STUDY REPORT SYNOPSIS

ZENSHIN study
Prevalence of HRR-related genes mutations and prognosis in metastatic castration resistant prostate cancer (mCRPC) patients in real world setting

Background/rationale: The incidence of prostate cancer (PC) in Japan is increasing, and the PC is currently the cause of death of more than 12,000 patients in Japan. In general, most PC patients initially respond to hormone therapy. However, the majority succumb to disease progression despite hormone therapy, which has been termed hormone-refractory prostate cancer. The prevalence of homologous recombination repair (HRR)-related gene mutation and the relationships between HRR-related gene mutation status and prognosis are not well reported in the real world setting. In addition, treatment pattern after diagnosis of metastatic castration resistant prostate cancer (mCRPC) is not clear in the real world setting in Japanese patients.

Objectives: The purpose of this study was to investigate the prevalence of tissue HRR-related gene mutations (positive/negative/variant of uncertain significance [VUS]), clinical outcomes such as prostate-specific antigen (PSA)-progression free survival (PFS), overall survival (OS) and treatment pattern in mCRPC patients.

Study design: This was a multi-center, prospective cohort study in patients with mCRPC.

Data source: A total of 20 to 30 Japanese study sites were planned to participate in the study. The cases with valid results of HRR-related gene mutations based on the Myriad Genetics Inc. test were analyzed and the extracted data were recorded into an electronic case report form (eCRF).

Study population: We planned to enroll 155 patients who were diagnosed with mCRPC between 2014 and 2018 and had confirmed HRR-related gene mutation data from archived primary or metastatic tumor sample.

Inclusion criteria:

1. Japanese men aged >20 at the time of informed consent.
2. Patients who provided informed consent. If the patient died, opt-out was

applicable.

3. Patients who were diagnosed with mCRPC between 1st January, 2014 and 31st December, 2018.
4. Patients who had Formalin fixed paraffin embedded (FFPE) tumor samples (primary or metastatic) with Formalin Neutral Buffer Solution.
5. Patients who had enough tumor samples based on the assessment of the investigator for future laboratory test.

Exclusion criteria:

1. Patients who failed HRR-related gene mutation testing with the myChoice HRD plus in screening period.
2. Patients who only had FFPE tumor sample (primary or metastatic) with unbuffered formalin including acidic formalin.
3. Patients who took an investigational medical product for prostate cancer between 1st January, 2014 and 31st December, 2020.

Statistical methods: This study summarized the result in a descriptive manner. Categorical variables were summarized using frequency and proportion. Continuous variables were summarized using descriptive statistics (mean, and standard deviation, median, minimum, and maximum). The number and prevalence of each HRR-related gene mutation status (Positive/Negative/VUS), as well as the number and proportion of patients by treatment pattern in 1st, 2nd and 3rd line treatment after the diagnosis of mCRPC, respectively, were calculated. As exploratory objectives, patient characteristics, PSA_{50} response based on baseline and nadir PSA value in each line of treatment, and PSA-PFS and OS were calculated by the Kaplan-Meier (K-M) method.

Results and Conclusion:

This study enrolled patients with metastatic castration resistant prostate cancer (mCRPC) from 24 investigational sites across Japan From July 2020 to December 2020. 143 patients were included in the full analysis set (FAS). The mean (SD) age at mCRPC diagnosis was 73.1 (7.7) years. Sample collection methods for archived tumor were by biopsy in 130 (90.9%) patients and surgery in 13 (9.1%) patients, and anatomical sites of the sampling were from primary tumor site in 137 patients and metastatic site in 6 (4.2%) patients. The final results will be reported at the end of 2022.

Publications: None

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