Real-World Outcomes in First-Line Treatment of Metastatic Castration-Resistant Prostate Cancer: the Prostate Cancer Registry

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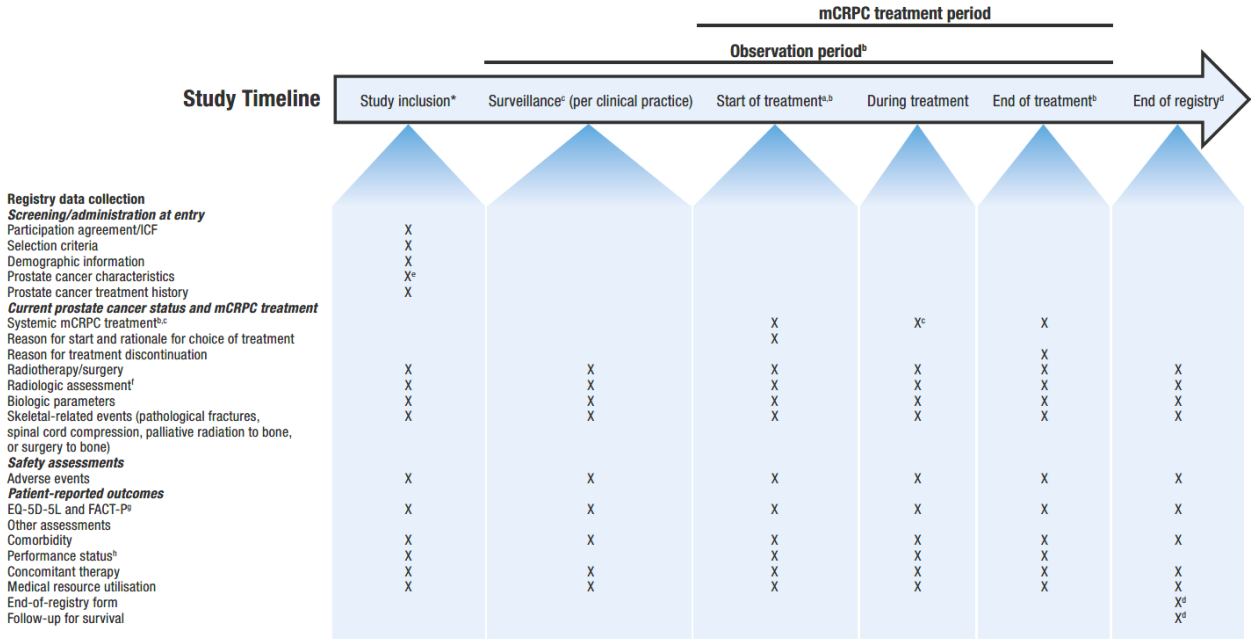
Fig. S1 Data collection schedule



Note: Patients could enter multiple systemic mCRPC treatment periods and periods of surveillance during the Registry

[a]For patients entering the Registry, the data from the baseline data collection and start of data collection may be the same; at enrollment, initiation of a new systemic mCRPC treatment was considered at ±30 days from a patient's baseline data collection

[b]Data were collected at the points of initiation and termination of each new systemic mCRPC treatment during the observational period. Recorded information included the type of treatment, start and stop dates, dose, and frequency of administration. The maximum duration of follow-up for individual patients in the observational period of the Registry was 3 years, regardless of when they enrolled

[c]For patients undergoing long-term (>3 months) systemic mCRPC treatment or in surveillance, data were collected at suggested intervals of 3 months

[d]The end of Registry was the last data collection time point for an individual patient, a maximum of 3 years after their enrollment. The close of Registry will be approximately 5.5 years after the first patient was enrolled. Survival data will be collected for all patients 3 years after their enrollment or at the close of the Registry, whichever occurs first, except for those patients who withdraw their consent prior to completing the Registry

[e]Including dates of initial diagnosis, first metastatic diagnosis and castration resistance, TNM stage and Gleason score at diagnosis, and most recent Gleason score

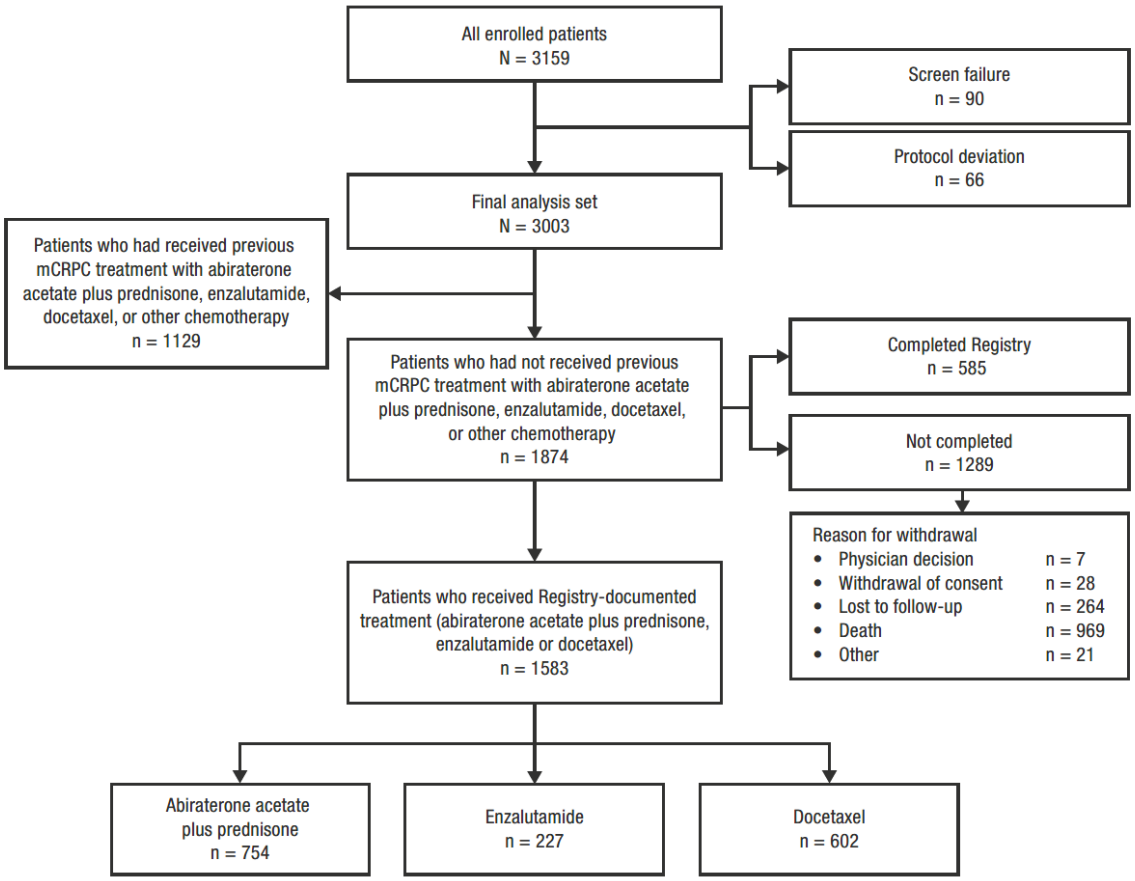
[f]Prostate Cancer Working Group 2 and Response Evaluation Criteria In Solid Tumors are recommended guidelines for radiologic assessment

[g]Where permitted per local regulations

[h]Performance status was collected using the ECOG scale

ECOG Eastern Cooperative Oncology Group, *EQ-5D-5L* European Quality of Life-5 Dimensions, 5 Levels, *FACT-P* Functional Assessment of Cancer Therapy-Prostate, *ICF* International Classification of Functioning, Disability and Health, *mCRPC* metastatic castration-resistant prostate cancer, *TNM* tumor, node, metastasis

Fig. S2 Study flow



mCRPC metastatic castration-resistant prostate cancer

Supplementary Table S1. Duration of treatment in the first-line treatment population, including subgroups

Kaplan-Meier estimates (ongoing treatment is censored at the data cut)	Abiraterone	Enzalutamide	Docetaxel[a]
First-line population			
N	754	227	602
Median (95% CI) duration of treatment, months	11.2 (9.8–12.2)	13.0 (10.4–15.9)	4.8 (4.4–5.0)
Patients with cardiovascular disease			
N	504	161	351
Median (95% CI) duration of treatment, months	11.1 (9.5–12.7)	12.7 (9.1–15.3)	4.6 (4.3–5.0)
Patients with diabetes mellitus			
N	121	47	100
Median (95% CI) duration of treatment, months	11.5 (9.1–16.1)	12.2 (8.2–17.5)	4.3 (3.6–4.9)
Patients with visceral metastases			
N	59	–	88
Median (95% CI) duration of treatment, months	7.9 (5.5–10.9)	–	4.3 (3.5–5.1)

[a]Docetaxel treatment was restricted to a limited number of cycles; therefore, duration of treatment in the docetaxel group cannot be compared with that in the abiraterone or enzalutamide treatment groups

CI confidence interval, *N* number of evaluable patients for each specific parameter

Supplementary Table S2. Reason for stopping systemic mCRPC treatment in the first-line treatment population, including subgroups

	Abiraterone	Enzalutamide	Docetaxel[a]
All patients	754	227	602
Reason for stopping systemic mCRPC treatment, *n* (%)			
N	607	171	586
Completed therapy	11 (1.8)	5 (2.9)	293 (50.0)
Toxicity	43 (7.1)	23 (13.5)	83 (14.2)
Disease progression	442 (72.8)	115 (67.3)	158 (27.0)
Death	44 (7.2)	19 (11.1)	22 (3.8)
Other	67 (11.0)	9 (5.3)	30 (5.1)
Patients with cardiovascular disease			
All	504	161	351
Reason for stopping systemic mCRPC treatment, *n* (%)			
N	403	126	342
Completed therapy	7 (1.7)	3 (2.4)	169 (49.4)
Toxicity	36 (8.9)	21 (16.7)	50 (14.6)
Disease progression	290 (72.0)	79 (62.7)	83 (24.3)
Death	28 (6.9)	15 (11.9)	19 (5.6)
Other	42 (10.4)	8 (6.3)	21 (6.1)
Patients with diabetes mellitus			
All	121	47	100
Reason for stopping systemic mCRPC treatment, *n* (%)			
N	92	38	100
Completed therapy	2 (2.2)	2 (5.3)	44 (44.0)
Toxicity	11 (12.0)	5 (13.2)	19 (19.0)
Disease progression	61 (66.3)	22 (57.9)	24 (24.0)
Death	9 (9.8)	7 (18.4)	5 (5.0)
Other	9 (9.8)	2 (5.3)	8 (8.0)
Patients with visceral metastases			

All	59	–	88
Reason for stopping systemic mCRPC treatment, *n* (%)			
N	48	–	86
Completed therapy	1 (2.1)	–	42 (48.8)
Toxicity	5 (10.4)	–	10 (11.6)
Disease progression	34 (70.8)	–	23 (26.7)
Death	5 (10.4)	–	4 (4.7)
Other	3 (6.3)	–	7 (8.1)

[a]Docetaxel treatment was restricted to a limited number of cycles; therefore, the reasons for stopping treatment in the docetaxel group cannot be compared with that in the abiraterone or enzalutamide treatment groups

mCRPC metastatic castration-resistant prostate cancer; *N* number of evaluable patients for each specific parameter

Table S3A. Patient demographics and disease and biological characteristics at study inclusion in patients with cardiovascular disease in the first-line treatment population

Characteristic	Abiraterone *N* = 504	Enzalutamide *N* = 161	Docetaxel *N* = 351
Age			
Mean (SD), years	76.5 (7.46)	76.4 (7.28)	70.7 (7.41)
Median (range), years	77.0 (50–94)	77.0 (59–91)	71.0 (47–88)
Age group, n (%)			
<65 years	35 (6.9)	10 (6.2)	73 (20.8)
65–74 years	133 (26.4)	52 (32.3)	162 (46.2)
≥75 years	336 (66.7)	99 (61.5)	116 (33.0)
ECOG performance status, n (%)			
N	477	130	314
0	218 (45.7)	62 (47.7)	110 (35.0)
1	214 (44.9)	51 (39.2)	171 (54.5)
≥2	45 (9.4)	17 (13.1)	33 (10.5)
Gleason score at initial diagnosis, n (%)			
N	448	144	332
≤6	71 (15.8)	20 (13.9)	41 (12.3)
7	154 (34.4)	39 (27.1)	103 (31.0)
8–10	223 (49.8)	85 (59.0)	188 (56.6)
M stage at initial diagnosis, n (%)			
N	488	156	341
Mx	114 (23.4)	27 (17.3)	48 (14.1)
M0	217 (44.5)	67 (42.9)	127 (37.2)
M1, M1a, M1b, M1c	157 (32.2)	62 (39.7)	166 (48.7)
Time from initial prostate cancer diagnosis to start of the study			

N	504	161	351
Median years (range)	5.3 (0–29)	4.9 (0–21)	3.1 (0–22)
Presence of bone metastases, n (%)			
N	374	131	269
Any	328 (87.7)	118 (90.1)	238 (88.5)
≥5	134 (35.8)	46 (35.1)	113 (42.0)
Visceral metastases, n (%)			
N	402	113	301
Liver only	7 (1.7)	6 (5.3)	27 (9.0)
Lung only	25 (6.2)	4 (3.5)	21 (7.0)
Liver and lung	5 (1.2)	0	5 (1.7)
Biological parameters			
PSA, ng/mL			
N	493	160	341
Mean (SD)	129.78 (559.819)	86.76 (188.571)	162.66 (541.211)
Lactic acid dehydrogenase, U/L			
N	227	60	148
Mean (SD)	324.3 (290.17)	265.3 (158.48)	371.3 (352.14)
Hemoglobin, g/dL			
N	438	143	319
Mean (SD)	12.6 (1.61)	12.8 (1.38)	12.5 (1.72)
Alkaline phosphatase, U/L			
N	392	137	252
Mean (SD)	197.8 (286.62)	148.9 (249.46)	213.4 (283.95)
Comorbidities requiring treatment, n (%)			
Any	504	161	351
Cardiovascular	504 (100.0)	161 (100.0)	351 (100.0)
Hypertension	411 (81.5)	129 (80.1)	289 (82.3)

Angina pectoris	34 (6.7)	12 (7.5)	35 (10.0)
Myocardial infarction	48 (9.5)	21 (13.0)	32 (9.1)
Arrhythmia	62 (12.3)	22 (13.7)	41 (11.7)
Thromboembolic disease	21 (4.2)	8 (5.0)	18 (5.1)
Cerebrovascular accident	19 (3.8)	3 (1.9)	17 (4.8)
Transient ischemic attack	14 (2.8)	5 (3.1)	9 (2.6)
Other cardiovascular	139 (27.6)	39 (24.2)	80 (22.8)
Respiratory	46 (9.1)	23 (14.3)	38 (10.8)
Chronic obstructive pulmonary disease	31 (6.2)	16 (9.9)	22 (6.3)
Other respiratory	16 (3.2)	8 (5.0)	16 (4.6)
Renal	43 (8.5)	20 (12.4)	32 (9.1)
Chronic renal disease	27 (5.4)	14 (8.7)	16 (4.6)
Other renal	16 (3.2)	6 (3.7)	16 (4.6)
Hepatic	15 (3.0)	3 (1.9)	6 (1.7)
Chronic hepatic disease	8 (1.6)	3 (1.9)	3 (0.9)
Other hepatic	7 (1.4)	0	3 (0.9)
Neurologic	52 (10.3)	17 (10.6)	37 (10.5)
Peripheral sensory impairment	1 (0.2)	0	5 (1.4)
Memory impairment	3 (0.6)	4 (2.5)	2 (0.6)
Cognitive disorder	3 (0.6)	2 (1.2)	0
Convulsion	3 (0.6)	0	0
Other neurologic	15 (3.0)	4 (2.5)	7 (2.0)
Infections	5 (1.0)	3 (1.9)	1 (0.3)
Other infection	5 (1.0)	3 (1.9)	1 (0.3)
Diabetes mellitus	101 (20.0)	36 (22.4)	84 (23.9)
Type 2	75 (14.9)	28 (17.4)	72 (20.5)
Type 1	26 (5.2)	8 (5.0)	12 (3.4)
Investigations			

Hypercholesterolemia	110 (21.8)	48 (29.8)	53 (15.1)

ECOG Eastern Cooperative Oncology Group, *M* metastatic status, *N* number of evaluable patients for each specific parameter, *PSA* prostate-specific antigen, *SD* standard deviation

Table 3B. Treatment history at study inclusion in patients with cardiovascular disease in the first-line treatment population

Prior treatment, *n* (%)	Abiraterone *N* = 504	Enzalutamide *N* = 161	Docetaxel *N* = 351
Orchiectomy since initial diagnosis	27 (5.4)	8 (5.0)	21 (6.0)
Radical prostatectomy/prostate-specific radiotherapy since initial diagnosis			
Both radical prostatectomy and prostate-specific radiotherapy	48 (9.5)	12 (7.5)	33 (9.4)
Radical prostatectomy only	59 (11.7)	18 (11.2)	33 (9.4)
Prostate-specific radiotherapy only	123 (24.4)	32 (19.9)	81 (23.1)
None	274 (54.4)	99 (61.5)	204 (58.1)
Prior systemic anticancer therapy			
Any	483 (95.8)	152 (94.4)	330 (94.0)
Endocrine therapy	479 (95.0)	150 (93.2)	327 (93.2)
Antiandrogen	432 (85.7)	134 (83.2)	300 (85.5)
GnRH agonist	314 (62.3)	109 (67.7)	259 (73.8)
Steroids	51 (10.1)	15 (9.3)	44 (12.5)
GnRH antagonist	43 (8.5)	4 (2.5)	20 (5.7)
Estrogens and derivatives	18 (3.6)	5 (3.1)	4 (1.1)
Adrenal synthesis inhibitors	6 (1.2)	0 (0)	7 (2.0)
Other	0 (0)	3 (1.9)	2 (0.6)
Bone-targeted			
Any	104 (20.6)	26 (16.1)	88 (25.1)
Zoledronic acid	76 (15.1)	14 (8.7)	60 (17.1)
Denosumab	29 (5.8)	9 (5.6)	20 (5.7)
Other	8 (1.6)	6 (3.7)	15 (4.3)

Other	8 (1.6)	5 (3.1)	6 (1.7)

GnRH gonadotropin-releasing hormone

Table S4A. Patient demographics and disease and biological characteristics at study inclusion in patients with diabetes mellitus in the first-line treatment population

Characteristic	Abiraterone	Enzalutamide	Docetaxel
	N = 121	*N* = 47	*N* = 100
Age			
Mean (SD) years	76.2 (7.20)	76.7 (7.04)	69.2 (6.96)
Median (range), years	77.0 (54–93)	77.0 (62–91)	69.0 (51–88)
Age group, years, *n* (%)			
<65 years	7 (5.8)	3 (6.4)	26 (26.0)
65–74 years	37 (30.6)	14 (29.8)	50 (50.0)
≥75 years	77 (63.6)	30 (63.8)	24 (24.0)
ECOG performance status, n (%)			
N	116	38	92
0	48 (41.4)	19 (50.0)	25 (27.2)
1	48 (41.4)	14 (36.8)	55 (59.8)
≥2	20 (17.2)	5 (13.2)	12 (13.0)
Gleason score at initial diagnosis, n (%)			
N	109	43	96
≤6	13 (11.9)	7 (16.3)	15 (15.6)
7	44 (40.4)	12 (27.9)	34 (35.4)
8–10	52 (47.7)	24 (55.8)	47 (49.0)
M stage at initial diagnosis, n (%)			
N	118	46	97
Mx	31 (26.3)	6 (13.0)	16 (16.5)
M0	50 (42.4)	22 (47.8)	35 (36.1)
M1, M1a, M1b, M1c	37 (31.4)	18 (39.1)	46 (47.4)

Time from initial prostate cancer diagnosis to start of the study			
N	121	47	100
Median years (range)	5.7 (0–29)	5.4 (1–20)	4.0 (0–18)
Presence of bone metastases, n (%)			
N	92	36	78
Any	79 (85.9)	31 (86.1)	70 (89.7)
≥5	31 (33.7)	14 (38.9)	31 (39.7)
Visceral metastases, n (%)			
N	99	31	87
Liver only	3 (3.0)	1 (3.2)	9 (10.3)
Lung only	9 (9.1)	1 (3.2)	11 (12.6)
Liver and lung	2 (2.0)	0	1 (1.1)
Biological parameters			
PSA, ng/mL			
N	118	47	99
Mean (SD)	85.70 (174.249)	54.80 (69.398)	174.45 (314.797)
Lactic acid dehydrogenase, U/L			
N	56	15	38
Mean (SD)	336.8 (313.73)	288.8 (151.54)	357.1 (343.87)
Hemoglobin, g/dL			
N	108	38	92
Mean (SD)	12.4 (1.62)	12.9 (1.49)	12.4 (1.78)
Alkaline phosphatase, U/L			
N	92	39	73
Mean (SD)	193.6 (294.45)	177.4 (243.16)	256.7 (302.12)
Comorbidities requiring treatment, *n* (%)			

Any	121 (100.0)	47 (100.0)	100 (100.0)
Cardiovascular	101 (83.5)	36 (76.6)	84 (84.0)
Hypertension	84 (69.4)	31 (66.0)	76 (76.0)
Angina pectoris	7 (5.8)	5 (10.6)	7 (7.0)
Myocardial infarction	18 (14.8)	4 (8.5)	11 (11.0)
Arrhythmia	9 (7.4)	6 (12.8)	12 (12.0)
Thromboembolic disease	5 (4.1)	0	3 (3.0)
Cerebrovascular accident	6 (5.0)	2 (4.3)	5 (5.0)
Transient ischemic attack	2 (1.7)	0	3 (3.0)
Other cardiovascular	29 (24.0)	10 (21.3)	13 (13.0)
Respiratory	14 (11.6)	6 (12.8)	11 (11.0)
Chronic obstructive pulmonary disease	9 (7.4)	5 (10.6)	9 (9.0)
Other respiratory	5 (4.1)	2 (4.3)	2 (2.0)
Renal	10 (8.3)	12 (25.5)	7 (7.0)
Chronic renal disease	7 (5.8)	6 (12.8)	4 (4.0)
Other renal	3 (2.5)	6 (12.8)	3 (3.0)
Hepatic	2 (1.7)	0	4 (4.0)
Chronic hepatic disease	1 (0.8)	0	2 (2.0)
Other hepatic	1 (0.8)	0	2 (2.0)
Neurologic	13 (10.7)	4 (8.5)	12 (12.0)
Peripheral sensory impairment	0	0	1 (1.0)
Memory impairment	1 (0.8)	1 (2.1)	1 (1.0)
Cognitive disorder	1 (0.8)	1 (2.1)	0
Other neurologic	5 (4.1)	0	2 (2.0)
Infections	0	1 (2.1)	0
Other infection	0	1 (2.1)	0
Diabetes mellitus	121 (100.0)	47 (100.0)	100 (100.0)

Type 2	87 (71.9)	36 (76.6)	82 (82.0)
Type 1	34 (28.1)	11 (23.4)	18 (18.0)
Investigations			
Hypercholesterolemia	24 (19.8)	11 (23.4)	21 (21.0)

ECOG Eastern Cooperative Oncology Group, *M* metastatic status, *N* number of evaluable patients for each specific parameter, *PSA* prostate-specific antigen, *SD* standard deviation

Table S4B. Treatment history at study inclusion in patients with diabetes mellitus in the first-line treatment population

Prior treatment, *n* (%)	Abiraterone *N* = 121	Enzalutamide *N* = 47	Docetaxel *N* = 100
Orchiectomy since initial diagnosis	7 (5.8)	4 (8.5)	7 (7.0)
Radical prostatectomy/prostate-specific radiotherapy since initial diagnosis			
Both radical prostatectomy and prostate-specific radiotherapy	10 (8.3)	4 (8.5)	14 (14.0)
Radical prostatectomy only	15 (12.4)	4 (8.5)	10 (10.0)
Prostate-specific radiotherapy only	36 (29.8)	12 (25.5)	23 (23.0)
None	60 (49.6)	27 (57.4)	53 (53.0)
Prior systemic anticancer therapy			
Any	115 (95.0)	46 (97.9)	94 (94.0)
Endocrine therapy	112 (92.6)	45 (95.7)	93 (93.0)
Antiandrogen	96 (79.3)	42 (89.4)	81 (81.0)
GnRH-agonist	74 (61.2)	30 (63.8)	73 (73.0)
Steroids	6 (5.0)	4 (8.5)	14 (14.0)
GnRH antagonist	12 (9.9)	1 (2.1)	5 (5.0)
Estrogens and derivatives	2 (1.7)	2 (4.3)	2 (2.0)
Adrenal synthesis inhibitors	2 (1.7)	0	1 (1.0)
Other	0	1 (2.1)	0
Bone-targeted			
Any	21 (17.4)	9 (19.1)	24 (24.0)
Zoledronic acid	16 (13.2)	5 (10.6)	18 (18.0)
Denosumab	5 (4.1)	3 (6.4)	3 (3.0)
Other	1 (0.8)	3 (6.4)	4 (4.0)

Other	3 (2.5)	1 (2.1)	1 (1.0)

GnRH gonadotropin-releasing hormone

Table S5A. Patient demographics and disease and biological characteristics at study inclusion in patients with visceral metastases in the first-line treatment population

Characteristic	Abiraterone *N* = 59	Docetaxel *N* = 88
Age		
Mean (SD) years	75.9 (7.54)	69.3 (8.07)
Median (range), years	76.0 (49–93)	70.0 (53–83)
Age group, *n* (%)		
<65 years	2 (3.4)	28 (31.8)
65–74 years	25 (42.4)	33 (37.5)
≥75 years	32 (54.2)	27 (30.7)
ECOG performance status, *n* (%)		
N	55	87
0	23 (41.8)	34 (39.1)
1	26 (47.3)	46 (52.9)
≥2	6 (10.9)	7 (8.0)
Gleason score at initial diagnosis, *n* (%)		
N	52	85
≤6	8 (15.4)	7 (8.2)
7	15 (28.8)	26 (30.6)
8–10	29 (55.8)	52 (61.2)
M stage at initial diagnosis, *n* (%)		
N	57	86
Mx	13 (22.8)	12 (14.0)
M0	23 (40.4)	31 (36.0)
M1, M1a, M1b, M1c	21(36.8)	43 (50.0)
Time from initial prostate cancer diagnosis to start of the study		

N	59	88
Median years (range)	5.3 (1–29)	2.6 (0–22)
Presence of bone metastases, n (%)		
N	37	61
Any	32 (86.5)	56 (91.8)
≥5	17 (45.9)	30 (49.2)
Visceral metastases, n (%)		
N	59	88
Liver only	13 (22.0)	39 (44.3)
Lung only	39 (66.1)	40 (45.5)
Liver and lung	7 (11.9)	9 (10.2)
Biological parameters		
PSA, ng/mL		
N	58	83
Mean (SD)	192.25 (663.193)	187.05 (395.683)
Lactic acid dehydrogenase, U/L		
N	25	44
Mean (SD)	365.8 (386.82)	381.8 (275.10)
Hemoglobin, g/dL		
N	52	73
Mean (SD)	12.1 (2.03)	12.5 (1.82)
Alkaline phosphatase, U/L		
N	45	58
Mean (SD)	232.9 (422.23)	181.1 (137.80)
Comorbidities requiring treatment, n (%)		
Any	46 (78.0)	57 (64.8)
Cardiovascular	37 (62.7)	53 (60.2)
Hypertension	26 (44.1)	43 (48.9)

Angina pectoris	1 (1.7)	7 (8.0)
Myocardial infarction	4 (6.8)	5 (5.7)
Arrhythmia	7 (11.9)	10.(11.4)
Thromboembolic disease	2 (3.4)	7 (8.0)
Cerebrovascular accident	1 (1.7)	1 (1.1)
Other cardiovascular	15 (25.4)	12 (13.6)
Respiratory	11 (18.6)	5 (5.7)
Chronic obstructive pulmonary disease	9 (15.3)	2 (2.3)
Other respiratory	2 (3.4)	3 (3.4)
Renal	3 (5.1)	7 (8.0)
Chronic renal disease	1 (1.7)	3 (3.4)
Other renal	2 (3.4)	4 (4.5)
Hepatic	1 (1.7)	1 (1.1)
Other hepatic	1 (1.7)	1 (1.1)
Neurologic	2 (3.4)	3 (3.4)
Peripheral sensory impairment	0	1 (1.1)
Other neurologic	1 (1.7)	1 (1.1)
Infections	1 (1.7)	0
Other infection	1 (1.7)	0
Diabetes mellitus	14 (23.7)	21 (23.9)
Type 2	9 (15.3)	15 (17.0)
Type 1	5 (8.5)	6 (6.8)
Investigations		
Hypercholesterolemia	11 (18.6)	13 (14.8)

ECOG Eastern Cooperative Oncology Group, *M* metastatic status, *N* number of evaluable patients for each specific parameter, *PSA* prostate-specific antigen, *SD* standard deviation

Table S5B. Treatment history at study inclusion in patients with visceral metastases in the first-line treatment population

Prior treatment, n (%)	Abiraterone N = 59	Docetaxel N = 88
Orchiectomy since initial diagnosis	1 (1.7)	6 (6.8)
Radical prostatectomy/prostate-specific radiotherapy since initial diagnosis		
Both radical prostatectomy and prostate-specific radiotherapy	8 (13.6)	9 (10.2)
Radical prostatectomy only	6 (10.2)	10 (11.4)
Prostate-specific radiotherapy only	12 (20.3)	19 (21.6)
None	33 (55.9)	50 (56.8)
Prior systemic anticancer therapy		
Any	57 (96.6)	82 (93.2)
Endocrine therapy	56 (94.9)	82 (93.2)
Antiandrogen	50 (84.7)	71 (80.7)
GnRH-agonist	31 (52.5)	58 (65.9)
Steroids	5 (8.5)	8 (9.1)
GnRH antagonist	6 (10.2)	5 (5.7)
Estrogens and derivatives	2 (3.4)	2 (2.3)
Adrenal synthesis inhibitors	0	2 (2.3)
Bone-targeted		
Any	9 (15.3)	24 (27.3)
Zoledronic acid	6 (10.2)	20 (22.7)
Denosumab	2 (3.4)	5 (5.7)
Other	2 (3.4)	1 (1.1)

GnRH gonadotropin-releasing hormone