Treatment strategies and outcomes in a long-term registry study of patients with high-risk metastatic hormone-naive prostate cancer in Japan: An interim analysis of the J-ROCK study

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Objective: The prognosis of high-risk metastatic hormone-naive prostate cancer is poor, and real-world evidence of therapeutic options and sequences is lacking. The J-ROCK study aimed to evaluate the outcomes in a real-world setting in Japan.

Methods: Patients with high-risk metastatic hormone-naive prostate cancer diagnosed after May 2019 were eligible. Based on their treatment within 3 months after diagnosis, patients were allocated to either cohort 1 (androgen deprivation therapy alone or combined androgen blockade with bicalutamide) or cohort 2 (androgen deprivation therapy with abiraterone acetate+prednisolone, docetaxel, enzalutamide, or apalutamide).

Results: In this first interim analysis (cut-off January 2021), 410 patients were enrolled, including 163 patients in cohort 1 and 247 in cohort 2. The median follow-up period was 7.6 (range 0.1–20.5) months. A higher proportion of patients in cohort 2 (42.5%) achieved nadir prostate-specific antigen levels ≤0.2 ng/ml within a year, compared with cohort 1 (22.1%). Prostate-specific antigen-progression-free survival was also more favorable in cohort 2 (adjusted hazard ratio 0.629 [95% confidence interval 0.345–1.147]).

Conclusions: The higher proportion of cohort 2 suggest a paradigm shift has occurred in the real-world treatment of high-risk metastatic hormone-naive prostate cancer in Japan. Some factors including prostate-specific antigen may affect treatment selection but need further observation. Most patients in cohort 2 received abiraterone acetate+prednisolone. The proportion of patients in cohort 1 receiving combined androgen blockade was lower than previously reported in Japan. This analysis suggest that more intensive therapy tends to prolong prostate-specific antigen-progression-free survival in patients with high-risk metastatic hormone-naive prostate cancer.

Key words: androgen antagonists, androgen receptor antagonists, prostatic neoplasms, registries, treatment outcome.

Introduction

PC was the second most frequently diagnosed cancer (14.1%) and the fifth leading cause of cancer mortality (6.8%) worldwide among men in 2020. In Japan, it is the most frequently diagnosed cancer in men (16%) in 2020. Although the prognosis of stage I–III PC is relatively favorable, with a 5-year survival rate of approximately 90%, that of stage IV PC is poor (5-year survival rate, only 51.3%). Especially, high-risk factors based on the LATITUDE study are associated with poor prognosis.
ADT is a standard treatment for mHNPC. CAB involving ADT plus bicalutamide, a first-generation antiandrogen, has been widely used in Japan but has not demonstrated clear benefit in patients with mHNPC. ADT plus docetaxel was recently shown to significantly improve OS in patients with high-volume mHNPC, defined as the presence of visceral metastases, or at least four bone metastases, including vertebral or pelvic bone metastases. LATITUDE also found that ADT plus abiraterone acetate plus prednisolone/prednisone (AAP) prolonged survival by 16.8 months in patients with high-risk mHNPC. In this study, high-risk criteria were defined as at least two out of the following: Gleason score ≥8, at least three bone lesions, and the presence of visceral metastasis.

Treatment options for mHNPC in Japan have expanded since the approval of enzalutamide and apalutamide in May 2020. These treatment options are recommended by various guidelines as first-line therapy for patients with PC and distant metastasis. However, recommendations based on the results of the LATITUDE have not been reflected to the guideline in Japan to date, and real-world evidence of therapeutic options and sequences in patients with high-risk mHNPC is still lacking. In addition, no studies have reported the effect of PC therapies on PROs in patients with mHNPC, although a study of metastatic CRPC reported better PROs for AAP over enzalutamide. It is therefore necessary to understand the efficacy and safety, including the impacts on QoL, of the therapeutic options and treatment sequences in high-risk mHNPC patients.

The J-ROCK study was designed as a longitudinal registry study to observe the clinical outcomes and PROs in high-risk mHNPC patients in a real-world setting in Japan. Here we report the first interim results after 18 months of the J-ROCK study.

Methods

Ethics

The study protocol and its amendment were submitted to and approved by the central ethics committee of each participating institution, as required by local regulations. All participating patients were informed of the observational nature of the study and provided written consent before the start of data collection. If independent ethics committees or institutional review boards approved, the informed consent requirement could be waived for participants who died. All procedures were conducted in accordance with the Declaration of Helsinki ethical principles and related regulations. The study was registered at ClinicalTrial.gov (NCT04034095) and University Hospital Medical Information Network-Clinical Trial Registration (UMIN-CTR, UMIN00037127).

Patients

The eligibility criteria for this study were: (1) patients diagnosed after 1 May 2019 with high-risk mHNPC (defined as mHNPC with at least two of the following at diagnosis: Gleason score ≥8, at least three bone lesions, and/or the presence of visceral metastasis); (2) men aged ≥20 years; and (3) willing to receive or received ADT (e.g., bilateral orchiectomy and luteinizing hormone-releasing hormone agonists/antagonists) containing regimens.

Study design

This was a multicenter, observational, real-world, registry study conducted at 77 sites in Japan. Enrollment was planned for approximately 1000 patients. Patients were allocated to two cohorts based on the routine clinical practice within the 3 months after their diagnosis of high-risk mHNPC. Cohort 1 included patients treated with either ADT alone or CAB. Cohort 2 included patients who received ADT plus additional intensive therapies (AAP, docetaxel, enzalutamide, or apalutamide). All patients who received intensive therapy at least once within the 3 months after diagnosis were allocated to cohort 2.

A registration period from August 2019 to August 2021, observation period until August 2024, two interim analyses and one final analysis were planned.

Medical records entered into the electronic case report form were collected. PROs were assessed at enrollment and every 6 months during the observation period. Later enrollment and retrospective data collection are allowed if the data are available.

Outcome measures

This analysis was conducted as follows: patient demographics and baseline characteristics at the diagnosis of high-risk mHNPC, therapeutic option, proportion of patients who achieved a nadir PSA ≤0.2 ng/ml, PSA-PFS, OS, PROs, and safety. PSA-PFS was defined as the duration from diagnosis of high-risk mHNPC to either PSA progression or death, whichever occurred first. PSA progression was defined as an increase of 2.0 ng/ml and 25% from nadir, confirmed at least once. PROs were evaluated using three established instruments: Patient Health Questionnaire-9, Functional Assessment of Cancer Therapy for Prostate Cancer, and the Montreal Cognitive Assessment.

Safety was evaluated by ADRs of special interest and SAEs. ADRs of special interest in this study included fluid retention or edema, hypokalemia, hypertension, hyperglycemia, cardiac disorder, increased alanine aminotransferase, increased aspartate transaminase, fatigue, rash, fracture, and seizure. AEs were encoded using the Medical Dictionary for Regulatory Activities version 23.0 and presented the worst grades based on the Common Terminology Criteria for Adverse Events version 5.0. This analysis included all documented SADRs and ADRs of special interest that occurred from the first administration of treatment that decided which cohort the patient was allocated to, up to 30 days after the last administration.

Statistical analysis

Patient demographics and baseline characteristics were summarized descriptively. Nadir PSA values were assessed at 3,
6, 7, or 12 months after initiation of cohort treatment. PSA-PFS was estimated using the Kaplan–Meier method and compared between the cohorts and between patients who did and did not achieve nadir PSA ≤0.2 ng/ml at 3 months after first administration of cohort treatment. Patients with no PD based on PSA measurements or death, and patients lost to follow-up or who withdrew from the study were censored at the last measurement prior to PD. Patients diagnosed with CRPC for reasons other than PSA progression were censored at the last measurement with no progression before or on the date of diagnosis of CRPC. Assessment of treatment effectiveness considered various confounding clinical factors, including number of bone metastases, visceral metastasis, Gleason score, age, PSA level, and bone surgery for symptomatic skeletal events. Stratified or univariate/multivariate analyses were performed for each treatment cohort.

We conducted a sensitivity analysis for effectiveness to avoid confounding due to treatment after 3 months from the diagnosis of high-risk mHNPC. Patients were allocated to sensitivity analysis cohorts based on their treatment from the diagnosis of high-risk mHNPC to the development of castration resistance.

No formal statistical hypothesis testing was performed for this study. The sample size was determined based on feasibility.

**Results**

**Patient demographics**

At the time of the first interim cut-off date (8 January 2021), 410 patients were eligible for this interim analysis. Based on their treatment within 3 months after the diagnosis of high-risk mHNPC, 163 patients were included in cohort 1 and 247 were included in cohort 2 (Figure 1). The most common therapy in cohort 1 was CAB (91/163, 55.8%) and that in cohort 2 was ADT plus AAP (178/247, 72.1%). The median follow-up period was 7.6 months (8.9 months for cohort 1 and 7.2 months for cohort 2). The median treatment durations were 5.7 months in cohort 1 and 5.9 months in cohort 2. Cohort treatment was discontinued in 57/163 patients (35.0%) in cohort 1 and 39/247 patients (15.8%) in cohort 2. The most frequent reasons for discontinuation were disease progression in each cohort.

Patient demographics and baseline characteristics (Tables 1 and S1) were similar in both cohorts, except for median number of bone metastases and median PSA, which were all higher in cohort 2. There was no difference in the proportion of patients in Gleason grade group 5 between both cohorts (57.7% vs. 60.3%), but the proportion of patients with Gleason score 10 was higher in cohort 2.

Regarding demographics at the first diagnosis of PC, median PSA values tended to be higher in cohort 2 compared with cohort 1 (351.0 ng/ml vs. 284.2 ng/ml, respectively). Other values were similar between the two cohorts (data not shown).

The demographics of the sensitivity analysis cohort at diagnosis were similar to the original cohort (data not shown).

**Clinical outcomes**

PSA response rates within 3, 6, 7, and 12 months after diagnosis of high-risk mHNPC in the original cohort were summarized in Table 2. In all treatment periods, the rate of patients who achieved a PSA ≤0.2 ng/ml tended to be higher in cohort 2 compared with cohort 1. The sensitivity analysis cohort also tended to be similar to the original cohort (data not shown). The PSA response was thus favorable in cohort 2.

**FIGURE 1** Patient flow chart. Number of patients in original cohort (sensitivity analysis cohort). A registration period from August 2019 to August 2021, observation period until August 2024, minimum and maximum follow-up periods of 3 and 5 years after registration, respectively.
## TABLE 1 Patient demographics and baseline characteristics at diagnosis of high-risk mHNC

|                          | Cohort 1 | Cohort 2 |
|--------------------------|----------|----------|
|                          | (n = 163) | (n = 247) |
| **Age, years**           |          |          |
| Median (range)            | 74.0 (47–94) | 7.0 (47–94) |
| **Number of bone metastases** |          |          |
| Median (range)            | 8.0 (0–Superscan) | 10.0 (0–Superscan) |
| Gleason score, (median)   |          |          |
| **Visceral metastases, n (%)** |          |          |
| No                        | 106 (65.0) | 258.7 (3.5–7640.0) |
| Yes                       | 57 (35.0)  | 232.0 (3.5–7640.0) |
| **Serum total testosterone, ng/ml** |          |          |
| n                         | 52        | 258.7 (3.5–7640.0) |
| Median (range)            | 3.5 (0.0–8.6) | 3.5 (0.0–8.6) |
| **Comorbidities, n (%)**  |          |          |
| Cardiovascular disorders  |          |          |
| No                        | 26 (21.8) | 110 (92.4) |
| Yes                       | 93 (78.2) | 6 (11.5)   |
| Respiratory disorders     |          |          |
| No                        | 110 (92.4) | 46 (88.5) |
| Yes                       | 9 (7.6)   | 6 (11.5)   |
| Renal disorders           |          |          |
| No                        | 103 (86.6) | 44 (84.6) |
| Yes                       | 16 (13.4) | 8 (11.9)   |
| Hepatic disorders         |          |          |
| No                        | 114 (95.8) | 64 (95.5) |
| Yes                       | 5 (4.2)   | 3 (4.5)    |
| Neurological disorders    |          |          |
| No                        | 108 (90.8) | 51 (98.1) |
| Yes                       | 11 (9.2)  | 1 (1.9)    |
| Diabetes                  |          |          |
| No                        | 88 (73.9) | 39 (75.0) |
| Yes                       | 31 (26.1) | 13 (25.0) |
| Other clinically important comorbidities |          |          |
| No                        | 92 (77.3) | 41 (78.8) |
| Yes                       | 27 (22.7) | 11 (21.2) |
| Eastern Cooperative Oncology Group - Performance Status | |          |
| No                        | 100 (61.3) | 33 (45.8) |
| Yes                       | 63 (38.7) | 39 (54.2) |
| 0                         | 35 (55.6) | 24 (61.5) |
| 2                         | 2 (4.8)   | 2 (5.1)    |
| 3                         | 0 (0.0)   | 0 (0.0)    |
| 4                         | 0 (0.0)   | 0 (0.0)    |
This tendency was also evident in the proportion of patients with percent-reduction of PSA values from baseline. PSA-PFS was more favorable in cohort 2 (Figure 2a) (HR 0.653, 95% CI 0.366, 1.166 by univariate analysis and 0.629 [0.345, 1.147] by multivariate analysis). PSA-PFS was similar in the original cohort and the sensitivity analysis cohort (Figure 2b). Sub-group analysis showed PSA-PFS was favored in patients who achieved nadir PSA ≤ 0.2 ng/ml within 3 months after the diagnosis of high-risk mHNPC (Figure 3a), regardless of the cohort (Figure 3b,c). PSA-PFS
was also favorable in patients who achieved a nadir PSA ≤0.2 ng/ml at 7 months (HR 0.998 [95% CI 0.930, 1.067]) overall, 0.150 [0.020, 1.111] in cohort 1, and 0.084 [0.020, 0.362] in cohort 2).

Regarding OS, five patients (3.1%) in cohort 1 and three (1.2%) in cohort 2 died. There was no difference between both cohorts (non-adjusted HR 0.462 [95% CI 0.110, 1.940]) in original cohort, 0.364 [0.087, 1.527] in sensitivity analysis cohort) (Figure 4a,b). The results of multivariate analysis were insufficient to discuss the clinical significance because death events were only observed in eight patients at this first interim cut-off.

Safety
Safety results are summarized in Table 3. Three ADRs of special interest (edema, alanine aminotransferase increased, and aspartate aminotransferase increased) were observed in two patients (1.2%) in cohort 1 and 20 events (hypokalemia, seizure, dermatitis exfoliative generalized, erythema multiforme, rash, rash maculo-papular, edema, alanine aminotransferase increased, and aspartate aminotransferase increased) in 18 patients (7.3%) in cohort 2. SADRs of special interest were observed in no patients in cohort 1 and eight patients (3.2%) in cohort 2. Two patients (1.2%) in cohort 1 died from AEs.

Two patients (1.2%) in cohort 1 and 10 patients (4.0%) in cohort 2 experienced AEs requiring treatment discontinuation. No patient in cohort 1 and 16 patients (6.5%) in cohort 2 experienced AEs leading to dose reduction, and no patient in cohort 1 and 12 patients (4.9%) in cohort 2 experienced AEs leading to dose interruption.

Discussion
We report the results of an interim analysis after 18 months of the J-ROCK study. Regarding to the treatment selection, higher proportion of patients with high-risk mHNPC received additional intensive treatments than ADT alone or CAB. It was suggested that PSA levels and the number of bone metastases may influence treatment selection. On the other hand, there was no difference between both cohorts in the proportion of patients with Gleason group grade 5, but the proportion of Gleason score 10 was higher in cohort 2.

In cohort 1, the proportion of patients receiving CAB was lower than previously reported. This may be because the patients in the current study had high-risk mHNPC, and some patients may have tentatively initiated ADT alone, so that intensive therapy could be added depending on their condition after the treatment initiation. Additionally, previous reports showing that there is no significant difference in clinical outcome between CAB and ADT alone, which may indicate that the trend of treatment selection has changed in recent years.

Most patients in cohort 2 received ADT plus AAP and fewer patients received enzalutamide and apalutamide. Because AAP is indicated for high-risk mHNPC in the Japanese national health insurance scheme, and enzalutamide and apalutamide are indicated for PC with distant metastasis, suggesting that AAP might be selected more frequently for patients with high-risk mHNPC. In addition, enzalutamide and apalutamide were approved as therapy for PCs with distant metastases in May 2020, although the start of enrollment in this study was August 2019. This may account for the relatively few enrolled patients at this interim cut-off date. About the infrequently uses of docetaxel, previous report shows comparing the efficacy of AAP and docetaxel under ADT by network meta-analyses shows AAP improved OS, PFS, and QoL. This report may affect treatment selection in the clinical practice.

At the 18-month interim cut-off date, few patients had changed treatment from cohort 1 to 2 or from ADT alone to CAB more than 3 months after their diagnosis of high-risk
mHNPC, and the results based on the sensitivity analysis cohorts were therefore similar to those for the original cohort. However, sensitivity analyses may subsequently detect differences as patients with delayed cohort 2 treatment increase at the second interim cut-off.

PSA-PFS tended to favor in cohort 2. Patients who achieved a nadir PSA ≤0.2 ng/ml within 3 months after first administration of cohort treatment showed favorable PSA-PFS than those who did not achieve, regardless of the treatment selection. In previous studies in Japanese patients with mHNPC, ADT plus AAP, ADT plus enzalutamide, and ADT plus apalutamide were associated with improved time-to-PSA progression or PSA-PFS compared with ADT alone or CAB.9,20–22 In this analysis, higher proportions of patients in cohort 2 achieved nadir PSA ≤0.2 ng/ml compared with cohort 1, which may have led to the favorable PSA-PFS in cohort 2. Previous reports identified PSA-related outcomes including decreased PSA levels after hormone therapy and PSA progression as independent predictors of survival.23–26

Similarly, the CHAARTED study reported a correlation between PSA levels at 7 months and mortality risk.27 These results suggest that intensive first-line treatment for metastatic PC may improve survival among patients with high-risk mHNPC. Previous reports of retrospective comparisons of CAB and AAP in patients with high-risk metastatic hormone sensitive prostate cancer also showed that PSA-PFS and OS were prolonged in patients who received AAP.28 Therefore, subsequent analysis will provide further result about prolonged OS and PSA-PFS.

Overall, the safety profiles in terms of ADRs and AEs were similar to previous reports in both cohorts. ADRs of special interest occurred in a higher proportion of patients in cohort 2 compared with cohort 1. However, ADRs of special interest of grade 3 or higher (1.2%) and SADRs (3.2%) were infrequent in cohort 2. One of the reasons is that ADR grade corresponds to the grade given to the most serious event; therefore, it is considered that the dose modification suppressed the increase in grade. Actually, in cohort 2, compared
Patients with AEs leading to dose interruption, n (%) 0 (0.0) 0 (0.0) 0 (0.0) 12 (4.9) 8 (4.5) 0 (0.0) 0 (0.0) 4 (8.5)

TABLE 3 Summary of ADRs and AEs

| Cohort 1 | Cohort 2 |
|----------|----------|
| Total (n = 163) | Total (n = 247) |
| ADT (n = 72) | ADT + AAP (n = 178) |
| CAB (n = 91) | ADT + docetaxel (n = 9) |
| ADT + enzalutamide (n = 13) | ADT + apalutamide (n = 47) |

Subjects at risk

Cohort 1 163 109 58 18 0
Cohort 2 247 149 75 16 0
Overall cohort 410 258 133 34 0

Subjects at risk

Cohort 1 146 94 50 14 0
Cohort 2 264 164 83 20 0
Overall cohort 410 258 133 34 0

FIGURE 4 Kaplan–Meier plots of OS in (a) original cohort and (b) sensitivity analysis cohort. Red line: cohort 1, blue line: cohort 2, green line: overall cohort.

to the incidence of grade 3/4 ADR of special interest, AEs leading to dose modification were observed more frequently.

The main limitation was the short follow-up period. Because of the interim analysis at 18 months, only 410 patients were included, which was less than the planned 1000 patients, and only parts of the planned analyses were performed. There was no difference in OS between both cohorts because of a lack of data. We expect that additional data will be available for the second interim and final analyses, which will allow factors such as PROs and treatment sequence, including treatment for metastatic CRPC, to be analyzed. The study was also limited by its observational nature, and the patient demographics and baseline characteristics may have differed between both cohorts. However, the data reflected real-world practice. Moreover, PSA-PFS was adjusted by using confounding factors. In addition, most of the sites participating in this study are relatively large-scale hospitals, such as university hospitals, and the results may not adequately reflect the treatment conditions at regional facilities responsible for primary care.

In conclusion, we report a first interim analysis of the long-term J-ROCK study to assess the treatment options and clinical outcomes in patients with high-risk mHNPC in a real-world setting in Japan. Although the sample size was small, intensive treatment appeared to reduce PSA levels and tended to lead to a more favorable PSA-PFS. Subsequent analyses with more patients and longer observation will further clarify the real-world outcomes of different treatments in Japanese patients with high-risk mHNPC.
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Author contributions

Hirotsgu Uemura: Conceptualization; investigation; methodology; visualization; writing – review and editing. Rikiya Matsumoto: Investigation; visualization; writing – review and editing. Atsushi Mizokami: Conceptualization; investigation; methodology; visualization; writing – review and editing. Hideaki Miyake: Conceptualization; investigation; methodology; visualization; writing – review and editing. Mutsushi Kawakita: Investigation; visualization; writing. Miku Ito: Data curation; formal analysis; project administration; visualization; writing.

Hiroji Uemura: Conceptualization; investigation; methodology; visualization; writing – review and editing. Hideyasu Matsuyama: Conceptualization; investigation; methodology; visualization; writing – review and editing. Kazuyoshi Nakamura: Investigation; visualization; writing – review and editing. Kazutaka Saito: Investigation; visualization; writing – review and editing. Mutsushi Kawakita: Investigation; visualization; writing – review and editing. Hideki Takeshita: Investigation; visualization; writing – review and editing. Yosuke Koroki, Shintaro Ono, Maiko Murota, Miku Ito are employees of Janssen. Toshiyuki Kamoto has received grants or contracts from Takeda, Bayer, Sanofi, Ono, and Astellas; consulting fees from Janssen, AstraZeneca, and Astellas; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Takeda, Sanofi, MSD, Janssen, AstraZeneca, Bayer, and Chugai. Kazuyoshi Nakamura has received lecture fees from Astellas, AstraZeneca, Bayer, Janssen, and Takeda. Kazutaka Saito has received grants or contracts from Takeda; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Janssen, Astellas, Takeda, Bayer, and AstraZeneca.

Approval of the research protocol by an Institutional Reviewer Board

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki and related regulations. The study was conducted at 77 sites in Japan. In all participating sites obtained approval from the Ethical Committee before initiation. In the institution to which the first author of this manuscript affiliates was approved by the Ethics Committee of Kindai University Faculty of Medicine (31-099).

Conflict of interest

Hirotsgu Uemura has received grants or contracts from Asahi Kasei, Sanofi, Kissei, Daiichi-Sankyo, Takeda, Astellas, and Ono; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Pfizer, Bayer, Janssen, MSD, Ono, and Bristol Myers Squibb; support for attending meetings and/or travel from Pfizer, Bayer, Janssen, MSD, Ono, and Bristol Myers Squibb; participation on a data safety monitoring board or advisory board for Janssen. Atsushi Mizokami has received grants or contracts from Sanofi, Ono, Nippon Shinyaku, Takeda, and Astellas; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Janssen; support for attending meetings and/or travel from Janssen; participation on a data safety monitoring board or advisory board for Janssen. Hiroji Uemura has received lecture fees from Janssen, Bayer, and Takeda; scholarship/encouragement donations from Takeda; travel fees from Janssen, Bayer, Takeda, Astellas, Sanofi, Daiichi-Sankyo, and Kyowa Kirin. Hideyasu Matsuyama has received grants or contracts from MSD, Astellas, Janssen, Pfizer, Bayer, Kyowa Kirin, Takeda, and Baxter; consulting fees from Sanofi and Janssen; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Sanofi, MSD, Janssen, AstraZeneca, Bayer, and Chugai. Kazuyoshi Nakamura has received lecture fees from Astellas, AstraZeneca, Bayer, Janssen, and Takeda. Kazutaka Saito has received grants or contracts from Takeda; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Janssen, Astellas, Takeda, Bayer, and AstraZeneca.

Informed consent

All participating patients were informed of the observational nature of the study and provided written consent before the start of data collection. For dead cases, the need for informed consent could be waived after approval by the independent ethics committees or institutional review boards.

Animal studies

Not applicable.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Table S1. Laboratory characteristics at diagnosis of high-risk metastatic hormone-naive prostate cancer

Editorial Comment

Editorial Comment to Treatment strategies and outcomes in a long-term registry study of patients with high-risk metastatic hormone-naive prostate cancer in Japan: An interim analysis of the J-ROCK study

Recent advancement in androgen receptor axis-targeted agents (ARATs) has drastically changed the treatment paradigm for hormone naïve metastatic prostate cancer (mHNPC). The prognostic benefit of the early intensive...