Real-World Treatment Patterns and Treatment Sequences in the Metastatic Castration-Resistant Prostate Cancer Setting Across Europe: a Real-World Survey

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Background

- Prostate cancer (PC) is the second most common cancer worldwide in men[1] with the most common treatments for PC aiming to deprive the cancer of testosterone. However, PC can continue to grow despite castrate levels of testosterone (<20 ng/dL)[2], leading to the development of castrate-resistant PC (CRPC).
- Prior to the Food and Drug Administration's and the European Medicines Agency's approval of novel hormone agents (NHAs) in 2011 for metastatic CRPC (mCRPC)[3], CRPC treatment was limited to the chemotherapy agent docetaxel.[4]
- NHAs have since been approved for the treatment of metastatic hormone-sensitive PC (mHSPC), and are used earlier in the treatment pathway, but evidence for the effectiveness of retreatment with an NHA is limited; there remains a need for advances in novel treatments in the first-line (1L) mCRPC setting or later.[5-6]
- Poly-ADP ribose polymerase (PARP) inhibitors have recently been approved for use in mCRPC, (as a monotherapy and in combination with abiraterone or with enzalutamide). PARP inhibitors are effective in the treatment of patients with mCRPC with homologous recombination repair (HRR) mutations.[7]
- As the treatment landscape in the mCRPC setting continue to evolve, there is a need to understand how patients are being treated in the real-world setting.

Objective

- To describe treatment patterns and sequencing between different lines of treatment in the mCRPC setting, as well as sequencing from mHSPC to 1L mCRPC for patients with mCRPC.

Methods

Study design

- Data were drawn from the Adelphi Real World PC Disease Specific Programme™ (DSP™).
- Descriptive statistics were used, and statistical comparisons were not conducted.

Data source

- The Adelphi Real World PC DSP is a cross-sectional survey, with elements of retrospective data collection, of physicians and their adult patients with metastatic PC (mPC) in France, Germany, Italy, Spain, and the United Kingdom (UK) from November 2022 – May 2023.
- Data sources used for analysis included electronic patient record forms (PRFs), and the physician attitudinal survey from the mCRPC arm only. Both surveys captured physician-reported data.
- The methodology has been previously described,[8-9] validated,[10] and demonstrated to be representative and consistent over time.[11]

Eligibility

- The DSP recruited physicians who met the following criteria:
  - Specialty in medical oncology or urology; saw a minimum of four mPC patients per month; and personally responsible for prescribing decisions for patients with mPC.
- Regarding the mCRPC arm of the DSP, physicians reported data on the next eight consecutively consulting patients with mCRPC meeting the eligibility criteria:
  - Age ≥18 years at diagnosis; physician-confirmed diagnosis of mCRPC; receiving active drug treatment for mCRPC; and not participating or ever participated, in a clinical trial at time of data collection.
- Patients with PC as their only malignancy were included in the analysis.

Study variables

- Study variables included patient demographics/clinical characteristics, treatment patterns and reasons for treatment. Descriptive statistics were used to describe demographics/clinical characteristics, treatment patterns, treatment sequencing and physician-stated reasons for treatment.

Results

- Overall, 221 physicians (France n=48; Germany n=50; Italy n=42; Spain n=47; UK n=34) reported data on a total of n=1737 patients.
- Of the physicians surveyed, 84% were medical oncologists and 16% were urologists; 60% of physicians worked in an academic setting and 40% worked in a community setting.

Patient demographics and clinical characteristics

- At data collection, median (interquartile range; IQR) patient age was 73.0 (68.0–78.0) years, 46% of patients had high-volume disease, and 77% had an ECOG score 0–1. Initial PC diagnosis was localized/locally advanced disease (50%) and median (IQR) time since mCRPC diagnosis was 159.2 (79.0–359.2) days (Table 1).
- Of all patients with mCRPC, 69% (n=1194) had recorded mHSPC treatment history.

Table 1. Patient demographics and clinical characteristics

	All patients (n=1737)	France (n=388)	Germany (n=394)	Italy (n=335)	Spain (n=348)	UK (n=272)
Patient demographics						
Age in years, median (IQR)	73.0 (68.0–78.0)	75.0 (69.2–79.0)	70.0 (68.0–73.2)	74.0 (70.0–80.0)	73.0 (68.0–78.0)	73.0 (68.0–78.0)
Days since mCRPC diagnosis (IQR)	159.5 (79.0–359.2)	156.5 (79.0–356.8)	153.0 (95.0–252.0)	148.0 (50.0–426.0)	182.0 (81.5–374.5)	159.5 (79.0–359.2)
Gleason score at initial diagnosis (IQR)	8.0 (7.0–8.0)	8.0 (7.0–8.0)	7.0 (7.0–8.0)	8.0 (7.0–8.8)	8.0 (7.0–9.0)	8.0 (7.0–9.0)
ECOG score at data collection, n (%)						
0–1	1337 (77)	278 (72)	245 (62)	278 (83)	302 (87)	234 (86)
2–4	397 (23)	109 (28)	147 (37)	57 (17)	46 (13)	38 (14)
Unknown	3 (<1)	1 (<1)	2 (<1)	0 (0)	0 (0)	0 (0)
Patient family history of cancer, n (%)						
Family history	205 (12)	44 (11)	35 (9)	56 (17)	54 (16)	16 (6)
No family history	1413 (81)	325 (84)	316 (80)	263 (79)	277 (80)	232 (85)
Unknown	119 (7)	19 (5)	43 (11)	16 (5)	17 (5)	24 (9)
Disease stage at initial diagnosis, n (%)						
Localized / Locally advanced disease	864 (50)	190 (49)	268 (68)	189 (56)	137 (39)	80 (29)
Metastatic disease	844 (49)	197 (51)	119 (30)	139 (41)	200 (57)	189 (69)
Unknown / Not assessed	24 (1)	1 (<1)	7 (2)	7 (2)	11 (3)	3 (1)
Physician-reported high-volume disease, n (%)						
High-volume disease	805 (46)	166 (43)	111 (28)	174 (52)	205 (59)	149 (55)
Not high-volume disease	876 (50)	212 (55)	257 (65)	148 (44)	140 (40)	119 (44)
Don't know	56 (3)	10 (3)	26 (7)	13 (4)	3 (1)	4 (1)
Metastases, n (%)						
Visceral metastases	478 (28)	96 (25)	95 (24)	126 (38)	91 (26)	70 (26)
Non-visceral metastases	1259 (72)	292 (75)	299 (76)	209 (62)	257 (74)	202 (74)

ECOG – Eastern Cooperative Oncology Group; IQR – interquartile range; mCRPC – metastatic castration-resistant prostate cancer; UK – United Kingdom.

Treatment patterns in the mCRPC setting

- At data collection, 83% of patients (n=1436) were receiving first-line (1L) treatment, 15% (n=260) were at second-line (2L), and 2% (n=41) were at third-line (3L) or later.
- Overall, at 1L (of all patients with recorded 1L treatment history; n=1737), 60% of patients received an NHA (abiraterone [abi] 31%; enzalutamide [enza] 28%; darolutamide [daro] 1%; Figure 1) ± androgen deprivation therapy (ADT), and 24% received chemotherapy (docetaxel [doce] 22%; cabazitaxel [caba] 2%; Figure 1) ± ADT.
- In Germany, usage of NHA ± ADT was present in less than half of patients (42%; Figure 1).
- Overall, at 2L (of all patients with recorded 2L treatment history; n=301) 42% of patients received chemotherapy ± ADT (doce 28%; caba 14%; Figure 1), and 35% received NHA ± ADT (enza 20%; abi 13%; daro 1%; Figure 1).
- Overall, at 3L (of all patients with recorded 3L treatment history) (n=41), 46% of patients received chemotherapy ± ADT (caba 32%; doce 15%; Figure 1) and 29% received NHA ± ADT (abi 12%; enza 12%; daro 5%).

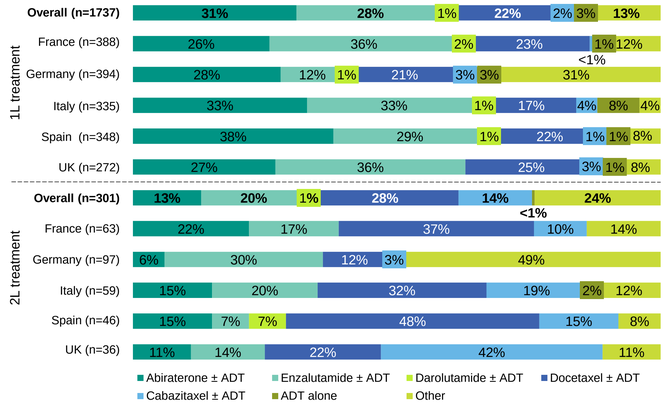
Duration of mCRPC treatment at first-line and second-line

- Overall, median (IQR) treatment duration for 1L mCRPC treatment for patients with known start and end dates of treatment (n=220) was 304.0 (173.2–610.0) days, and median (IQR) treatment duration for 2L mCRPC treatment (n=38) was 204.0 (128.2–426.0) days.
- For patients who had received 1L NHA ± ADT and with known treatment start and end dates (n=142), median (IQR) treatment duration was 452.5 (241.0–735.2) days, and for patients who had received 2L NHA ± ADT (n=12) it was 466.5 (417.8–625.5) days.
- For patients who had received 1L chemotherapy ± ADT and with known treatment start and end dates, median (IQR) treatment duration was 154.0 (122.0 – 192.0; n=57) days, whilst for 2L chemotherapy ± ADT, the treatment duration was 161.0 (126.8-230.8, n=20) days.

Reasons for treatment choice (physician-stated)

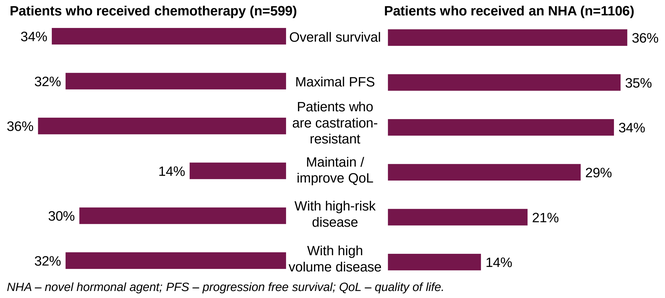
- Overall, the most common reasons cited for why NHAs were prescribed were: their suitability for patients for whom the priority is "overall survival" (36%), and "maximal progression-free survival" (35%; Figure 2).
- In relation, chemotherapy was regarded as being suitable for patients who have "become castration-resistant" and "whose priority is overall survival" (36% and 34% of physicians, respectively; Figure 2).

Figure 1. Treatment regimens (individual agents) received by patients with mCRPC, by line of therapy



1L – First-line; 2L – Second-line; ADT – androgen deprivation therapy; NHA – novel hormonal agent; UK – United Kingdom. Other includes: darolutamide ± ADT; other NHA ± ADT; other chemotherapy ± ADT; NHA + chemotherapy + ADT; other combinations with NHA; other combinations with chemotherapy; other drugs (see list) ± ADT; NHA + Chemotherapy + ADT (where there are multiple of one of the drug types); and NHA + Chemotherapy + ADT + other drugs (see list). Other drug list: bicalutamide, flutamide, nilutamide, ketoconazole, cyproterone, abarelix, buserelin acetate, sipuleucel-T, pembrolizumab, strontium-89, lutetium lu-177 vipivotide tetraxetan, olaparib, rucaparib.

Figure 2. Physician-reported reasons for treatment choice

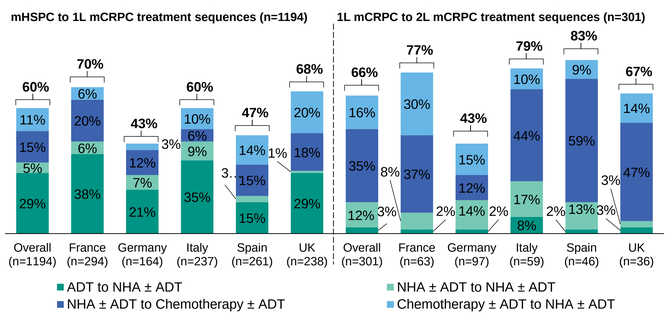


NHA – novel hormonal agent; PFS – progression free survival; QoL – quality of life.

Treatment sequencing: mCRPC treatment and mHSPC treatment immediately prior [Figures 3a-3d]

- For mCRPC patients with a recorded treatment history of mHSPC (n=1194), 29% of these received ADT alone at mHSPC followed by NHA ± ADT at 1L mCRPC (enza 14%; abi 13%; daro <1%). Whilst 15% received NHA ± ADT at mHSPC then chemotherapy ± ADT (doce 14%; caba <1%) at 1L mCRPC.
  - For patients who received NHA ± ADT in the mHSPC setting (24%, n=291; abi 12%; enza 7%; apalutamide 5%), 60% received chemotherapy ± ADT (doce 58%; caba 2%) at 1L mCRPC, and 21% were rechallenged with NHA ± ADT (abi 12%; enza 9%). NHA + chemotherapy + ADT was received by 9%, 2% received ADT alone and 8% received other treatments at 1L mCRPC.
- For all patients who had received 2L mCRPC treatment (n=301), the most common 1L to 2L sequence was NHA ± ADT to chemotherapy ± ADT (35%). The second most common sequence was chemotherapy ± ADT to NHA ± ADT (16%).
- For all patients who were receiving 3L mCRPC treatment (n=41), the most common 2L to 3L sequence was NHA ± ADT to chemotherapy ± ADT (27%).

Figure 3a. Proportion of patients who received key treatment sequences



The proportions of each stacked bar represent the proportion of patients, compared to the respective base, who were treated with the most common treatment sequences depicted in the figure. The proportion of patients not shown were treated with other, less common, sequences.

Figure 3b. Treatment sequencing: mHSPC to 1L mCRPC

Figure 3c. Treatment sequencing: 1L mCRPC to 2L mCRPC

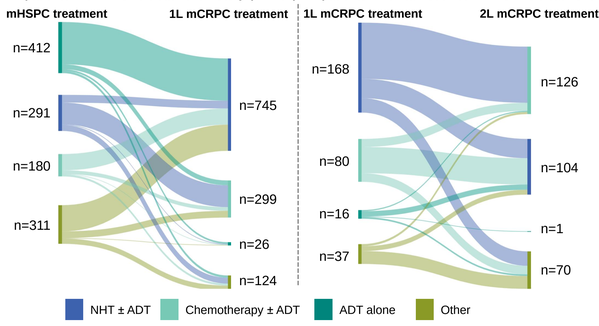
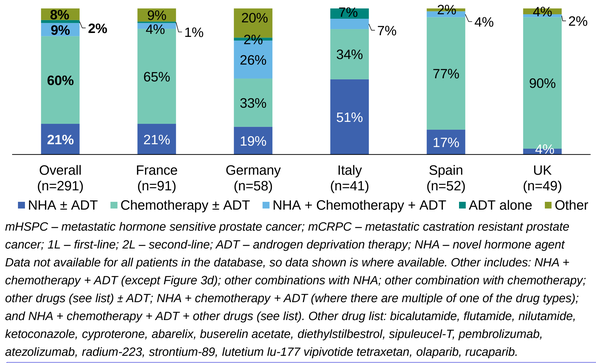


Figure 3d. 1L mCRPC regimen for patients treated with NHA at the mHSPC setting



mHSPC – metastatic hormone sensitive prostate cancer; mCRPC – metastatic castration resistant prostate cancer; 1L – first-line; 2L – second-line; ADT – androgen deprivation therapy; NHA – novel hormone agent Data not available for all patients in the database, so data shown is where available. Other includes: NHA + chemotherapy + ADT (except Figure 3d); other combinations with NHA; other combination with chemotherapy; other drugs (see list) ± ADT; NHA + chemotherapy + ADT (where there are multiple of one of the drug types); and NHA + chemotherapy + ADT + other drugs (see list). Other drug list: bicalutamide, flutamide, nilutamide, ketoconazole, cyproterone, abarelix, buserelin acetate, diethylstilbestrol, sipuleucel-T, pembrolizumab, atezolizumab, radium-223, strontium-89, lutetium lu-177 vipivotide tetraxetan, olaparib, rucaparib.

Conclusions

- This real-world analysis shows that NHA usage frequently occurs prior to chemotherapy use in the mCRPC setting.
  - Alternatively, for patients who received chemotherapy at 1L mCRPC treatment, most patients went on to receive an NHA at 2L mCRPC treatment.
- However, most patients are NHA naïve at mCRPC diagnosis, despite guideline recommendations for NHA usage at the mHSPC setting.
  - Patients with an mHSPC treatment history who received ADT alone in the mHSPC setting often went on to receive an NHA at 1L mCRPC treatment.
- Where data was available, median duration of 1L treatment was, on average, 100 days longer than 2L treatment duration.
  - Across 1L and 2L, treatment duration was longer with an NHA than with chemotherapy.

Limitations

- Participating patients may not reflect the general mCRPC population since the DSP only includes patients who are consulting with their physician. This means that patients who consult more frequently have a higher likelihood of being included. Recall bias, a common limitation of surveys, might also have affected responses of both physicians and patients. However, physicians did have the ability to refer to the patients' records while completing the PRF, thus minimizing the possibility of recall bias.

Disclosures

- Data collection was undertaken by Adelphi Real World as part of an independent survey, entitled the Adelphi Real World Prostate Cancer Disease Specific Programme. Merck & Co., Inc., Rahway, NJ, USA. did not influence the original survey through either contribution to the design of questionnaires or data collection. The analysis described here used data from the Adelphi Real World Prostate Cancer DSP. The DSP is a wholly owned Adelphi Real World product. Merck & Co., Inc., Rahway, NJ, USA.. is one of multiple subscribers to the DSP. Publication of survey results was not contingent on the subscriber's approval or censorship of the publication.
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