Treatment Patterns after Castration-Resistant Prostate Cancer (CRPC) Diagnosis: A European Physician Survey

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Treatment patterns of castration-resistant prostate cancer in Europe are not well studied

- **Prostate cancer** is the most common solid neoplasm in European patients. Androgen deprivation therapy is typically used to treat recurring or metastatic prostate cancer.

- However, approximately 10-20% of prostate cancer patients develop **castration-resistant prostate cancer (CRPC)** within ~5 years of follow-up. CRPC is defined as disease progression despite androgen deprivation therapy.

- CRPC may present as any one or combination of continuous rise in PSA, progression of pre-existing disease or appearance of new metastases and patients have poor survival prognosis (~9-30 months, median of 14 months).

- **Current therapeutic options** for CRPC include continued androgen deprivation, secondary hormonal therapies, immunotherapy (US), and chemotherapy etc.

- Current treatment guidelines are non-specific with respect to sequence of agents, and the few recent studies from the EU have focused on chemotherapy treatment patterns alone
  - After CRPC diagnosis, up to 1/3 receive chemotherapy alone, and another 10-30% chemo with hormonal therapy
  - After 1L docetaxel, other chemotherapies used are mitoxantrone (44%), vinorelbine (22%) and docetaxel (3%), with docetaxel rechallenge being uncommon

- However, there have been **recent drug approvals** in CRPC that call for a re-evaluation of treatment patterns, including cabazitaxel and abiraterone (both approved 2011)

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**Our objectives were to describe clinical treatment patterns of patients after CRPC diagnosis in the EU-5 countries**

Patient level data were derived from IMS Oncology Analyzer: a structured survey of treated prevalence available in 11 countries.

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Physician surveys from 3Q2011, 4Q2011, 1Q2012 and 2Q2012 from the United Kingdom, Germany, France, Italy and Spain</th>
</tr>
</thead>
</table>
| Sampling method | • The survey proportionally covers physician specialties treating targeted cancers in each country  
• The number of patients included is based on epidemiological data for each tumor type and country |
| Physician panel | • Included physicians must be educated and practicing in specialty and meet statistically set reporting cap for each period, and personally treat patients  
• There is high respondent stability across panels and geographic representativeness |
| Data Collection Method | • Physicians consult patients’ charts to complete the medical record abstraction form  
• Data collected are cross-sectional in nature, but also longitudinal as the entire history of the patient’s cancer diagnosis and treatment available to the reporting physician are collected up to the point of the survey |
| Data Elements | Patient demographics, tumor stage and diagnostic test results at various points during past treatment, past surgery and radiotherapy, and past and current chemotherapy, hormonal therapy, and supportive care. |

All data files contain de-identified patient-level data and comply with relevant rules for protecting patient privacy.
We identified 624 CRPC patients who met the study criteria.

**Patient Selection Criteria**

**Inclusion Criteria**
- Subjects of male gender and designated as having prostate cancer, and
- Subject designated by the physician as having castration resistance

**Exclusion Criteria**
- Incomplete date designation for history of castration resistance.
- Patients under 18 years of age

**Patient Treatment Statistics**

- Prostate cancer patients identified: 4479
- CRPC patients identified (14%): 624
- Received 1 treatment (89%): 556
  - 313 of these continued 1st treatment
- Received 2nd treatment (41%): 229
  - 137 of these continued on second treatment
- Received a 3rd treatment (37%): 85

Region-wise distribution:
- UK: 202
- Germany: 128
- Spain: 110
- Italy: 94
- France: 90
Results

• The majority of physicians reporting on MCRPC were medical oncologists (55%), followed by urologists (22%), and radiologists (20%). However, there were variations between countries.*

• More than 3/4 of patients were over 65 years of age, and 58% had been diagnosed with CRPC within the past year.

• Most recent mean Gleason Score (7.77) and PSA levels (88.59 ng/mL) were consistent with CRPC.

• Approximately 90% of patients had at least one metastasis, most commonly to bone (80%), followed by lymph nodes (57%), and lung (8%).

* Differences between countries in terms of patient characteristics or treatment patterns were not tested for significance.

59% had at least 1 co-morbidity

- Diabetes: 20.8%
- Other: 16.5%
- Cardiac Dysfunction: 16.3%
- COPD: 12.0%
- Renal Dysfunction: 5.3%
- Parkinson's: 2.1%
- Liver Dysfunction: 1.9%

Reporting Physician Specialty

- Medical Oncology
- Radiology
- Urology
- Other
Chemotherapy and hormonal therapy were the most frequently used treatments after the diagnosis of CRPC.

### All countries and lines of therapy combined

- **Chemotherapy**: 67.3%
- **Hormonal Therapy**: 48.6%
- **Bone Agents**: 29.8%
- **Corticosteroids**: 28.7%
- **Antiemetics**: 25.6%
- **Radiotherapy**: 21.8%
- **Surgical Procedures**: 12.5%
- **Narcotic Analgesics**: 8.7%
- **Any Other Supportive Treatments**: 6.9%
- **Any Other Treatments**: 2.6%

Note: Percentages are not mutually exclusive. Patients typically will have multiple therapeutic agents.

### Chemotherapy

- **Docetaxel**: 65.4%
- **Cabazitaxel**: 7.9%
- **Others**: 12.2%

### Hormonal Therapy

- **Goserelin**: 20.5%
- **Bicalutamide**: 16.0%
- **Leuprolelin**: 11.1%
- **Abiraterone Acetate**: 10.7%
- **Diethylstilbestrol**: 7.7%
- **Triptorelin**: 5.0%
- **Others**: 5.60%

Other chemotherapy agents include: Mitoxantrone, Estramustine, Carboplatin, Etoposide, Cyclophosphamide, Vinorelbine, Fluorouracil, Paclitaxel, Cisplatin, Vincristine, Mitoxantrone.

Other hormonal agents include: Degarelix, Cyproteroone, Buserelin, Ketoconazole, Flutamide.
Docetaxel was the dominant first and second treatment after CRPC diagnosis, followed by hormonal treatments.
The second treatment after docetaxel and hormonal regimens were mainly single chemotherapy agents.

**First Treatment**
- **D**
- **H** or **H**
- 280
- 225

**Second Treatment (n=97, 35%)**
- **C**
  - 47.4%
- **H**
  - 28.9%
- **C**
  - 5.2%
- **H**
  - 11.3%
- **T**
  - 7.2%
- **N**
  - 3.5%

**Second Treatment (n=110, 49%)**
- **C**
  - 47.3%
- **H**
  - 25.5%
- **C**
  - 1.8%
- **H**
  - 15.5%
- **C + H**
  - 9.1%
- **T**
  - 0.9%
- **N**
  - 0.4%

*Single agent chemotherapies, including docetaxel*
Only 1/3 of patients with bone metastases received bone agents and <20% radiotherapy after CRPC diagnosis

For the management of skeletal metastases EAU guidelines recommend that:
(1) Bisphosphonates should be offered to prevent skeletal complications while balancing the toxicity of these agents.
(2) Palliative radiotherapy and adequate use of analgesics to improve quality of life and provide pain reduction should be considered early.

Possible explanations
(1) Greater prevalence of radiologists treating in UK (42% vs. 20% average)
(2) UK’s NICE recommends against the regular use of bisphosphonates for bone metastases, but indicates that they may be considered for pain relief if analgesics and palliative radiotherapy have failed.

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=502)</th>
<th>UK (n=166)</th>
<th>Germany (n=109)</th>
<th>Spain (n=93)</th>
<th>Italy (n=77)</th>
<th>France (n=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid</td>
<td>34.1%</td>
<td>25.9%</td>
<td>17.6%</td>
<td>17.2%</td>
<td>13.0%</td>
<td>17.5%</td>
</tr>
<tr>
<td>Pamidronic acid</td>
<td>16.5%</td>
<td>17.5%</td>
<td>7.3%</td>
<td>4.6%</td>
<td>1.1%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Denosumab</td>
<td>2.0%</td>
<td>1.0%</td>
<td>0.9%</td>
<td>0.9%</td>
<td>1.1%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Ibandronic acid</td>
<td>0.9%</td>
<td>1.1%</td>
<td>1.1%</td>
<td>1.1%</td>
<td>1.1%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>
Limitations

- Data are obtained through **physician report**, and consequently are dependent on the physician to assign castration-resistant status, and report patient-related and treatment details.

- **Treatments evaluated in this study are those initiated after physician-determined CRPC diagnosis.** Treatments initiated prior to CRPC diagnosis and that may have been ongoing after diagnosis are not the focus of this analysis and are not reported. However, the low rates of treatment for bone metastases and potentially other agents may be attributed to this element of the study design.

- Since the data is based on patient chart abstractions, the **length of patient history after CRPC diagnosis is variable**. Although most patients were diagnosed within 1-4 calendar quarters prior to survey completion, some (1/10) were diagnosed in the same quarter as survey completion, providing limited time to assess long term treatment patterns. As such, this study can only claim to present a picture of **short term treatment patterns post-CRPC diagnosis in the EU-5**.

- Differences between countries in terms of patient characteristics or treatment patterns were **not tested for significance**.
This is the first study to comprehensively describe treatments patterns post-CRPC diagnosis in EU-5

- This study uses the latest survey data on a large sample of European patients and presents a picture of current patient characteristics and detailed treatment patterns in the region.

- Docetaxel was the most common first treatment initiated after CRPC diagnosis (50% of cases), consistent with it being the preferred treatment per European guidelines.

- About 35% of patients receive second treatment after docetaxel, consistent with findings from other countries (37-44%).

- As patients progressed through lines of treatment, docetaxel was used less frequently and supplanted by other chemotherapeutic agents.

- Third treatments were more varied with patients receiving different chemo and hormonal therapies, due to the lack of clinical consensus in this setting.

- Low rates of initiation of bone agents in patients with bone metastases (36%) warrants study on alternative timing and choices.
Questions?

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