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## Supplementary Material

# Insights into Treatment Patterns in the Routine Care of Patients Diagnosed with Metastatic Castration-Resistant Prostate Cancer in Germany After the Introduction of New Therapies

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ABSTRACT

**Background:** Clinical treatment guidelines for metastatic castration-resistant prostate cancer (mCRPC) predominantly rely on the evidence from clinical trials, which frequently apply restrictive eligibility criteria resulting in selected patient populations. Therefore, real world treatment pattern may deviate from recommendations. We aimed to describe treatment patterns including sequencing and treatment duration of patients diagnosed with mCRPC in Germany, by characterizing the demographic and clinical characteristics of patients.

**Methods:** A large German claims database was used to identify males who were diagnosed and treated for mCRPC (ICD-10-GM code C61) between January 2013 and December 2015. Patients were required to be continuously enrolled 12 months before initiation of treatment with abiraterone, cabazitaxel, docetaxel, or enzalutamide. Study endpoints included lines of therapy, treatment duration and treatment sequencing. Treatment duration was calculated via Kaplan-Meier estimates.

**Results:** There were n=447 patients meeting all inclusion criteria in the database. Mean age (±SD) was 72.9 (±8.8) years, mean Charlson comorbidity index was 8.1, there were on average 1.9 hospitalizations within the 12 months before the index, and 70% of patients presented with bone metastasis. Overall, abiraterone was the most commonly prescribed treatment across lines of therapy while cabazitaxel, was the least utilized therapy. The longest treatment duration was seen in abiraterone patients (median duration of 8.3 months in first and 7.4 months in second line). Switches between abiraterone and docetaxel in first and second line were common. Among the 447 patients more than 70 different pathways were identified.

**Conclusion:** There was a significant variability in treatment pathways pointing to a highly individualized treatment approach in spite of detailed treatment algorithms. Even in third line, systemic therapies were still being prescribed. Furthermore, this study showed that routine-care data are a valuable source to assess the actual treatment pathways on a cohort but also on an individual level.



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**Supplementary Table 1:** Comorbidities by treatment of index line.

| **Abiraterone** | | **Cabazitaxel** | | **Docetaxel** | | **Enzalutamide** | |
|---|---|---|---|---|---|---|---|
| **Description** | **N (%)** | **Description** | **N (%)** | **Description** | **N (%)** | **Description** | **N (%)** |
| Essential (primary) hypertension | 198 (79%) | Secondary malignant neoplasm of other and unspecified sites | 2 (100%) | Essential (primary) hypertension | 92 (69%) | Essential (primary) hypertension | 45 (74%) |
| Secondary malignant neoplasm of other and unspecified sites | 166 (66%) | Disorders of lipoprotein metabolism and other lipidaemias | 2 (100%) | Dorsalgia | 65 (49%) | Secondary malignant neoplasm of other and unspecified sites | 41 (67%) |
| Disorders of lipoprotein metabolism and other lipidaemias | 122 (49%) | Obesity | 1 (50%) | Disorders of lipoprotein metabolism and other lipidaemias | 63 (47%) | Disorders of lipoprotein metabolism and other lipidaemias | 40 (66%) |
| Dorsalgia | 108 (43%) | Non-insulin-dependent diabetes mellitus | 1 (50%) | Secondary and unspecified malignant neoplasm of lymph nodes | 52 (39%) | Dorsalgia | 27 (44%) |
| Disorders of refraction and accommodation | 88 (35%) | Other aplastic anaemias | 1 (50%) | Hyperplasia of prostate | 41 (31%) | Disorders of refraction and accommodation | 22 (36%) |
| Other disorders of urinary system | 80 (32%) | Anaemia in chronic diseases classified elsewhere | 1 (50%) | Disorders of refraction and accommodation | 41 (31%) | Hyperplasia of prostate | 21 (34%) |
| Non-insulin-dependent diabetes mellitus | 78 (31%) | Secondary and unspecified malignant neoplasm of lymph nodes | 1 (50%) | Pain, not elsewhere classified | 38 (28%) | Chronic ischaemic heart disease | 17 (28%) |
| Chronic ischaemic heart disease | 71 (28%) | Secondary malignant neoplasm of respiratory and digestive organs | 1 (50%) | Other disorders of urinary system | 38 (28%) | Non-insulin-dependent diabetes mellitus | 14 (23%) |
| Hyperplasia of prostate | 62 (25%) | Depressive episode | 1 (50%) | Non-insulin-dependent diabetes mellitus | 36 (27%) | Chronic kidney disease | 14 (23%) |
| Secondary and unspecified malignant neoplasm of lymph nodes | 60 (24%) | Disorders of purine and pyrimidine metabolism | 1 (50%) | Chronic ischaemic heart disease | 36 (27%) | Other disorders of urinary system | 12 (20%) |
| Spondylosis | 55 (22%) | Other anxiety disorders | 1 (50%) | Secondary malignant neoplasm of respiratory and digestive organs | 32 (24%) | Unspecified urinary incontinence | 12 (20%) |
| Depressive episode | 54 (22%) | Sexual dysfunction, not caused by organic disorder or disease | 1 (50%) | Obstructive and reflux uropathy | 28 (21%) | Secondary and unspecified malignant neoplasm of lymph nodes | 12 (20%) |
| Disorders of purine and pyrimidine metabolism | 53 (21%) | Essential (primary) hypertension | 1 (50%) | Obesity | 27 (20%) | Other retinal disorders | 12 (20%) |
| Pain, not elsewhere classified | 52 (21%) | Other conduction disorders | 1 (50%) | Disorders of purine and pyrimidine metabolism | 27 (20%) | Senile cataract | 12 (20%) |
| Unspecified urinary incontinence | 48 (19%) | Atrioventricular and left bundle-branch block | 1 (50%) | Sleep disorders | 26 (19%) | Atrial fibrillation and flutter | 11 (18%) |
| Somatoform disorders | 47 (19%) | Pulmonary embolism | 1 (50%) | Depressive episode | 25 (19%) | Other cardiac arrhythmias | 11 (18%) |
| Gonarthrosis [arthrosis of knee] | 47 (19%) | Complications and ill-defined descriptions of heart disease | 1 (50%) | Senile cataract | 24 (18%) | Heart failure | 11 (18%) |
| Other retinal disorders | 46 (18%) | Phlebitis and thrombophlebitis | 1 (50%) | Other diseases of liver | 24 (18%) | Other chronic obstructive pulmonary disease | 11 (18%) |
| Other dorsopathies, not elsewhere classified | 46 (18%) | Other venous embolism and thrombosis | 1 (50%) | Gastritis and duodenitis | 24 (18%) | Pain, not elsewhere classified | 10 (16%) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Other cataract | 45 (18%) | Other disorders of urinary system | 1 (50%) | Gastro-oesophageal reflux disease | 23 (17%) | Spondylosis | 10 (16%) |

**Supplementary Table 2:** Number of patients for all determined treatment paths with n=>2.

| **Regimen** | **Number of Patients** |
|---|---|
| Abiraterone | 131 |
| Docetaxel | 57 |
| Enzalutamide | 43 |
| Docetaxel-Abiraterone | 36 |
| Abiraterone-Docetaxel | 18 |
| Abiraterone-Enzalutamide | 18 |
| Abiraterone-Abiraterone | 14 |
| Docetaxel-Enzalutamide | 11 |
| Docetaxel-Abiraterone-Enzalutamide | 9 |
| Abiraterone-Docetaxel-Enzalutamide | 6 |
| Abiraterone-Abiraterone-Abiraterone | 4 |
| Docetaxel-Abiraterone-Cabazitaxel | 4 |
| Docetaxel-Cabazitaxel | 4 |
| Abiraterone-Abiraterone-Enzalutamide | 3 |
| Docetaxel-Abiraterone-Abiraterone | 3 |
| Docetaxel-Abiraterone-Cabazitaxel-Enzalutamide | 3 |
| Docetaxel-Abiraterone-Enzalutamide-Abiraterone | 3 |
| Docetaxel-Cabazitaxel-Abiraterone | 3 |
| Enzalutamide-Abiraterone | 3 |
| Abiraterone-Docetaxel-Enzalutamide-Cabazitaxel | 2 |
| Abiraterone-Enzalutamide-Abiraterone | 2 |
| Docetaxel-Docetaxel | 2 |
| Docetaxel-Docetaxel-Abiraterone-Enzalutamide | 2 |
| Docetaxel-Enzalutamide-Enzalutamide | 2 |
| Enzalutamide-Docetaxel | 2 |
| Enzalutamide-Docetaxel-Enzalutamide | 2 |
| Enzalutamide-Enzalutamide | 2 |
| Enzalutamide-Enzalutamide-Enzalutamide-Enzalutamide | 2 |
| Truncated treatment paths used in only one patient | 49 |

**Supplementary Table 3:** Overview of pivotal trial eligibly criteria in key mCRPC trials.

| **Therapy** | **Docetaxel** | **Abiraterone** | **Cabazitaxel** | **Enzalutamide** |
|---|---|---|---|---|
| Trial name (ref) | Tax 327[29, 30] | COU-AA-301[31] | TROPIC[32] | AFFIRM [33] |
| **Age** | | | | |
| For inclusion | 30+ | none | 18+ | none |
| Median age | 68 (range: 36-92) | 69 (range: 39-95) | 68 (IQR 61-73) | 69 (SD 8.1) |
| **Progression** | 3 cons increases in PSA | 2 cons. Increases in PSA | Acc. to RECIST criteria or 2 cons. Increases in PSA | 3 cons. Increases in PSA or radiographically confirmed |
| **Condition** | Karnofsky performance status score of >= 60% | ECOG ≤ 2 | ECOG ≤ 2 | ECOG ≤ 2 |
| **Pre-treatment** | no prior chemo except estramustine or radioisotopes | Docetaxel | Docetaxel | One or two chemo. at least one of which containing docetaxel |
| **Comorbidities** | No prior cancer within the preceding five years, no brain or leptomeningeal metastases, no symptomatic peripheral neuropathy of grade 2 or higher, and no other serious medical condition. | Excluded if abnormal aminotransferase levels serious coexisting nonmalignant disease, active or symptomatic viral hepatitis or chronic liver disease, uncontrolled hypertension, a history of pituitary or adrenal dysfunction, clinically significant heart disease, or previous therapy with ketoconazole | Included if adequate hepatic, renal, and cardiac function; and a left-ventricular ejection fraction of more than 50%<br><br>Excluded if active grade 2 or higher peripheral neuropathy or stomatitis, other serious illness (including secondary cancer), or a history of hypersensitivity to polysorbate 80-containing drugs or prednisone | Excluded if metastases in the brain or active epidural disease Another malignancy within the previous 5 years Clinically significant cardiovascular disease. Gastrointestinal disorder affecting absorption |