase from the second line onwards, with respective usage rates of 13%, 6.5%, and 17.4% in lines beyond the third. Among patients who received first-line (1L) treatment with either Docetaxel, Enzalutamide, Abiraterone, or Bicalutamide, the most common subsequent sequence was often no additional line of therapy (LOT), ranging from 43.5% to 58.2% of cases. Individuals who had received

docetaxel as their initial treatment were more inclined to be prescribed enzalutamide (21.7%) in the second-line setting, followed by abiraterone, the subsequent most common choice at 15.7%. On the other hand, patients treated with abiraterone as a first-line therapy were equally likely to switch to docetaxel or enzalutamide, each at a rate of 21.2%, when receiving second-line treatment. Conversely, those initially treated with enzalutamide were more prone to be prescribed docetaxel (20.6%) in the second-line setting, with abiraterone (15.1%) being the next favored option. The medium treatment duration for 1L, 2L, and 3L was 5.5, 4.7, and 4.1 months, respectively. Disease progression was identified as the primary reason for discontinuing treatment across regimens. In the usage of new hormonal agents, a majority of discontinuations were due to disease progression (66.5%), with a relatively low incidence of toxicity (4.2%) and death (5.6%). Cytotoxic chemotherapy demonstrated a distinct pattern, with 52.1% discontinuing due to disease progression and 12.2% due to toxicity. Half of the patients with mCSPC (53%) and a few patients with nmCRPC (11%) received life-prolonging therapy, mainly androgen deprivation therapy (ADT).

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