Supplementary Material

Title: Real-world longitudinal treatment outcomes for patients with metastatic castration-sensitive prostate cancer in Japan

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Supplementary results

Exploratory endpoints

TTD of first-line and second-line therapy

Among patients who initiated treatment with an ARSI, the most common second-line treatment pattern for those starting with ADT + ENZA, was ADT + others (non-ARSI); for those starting with other ARSIs, ADT + ENZA was the most common (**Supplementary Table 7**).

Among patients who started therapy with ADT + ENZA (n = 255) as first-line therapy followed by a second-line therapy, most frequently transitioned to ADT + others (n = 89), followed by ADT + ABI (n = 74), ADT + DOC (n = 59), ADT + APA (n = 25), and ADT + DARO ± DOC (n = 8). Within this subgroup, the median TTD for first-line and second-line therapies was longest for ADT + DARO ± DOC at 601.5 days (95%CI: 42.0–1,008.0).

For those starting with ADT + APA (n = 366) as first-line therapy followed by a second-line therapy, the most frequently selected regimens were ADT + ENZA (n = 154), followed by ADT + others (n = 92), ADT + ABI (n = 72), ADT + DOC (n = 42), and ADT + DARO ± DOC (n = 6). In this group, the median TTD for first-line and second-line therapies was longest for ADT + ENZA at 1,140 days (95% CI: 642.0–NR).

Among patients who initiated therapy with ADT + ABI (n = 247) as first-line therapy followed by a second-line therapy, the most selected regimens were ADT + ENZA (n = 129), followed by ADT + DOC (n = 65), ADT + others (n = 34), ADT + APA (n = 17), and ADT + DARO ± DOC (n = 2). The longest median TTD for first-line and second-line therapies in this group was observed for ADT + DARO ± DOC at 1,371 days (95% CI: 1,321.0–1,421.0).

Patients who started with ADT + DARO + DOC (n = 35) as first-line therapy followed by second-line therapy, the most frequently selected regimens were ADT + ENZA (n = 12), followed by ADT + ABI and ADT + others (n = 8, each), ADT + cabazitaxel (n = 4), and ADT + APA (n = 3). The median time to discontinuation for first-line and second-line therapies was longest for ADT + ENZA at 455 days (95% CI: 344.0–455.0).

Sensitivity analyses

The results of the sensitivity analyses are consistent with the main analysis under all conditions for achieving PSA90 during the first-line period, confirming the robustness of the data. The unadjusted cumulative PSA90 response rates were higher in the ADT + ARSI group

compared with the ADT alone and ADT + NSAA groups. There were no significant differences among the ARSI therapies.

Standardizing the gap period to 60 days for ADT drugs and other drugs

Despite modifications to the study conditions, the proportion of the total population experiencing the event was comparable to the result of the main analysis: ADT alone (63.1%), ADT + NSAA (68.9%), ADT + ENZA (82.6%), ADT + APA (84.6%), ADT + ABI (83.5%), and ADT + DARO + DOC (78.0%). The unadjusted point estimates at 3, 6, and 12 months indicated that the cumulative PSA90 response rates after the study index date were higher in the ADT + ARSI group compared with the ADT alone and ADT + NSAA groups. Specifically, at 3 months, the cumulative PSA90 response rates were 91.8% (95% CI: 86.3–95.8) for ADT + ENZA, 90.9% (95% CI: 84.8–95.3) for ADT + APA, 90.7% (95% CI: 82.3–96.2) for ADT + ABI, and 81.2% (95% CI: 68.0–91.4) for ADT + DARO + DOC. In contrast, the rates for ADT alone and ADT + NSAA were 64.2% (95% CI: 57.0–71.3) and 69.3% (95% CI: 65.1–73.4), respectively.

After adjusting for patient background characteristics, treatment with ADT + ENZA (P<0.001), ADT + APA (P<0.001), and ADT + ABI (P<0.001) were significantly associated with a higher probability of achieving PSA90 compared with ADT alone and ADT + NSAA with no significant differences among ARSIs.

Defining the gap period as double the original duration (ADT: 90 days to 180 days, other drugs: 60 days to 120 days)

Despite modifications to the study conditions, the proportion of the total population experiencing the event was comparable to the results reported in the main analysis: ADT alone (64.8%), ADT + NSAA (70.0%), ADT + ENZA (82.6%), ADT + APA (86.0%), ADT + ABI (83.5%), and ADT + DARO + DOC (78.0%). The unadjusted point estimates at 3, 6, and 12 months indicated that the unadjusted PSA90 response rates after the study index date were higher in the ADT + ARSI group compared with the ADT alone and ADT + NSAA groups. Specifically, at 3 months, the cumulative PSA90 response rates were 91.8% (95% CI: 86.3–95.8) for ADT + ENZA, 91.9% (95% CI: 85.1–95.4) for ADT + APA, 90.7% (95% CI: 82.3–96.2) for ADT + ABI, and 81.2% (95% CI: 68.0–91.4) for ADT + DARO + DOC. In contrast, the rates for ADT alone and ADT + NSAA were 62.9% (95% CI: 55.8–70.0) and 68.0% (95% CI: 63.9–72.2), respectively.

After adjusting for patient background characteristics, treatment with ADT + ENZA (*P*<0.001), ADT + APA (*P*<0.001), and ADT + ABI (*P*<0.001) were significantly associated with a higher probability of achieving PSA90 compared with ADT alone and ADT + NSAA with no significant differences among ARSIs.

Patients with a follow-up period of ≥ 12 weeks

As a result of modifications to the study conditions, the sample size for each first-line therapy decreased, and the proportion of the total population experiencing the event increased compared with the main analysis results: ADT alone (70.2%), ADT + NSAA (73.9%), ADT + ENZA (88.4%), ADT + APA (86.8%), ADT + ABI (88.7%), and ADT + DARO + DOC (82.2%). The unadjusted point estimates at 3, 6, and 12 months indicated that the unadjusted PSA90 response rates after the study index date were higher in the ADT + ARSI group compared with the ADT alone and ADT + NSAA groups. Specifically, at 3 months, the cumulative PSA90 response rates were 92.0% (95% CI: 86.4–95.8) for ADT + ENZA, 91.0% (95% CI: 82.8–96.4) for ADT + ABI, 90.5% (95% CI: 84.1–95.0) for ADT + APA, and 82.3% (95% CI: 68.9–92.3) for ADT + DARO + DOC. In contrast, the rates for ADT alone and ADT + NSAA were 60.0% (95% CI: 52.4–67.7) and 69.6% (95% CI: 65.3–73.7), respectively.

After adjusting for patient background characteristics, treatment with ADT + ENZA (*P*<0.001), ADT + APA (*P*<0.001), ADT + ABI (*P*<0.001), were significantly associated with a higher probability of achieving PSA90 compared with ADT alone and ADT + NSAA. Additionally, ADT + DARO + DOC (*P*=0.002) and ADT + NSAA (*P*=0.009) demonstrated higher probabilities of achieving PSA90 compared with ADT alone. No significant differences were observed among ARSIs.

Excluding patients who discontinued treatment within 30 days of the study index date for first-line therapy

As a result of modifications to the study conditions, the sample size for each first-line therapy decreased, and the proportion of the total population experiencing the event increased compared with the main analysis results: ADT alone (70.0%), ADT + NSAA (77.5%), ADT + ENZA (91.9%), ADT + APA (91.4%), ADT + ABI (90.3%), and ADT + DARO + DOC (83.0%). The unadjusted point estimates at 3, 6, and 12 months indicated that the unadjusted PSA90 response rates after the study index date were higher in the ADT + ARSI group compared with

the ADT alone and ADT + NSAA groups. Specifically, at 3 months, the cumulative PSA90 response rates were 92.0% (95% CI: 86.5–95.8) for ADT + ENZA, 90.7% (95% CI: 84.4–95.1) for ADT + APA, 90.6% (95% CI: 82.1–96.1) for ADT + ABI, and 81.5% (95% CI: 68.4–91.5) for ADT + DARO + DOC, and 46.4% (95% CI: 17.5–86.8) for ADT + DOC. In contrast, the rates for ADT alone and ADT + NSAA were 62.7% (95% CI: 55.5–69.9) and 69.2% (95% CI: 65.0–73.3), respectively.

After adjusting for patient background characteristics, treatment with ADT + ENZA (*P*<0.001), ADT + APA (*P*<0.001), and ADT + ABI (*P*<0.001) were significantly associated with a higher probability of achieving PSA90 compared with ADT alone and ADT + NSAA. Additionally, ADT + DARO + DOC (P=0.003) and ADT + NSAA (P=0.026) demonstrated higher probabilities of achieving PSA90 compared with ADT alone. No significant differences were observed among ARSIs.

Excluding patients who discontinued treatment within 60 days of the study index date for first-line therapy

As a result of the modifications to the study conditions, the sample size for each first-line therapy decreased, and the proportion of the total population experiencing the event increased compared with the main analysis results: ADT alone (73.0%), ADT + NSAA (82.2%), ADT + ENZA (95.5%), ADT + APA (93.3%), ADT + ABI (92.2%), and ADT + DARO + DOC (83.7%). The unadjusted point estimates at 3, 6, and 12 months indicated that the unadjusted PSA90 response rates after the study index date were higher in the ADT + ARSI group compared with the ADT alone and ADT + NSAA groups. Specifically, at 3 months, the cumulative PSA90 response rates were 92.0% (95% CI: 86.4–95.8) for ADT + ENZA, 90.6% (95% CI: 84.2–95.1) for ADT + APA, 90.0% (95% CI: 81.0–95.9) for ADT + ABI, and 80.1% (95% CI: 66.3–90.9) for ADT + DARO + DOC. In contrast, the rates for ADT alone and ADT + NSAA were 59.4% (95% CI: 51.8–67.1) and 68.2% (95% CI: 63.9–72.4), respectively.

After adjusting for patient background characteristics, treatment with ADT + ENZA (*P*<0.001), ADT + APA (*P*<0.001), and ADT + ABI (*P*<0.001) were significantly associated with a higher probability of achieving PSA90 compared with ADT alone and ADT + NSAA. Additionally, ADT + DARO + DOC (*P*=0.003) and ADT + NSAA (*P*=0.018) demonstrated higher probabilities of achieving PSA90 compared with ADT alone. No significant differences were observed among ARSIs.

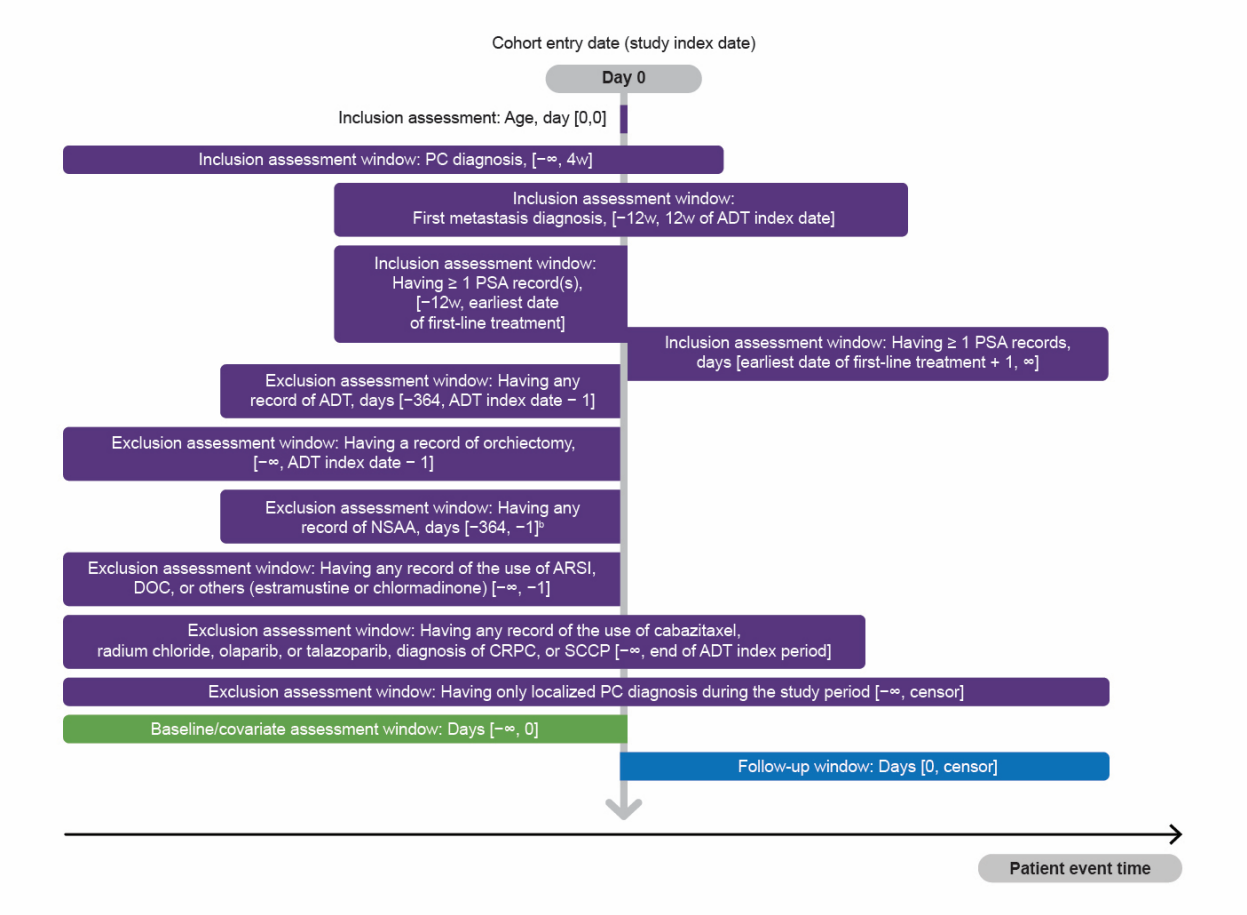
The updated definition of the baseline PSA value

The baseline PSA was redefined as the value measured closest to the earliest date among the following: the ADT index date; the study index date, or the start date of testosterone flare-preventive NSAA therapy. Across the various treatment groups, with the exception of ADT alone, the proportion of the total population experiencing the event showed some fluctuations compared with the primary analysis; however, the differences were not considered substantial: ADT alone (64.4%), ADT + NSAA (71.3%), ADT + ENZA (83.2%), ADT + APA (88.1%), ADT + ABI (82.3%), and ADT + DARO + DOC (84.0%). The unadjusted point estimates at 3, 6, and 12 months indicated that the unadjusted PSA90 response rates after the study index date were higher in the ADT + ARSI group compared with the ADT alone and ADT + NSAA groups. Specifically, at 3 months, the cumulative PSA90 response rates were 95.6% (95% CI: 90.5–98.4) for ADT + APA, 94.9% (95% CI: 82.0–99.4) for ADT + DARO + DOC, 90.8% (95% CI: 85.1–94.9) for ADT + ENZA, 90.3% (95% CI: 81.8–95.9) for ADT + ABI, and 61.9% (95% CI: 28.4–93.9) for ADT +
DOC. In contrast, the rates for ADT alone and ADT + NSAA were 63.2% (95% CI: 56.1–70.3) and 75.0% (95% CI: 71.1–78.8), respectively.

After adjusting for patient background characteristics, treatment with ADT + ENZA (P<0.001), ADT + APA (P<0.001), ADT + ABI (P<0.001), ADT + DARO + DOC (P<0.001), and ADT + NSAA (P<0.001; vs ADT alone) were significantly associated with a higher probability of achieving PSA90 compared with ADT alone and ADT + NSAA with no significant differences among ARSIs.

Supplementary figure

Supplementary Figure 1. Study design schematic



[a] Covariate assessment window may vary by covariates.

[b] If patients who were prescribed NSAA within 28 days prior to the ADT index date and the length of duration was less than or equal to 90 days, they were not excluded.

ADT androgen-deprivation therapy, *ARSI* androgen receptor signaling inhibitor, *CRPC* castration-resistant prostate cancer, *NSAA* nonsteroidal antiandrogens, *PC* prostate cancer, *PSA* prostate-specific antigen, *SCCP* small cell carcinoma of the prostate, *w* weeks.

Supplementary tables

Supplementary Table 1. Patient disposition, cohort 1

Criteria	#	Condition	N
Inclusion	1	Having an ADT record (drugs or orchiectomy) on or after June 1, 2020	166,639
Inclusion	2	Male and aged 18 years or older at the study index date	146,267
Inclusion	3	Having a record of PC diagnosis (excluding suspicious diagnosis) prior to the study index date (inclusive) to 4 weeks after the study index date	144,147
Inclusion	4	Having a first[a] record of metastasis between 12 weeks before ADT index date and 12 weeks after the ADT index date	17,105
Inclusion	5	Having at least one PSA record within 12 weeks prior to the study index date (inclusive)	2,084
Inclusion	6	Having at least one PSA record after the study index date (exclusive)	1,915
Exclusion	1	Having a record of use of an ADT drug within 1 year prior to the ADT index date (exclusive)	1,837
Exclusion	2	Having a record of orchiectomy prior to the ADT index date (exclusive)	1,837
Exclusion	3	Having a record of use of NSAA within 1 year prior to the study index date (exclusive). However, if patients who are prescribed NSAA within 28 days prior to ADT index date and the length of duration was less than or equal to 90 days, they are not excluded	1,755
Exclusion	4	Having a record of the use of ARSI, DOC, or others (estramustine or chlormadinone) prior to the study index date (exclusive)	1,686
Exclusion	5	Having a record of the use of cabazitaxel, Ra-223, olaparib, or talazoparib on or before the end of the ADT index period	1,673
Exclusion	6	Having a diagnosis of CRPC or SCCP on or before the end of the ADT index period	1,307
Exclusion	7	Having only localized PC diagnosis during the study period	1,306

[a] First in the whole data period since 2008.

ADT androgen-deprivation therapy, *ARSI* androgen receptor signaling inhibitor, *CRPC* castration-resistant prostate cancer, *DOC* docetaxel, *NSAA* nonsteroidal antiandrogen, *PC* prostate cancer, *PSA* prostate-specific antigen, *RA-223* Radium (223Ra) chloride, *SCCP* small cell carcinoma of the prostate.

Supplementary Table 2. Patient disposition, cohort 2

Criteria	#	Condition	N
Inclusion	1	Having an ADT record (drugs or orchiectomy) on or after June 1. 2020	166,639
Inclusion	2	Male and aged 18 years or older at the study index date	146,267
Inclusion	3	Having a record of PC diagnosis (excluding suspicious diagnosis) prior to the study index date (inclusive) to 4 weeks after the study index date	144,147
Inclusion	4	Having a first[a] record of metastasis between 12 weeks before ADT index date and 12 weeks after the ADT index date	17,105
Exclusion	1	Having a record of use of an ADT drug within 1 year prior to the ADT index date (exclusive)	15,975
Exclusion	2	Having a record of orchiectomy prior to the ADT index date (exclusive)	15,972
Exclusion	3	Having a record of use of NSAA within 1 year prior to the study index date (exclusive). However, if patients who are prescribed NSAA within 28 days prior to ADT index date and the length of duration was less than or equal to 90 days, they are not excluded	15,217
Exclusion	4	Having a record of the use of ARSI, DOC, or others (estramustine or chlormadinone) prior to the study index date (exclusive)	14,503
Exclusion	5	Having a record of the use of cabazitaxel, Ra-223, olaparib, or talazoparib on or before the end of the ADT index period	14,344
Exclusion	6	Having a diagnosis of CRPC or SCCP on or before the end of the ADT index period	11,792
Exclusion	7	Having only localized PC diagnosis during the study period	11,737

[a] First in the whole data period since 2008.

ADT androgen-deprivation therapy, *ARSI* androgen receptor signaling inhibitor, *CRPC* castration-resistant prostate cancer, *DOC* docetaxel, *NSAA* nonsteroidal antiandrogen, *PC* prostate cancer, *PSA* prostate-specific antigen, *RA-223* Radium (223Ra) chloride, *SCCP* small cell carcinoma of the prostate.

Supplementary Table 3. Patient characteristics during the baseline period, cohort 1

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
Age at index date (years)	Mean (SD)	76.2 (8.6)	77.8 (8.7)	78.2 (8.2)	72.4 (8.4)	73.4 (7.6)	74.0 (7.4)	69.5 (6.9)	73.3 (10.7)	69.0 (7.2)	65.0 (-)	-
	Median (Q1–Q3)	76.0 (71.0–82.0)	78.0 (72.0–84.0)	79.0 (73.0–84.0)	73.0 (68.0–79.0)	73.0 (69.0–78.0)	75.0 (68.0–80.0)	70.0 (64.0–75.0)	76.0 (66.5–80.0)	67.5 (63.0–74.5)	65.0 (65.0–65.0)	-
	Range (min–max)	47–99	52–96	47–99	50–91	49–91	57–88	52–81	58–83	61–81	65–65	-
Age Group at index date (years)	18–44	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	45–54	19 (1.5%)	3 (1.3%)	4 (0.6%)	6 (3.6%)	4 (2.8%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	55–64	90 (6.9%)	9 (3.9%)	25 (4.0%)	19 (11.4%)	13 (9.1%)	9 (11.4%)	11 (22.0%)	1 (25.0%)	3 (37.5%)	0 (0.0%)	0 (0.0%)
	65–74	436 (33.4%)	70 (30.0%)	175 (28.2%)	75 (44.9%)	61 (42.7%)	28 (35.4%)	23 (46.0%)	0 (0.0%)	3 (37.5%)	1 (100.0%)	0 (0.0%)
	≥75	761 (58.3%)	151 (64.8%)	417 (67.1%)	67 (40.1%)	65 (45.5%)	42 (53.2%)	14 (28.0%)	3 (75.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)
Charlson Comorbidity Index (CCI)[b]	n (%)	1,306 (100.0%)	233 (100.0%)	621 (100.0%)	167 (100.0%)	143 (100.0%)	79 (100.0%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Mean (SD)	1.5 (2.0)	1.9 (2.1)	1.5 (2.0)	1.5 (2.1)	1.3 (1.7)	1.1 (1.6)	1.4 (1.6)	3.3 (2.9)	1.1 (2.4)	2.0 (-)	-
	Median (Q1–Q3)	1.0 (0.0–2.0)	1.0 (0.0–3.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	0.0 (0.0–2.0)	1.0 (0.0–2.0)	2.5 (1.0–5.5)	0.0 (0.0–1.0)	2.0 (2.0–2.0)	-
	Range (min–max)	0–11	0–9	0–10	0–11	0–8	0–8	0–5	1–7	0–7	2–2	-
Comorbidities, n (%)												
CCI group[b]	≤1	811 (62.1%)	124 (53.2%)	387 (62.3%)	104 (62.3%)	96 (67.1%)	59 (74.7%)	32 (64.0%)	2 (50.0%)	7 (87.5%)	0 (0.0%)	0 (0.0%)
	>1	495 (37.9%)	109 (46.8%)	234 (37.7%)	63 (37.7%)	47 (32.9%)	20 (25.3%)	18 (36.0%)	2 (50.0%)	1 (12.5%)	1 (100.0%)	0 (0.0%)
Individual components of CCI[b], n (%)												
Myocardial infarction	No	1,270 (97.2%)	231 (99.1%)	600 (96.6%)	163 (97.6%)	140 (97.9%)	76 (96.2%)	48 (96.0%)	4 (100.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	36 (2.8%)	2 (0.9%)	21 (3.4%)	4 (2.4%)	3 (2.1%)	3 (3.8%)	2 (4.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
Congestive	No	1,175 (90.0%)	211 (90.6%)	555 (89.4%)	149 (89.2%)	134 (93.7%)	75 (94.9%)	40 (80.0%)	2 (50.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
heart failure	Yes	131 (10.0%)	22 (9.4%)	66 (10.6%)	18 (10.8%)	9 (6.3%)	4 (5.1%)	10 (20.0%)	2 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peripheral vascular disease	No	1,256 (96.2%)	226 (97.0%)	594 (95.7%)	159 (95.2%)	139 (97.2%)	77 (97.5%)	48 (96.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	50 (3.8%)	7 (3.0%)	27 (4.3%)	8 (4.8%)	4 (2.8%)	2 (2.5%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cerebrovascular disease	No	1,187 (90.9%)	210 (90.1%)	550 (88.6%)	157 (94.0%)	136 (95.1%)	75 (94.9%)	46 (92.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	119 (9.1%)	23 (9.9%)	71 (11.4%)	10 (6.0%)	7 (4.9%)	4 (5.1%)	4 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dementia	No	1,271 (97.3%)	225 (96.6%)	597 (96.1%)	166 (99.4%)	141 (98.6%)	79 (100.0%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	35 (2.7%)	8 (3.4%)	24 (3.9%)	1 (0.6%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic pulmonary disease	No	1,196 (91.6%)	205 (88.0%)	571 (91.9%)	148 (88.6%)	135 (94.4%)	77 (97.5%)	47 (94.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	110 (8.4%)	28 (12.0%)	50 (8.1%)	19 (11.4%)	8 (5.6%)	2 (2.5%)	3 (6.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatologic disease	No	1,284 (98.3%)	228 (97.9%)	610 (98.2%)	163 (97.6%)	142 (99.3%)	78 (98.7%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	22 (1.7%)	5 (2.1%)	11 (1.8%)	4 (2.4%)	1 (0.7%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peptic ulcer disease	No	1,119 (85.7%)	198 (85.0%)	535 (86.2%)	139 (83.2%)	125 (87.4%)	65 (82.3%)	44 (88.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	187 (14.3%)	35 (15.0%)	86 (13.8%)	28 (16.8%)	18 (12.6%)	14 (17.7%)	6 (12.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mild liver disease	No	1,181 (90.4%)	210 (90.1%)	566 (91.1%)	154 (92.2%)	125 (87.4%)	71 (89.9%)	42 (84.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	125 (9.6%)	23 (9.9%)	55 (8.9%)	13 (7.8%)	18 (12.6%)	8 (10.1%)	8 (16.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diabetes (mild to moderate)	No	1,014 (77.6%)	170 (73.0%)	496 (79.9%)	132 (79.0%)	107 (74.8%)	63 (79.7%)	38 (76.0%)	1 (25.0%)	6 (75.0%)	1 (100.0%)	0 (0.0%)
	Yes	292 (22.4%)	63 (27.0%)	125 (20.1%)	35 (21.0%)	36 (25.2%)	16 (20.3%)	12 (24.0%)	3 (75.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
Diabetes with chronic complications[c]	No	1,266 (96.9%)	224 (96.1%)	603 (97.1%)	160 (95.8%)	140 (97.9%)	78 (98.7%)	48 (96.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	40 (3.1%)	9 (3.9%)	18 (2.9%)	7 (4.2%)	3 (2.1%)	1 (1.3%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hemiplegia or paraplegia	No	1,287 (98.5%)	224 (96.1%)	614 (98.9%)	167 (100.0%)	141 (98.6%)	79 (100.0%)	49 (98.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	19 (1.5%)	9 (3.9%)	7 (1.1%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Renal disease	No	1,240 (94.9%)	226 (97.0%)	583 (93.9%)	158 (94.6%)	138 (96.5%)	74 (93.7%)	49 (98.0%)	3 (75.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	66 (5.1%)	7 (3.0%)	38 (6.1%)	9 (5.4%)	5 (3.5%)	5 (6.3%)	1 (2.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Any malignancy, including lymphoma and leukemia	No	1,098 (84.1%)	185 (79.4%)	521 (83.9%)	140 (83.8%)	125 (87.4%)	72 (91.1%)	43 (86.0%)	4 (100.0%)	8 (100.0%)	0 (0.0%)	0 (0.0%)
	Yes	208 (15.9%)	48 (20.6%)	100 (16.1%)	27 (16.2%)	18 (12.6%)	7 (8.9%)	7 (14.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
Moderate or severe liver disease	No	1,304 (99.8%)	233 (100.0%)	620 (99.8%)	166 (99.4%)	143 (100.0%)	79 (100.0%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	2 (0.2%)	0 (0.0%)	1 (0.2%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Metastatic solid tumor	No	1,268 (97.1%)	220 (94.4%)	606 (97.6%)	164 (98.2%)	139 (97.2%)	78 (98.7%)	50 (100.0%)	3 (75.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	38 (2.9%)	13 (5.6%)	15 (2.4%)	3 (1.8%)	4 (2.8%)	1 (1.3%)	0 (0.0%)	1 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
HIV	No	1,306 (100.0%)	233 (100.0%)	621 (100.0%)	167 (100.0%)	143 (100.0%)	79 (100.0%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other comorbidities, n (%)												
Hypertension	No	911 (69.8%)	167 (71.7%)	413 (66.5%)	116 (69.5%)	109 (76.2%)	66 (83.5%)	33 (66.0%)	2 (50.0%)	5 (62.5%)	0 (0.0%)	0 (0.0%)

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
	Yes	395 (30.2%)	66 (28.3%)	208 (33.5%)	51 (30.5%)	34 (23.8%)	13 (16.5%)	17 (34.0%)	2 (50.0%)	3 (37.5%)	1 (100.0%)	0 (0.0%)
Hyperlipidemia	No	1,110 (85.0%)	204 (87.6%)	524 (84.4%)	134 (80.2%)	124 (86.7%)	70 (88.6%)	43 (86.0%)	3 (75.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	196 (15.0%)	29 (12.4%)	97 (15.6%)	33 (19.8%)	19 (13.3%)	9 (11.4%)	7 (14.0%)	1 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
Metastasis site, n (%)												
Bone	No	426 (32.6%)	99 (42.5%)	234 (37.7%)	29 (17.4%)	36 (25.2%)	21 (26.6%)	5 (10.0%)	1 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
	Yes	880 (67.4%)	134 (57.5%)	387 (62.3%)	138 (82.6%)	107 (74.8%)	58 (73.4%)	45 (90.0%)	3 (75.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
Lymph	No	1,032 (79.0%)	189 (81.1%)	477 (76.8%)	135 (80.8%)	121 (84.6%)	59 (74.7%)	39 (78.0%)	4 (100.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	274 (21.0%)	44 (18.9%)	144 (23.2%)	32 (19.2%)	22 (15.4%)	20 (25.3%)	11 (22.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
Lung	No	1,200 (91.9%)	210 (90.1%)	580 (93.4%)	154 (92.2%)	131 (91.6%)	68 (86.1%)	45 (90.0%)	4 (100.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	106 (8.1%)	23 (9.9%)	41 (6.6%)	13 (7.8%)	12 (8.4%)	11 (13.9%)	5 (10.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
Liver	No	1,278 (97.9%)	228 (97.9%)	606 (97.6%)	166 (99.4%)	142 (99.3%)	77 (97.5%)	47 (94.0%)	4 (100.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	28 (2.1%)	5 (2.1%)	15 (2.4%)	1 (0.6%)	1 (0.7%)	2 (2.5%)	3 (6.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
Others	No	1,241 (95.0%)	223 (95.7%)	604 (97.3%)	156 (93.4%)	131 (91.6%)	71 (89.9%)	45 (90.0%)	3 (75.0%)	7 (87.5%)	1 (100.0%)	0 (0.0%)
	Yes	65 (5.0%)	10 (4.3%)	17 (2.7%)	11 (6.6%)	12 (8.4%)	8 (10.1%)	5 (10.0%)	1 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
Previous treatment, n (%)												
Prostatectomy (radical)	No	1,277 (97.8%)	222 (95.3%)	610 (98.2%)	164 (98.2%)	140 (97.9%)	79 (100.0%)	49 (98.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	29 (2.2%)	11 (4.7%)	11 (1.8%)	3 (1.8%)	3 (2.1%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
EBRT or SBRT	No	1,236 (94.6%)	213 (91.4%)	593 (95.5%)	163 (97.6%)	136 (95.1%)	74 (93.7%)	47 (94.0%)	3 (75.0%)	6 (75.0%)	1 (100.0%)	0 (0.0%)
	Yes	70 (5.4%)	20 (8.6%)	28 (4.5%)	4 (2.4%)	7 (4.9%)	5 (6.3%)	3 (6.0%)	1 (25.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)
EBRT	No	1,248 (95.6%)	218 (93.6%)	595 (95.8%)	163 (97.6%)	137 (95.8%)	76 (96.2%)	48 (96.0%)	4 (100.0%)	6 (75.0%)	1 (100.0%)	0 (0.0%)
	Yes	58 (4.4%)	15 (6.4%)	26 (4.2%)	4 (2.4%)	6 (4.2%)	3 (3.8%)	2 (4.0%)	0 (0.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)
SBRT	No	1,294 (99.1%)	228 (97.9%)	619 (99.7%)	167 (100.0%)	142 (99.3%)	77 (97.5%)	49 (98.0%)	3 (75.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	12 (0.9%)	5 (2.1%)	2 (0.3%)	0 (0.0%)	1 (0.7%)	2 (2.5%)	1 (2.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BT	No	1,306 (100.0%)	233 (100.0%)	621 (100.0%)	167 (100.0%)	143 (100.0%)	79 (100.0%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Laboratory data												
PSA levels (ng/ml)	n (%)	1,306 (100.0%)	233 (100.0%)	621 (100.0%)	167 (100.0%)	143 (100.0%)	79 (100.0%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Mean (SD)	652.18 (2,039.68)	895.93 (3,321.17)	637.30 (1,756.36)	418.67 (938.43)	460.83 (1,274.50)	716.81 (1,872.69)	732.13 (1,531.42)	4366.82 (5,918.41)	82.09 (106.82)	61.40 (-)	-
	Median (Q1–Q3)	97.81 (16.60–471.04)	93.62 (14.01–556.00)	110.00 (17.89–524.02)	93.20 (14.30–441.08)	68.85 (9.91–258.00)	171.00 (48.02–469.09)	80.99 (11.78–678.00)	2226.93 (517.70–8,215.93)	49.86 (3.65–120.30)	61.40 (61.40–61.40)	-
	Range (min–max)	0.0–43,900.0	0.0–43,900.0	0.0–29,139.0	0.0–7,366.0	0.0–8,756.4	0.4–10,804.3	0.2–8,930.8	35.4–12,978.0	0.1–309.0	61.4–61.4	-
ALP levels (U/L)	n (%)	1,262 (96.6%)	223 (95.7%)	593 (95.5%)	167 (100.0%)	141 (98.6%)	75 (94.9%)	50 (100.0%)	4 (100.0%)	8 (100.0%)	1 (100.0%)	0 (0.0%)
	Mean (SD)	873.01 (1,595.63)	793.24 (1,875.62)	788.09 (1,315.18)	1043.24 (1,965.55)	922.36 (1,590.34)	969.64 (1,496.30)	1265.84 (1,889.78)	3254.50 (2,901.93)	469.63 (334.02)	446.00 (-)	-
	Median (Q1–Q3)	327.00 (230.00–772.00)	290.00 (207.00–574.00)	324.00 (230.00–745.00)	352.00 (222.00–1,105.00)	346.00 (239.00–912.00)	338.00 (250.00–787.00)	465.50 (267.00–1,366.00)	2737.50 (950.00–5,559.00)	342.00 (287.00–542.50)	446.00 (446.00–446.00)	-

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
	Range (min–max)	54.0–20,147.0	74.0–20,147.0	54.0–13,984.0	94.0–15,626.0	133.0–1,2718.0	137.0–6,867.0	190.0–10,920.0	608.0–6,935.0	187.0–1,227.0	446.0–446.0	-
Hb levels (g/dL)	n (%)	1,257 (96.2%)	219 (94.0%)	610 (98.2%)	156 (93.4%)	137 (95.8%)	77 (97.5%)	48 (96.0%)	3 (75.0%)	7 (87.5%)	0 (0.0%)	0 (0.0%)
	Mean (SD)	12.47 (2.17)	12.53 (2.22)	12.40 (2.19)	12.60 (2.24)	12.69 (2.02)	12.49 (1.98)	12.06 (2.08)	9.53 (2.36)	13.73 (2.08)	-	-
	Median (Q1–Q3)	12.70 (11.20–14.00)	12.70 (11.10–14.30)	12.60 (11.00–14.00)	12.90 (11.50–14.15)	13.10 (11.70–14.20)	12.80 (11.50–13.80)	12.10 (10.55–13.65)	8.70 (7.70–12.20)	13.20 (12.50–14.40)	-	-
	Range (min–max)	5.3–19.4	5.5–17.6	6.0–19.4	6.4–17.4	5.3–16.2	8.3–17.2	7.0–15.7	7.7–12.2	11.3–17.9	-	-
LDH levels (U/L)	n (%)	255 (19.5%)	51 (21.9%)	140 (22.5%)	18 (10.8%)	27 (18.9%)	13 (16.5%)	5 (10.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
	Mean (SD)	199.30 (52.28)	199.61 (54.17)	205.32 (56.67)	186.78 (45.93)	184.00 (30.34)	185.85 (36.22)	182.00 (37.98)	-	241.00 (-)	-	-
	Median (Q1–Q3)	188.00 (164.00–218.00)	190.00 (161.00–213.00)	191.00 (165.00–232.50)	174.50 (157.00–190.00)	183.00 (166.00–204.00)	187.00 (157.00–197.00)	184.00 (165.00–216.00)	-	241.00 (241.00–241.00)	-	-
	Range (min–max)	88.0–413.0	126.0–339.0	88.0–413.0	138.0–311.0	128.0–263.0	130.0–246.0	127.0–218.0	-	241.0–241.0	-	-
BMI (kg/m^2)	n (%)	930 (71.2%)	145 (62.2%)	424 (68.3%)	127 (76.0%)	123 (86.0%)	60 (75.9%)	41 (82.0%)	3 (75.0%)	7 (87.5%)	0 (0.0%)	0 (0.0%)
	Mean (SD)	22.80 (3.44)	23.06 (4.24)	22.58 (3.30)	22.71 (3.53)	23.05 (3.03)	22.75 (3.18)	23.29 (2.76)	25.37 (2.39)	24.96 (3.49)	-	-
	Median (Q1–Q3)	22.64 (20.50–24.82)	22.87 (20.41–25.55)	22.27 (20.36–24.55)	22.48 (20.08–24.66)	22.91 (20.89–25.14)	22.33 (20.51–24.16)	22.97 (21.45–25.34)	26.04 (22.72–27.35)	24.82 (21.44–27.24)	-	-
	Range (min–max)	13.6–46.9	13.9–46.9	13.6–35.1	14.7–33.2	14.8–30.1	16.7–31.4	18.2–29.9	22.7–27.4	21.3–31.3	-	-
Inpatient/Outpatient, n (%)	Inpatient	262 (20.1%)	73 (31.3%)	147 (23.7%)	9 (5.4%)	6 (4.2%)	5 (6.3%)	16 (32.0%)	0 (0.0%)	6 (75.0%)	0 (0.0%)	0 (0.0%)
	Outpatient	1,044 (79.9%)	160 (68.7%)	474 (76.3%)	158 (94.6%)	137 (95.8%)	74 (93.7%)	34 (68.0%)	4 (100.0%)	2 (25.0%)	1 (100.0%)	0 (0.0%)
Size of hospital (number of beds), n (%)	≤199	16 (1.2%)	0 (0.0%)	13 (2.1%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)
	200–499	690 (52.8%)	109 (46.8%)	348 (56.0%)	66 (39.5%)	94 (65.7%)	43 (54.4%)	26 (52.0%)	3 (75.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)

Parameter	Category/ Statistic	Overall (N = 1,306, 100.0%)	ADT alone (N = 233, 17.8%)	ADT + NSAA (N = 621, 47.5%)	ADT + ENZA (N = 167, 12.8%)	ADT + APA (N = 143, 10.9%)	ADT + ABI (N = 79, 6.0%)	ADT + DARO + DOC (N = 50, 3.8%)	ADT + DARO without DOC (N = 4, 0.3%)	ADT + DOC (N = 8, 0.6%)	ADT + others (N = 1, 0.1%)	Multiple treatments[a] (N = 0, 0.0%)
	≥500	600 (45.9%)	124 (53.2%)	260 (41.9%)	100 (59.9%)	49 (34.3%)	36 (45.6%)	23 (46.0%)	1 (25.0%)	6 (75.0%)	1 (100.0%)	0 (0.0%)
Year of index date, n (%)	2020	89 (6.8%)	12 (5.2%)	63 (10.1%)	1 (0.6%)	9 (6.3%)	4 (5.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	2021	215 (16.5%)	52 (22.3%)	117 (18.8%)	14 (8.4%)	20 (14.0%)	12 (15.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	2022	344 (26.3%)	57 (24.5%)	180 (29.0%)	37 (22.2%)	38 (26.6%)	27 (34.2%)	0 (0.0%)	0 (0.0%)	5 (62.5%)	0 (0.0%)	0 (0.0%)
	2023	395 (30.2%)	71 (30.5%)	172 (27.7%)	62 (37.1%)	41 (28.7%)	25 (31.6%)	22 (44.0%)	0 (0.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)
	2024	263 (20.1%)	41 (17.6%)	89 (14.3%)	53 (31.7%)	35 (24.5%)	11 (13.9%)	28 (56.0%)	4 (100.0%)	1 (12.5%)	1 (100.0%)	0 (0.0%)
Length of follow-up period (days)	Mean (SD)	464.0 (363.7)	415.2 (355.1)	503.5 (384.1)	372.7 (281.3)	516.8 (379.8)	537.6 (356.0)	261.9 (143.5)	74.0 (58.3)	554.9 (341.6)	169.0 (-)	-
	Median (Q1–Q3)	372.0 (167.0–688.0)	317.0 (116.0–680.0)	431.0 (184.0–735.0)	309.0 (148.0–554.0)	410.0 (184.0–778.0)	533.0 (241.0–773.0)	256.5 (155.0–345.0)	63.5 (30.0–118.0)	700.0 (225.5–826.0)	169.0 (169.0–169.0)	-
	Range (min–max)	5–1,558	16–1,545	5–1,550	15–1,268	15–1,516	21–1,558	29–575	18–151	44–892	169–169	-

[a] If treatments for multiple groups (three or more than three first-line treatment classes) were initiated at the same date, those patients were categorized as “multiple therapies”, as distinct from those in single group.

[b] Diagnosis of PC was excluded from calculation of CCI.

[c] Chronic complications included those with the following ICD codes: E10.2–E10.5, E10.7, E11.2–E11.5, E11.7, E12.2–E12.5, E12.7, E13.2–E13.5, E13.7, E14.2–E14.5, E14.7.

ABI abiraterone, *ADT* androgen-deprivation therapy, *ALP* alkaline phosphatase, *APA* apalutamide, *BMI* body mass index, *BT* brachytherapy, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *EBRT* external beam radiation therapy, *ENZA* enzalutamide, *Hb* hemoglobin, *HIV* human immunodeficiency virus, *ICD* International Classification of Diseases, *LDH* lactate dehydrogenase, *max* maximum, *min* minimum, *NSAA* nonsteroidal antiandrogen, *PC* prostate cancer, *PSA* prostate-specific antigen, *Q1* first quartile, *Q3* third quartile, *SBRT* stereotactic body radiation therapy.

Supplementary Table 4. Patient characteristics during the baseline period, cohort 2

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
Age at index date (years)	Mean (SD)	76.3 (8.3)	78.0 (8.5)	77.6 (8.2)	74.9 (7.8)	74.1 (7.4)	73.6 (7.8)	70.3 (6.9)	72.7 (7.7)	70.2 (7.7)	76.9 (7.1)	79.6 (8.7)
	Median (Q1–Q3)	76.0 (71.0–82.0)	79.0 (73.0–84.0)	78.0 (72.0–83.0)	75.0 (70.0–80.0)	75.0 (70.0–79.0)	74.0 (69.0–79.0)	71.0 (66.0–75.0)	73.0 (68.0–77.0)	71.0 (65.0–75.0)	77.0 (72.0–82.0)	81.0 (77.0–86.0)
	Range (min–max)	43–99	46–99	43–99	47–96	47–94	47–93	51–87	48–89	52–87	60–94	66–88
Age group at index date (years), n (%)	18–44	1 (0.0%)	0 (0.0%)	1 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	45–54	122 (1.0%)	15 (0.8%)	41 (0.7%)	19 (1.3%)	17 (1.4%)	13 (1.5%)	10 (2.4%)	2 (2.5%)	5 (5.7%)	0 (0.0%)	0 (0.0%)
	55–64	816 (7.0%)	103 (5.2%)	298 (5.3%)	118 (8.3%)	109 (8.9%)	93 (10.8%)	70 (16.9%)	7 (8.9%)	15 (17.0%)	3 (3.9%)	0 (0.0%)
	65–74	3,856 (32.9%)	553 (28.1%)	1,622 (29.0%)	531 (37.1%)	479 (38.9%)	346 (40.3%)	219 (52.9%)	39 (49.4%)	42 (47.7%)	24 (31.2%)	1 (20.0%)
	≤75	6,942 (59.1%)	1,296 (65.9%)	3,625 (64.9%)	762 (53.3%)	626 (50.9%)	407 (47.4%)	115 (27.8%)	31 (39.2%)	26 (29.5%)	50 (64.9%)	4 (80.0%)
CCI[b]	n (%)	11,737 (100.0%)	1,967 (100.0%)	5,587 (100.0%)	1,430 (100.0%)	1,231 (100.0%)	859 (100.0%)	414 (100.0%)	79 (100.0%)	88 (100.0%)	77 (100.0%)	5 (100.0%)
	Mean (SD)	1.6 (2.1)	1.9 (2.2)	1.7 (2.1)	1.5 (2.0)	1.5 (2.0)	1.3 (1.8)	1.4 (1.8)	1.8 (2.1)	1.8 (2.3)	1.9 (2.3)	1.4 (2.1)
	Median (Q1–Q3)	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–1.0)
	Range (min–max)	0–14	0–13	0–14	0–12	0–11	0–11	0–9	0–9	0–11	0–10	0–5
Comorbidities, n (%)												
CCI group[b]	≤1	7094 (60.4%)	1076 (54.7%)	3306 (59.2%)	908 (63.5%)	782 (63.5%)	594 (69.2%)	281 (67.9%)	47 (59.5%)	53 (60.2%)	43 (55.8%)	4 (80.0%)
	>1	4643 (39.6%)	891 (45.3%)	2281 (40.8%)	522 (36.5%)	449 (36.5%)	265 (30.8%)	133 (32.1%)	32 (40.5%)	35 (39.8%)	34 (44.2%)	1 (20.0%)
Individual components of CCI[b], n (%)												
Myocardial infarction	No	11,330 (96.5%)	1,901 (96.6%)	5,370 (96.1%)	1,387 (97.0%)	1,180 (95.9%)	843 (98.1%)	407 (98.3%)	79 (100.0%)	85 (96.6%)	73 (94.8%)	5 (100.0%)
	Yes	407 (3.5%)	66 (3.4%)	217 (3.9%)	43 (3.0%)	51 (4.1%)	16 (1.9%)	7 (1.7%)	0 (0.0%)	3 (3.4%)	4 (5.2%)	0 (0.0%)

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
Congestive heart failure	No	10,299 (87.7%)	1,716 (87.2%)	4,847 (86.8%)	1,260 (88.1%)	1,100 (89.4%)	783 (91.2%)	371 (89.6%)	70 (88.6%)	82 (93.2%)	65 (84.4%)	5 (100.0%)
	Yes	1,438 (12.3%)	251 (12.8%)	740 (13.2%)	170 (11.9%)	131 (10.6%)	76 (8.8%)	43 (10.4%)	9 (11.4%)	6 (6.8%)	12 (15.6%)	0 (0.0%)
Peripheral vascular disease	No	11,104 (94.6%)	1,865 (94.8%)	5,261 (94.2%)	1,350 (94.4%)	1,177 (95.6%)	819 (95.3%)	394 (95.2%)	76 (96.2%)	84 (95.5%)	73 (94.8%)	5 (100.0%)
	Yes	633 (5.4%)	102 (5.2%)	326 (5.8%)	80 (5.6%)	54 (4.4%)	40 (4.7%)	20 (4.8%)	3 (3.8%)	4 (4.5%)	4 (5.2%)	0 (0.0%)
Cerebrovascular disease	No	10,597 (90.3%)	1,769 (89.9%)	4,951 (88.6%)	1,304 (91.2%)	1,148 (93.3%)	807 (93.9%)	391 (94.4%)	74 (93.7%)	83 (94.3%)	66 (85.7%)	4 (80.0%)
	Yes	1,140 (9.7%)	198 (10.1%)	636 (11.4%)	126 (8.8%)	83 (6.7%)	52 (6.1%)	23 (5.6%)	5 (6.3%)	5 (5.7%)	11 (14.3%)	1 (20.0%)
Dementia	No	11,394 (97.1%)	1,875 (95.3%)	5,402 (96.7%)	1,405 (98.3%)	1,209 (98.2%)	847 (98.6%)	413 (99.8%)	76 (96.2%)	87 (98.9%)	75 (97.4%)	5 (100.0%)
	Yes	343 (2.9%)	92 (4.7%)	185 (3.3%)	25 (1.7%)	22 (1.8%)	12 (1.4%)	1 (0.2%)	3 (3.8%)	1 (1.1%)	2 (2.6%)	0 (0.0%)
Chronic pulmonary disease	No	10,799 (92.0%)	1,772 (90.1%)	5,103 (91.3%)	1,322 (92.4%)	1,166 (94.7%)	818 (95.2%)	389 (94.0%)	75 (94.9%)	83 (94.3%)	67 (87.0%)	4 (80.0%)
	Yes	938 (8.0%)	195 (9.9%)	484 (8.7%)	108 (7.6%)	65 (5.3%)	41 (4.8%)	25 (6.0%)	4 (5.1%)	5 (5.7%)	10 (13.0%)	1 (20.0%)
Rheumatologic disease	No	11,555 (98.4%)	1,933 (98.3%)	5,506 (98.6%)	1,406 (98.3%)	1,214 (98.6%)	848 (98.7%)	405 (97.8%)	77 (97.5%)	87 (98.9%)	74 (96.1%)	5 (100.0%)
	Yes	182 (1.6%)	34 (1.7%)	81 (1.4%)	24 (1.7%)	17 (1.4%)	11 (1.3%)	9 (2.2%)	2 (2.5%)	1 (1.1%)	3 (3.9%)	0 (0.0%)
Peptic ulcer disease	No	10,050 (85.6%)	1,669 (84.9%)	4,803 (86.0%)	1,241 (86.8%)	1,055 (85.7%)	717 (83.5%)	349 (84.3%)	72 (91.1%)	75 (85.2%)	66 (85.7%)	3 (60.0%)
	Yes	1,687 (14.4%)	298 (15.1%)	784 (14.0%)	189 (13.2%)	176 (14.3%)	142 (16.5%)	65 (15.7%)	7 (8.9%)	13 (14.8%)	11 (14.3%)	2 (40.0%)
Mild liver disease	No	10,614 (90.4%)	1,791 (91.1%)	5,069 (90.7%)	1,290 (90.2%)	1,113 (90.4%)	778 (90.6%)	363 (87.7%)	66 (83.5%)	74 (84.1%)	65 (84.4%)	5 (100.0%)
	Yes	1,123 (9.6%)	176 (8.9%)	518 (9.3%)	140 (9.8%)	118 (9.6%)	81 (9.4%)	51 (12.3%)	13 (16.5%)	14 (15.9%)	12 (15.6%)	0 (0.0%)

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
Diabetes (mild to moderate)	No	9,208 (78.5%)	1,502 (76.4%)	4,428 (79.3%)	1,099 (76.9%)	944 (76.7%)	720 (83.8%)	327 (79.0%)	63 (79.7%)	65 (73.9%)	56 (72.7%)	4 (80.0%)
	Yes	2,529 (21.5%)	465 (23.6%)	1,159 (20.7%)	331 (23.1%)	287 (23.3%)	139 (16.2%)	87 (21.0%)	16 (20.3%)	23 (26.1%)	21 (27.3%)	1 (20.0%)
Diabetes with chronic complications[c]	No	11,222 (95.6%)	1,882 (95.7%)	5,339 (95.6%)	1,355 (94.8%)	1,177 (95.6%)	840 (97.8%)	397 (95.9%)	71 (89.9%)	83 (94.3%)	73 (94.8%)	5 (100.0%)
	Yes	515 (4.4%)	85 (4.3%)	248 (4.4%)	75 (5.2%)	54 (4.4%)	19 (2.2%)	17 (4.1%)	8 (10.1%)	5 (5.7%)	4 (5.2%)	0 (0.0%)
Hemiplegia or paraplegia	No	11,546 (98.4%)	1,914 (97.3%)	5,494 (98.3%)	1,417 (99.1%)	1,216 (98.8%)	850 (99.0%)	411 (99.3%)	78 (98.7%)	87 (98.9%)	74 (96.1%)	5 (100.0%)
	Yes	191 (1.6%)	53 (2.7%)	93 (1.7%)	13 (0.9%)	15 (1.2%)	9 (1.0%)	3 (0.7%)	1 (1.3%)	1 (1.1%)	3 (3.9%)	0 (0.0%)
Renal disease	No	11,002 (93.7%)	1,842 (93.6%)	5,201 (93.1%)	1,347 (94.2%)	1,160 (94.2%)	817 (95.1%)	395 (95.4%)	75 (94.9%)	87 (98.9%)	73 (94.8%)	5 (100.0%)
	Yes	735 (6.3%)	125 (6.4%)	386 (6.9%)	83 (5.8%)	71 (5.8%)	42 (4.9%)	19 (4.6%)	4 (5.1%)	1 (1.1%)	4 (5.2%)	0 (0.0%)
Any malignancy, including lymphoma and leukemia	No	9,747 (83.0%)	1,536 (78.1%)	4,594 (82.2%)	1,223 (85.5%)	1,059 (86.0%)	758 (88.2%)	367 (88.6%)	65 (82.3%)	74 (84.1%)	67 (87.0%)	4 (80.0%)
	Yes	1,990 (17.0%)	431 (21.9%)	993 (17.8%)	207 (14.5%)	172 (14.0%)	101 (11.8%)	47 (11.4%)	14 (17.7%)	14 (15.9%)	10 (13.0%)	1 (20.0%)
Moderate or severe liver disease	No	11,687 (99.6%)	1,954 (99.3%)	5,568 (99.7%)	1,421 (99.4%)	1,227 (99.7%)	857 (99.8%)	413 (99.8%)	79 (100.0%)	87 (98.9%)	76 (98.7%)	5 (100.0%)
	Yes	50 (0.4%)	13 (0.7%)	19 (0.3%)	9 (0.6%)	4 (0.3%)	2 (0.2%)	1 (0.2%)	0 (0.0%)	1 (1.1%)	1 (1.3%)	0 (0.0%)
Metastatic solid tumor	No	11,438 (97.5%)	1,898 (96.5%)	5,467 (97.9%)	1,404 (98.2%)	1,196 (97.2%)	834 (97.1%)	403 (97.3%)	75 (94.9%)	81 (92.0%)	75 (97.4%)	5 (100.0%)
	Yes	299 (2.5%)	69 (3.5%)	120 (2.1%)	26 (1.8%)	35 (2.8%)	25 (2.9%)	11 (2.7%)	4 (5.1%)	7 (8.0%)	2 (2.6%)	0 (0.0%)
HIV	No	11,732 (100.0%)	1,966 (99.9%)	5,586 (100.0%)	1,430, (100.0%)	1,228 (99.8%)	859 (100.0%)	414 (100.0%)	79 (100.0%)	88 (100.0%)	77 (100.0%)	5 (100.0%)
	Yes	5 (0.0%)	1 (0.1%)	1 (0.0%)	0 (0.0%)	3 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other Comorbidities, n (%)												
Hypertension	No	7,898 (67.3%)	1,311 (66.6%)	3,673 (65.7%)	999 (69.9%)	850 (69.0%)	617 (71.8%)	288 (69.6%)	56 (70.9%)	57 (64.8%)	44 (57.1%)	3 (60.0%)

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
	Yes	3,839 (32.7%)	656 (33.4%)	1,914 (34.3%)	431 (30.1%)	381 (31.0%)	242 (28.2%)	126 (30.4%)	23 (29.1%)	31 (35.2%)	33 (42.9%)	2 (40.0%)
Hyperlipidemia	No	9,666 (82.4%)	1,630 (82.9%)	4,559 (81.6%)	1,161 (81.2%)	1,029 (83.6%)	734 (85.4%)	351 (84.8%)	64 (81.0%)	75 (85.2%)	59 (76.6%)	4 (80.0%)
	Yes	2,071 (17.6%)	337 (17.1%)	1,028 (18.4%)	269 (18.8%)	202 (16.4%)	125 (14.6%)	63 (15.2%)	15 (19.0%)	13 (14.8%)	18 (23.4%)	1 (20.0%)
Metastasis site, n (%)												
Bone	No	3,649 (31.1%)	715 (36.3%)	1,976 (35.4%)	355 (24.8%)	296 (24.0%)	161 (18.7%)	78 (18.8%)	13 (16.5%)	24 (27.3%)	31 (40.3%)	0 (0.0%)
	Yes	8,088 (68.9%)	1,252 (63.7%)	3,611 (64.6%)	1,075 (75.2%)	935 (76.0%)	698 (81.3%)	336 (81.2%)	66 (83.5%)	64 (72.7%)	46 (59.7%)	5 (100.0%)
Lymph	No	8,955 (76.3%)	1,585 (80.6%)	4,269 (76.4%)	1,050 (73.4%)	894 (72.6%)	675 (78.6%)	295 (71.3%)	63 (79.7%)	61 (69.3%)	59 (76.6%)	4 (80.0%)
	Yes	2,782 (23.7%)	382 (19.4%)	1,318 (23.6%)	380 (26.6%)	337 (27.4%)	184 (21.4%)	119 (28.7%)	16 (20.3%)	27 (30.7%)	18 (23.4%)	1 (20.0%)
Lung	No	10,635 (90.6%)	1,779 (90.4%)	5,138 (92.0%)	1,291 (90.3%)	1,104 (89.7%)	748 (87.1%)	354 (85.5%)	72 (91.1%)	73 (83.0%)	72 (93.5%)	4 (80.0%)
	Yes	1,102 (9.4%)	188 (9.6%)	449 (8.0%)	139 (9.7%)	127 (10.3%)	111 (12.9%)	60 (14.5%)	7 (8.9%)	15 (17.0%)	5 (6.5%)	1 (20.0%)
Liver	No	11,501 (98.0%)	1,897 (96.4%)	5,493 (98.3%)	1,409 (98.5%)	1,219 (99.0%)	844 (98.3%)	395 (95.4%)	79 (100.0%)	84 (95.5%)	76 (98.7%)	5 (100.0%)
	Yes	236 (2.0%)	70 (3.6%)	94 (1.7%)	21 (1.5%)	12 (1.0%)	15 (1.7%)	19 (4.6%)	0 (0.0%)	4 (4.5%)	1 (1.3%)	0 (0.0%)
Others	No	11,175 (95.2%)	1,867 (94.9%)	5,413 (96.9%)	1,330 (93.0%)	1,173 (95.3%)	796 (92.7%)	371 (89.6%)	67 (84.8%)	77 (87.5%)	76 (98.7%)	5 (100.0%)
	Yes	562 (4.8%)	100 (5.1%)	174 (3.1%)	100 (7.0%)	58 (4.7%)	63 (7.3%)	43 (10.4%)	12 (15.2%)	11 (12.5%)	1 (1.3%)	0 (0.0%)
Previous treatment, n (%)												
Prostatectomy (radical)	No	11,539 (98.3%)	1,891 (96.1%)	5,496 (98.4%)	1,422 (99.4%)	1,218 (98.9%)	855 (99.5%)	411 (99.3%)	76 (96.2%)	88 (100.0%)	77 (100.0%)	5 (100.0%)
	Yes	198 (1.7%)	76 (3.9%)	91 (1.6%)	8 (0.6%)	13 (1.1%)	4 (0.5%)	3 (0.7%)	3 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
EBRT or SBRT	No	11,236 (95.7%)	1,833 (93.2%)	5,401 (96.7%)	1,367 (95.6%)	1,177 (95.6%)	820 (95.5%)	399 (96.4%)	77 (97.5%)	81 (92.0%)	76 (98.7%)	5 (100.0%)
	Yes	501 (4.3%)	134 (6.8%)	186 (3.3%)	63 (4.4%)	54 (4.4%)	39 (4.5%)	15 (3.6%)	2 (2.5%)	7 (8.0%)	1 (1.3%)	0 (0.0%)
EBRT	No	11,297 (96.3%)	1,846 (93.8%)	5,427 (97.1%)	1,372 (95.9%)	1,181 (95.9%)	828 (96.4%)	403 (97.3%)	78 (98.7%)	81 (92.0%)	76 (98.7%)	5 (100.0%)
	Yes	440 (3.7%)	121 (6.2%)	160 (2.9%)	58 (4.1%)	50 (4.1%)	31 (3.6%)	11 (2.7%)	1 (1.3%)	7 (8.0%)	1 (1.3%)	0 (0.0%)
SBRT	No	11,674 (99.5%)	1,954 (99.3%)	5,560 (99.5%)	1,425 (99.7%)	1,226 (99.6%)	851 (99.1%)	410 (99.0%)	78 (98.7%)	88 (100.0%)	77 (100.0%)	5 (100.0%)
	Yes	63 (0.5%)	13 (0.7%)	27 (0.5%)	5 (0.3%)	5 (0.4%)	8 (0.9%)	4 (1.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BT	No	11,730 (99.9%)	1,962 (99.7%)	5,586 (100.0%)	1,429 (99.9%)	1,231 (100.0%)	859 (100.0%)	414 (100.0%)	79 (100.0%)	88 (100.0%)	77 (100.0%)	5 (100.0%)
	Yes	7 (0.1%)	5 (0.3%)	1 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Laboratory data												
PSA levels (ng/ml)	n (%)	1,454 (12.4%)	290 (14.7%)	693 (12.4%)	177 (12.4%)	146 (11.9%)	80 (9.3%)	53 (12.8%)	6 (7.6%)	8 (9.1%)	1 (1.3%)	0 (0.0%)
	Mean (SD)	727.13 (2,197.72)	1,142.99 (3,674.52)	676.84 (1,741.34)	413.20 (920.05)	460.77 (1,264.48)	740.24 (1,872.57)	734.15 (1,500.05)	2,911.80 (5,108.57)	82.09 (106.82)	61.40 (–)	-
	Median (Q1–Q3)	106.34 (16.70–556.81)	114.50 (14.68–709.00)	130.00 (18.00–646.53)	93.20 (14.68–441.08)	68.72 (9.91–258.00)	176.71 (49.51–481.05)	83.80 (14.21–678.00)	517.70 (3.10–3,453.87)	49.86 (3.65–120.30)	61.40 (61.40–61.40)	-
	Range (min–max)	0.0–43,900.0	0.0–43,900.0	0.0–29,139.0	0.0–7,366.0	0.0–8,756.4	0.4–10,804.3	0.2–8,930.8	0.5–12,978.0	0.1–309.0	61.4–61.4	-
ALP levels (U/L)	n (%)	1,778 (15.1%)	353 (17.9%)	861 (15.4%)	216 (15.1%)	166 (13.5%)	98 (11.4%)	62 (15.0%)	8 (10.1%)	9 (10.2%)	5 (6.5%)	0 (0.0%)
	Mean (SD)	800.82 (1,468.78)	683.53 (1,539.65)	745.73 (1,301.58)	917.83 (1,772.18)	907.98 (1,561.88)	910.30 (1,372.62)	1,179.11 (1,747.91)	2,760.75 (2,377.90)	527.00 (356.72)	474.40 (313.84)	-
	Median (Q1–Q3)	312.00 (223.00–682.00)	288.00 (204.00–514.00)	306.00 (222.00–667.00)	311.00 (219.00–775.00)	342.50 (239.00–886.00)	336.50 (244.00–787.00)	460.00 (250.00–1,366.00)	1,961.00 (899.00–4,566.50)	349.00 (287.00–636.00)	446.00 (267.00–517.00)	-
	Range (min–max)	54.0–20,147.0	74.0–20,147.0	54.0–13,984.0	94.0–15,626.0	133.0–12,718.0	131.0–6,867.0	160.0–10,920.0	298.0–6,935.0	187.0–1,227.0	165.0–977.0	-

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
Hb levels (g/dL)	n (%)	1,822 (15.5%)	354 (18.0%)	897 (16.1%)	215 (15.0%)	167 (13.6%)	107 (12.5%)	60 (14.5%)	7 (8.9%)	11 (12.5%)	4 (5.2%)	0 (0.0%)
	Mean (SD)	12.52 (2.20)	12.59 (2.21)	12.42 (2.24)	12.71 (2.25)	12.72 (1.95)	12.69 (2.06)	12.17 (2.14)	11.91 (2.76)	12.84 (2.29)	11.90 (2.30)	-
	Median (Q1–Q3)	12.70 (11.15–14.10)	12.80 (11.10–14.30)	12.60 (11.00–14.00)	12.90 (11.60–14.20)	13.00 (11.70–14.20)	12.80 (11.50–14.10)	12.20 (10.50–14.00)	12.20 (8.70–14.10)	13.00 (11.20–13.90)	11.85 (10.10–13.70)	-
	Range (min–max)	5.3–19.4	5.5–17.7	5.8–19.4	6.4–18.0	5.3–16.2	8.3–18.7	7.0–15.7	7.7–15.0	9.4–17.9	9.3–14.6	-
LDH levels (U/L)	n (%)	394 (3.4%)	92 (4.7%)	219 (3.9%)	25 (1.7%)	30 (2.4%)	20 (2.3%)	6 (1.4%)	0 (0.0%)	2 (2.3%)	0 (0.0%)	0 (0.0%)
	Mean (SD)	210.09 (95.65)	210.12 (133.39)	211.97 (71.90)	231.92 (172.20)	184.13 (32.86)	206.40 (53.24)	197.83 (51.56)	-	192.00 (69.30)	-	-
	Median (Q1–Q3)	193.00 (165.00–228.00)	194.50 (156.00–215.00)	195.00 (166.00–233.00)	178.00 (163.00–239.00)	186.00 (166.00–204.00)	193.00 (166.00–248.00)	200.00 (165.00–218.00)	-	192.00 (143.00–241.00)	-	-
	Range (min–max)	88.0–1,382.0	112.0–1,382.0	88.0–712.0	138.0–1,019.0	118.0–263.0	130.0–337.0	127.0–277.0	-	143.0–241.0	-	-
BMI (kg/m^2)	n (%)	8,645 (73.7%)	1,263 (64.2%)	4,074 (72.9%)	1,110 (77.6%)	1,004 (81.6%)	647 (75.3%)	364 (87.9%)	55 (69.6%)	79 (89.8%)	45 (58.4%)	4 (80.0%)
	Mean (SD)	22.82 (4.58)	22.84 (8.69)	22.74 (3.43)	23.01 (3.55)	22.92 (3.35)	22.65 (3.32)	22.82 (3.10)	23.19 (3.85)	23.95 (3.61)	22.83 (3.31)	22.28 (4.15)
	Median (Q1–Q3)	22.67 (20.45–24.86)	22.50 (20.20–24.77)	22.66 (20.45–24.83)	22.74 (20.58–25.14)	22.82 (20.62–24.95)	22.61 (20.23–24.76)	22.70 (20.61–24.75)	23.05 (20.76–24.81)	23.80 (21.71–25.46)	22.96 (20.34–24.51)	21.54 (19.37–25.19)
	Range (min–max)	10.0–304.4	12.1–304.4	10.0–38.1	13.7–46.0	13.4–51.2	13.9–35.3	15.8–32.0	16.3–34.1	15.4–41.7	16.4–32.0	18.1–27.9
Inpatient/Outpatient, n (%)	Inpatient	2,497 (21.3%)	623 (31.7%)	1,441 (25.8%)	116 (8.1%)	53 (4.3%)	78 (9.1%)	96 (23.2%)	3 (3.8%)	67 (76.1%)	18 (23.4%)	2 (40.0%)
	Outpatient	9,240 (78.7%)	1,344 (68.3%)	4,146 (74.2%)	1,314 (91.9%)	1,178 (95.7%)	781 (90.9%)	318 (76.8%)	76 (96.2%)	21 (23.9%)	59 (76.6%)	3 (60.0%)
Size of hospital (number of beds), n (%)	≤199	744 (6.3%)	113 (5.7%)	438 (7.8%)	76 (5.3%)	40 (3.2%)	50 (5.8%)	19 (4.6%)	2 (2.5%)	3 (3.4%)	3 (3.9%)	0 (0.0%)
	200–499	6,380 (54.4%)	957 (48.7%)	3,131 (56.0%)	804 (56.2%)	687 (55.8%)	471 (54.8%)	208 (50.2%)	44 (55.7%)	40 (45.5%)	35 (45.5%)	3 (60.0%)
	≥500	4,613 (39.3%)	897 (45.6%)	2,018 (36.1%)	550 (38.5%)	504 (40.9%)	338 (39.3%)	187 (45.2%)	33 (41.8%)	45 (51.1%)	39 (50.6%)	2 (40.0%)

Parameter	Category/Statistic	Overall (N = 11,737, 100.0%)	ADT alone (N = 1,967, 16.8%)	ADT + NSAA (N = 5,587, 47.6%)	ADT + ENZA (N = 1,430, 12.2%)	ADT +APA (N = 1,231, 10.5%)	ADT + ABI (N = 859, 7.3%)	ADT + DARO + DOC (N = 414, 3.5%)	ADT + DARO without DOC (N = 79, 0.7%)	ADT + DOC (N = 88, 0.7%)	ADT + others (N = 77, 0.7%)	Multiple treatments[a] (N = 5, 0.0%)
Year of index date, n (%)	2020	1,429 (12.2%)	248 (12.6%)	918 (16.4%)	57 (4.0%)	104 (8.4%)	89 (10.4%)	0 (0.0%)	0 (0.0%)	5 (5.7%)	7 (9.1%)	1 (20.0%)
	2021	2,217 (18.9%)	362 (18.4%)	1,217 (21.8%)	211 (14.8%)	199 (16.2%)	194 (22.6%)	0 (0.0%)	0 (0.0%)	12 (13.6%)	21 (27.3%)	1 (20.0%)
	2022	2,620 (22.3%)	444 (22.6%)	1,296 (23.2%)	303 (21.2%)	256 (20.8%)	255 (29.7%)	0 (0.0%)	3 (3.8%)	44 (50.0%)	19 (24.7%)	0 (0.0%)
	2023	2,967 (25.3%)	481 (24.5%)	1,292 (23.1%)	446 (31.2%)	311 (25.3%)	222 (25.8%)	159 (38.4%)	18 (22.8%)	19 (21.6%)	16 (20.8%)	3 (60.0%)
	2024	2,504 (21.3%)	432 (22.0%)	864 (15.5%)	413 (28.9%)	361 (29.3%)	99 (11.5%)	255 (61.6%)	58 (73.4%)	8 (9.1%)	14 (18.2%)	0 (0.0%)
Length of follow-up period (days)	Mean (SD)	514.7 (416.4)	432.8 (414.8)	563.6 (432.2)	458.3 (363.7)	530.7 (413.4)	613.4 (397.6)	232.8 (154.2)	174.3 (191.8)	591.9 (329.6)	545.6 (422.2)	370.0 (212.9)
	Median (Q1–Q3)	426.0 (155.0–799.0)	302.0 (84.0–687.0)	495.0 (183.0–876.0)	363.0 (156.0–687.0)	444.0 (174.0–824.0)	571.0 (302.0–887.0)	203.5 (98.0–340.0)	127.0 (27.0–262.0)	654.5 (315.5–826.0)	531.0 (137.0–888.0)	456.0 (301.0–489.0)
	Range (min–max)	1–1,621	1–1,610	2–1,621	1–1,540	1–1,571	1–1,576	3–613	1–918	2–1,425	1–1,555	32–572

[a] If treatments for multiple groups (three or more than three first-line treatment classes) were initiated at the same date, those patients were categorized as “multiple therapies”, as distinct from those in single group.

[b] Diagnosis of PC was excluded from calculation of CCI.

[c] Chronic complications included those with the following ICD codes: E10.2–E10.5, E10.7, E11.2–E11.5, E11.7, E12.2–E12.5, E12.7, E13.2–E13.5, E13.7, E14.2–E14.5, E14.7.

ABI abiraterone, *ADT* androgen-deprivation therapy, *ALP* alkaline phosphatase, *APA* apalutamide, *BMI* body mass index, *BT* brachytherapy, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *EBRT* external beam radiation therapy, *ENZA* enzalutamide, *Hb* hemoglobin, *HIV* human immunodeficiency virus, *ICD* International Classification of Diseases, *LDH* lactate dehydrogenase, *max* maximum, *min* minimum, *NSAA* nonsteroidal antiandrogen, *PC* prostate cancer, *PSA* prostate-specific antigen, *Q1* first quartile, *Q3* third quartile, *SBRT* stereotactic body radiation therapy.

Supplementary Table 5. Cumulative incidence of patients achieving a PSA response (PSA50) during the first-line period

	ADT alone	**ADT + NSAA**	**ADT + ENZA**	**ADT + APA**	**ADT + ABI**	**ADT + DARO + DOC**
N	233	621	167	143	79	50
Number (%) of events	186 (79.8)	519 (83.6)	150 (89.8)	130 (90.9)	71 (89.9)	47 (94.0)
Time to PSA response (months)[a]						
25% Percentile	1.0	0.8	0.7	0.5	0.5	0.5
Median (95% CI)	1.0 (1.0–1.1)	1.0 (1.0–1.0)	1.0 (NR–NR)	1.0 (0.9–1.0)	1.0 (NR–NR)	0.9 (0.7–1.0)
75% Percentile	1.4	1.4	1.0	1.0	1.0	1.0
Range (min–max)	0.0–33.2	0.0–41.0	0.0–5.8	0.0–9.5	0.0–5.5	0.0–2.9
Cumulative incidence rate[a]						
at 3 months (95% CI)	89.1 (84.2–93.1)	90.6 (87.9–92.9)	99.0 (95.5–99.9)	98.1 (94.1–99.6)	96.6 (89.9–99.3)	100.0 (NR–NR)
at 6 months (95% CI)	93.7 (89.5–96.6)	96.1 (94.0–97.6)	N/A	98.1 (94.1–99.6)	100.0 (NR–NR)	100.0 (NR–NR)
at 12 months (95% CI)	95.0 (91.0–97.5)	96.9 (94.8–98.3)	N/A	N/A	100.0 (NR–NR)	100.0 (NR–NR)
Adjusted HR (95% CI), *P*-value[b]						
vs ADT alone	–	1.13 (0.95–1.34), 0.175	1.77 (1.41–2.24), <0.001	1.82 (1.44–2.30), <0.001	1.67 (1.26–2.22), <0.001	1.91 (1.36–2.70), <0.001
vs ADT + NSAA	0.88 (0.75–1.05), 0.175	–	1.58 (1.29–1.92), <0.001	1.61 (1.32–1.98), <0.001	1.49 (1.15–1.92), 0.003	1.70 (1.23–2.34), 0.001
vs ADT + ENZA	0.56 (0.45–0.71), <0.001	0.63 (0.52–0.78), <0.001	–	1.02 (0.81–1.30), 0.841	0.94 (0.71–1.26), 0.689	1.08 (0.77–1.50), 0.661
vs ADT + APA	0.55 (0.43–0.69), <0.001	0.62 (0.51–0.76), <0.001	0.98 (0.77–1.23), 0.841	–	0.92 (0.69–1.23), 0.578	1.05 (0.75–1.48), 0.772
vs ADT + ABI	0.60 (0.45–0.79), <0.001	0.67 (0.52–0.87), 0.003	1.06 (0.79–1.41), 0.689	1.09 (0.81–1.45), 0.578	–	1.14 (0.78–1.67), 0.492
vs ADT + DARO + DOC	0.52 (0.37–0.74), <0.001	0.59 (0.43–0.81), 0.001	0.93 (0.67–1.30), 0.661	0.95 (0.68–1.33), 0.772	0.88 (0.60–1.28), 0.492	–

[a] Estimated by the Kaplan–Meier method.

[b] Adjusted HRs and *P*-values were calculated using the Cox proportional hazards model. The model included first-line drug class as a dependent variable and baseline PSA (ng/mL), age (years), CCI, history of hypertension (yes/no), history of hyperlipidemia (yes/no), metastasis site to bone (yes/no), metastasis site to lymph (yes/no), metastasis site to lung (yes/no), metastasis site to liver (yes/no), metastasis to other sites (yes/no), hospital size (≤199 beds, 200–499 beds, ≥500 beds), and year of index date (2020 through to 2024) as covariates.

ABI abiraterone, *ADT* androgen-deprivation therapy, *APA* apalutamide, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *ENZA* enzalutamide, *max* maximum, *min* minimum, *N/A* not applicable; *NR* not reached, *NSAA* nonsteroidal antiandrogen, *PSA* prostate-specific antigen, *PSA50* ≥50% PSA reduction, *vs* versus.

Supplementary Table 6. Cumulative incidence of patients achieving a PSA response (≤0.2 ng/mL) during the first-line period

	ADT alone	ADT + NSAA	ADT + ENZA	ADT + APA	ADT + ABI	ADT + DARO + DOC
N	233	621	167	143	79	50
Number (%) of events	45 (19.3)	195 (31.4)	87 (52.1)	80 (55.9)	39 (49.4)	26 (52.0)
Time to PSA response (months)[a]						
25% Percentile	5.6	4.1	2.3	2.1	2.8	2.1
Median (95% CI)	31.4 (13.4–31.4)	9.1 (7.2 –14.4)	3.9 (3.5–5.6)	3.7 (2.8–4.2)	5.1 (3.9–7.4)	4.9 (2.8–8.3)
75% Percentile	31.4	–	10.4	13.8	24.6	13.7
Range (min–max)	0.0–31.4	0.0–33.4	0.0–33.1	0.0–36.1	0.0–25.0	0.0–13.7
Cumulative incidence rate[a]						
at 3 months (95% CI)	14.5 (9.9–21.1)	13.2 (10.5–16.7)	36.5 (28.8–45.4)	47.0 (38.2–56.7)	28.9 (19.3–41.9)	41.1 (27.8–57.8)
at 6 months (95% CI)	25.2 (18.6 –33.7)	40.0 (35.2–45.2)	59.3 (50.5–68.3)	63.6 (54.2–73.0)	53.4 (40.9–66.9)	51.8 (37.4–68.0)
at 12 months (95% CI)	30.3 (22.3–40.4)	52.9 (47.2–58.9)	79.9 (69.8–88.3)	72.9 (62.6–82.4)	71.8 (58.1–84.1)	69.7 (52.4–85.4)
Adjusted HR (95% CI), *P*-value[b]						
vs ADT alone	–	1.52 (1.09–2.11), 0.013	2.51 (1.72–3.65), <0.001	2.76 (1.89–4.01), <0.001	2.27 (1.46–3.52), <0.001	2.49 (1.49–4.15), <0.001
vs ADT + NSAA	0.66 (0.47–0.92), 0.013	–	1.65 (1.25–2.19), <0.001	1.81 (1.37–2.40), <0.001	1.49 (1.04–2.13), 0.029	1.64 (1.05–2.57), 0.031
vs ADT + ENZA	0.40 (0.27–0.58), <0.001	0.61 (0.46–0.80), <0.001	–	1.10 (0.80–1.50), 0.553	0.90 (0.61–1.33), 0.608	0.99 (0.63–1.56), 0.974
vs ADT + APA	0.36 (0.25–0.53), <0.001	0.55 (0.42–0.73), <0.001	0.91 (0.67–1.25), 0.553	–	0.82 (0.56–1.21), 0.325	0.90 (0.57–1.43), 0.664
vs ADT + ABI	0.44 (0.28–0.68), <0.001	0.67 (0.47–0.96), 0.029	1.11 (0.75–1.64), 0.608	1.22 (0.83–1.79), 0.325	–	1.10 (0.66–1.84), 0.721
vs ADT + DARO + DOC	0.40 (0.24–0.67), <0.001	0.61 (0.39–0.95), 0.031	1.01 (0.64–1.59), 0.974	1.11 (0.70–1.75), 0.664	0.91 (0.54–1.52), 0.721	–

[a] Estimated by the Kaplan–Meier method.

[b] Adjusted HRs and *P*-values were calculated using the Cox proportional hazards model. The model included first-line drug class as a dependent variable and baseline PSA (ng/mL), age (years), CCI, history of hypertension (yes/no), history of hyperlipidemia (yes/no), metastasis site to bone (yes/no), metastasis site to lymph (yes/no), metastasis site to lung (yes/no), metastasis site to liver (yes/no), metastasis to other sites (yes/no), hospital size (≤199 beds, 200–499 beds, ≥500 beds), and year of index date (2020 through to 2024) as covariates.
ABI abiraterone, *ADT* androgen-deprivation therapy, *APA* apalutamide, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *ENZA* enzalutamide, *HR* hazard ratio, *max* maximum, *min* minimum, *NSAA* nonsteroidal antiandrogen, *PSA* prostate-specific antigen.

Supplementary Table 7. TTPP during the first-line period

	ADT alone	ADT + NSAA	ADT + ENZA	ADT + APA	ADT + ABI	ADT + DARO + DOC
N	233	621	167	143	79	50
Number (%) of events	44(18.9%)	195 (31.4%)	25 (15.0%)	24 (16.8%)	18 (22.8%)	4 (8.0%)
TTPP (months)[a]						
25% Percentile	10.9	8.8	15.4	11.2	11.8	11.3
Median (95% CI)	23.8 (14.1–NR)	15.2 (13.1–19.0)	35.0 (23.9–35.0)	33.4 (21.8–NR)	33.6 (17.1–NR)	NR (9.5–NR)
75% Percentile	NR	31.5	35.0	NR	NR	NR
Range (min–max)	0.0–41.3	0.0–50.9	0.0–35.0	0.0–40.8	0.0–41.4	0.0–18.1
Cumulative event-free rate[a]						
at 3 months (95% CI)	98.0 (94.0–99.4)	97.9 (96.2–98.9)	97.6 (92.9–99.2)	99.1 (93.5–99.9)	97.1 (88.8–99.3)	100.0 (100.0–100.0)
at 6 months (95% CI)	85.5 (77.9–90.7)	87.7 (84.0–90.5)	86.7 (78.5–92.0)	89.0 (80.5–94.0)	90.1 (79.1–95.4)	100.0 (100.0–100.0)
at 12 months (95% CI)	72.1 (61.9–80.0)	59.8 (54.0–65.0)	79.8 (69.8–86.8)	75.0 (62.6–83.8)	74.7 (59.9–84.6)	68.7 (34.1–87.7)
at 24 months (95% CI)	46.2 (32.8–58.5)	35.5 (29.2–41.9)	55.7 (30.5–74.9)	63.3 (47.6–75.4)	62.8 (46.1–75.7)	N/A
at 36 months (95% CI)	42.6 (28.8–55.8)	25.0 (18.3–32.3)	0.0 (NR–NR)	42.7 (16.4–67.0)	41.9 (10.3–71.6)	N/A
Adjusted HR (95% CI), *P*-value[b]						
vs ADT alone	–	1.37 (0.98–1.92), 0.067	0.70 (0.42–1.17), 0.169	0.69 (0.41–1.16), 0.163	0.71 (0.41–1.25), 0.237	0.46 (0.16–1.33), 0.152
vs ADT + NSAA	0.73 (0.52–1.02), 0.067	–	0.51 (0.32–0.80), 0.003	0.51 (0.32–0.79), 0.003	0.52 (0.32–0.86), 0.010	0.34 (0.12–0.94), 0.038
vs ADT + ENZA	1.43 (0.85–2.38), 0.169	1.96 (1.25–3.13), 0.003	–	1.00 (0.56–1.76), 0.989	1.02 (0.55–1.90), 0.938	0.66 (0.23–1.93), 0.451
vs ADT + APA	1.45 (0.86–2.44), 0.163	1.96 (1.27–3.13), 0.003	1.00 (0.57–1.79), 0.989	–	1.03 (0.56–1.91), 0.927	0.67 (0.23–1.96), 0.459
vs ADT + ABI	1.41 (0.8–2.44), 0.237	1.92 (1.16–3.1212), 0.010	0.98 (0.53–1.82), 0.938	0.97 (0.52–1.79), 0.927	–	0.65 (0.21–1.95), 0.439
vs ADT + DARO + DOC	2.17 (0.75–6.25), 0.152	2.94 (1.06–8.33), 0.038	1.52 (0.52–4.35), 0.451	1.49 (0.51–4.35), 0.459	1.54 (0.51–4.76), 0.439	–

[a] Estimated by the Kaplan–Meier method.

[b] Adjusted HRs and *P*-values were calculated using the Cox proportional hazards model. The model included first-line drug class as a dependent variable and baseline PSA (ng/mL), age (years), CCI, history of hypertension (yes/no), history of hyperlipidemia (yes/no), metastasis site to bone (yes/no), metastasis site to lymph (yes/no), metastasis site to lung (yes/no), metastasis site to liver (yes/no), metastasis to other sites (yes/no), hospital size (≤199 beds, 200–499 beds, ≥500 beds), and year of index date (2020 through to 2024) as covariates.

ABI abiraterone, *ADT* androgen-deprivation therapy, *APA* apalutamide, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *ENZA* enzalutamide, *max* maximum, *min* minimum, *N/A* not applicable; *NR* not reached, *NSAA* nonsteroidal antiandrogen, *PSA* prostate-specific antigen, *TTPP* time to PSA progression.

Supplementary Table 8. TTD of first-line treatment, cohort 1

	ADT alone	ADT + NSAA	ADT + ENZA	ADT + APA	ADT + ABI	ADT + DARO + DOC
N	233	621	167	143	79	50
Number (%) of events	89 (38.2%)	333 (53.6%)	47 (28.1%)	55 (38.5%)	31 (39.2%)	12 (24.0%)
Time to discontinuation (months)[a]						
25% Percentile	4.7	4.9	6.7	4.8	6.7	9.5
Median (95% CI)	11.9 (9.4–20.9)	11.9 (10.1–13.2)	32.4 (18.7–NR)	35.3 (11.4–NR)	20.7 (15.7–NR)	NR (10.4–NR)
75% Percentile	NR	24.3	NR	NR	35.2	NR
Range (min–max)	0.4–41.3	0.0–50.9	0.2–39.2	0.5–49.8	0.4–41.4	0.4–18.1
Cumulative event-free rate[a]						
at 3 months (95% CI)	86.3 (80.6–90.4)	82.7 (79.4–85.5)	87.4 (81.2–91.7)	83.8 (76.5–89.1)	85.5 (75.3–91.7)	83.0 (68.8–91.1)
at 6 months (95% CI)	68.1 (60.5–74.5)	71.8 (67.9–75.4)	79.4 (71.7–85.2)	72.4 (63.7–79.3)	77.8 (66.2–85.8)	83.0 (68.8–91.1)
at 12 months (95% CI)	49.2 (40.7–57.2)	49.4 (44.6–53.9)	69.2 (60.3–76.5)	58.8 (49.0–67.3)	69.4 (56.8–79.0)	57.6 (31.2–77.0)
at 24 months (95% CI)	38.1 (28.6–47.5)	26.3 (21.6–31.2)	60.6 (49.7–69.8)	54.3 (44.0–63.5)	44.5 (28.6–59.1)	N/A
at 36 months (95% CI)	35.8 (26.1–45.7)	18.6 (13.7–24.1)	45.4 (18.9–68.8)	46.7 (32.9–59.4)	22.2 (2.0–55.9)	N/A
Adjusted HR (95% CI), *P*-value[b]						
vs ADT only	–	1.29 (1.02–1.64), 0.035	0.62 (0.43–0.89), 0.010	0.75 (0.53–1.07), 0.118	0.76 (0.50–1.16), 0.205	0.65 (0.34–1.22), 0.178
vs ADT + NSAA	0.78 (0.61–0.98), 0.035	–	0.48 (0.34–0.66), <0.001	0.58 (0.43–0.79), <0.001	0.59 (0.40–0.86), 0.006	0.50 (0.27–0.92), 0.026
vs ADT + ENZA	1.61 (1.12–2.33), 0.010	2.08 (1.52–2.94), <0.001	–	1.22 (0.82–1.81), 0.319	1.24 (0.78–1.96), 0.362	1.05 (0.55–2.01), 0.880
vs ADT + APA	1.33 (0.93–1.89), 0.118	1.72 (1.27–2.33), <0.001	0.82 (0.55–1.22), 0.319	–	1.01 (0.65–1.58), 0.957	0.86 (0.45–1.63), 0.645
vs ADT + ABI	1.32 (0.86–2.00), 0.205	1.69 (1.16–2.50), 0.006	0.81 (0.51–1.28), 0.362	0.99 (0.63–1.54), 0.957	–	0.85 (0.43–1.68), 0.639
vs ADT + DARO + DOC	1.54 (0.82–2.94), 0.178	2.00 (1.09–3.70), 0.026	0.95 (0.50–1.82), 0.880	1.16 (0.61–2.22), 0.645	1.18 (0.60–2.33), 0.639	–

[a] Estimated by the Kaplan–Meier method.

[b] Adjusted HRs and *P*-values were calculated using the Cox proportional hazards model. The model included first-line drug class as a dependent variable and baseline PSA (ng/mL), age (years), CCI, history of hypertension (yes/no), history of hyperlipidemia (yes/no), metastasis site to bone (yes/no), metastasis site to

lymph (yes/no), metastasis site to lung (yes/no), metastasis site to liver (yes/no), metastasis to other sites (yes/no), hospital size (≤199 beds, 200–499 beds, ≥500 beds), and year of index date (2020 through to 2024) as covariates.

ABI abiraterone, *ADT* androgen-deprivation therapy, *APA* apalutamide, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *ENZA* enzalutamide, *max* maximum, *min* minimum, *NR* not reached, *NSAA* nonsteroidal antiandrogen, *PSA* prostate-specific antigen, *TTD* time-to-treatment discontinuation.

Supplementary Table 9. TTD of first-line and second-line therapies, cohort 2

				Time to discontinuation (day)			
First-line treatment	**Second-line treatment**	**N**	**Number (%) of events**	**25% Percentile (95% CI)[a]**	**Median (95% CI)[a]**	**75% Percentile (95% CI)[a]**	**Range (min–max)**
ADT + ENZA	ADT + DOC	59	42 (71.2%)	319.0 (252.0–407.0)	495.0 (407.0–811.0)	846.0 (781.0–1,017.0)	43.0–1,402.0
	ADT + ABI	74	45 (60.8%)	335.0 (247.0–434.0)	481.0 (434.0–545.0)	791.0 (532.0–1,228.0)	98.0–1,305.0
	ADT + APA	25	15 (60.0%)	175.0 (30.0–287.0)	308.0 (245.0–553.0)	553.0 (322.0–NR)	30.0–1,040.0
	ADT + DARO ± DOC	8	5 (62.5%)	86.5 (42.0–1,008.0)	601.5 (42.0–1,008.0)	1,008.0 (98.0–1,008.0)	42.0–1,008.0
	ADT + others[b]	89	44 (49.4%)	305.0 (168.0–406.0)	666.0 (545.0–812.0)	1,010.0 (812.0–NR)	10.0–1,368.0
	None	1,165	164 (14.1%)	884.0 (679.0–NR)	NR (NR–NR)	NR (NR–NR)	1.0–1,540.0
ADT + APA	ADT + DOC	42	27 (64.3%)	393.0 (252.0–482.0)	540.0 (397.0–742.0)	915.0 (592.0–1,024.0)	176.0–1,456.0
	ADT + ABI	72	45 (62.5%)	343.0 (231.0–427.0)	490.0 (427.0–648.0)	852.0 (648.0–NR)	56.0–1,446.0
	ADT + ENZA	154	51 (33.1%)	411.0 (320.0–469.0)	1,140.0 (642.0–NR)	NR (NR–NR)	28.0–1,443.0
	ADT + DARO ± DOC	6	2 (33.3%)	679.0 (229.0–NR)	679.0 (229.0–NR)	NR (229.0–NR)	142.0–912.0
	ADT + others[b]	92	65 (70.7%)	229.0 (161.0–266.0)	417.0 (315.0–554.0)	815.0 (607.0–909.0)	28.0–1,515.0
	None	852	129 (15.1%)	1,022.0 (607.0–1,270.0)	NR (NR–NR)	NR (NR–NR)	1.0–1,571.0
ADT + ABI	ADT + DOC	65	50 (76.9%)	378.0 (301.0–473.0)	579.0 (476.0–723.0)	910.0 (723.0–1,028.0)	203.0–1,421.0
	ADT + ENZA	129	65 (50.4%)	392.0 (342.0–505.0)	754.0 (645.0–939.0)	1,104.0 (948.0–1,477.0)	41.0–1,477.0
	ADT + APA	17	13 (76.5%)	175.0 (34.0–252.0)	354.0 (154.0–639.0)	639.0 (252.0–1,078.0)	34.0–1,078.0
	ADT + DARO ± DOC	2	2 (100.0%)	1,321.0 (1,321.0–1,421.0)	1,371.0 (1,321.0–1,421.0)	1,421.0 (1321.0–1,421.0)	1,321.0–1,421.0
	ADT + others[b]	34	23 (67.6%)	193.0 (50.0–231.0)	308.0 (217.0–667.0)	814.0 (431.0–NR)	36.0–1,485.0
	None	606	88 (14.5%)	NR (953.0–NR)	NR (NR–NR)	NR (NR–NR)	1.0–1,576.0
ADT + DARO ± DOC	ADT + DOC	0	0 (0.0%)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)

				Time to discontinuation (day)			
First-line treatment	**Second-line treatment**	**N**	**Number (%) of events**	**25% Percentile (95% CI)[a]**	**Median (95% CI)[a]**	**75% Percentile (95% CI)[a]**	**Range (min–max)**
	ADT + ABI	8	4 (50.0%)	336.0 (252.0–449.0)	449.0 (252.0–NR)	NR (336.0–NR)	252.0–613.0
	ADT + ENZA	12	3 (25.0%)	420.0 (344.0–455.0)	455.0 (344.0–455.0)	455.0 (420.0–455.0)	108.0–455.0
	ADT + APA	3	2 (66.7%)	103.0 (103.0–NR)	273.0 (103.0–NR)	NR (103.0–NR)	103.0–433.0
	ADT + cabazitaxel	4	2 (50.0%)	333.0 (333.0–NR)	378.0 (333.0–NR)	NR (333.0–NR)	266.0–591.0
	ADT + others[b]	8	5 (62.5%)	86.0 (14.0–385.0)	385.0 (14.0–NR)	413.0 (182.0–NR)	14.0–436.0
	None	376	19 (5.1%)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)	3.0–612.0
Others[a]	ADT + DOC	104	86 (82.7%)	277.0 (182.0–317.0)	402.0 (348.0–493.0)	672.0 (533.0–860.0)	11.0–1,479.0
	ADT + ENZA	1,003	430 (42.9%)	472.0 (432.0–504.0)	856.0 (783.0–972.0)	NR (NR–NR)	16.0–1,611.0
	ADT + APA	217	103 (47.5%)	294.0 (236.0–343.0)	595.0 (474.0–769.0)	NR (1,024.0–NR)	7.0–1,532.0
	ADT + ABI	369	213 (57.7%)	322.0 (281.0–364.0)	629.0 (547.0–700.0)	NR (1,148.0–NR)	42.0–1,621.0
	ADT + DARO ± DOC	52	33 (63.5%)	84.0 (43.0–142.0)	579.0 (142.0–1,086.0)	1,309.0 (948.0–NR)	8.0–1,551.0
	ADT + cabazitaxel	11	8 (72.7%)	287.0 (166.0–406.0)	406.0 (203.0–777.0)	777.0 (401.0–NR)	166.0–968.0
	ADT + others[b]	666	421 (63.2%)	292.0 (269.0–333.0)	532.0 (490.0–605.0)	958.0 (861.0–1,080.0)	7.0–1,604.0
	None	5,277	1,618 (30.7%)	203.0 (190.0–220.0)	761.0 (728.0–868.0)	NR (NR–NR)	1.0–1,597.0

[a] ADT alone, ADT + bicalutamide, ADT + flutamide, ADT + estramustine, or ADT + chlormadinone, or ADT + darolutamide without docetaxel.

[b] Bicalutamide, flutamide, estramustine, chlormadinone, olaparib, talazoparib, pembrolizumab, or Ra-223.

ABI abiraterone, *ADT* androgen-deprivation therapy, *APA* apalutamide, *CCI* Charlson Comorbidity Index, *DARO* darolutamide, *DOC* docetaxel, *ENZA* enzalutamide, *max* maximum, *min* minimum, *NR* not reached, *NSAA* nonsteroidal antiandrogen, *Ra-223* radium-223 dichloride, *TTD* time-to-treatment discontinuation.

Supplementary Table 10. OS by first-line therapy, cohort 2

	ADT alone	ADT + NSAA	ADT + ENZA	ADT + APA	ADT + ABI	ADT + DARO + DOC
N	1,967	5,587	1,430	1,231	859	414
Number (%) of events	192 (9.8%)	553 (9.9%)	70 (4.9%)	68 (5.5%)	72 (8.4%)	4 (1.0%)
OS (months)[a]						
25th Percentile	NR	49.8	NR	NR	NR	NR
Median (95% CI)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)
75th Percentile	NR	NR	NR	NR	NR	NR
Range (min–max)	0.0–52.9	0.1–53.3	0.0–50.6	0.0–51.6	0.0–51.8	0.1–20.1
Cumulative event-free rate[a]						
at 3 months (95% CI)	96.0 (94.9–96.8)	97.6 (97.2–98.0)	99.5 (98.9–99.7)	99.0 (98.2–99.4)	98.7 (97.6–99.3)	99.7 (98.0–100.0)
at 6 months (95% CI)	94.4 (93.1–95.4)	96.0 (95.5–96.6)	98.6 (97.7–99.1)	98.3 (97.4–99.0)	97.7 (96.4–98.6)	99.3 (97.3–99.8)
at 12 months (95% CI)	91.6 (90.0–92.9)	93.7 (92.9–94.4)	96.5 (95.1–97.5)	96.5 (95.0–97.5)	95.7 (94.0–96.9)	98.0 (94.5–99.3)
at 24 months (95% CI)	85.4 (83.0–87.4)	88.5 (87.4–89.5)	91.8 (89.4–93.7)	91.9 (89.4–93.8)	90.7 (88.1–92.8)	N/AA
at 36 months (95% CI)	81.2 (78.0–84.0)	82.9 (81.3–84.4)	87.5 (83.5–90.6)	88.3 (84.8–91.1)	85.7 (81.5–89.0)	N/A
Adjusted HR (95% CI), *P*-value[b]						
vs ADT alone	–	0.83 (0.70–0.98), 0.030	0.58 (0.44–0.76), <0.001	0.61 (0.46–0.80), 0.001	0.82 (0.62–1.08), 0.163	0.22 (0.08–0.59), 0.003
vs ADT + NSAA	1.20 (1.02–1.43), 0.030	–	0.69 (0.54–0.89), 0.005	0.73 (0.57–0.94), 0.016	0.99 (0.77–1.27), 0.919	0.26 (0.10–0.70), 0.008
vs ADT + ENZA	1.72 (1.32–2.27), <0.001	1.45 (1.12–1.85), 0.005	–	1.05 (0.75–1.47), 0.759	1.42 (1.02–1.98), 0.036	0.37 (0.14–1.03), 0.057
vs ADT + APA	1.64 (1.25–2.17), 0.001	1.37 (1.06–1.75), 0.016	0.95 (0.68–1.33), 0.759	–	1.35 (0.97–1.89), 0.076	0.35 (0.13–0.98), 0.045
vs ADT + ABI	1.22 (0.93–1.61), 0.163	1.01 (0.79–1.30), 0.919	0.70 (0.51–0.98), 0.036	0.74 (0.53–1.03), 0.076	–	0.26 (0.09–0.72), 0.010
vs ADT + DARO ± DOC	4.55 (1.69–12.50), 0.003	3.85 (1.43–10.00), 0.008	2.70 (0.97–7.14), 0.057	2.86 (1.02–7.69), 0.045	3.85 (1.39–11.11), 0.010	–

[a] Estimated by the Kaplan–Meier method.

[b] Adjusted HRs and *P*-values were calculated using the Cox proportional hazards model. The model included first-line drug class as a dependent variable and baseline PSA (ng/mL), age (years), CCI, history of hypertension (yes/no), history of hyperlipidemia (yes/no), metastasis site to bone (yes/no), metastasis site to

lymph (yes/no), metastasis site to lung (yes/no), metastasis site to liver (yes/no), metastasis to other sites (yes/no), hospital size (≤ 199 beds, 200–499 beds, ≥ 500 beds), and year of index date (2020 through to 2024) as covariates.

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