PROSTATE CANCER REGISTRY

Real-World Outcomes in First-Line Treatment of Metastatic Castration-Resistant Prostate Cancer (mCRPC): The Prostate Cancer Registry

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BACKGROUND

- In the management of metastatic castration-resistant prostate cancer (mCRPC), the availability of new therapeutic options is changing the treatment landscape,[1] while our understanding of the optimal use of chemotherapy is also evolving.[2]
- As such, there are important knowledge gaps around how to optimize the use of different treatment options within clinical practice to achieve maximum patient benefit.
- Observational studies can help address these gaps by providing valuable insights into real-world management that can complement data from interventional clinical trials.[3]
- The Prostate Cancer Registry is the first prospective, international, observational study of patients with mCRPC.[4-7]

OBJECTIVES

- The overall objective of the Prostate Cancer Registry is to document the characteristics, management, and outcomes of > 3000 men with mCRPC in routine clinical practice, independent of treatment used.
- This poster reports the results of an interim analysis in patients who received first-line mCRPC treatment on the Registry.

METHODS

Study Design

- The Prostate Cancer Registry is a prospective, noninterventional, multicenter registry of > 3000 men with mCRPC (ClinicalTrials.gov ID: NCT02236637), conducted at 199 centers in 16 countries in Europe.
- Enrollment was initiated in June 2013 and completed in early 2016. Study duration will be 5.5 years, with a maximum patient follow-up of 3 years.
- Eligible patients were male, aged ≥ 18 years, with confirmed diagnosis of adenocarcinoma of the prostate and documented castration-resistant metastatic disease, enrolled at any time after diagnosis; a history of disease progression despite surgical or chemical androgen deprivation therapy was confirmed in all patients.
- Patients were currently in surveillance according to clinical practice or were initiating a new systemic treatment for mCRPC within 30 days of baseline data collection.
- Signed informed consent/participation agreement, as applicable, was required.

Data Collection and Analysis

- Prior disease history and management data were collected at study inclusion.
- Clinical data were collected at study inclusion and prospectively every 3 months (where available) during follow-up.
- The analysis involved patients enrolled in the study up until and including 31 March 2015 with ≥ 12 months of follow-up (or less in case of early withdrawal, loss to follow-up, or death) who had received no prior systemic therapy for mCRPC and who received their first treatment for mCRPC on study.
- Due to the observational nature of the Registry, this analysis attempted to reduce the effects of confounding when evaluating comparative effectiveness between treatments, as measured by time to progression (TTP), by estimating an adjusted treatment effect using propensity scoring methods.

RESULTS

- There were 1906 evaluable patients with ≥ 12 months of follow-up data available as of June 2016 (median duration of follow-up 14.8 months, range 0.2-33.6).
- Of these 1906 patients, among those with no prior treatment for mCPRC, first mCRPC treatments (initiated in ≥ 50 patients) on study were abiraterone acetate plus prednisone (AAP) (n = 472), enzalutamide (n = 98), and docetaxel (n = 382).

Patient Demographics, Disease Characteristics, and Prior Treatments

- Patient demographics and disease and biological characteristics at study inclusion are summarized in Table 1.
- Patients who received docetaxel as first-line mCRPC treatment on study tended to be younger and to have had a shorter time from initial diagnosis to castration resistance than those who received the androgen inhibitors AAP and enzalutamide.
- A higher proportion of patients who received docetaxel had ≥ 5 bone metastases at study entry compared with patients who received androgen inhibitors. Baseline prostate-specific antigen (PSA) levels were also highest among patients who received docetaxel.

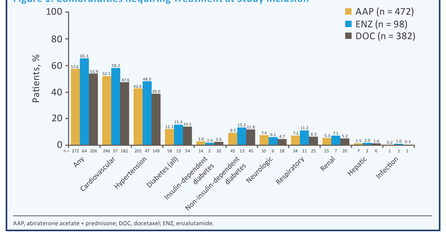
Table 1. Patient Demographics, Disease, and Biological Characteristics at Study Inclusion

Characteristic	AAP (n = 472)	ENZ (n = 98)	DOC (n = 382)
Age, mean (SD) years	n = 472 75.0 (8.3)	n = 98 73.6 (7.7)	n = 382 69.7 (7.7)
Age group, years, n (%)	n = 472	n = 98	n = 382
< 65	52 (11.0)	12 (12.2)	93 (24.3)
65-69	65 (13.8)	18 (18.4)	87 (22.8)
70-74	81 (17.2)	17 (17.3)	95 (24.9)
≥ 75	274 (58.1)	51 (52.0)	107 (28.0)
ECOG performance status, n (%)	n = 454	n = 87	n = 353
0	203 (44.7)	53 (60.9)	118 (33.4)
1	208 (45.8)	25 (28.7)	196 (55.5)
≥ 2	43 (9.5)	9 (10.3)	39 (11.0)
Gleason score at initial diagnosis, n (%)	n = 422	n = 93	n = 367
≤ 6	60 (14.2)	17 (18.3)	42 (11.4)
7	141 (33.4)	30 (32.3)	123 (33.5)
8-10	221 (52.4)	46 (49.5)	202 (55.0)
M stage at initial diagnosis, n (%)	n = 454	n = 96	n = 376
Mx	98 (21.6)	17 (17.7)	60 (16.0)
M0	187 (41.2)	46 (47.9)	138 (36.7)
M1, M1a, M1b, M1c	169 (37.2)	33 (34.4)	178 (47.3)
Time from initial diagnosis to castration resistance, median years (range)	n = 468 3.6 (0.0-28.0)	n = 97 3.9 (0.0-18.0)	n = 381 2.1 (0.0-18.0)
Presence of bone metastases, n (%)	n = 362	n = 79	n = 285
Any	328 (90.6)	68 (86.1)	254 (89.1)
≥ 5	143 (39.5)	23 (29.1)	124 (43.5)
PSA, median ng/mL (range)	n = 457 36.4 (0.0-10,710.0)	n = 97 22.0 (0.0-428.3)	n = 377 48.2 (0.0-8523.0)
Lactic acid dehydrogenase, median U/L (range)	n = 187 276.0 (116.0-2149.0)	n = 34 206.0 (131.0-636.0)	n = 139 321.0 (40.0-3232.0)
Hemoglobin, median g/dL (range)	n = 413 12.8 (8.0-17.0)	n = 87 13.1 (10.0-17.0)	n = 348 12.8 (7.0-16.0)
Alkaline phosphatase, median U/L (range)	n = 380 110.5 (2.0-2228.0)	n = 82 85.0 (1.0-536.0)	n = 272 119.5 (1.0-2023.0)
Serum testosterone, median ng/dL (range)	n = 351 0.30 (0.0-116.0)	n = 65 0.4 (0.0-19.4)	n = 307 0.15 (0.0-36.0)

AAP, abiraterone acetate + prednisone; DOC, docetaxel; ECOG, Eastern Cooperative Oncology Group; ENZ, enzalutamide; M, metastatic status; PSA, prostate-specific antigen.

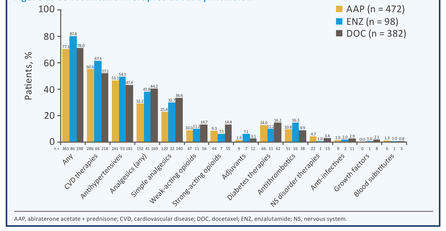
- Overall, more than 50% of patients had comorbid conditions at study inclusion and these were predominantly cardiovascular disorders (47.6-58.2%; 39.0-48.0% had hypertension) (Figure 1).
- More than 75% of patients were receiving concomitant medications, most commonly for cardiovascular disorders (especially antihypertensives) (Figure 2).
  - A higher proportion of patients who received docetaxel were receiving strong-acting opioid analgesics compared with patients who received androgen inhibitors.
- Patients who received docetaxel had received slightly less prior local therapy (radical prostatectomy and/or prostate radiotherapy) than those who received androgen inhibitors (Table 2).
- Almost all patients had received prior endocrine therapy in all treatment groups.

Figure 1. Comorbidities Requiring Treatment at Study Inclusion



AAP, abiraterone acetate + prednisone; DOC, docetaxel; ENZ, enzalutamide.

Figure 2. Concomitant Therapies at Study Inclusion



AAP, abiraterone acetate + prednisone; CVD, cardiovascular disease; DOC, docetaxel; ENZ, enzalutamide; NS, nervous system.

Table 2. Treatment History at Study Inclusion

Prior treatment, n (%)	AAP (n = 472)	ENZ (n = 98)	DOC (n = 382)
Radical prostatectomy/prostate-specific radiotherapy since initial diagnosis			
Both radical prostatectomy and prostate-specific radiotherapy	25 (5.3)	8 (8.2)	16 (4.2)
Only radical prostatectomy	84 (17.8)	24 (24.5)	58 (15.2)
Only prostate-specific radiotherapy	110 (23.3)	25 (25.5)	74 (19.4)
None	303 (64.2)	57 (58.2)	266 (69.6)
Prior systemic anticancer therapy			
Any	456 (96.6)	95 (96.9)	373 (97.6)
Chemotherapy	0	0	0
Endocrine therapy	452 (95.8)	95 (96.9)	369 (96.6)
Antiandrogen	394 (83.5)	84 (85.7)	333 (87.2)
GnRH agonist	341 (72.2)	72 (73.5)	307 (80.4)
Steroids	52 (11.0)	11 (11.2)	57 (14.9)
GnRH antagonist	43 (9.1)	5 (5.1)	26 (6.8)
Estrogens and derivatives	20 (4.2)	4 (4.1)	1 (0.3)
Adrenal synthesis inhibitors	5 (1.1)	0	6 (1.6)
Other	6 (1.3)	2 (2.0)	6 (1.6)
Bone-targeted agents			
Any	125 (26.5)	20 (20.4)	115 (30.1)
Zoledronic acid	89 (18.9)	15 (15.3)	76 (19.9)
Denosumab	36 (7.6)	4 (4.1)	26 (6.8)
Other	8 (1.7)	4 (4.1)	23 (6.0)
Other	11 (2.3)	5 (5.1)	11 (2.9)

AAP, abiraterone acetate + prednisone; DOC, docetaxel; ENZ, enzalutamide; GnRH, gonadotropin-releasing hormone.

Clinical Outcomes

- PSA response (≥ 50% decrease in PSA within 6 months from start of treatment) was generally higher for enzalutamide versus AAP or docetaxel, occurring in 52 (59.1%), 181 (42.6%), and 174 (49.3%) patients, respectively.
- Propensity scoring was applied to the results for TTP; potential confounders considered in the propensity score model are listed in Table 3, with those identified as confounders for each treatment comparison indicated.

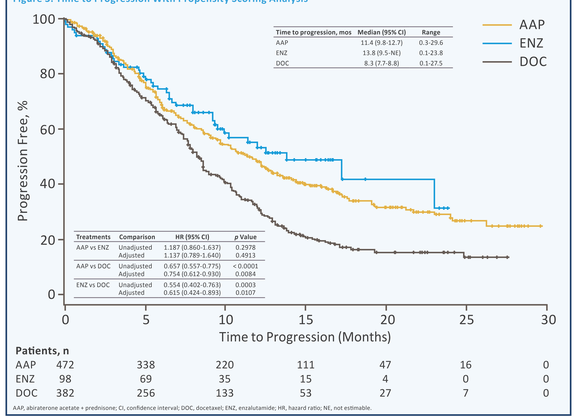
Table 3. Confounders for TTP for Each Treatment Comparison

Potential confounder	Treatment comparisons: AAP vs ENZ	AAP vs DOC	ENZ vs DOC
Age	✔	✔	✔
Time from initial diagnosis to CRPC, log		✔	✔
Time from initial diagnosis to mCRPC, log			✔
Time from mCRPC to study inclusion, log	✔		
Alkaline phosphatase, log IU/L	✔	✔	✔
PSA, log	✔	✔	✔
Hemoglobin, log	✔	✔	✔
Gleason score	✔	✔	
Diabetes disease	✔		✔
Strong opioid analgesic use	✔	✔	✔
Weak opioid analgesic use	✔	✔	✔
Cardiovascular disease	✔	✔	✔
ECOG performance status 2-3		✔	✔
ECOG performance status unknown	✔	✔	
Prior radical prostatectomy	✔	✔	✔
T class 3	✔	✔	✔
T class 4		✔	
T class unknown	✔		✔
N class 1			
N class unknown	✔	✔	
M class 1	✔	✔	✔
M class unknown	✔	✔	✔
Bone lesions 5-20			✔
Bone lesions > 20	✔	✔	✔
Bone lesions unknown		✔	✔

✔ = confounder identified and applied in propensity scoring analysis.
AAP, abiraterone acetate + prednisone; DOC, docetaxel; ECOG, Eastern Cooperative Oncology Group; ENZ, enzalutamide; M, metastatic status; N, node status; PSA, prostate-specific antigen; T, tumor status.

- Median TTP was significantly longer for both AAP (11.4 months) and enzalutamide (13.8 months) versus docetaxel (8.3 months) (Figure 3): $p < 0.0001$ and 0.0084 (unadjusted and adjusted hazard ratios, respectively) for AAP versus docetaxel and $p = 0.0003$ and 0.0107 for enzalutamide versus docetaxel; there was no significant difference in TTP between AAP and enzalutamide ($p = 0.2978$ and 0.4913 for unadjusted and adjusted hazard ratios, respectively).

Figure 3. Time to Progression With Propensity Scoring Analysis



AAP, abiraterone acetate + prednisone; CI, confidence interval; DOC, docetaxel; ENZ, enzalutamide; HR, hazard ratio; NE, not estimable.

CONCLUSIONS

- The study results provide unique insights into routine clinical presentation, treatment, and outcomes in a large, real-world population of patients with mCRPC.
- In the cohort of patients who received first-line mCRPC therapy on the Registry, patients who received docetaxel had more severe disease at study inclusion than those who received the androgen inhibitors AAP or enzalutamide.
- PSA response was generally greater for enzalutamide versus AAP or docetaxel.
- TTP was:
  - significantly longer in patients who received AAP versus docetaxel
  - significantly longer in patients who received enzalutamide versus docetaxel
  - not different between patients who received AAP and those who received enzalutamide.
- Although propensity scoring methods were used to accommodate differences in confounding factors, differences in TTP seen between treatments should be interpreted with caution.
- The TTP results in this analysis are consistent with those seen in randomized clinical trials for AAP and enzalutamide.[8,9]

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