Safety results of a phase III trial evaluating androgen deprivation therapy (ADT) + Docetaxel versus ADT alone in hormone-naïve metastatic prostate cancer

GETUG-15/0403 Trial

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A French national multicentric study sponsored by the National Federation of Comprehensive Cancer Centers (FNCLCC) with the collaboration of the French Association of Urologists (AFU).

ABSTRACT # 44666

Progression-free survival (PFS) and overall survival (OS) were evaluated. The target accrual of the GETUG-AFU 15/0403 phase III trial testing Docetaxel in hormone-naïve metastatic prostate cancer was completed from October 2004 to December 2009, 385 patients have been included.

Relative to ADT alone Docetaxel is associated with higher rates of toxicity.

Apart from a higher incidence of febrile neutropenia, overall toxicity was comparable to toxicity rates observed in previous studies in metastatic castration resistant prostate cancer patients.

Systematic use of G-CSF is recommended in this setting.

CONCLUSION

ACKNOWLEDGEMENTS

All the financial partners.

The patients who have accepted to participate in this study.

The IDMC members.

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The main results of the trial were as follows:

**Primary endpoints:**

- Progression-free survival (PFS)
- Overall survival (OS)

**Secondary endpoints:**

- Quality of life
- Hematological and non-hematological toxicity
- Economic evaluation
- Cost effectiveness
- Pathological studies

**Study population:**

- Patients with androgen naïve metastatic prostate cancer
- Age ≥ 45 years
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2
- Prior radiotherapy is allowed if achieved at least a day before inclusion
- Adequate hematological, renal and hepatic function
- Brain metastasis or distant bone metastasis
- No chemotherapy for metastatic disease

**Treatment:**

- ADT (n = 192)
- ADT + Docetaxel (n = 193)

**Results:**

- Adverse events: G3-G4
  - Alopecia: 54% (3% G ≥ 3)
  - Peripheral edema: 29% (1% G ≥ 3)
  - Diarrhea: 30% (1% G ≥ 3)
  - Septic death: 1%
- Systemic use of G-CSF is recommended in this setting.

**Hematologic toxicity grade 3-4**

<table>
<thead>
<tr>
<th>Grade 3-4</th>
<th>ADT alone</th>
<th>ADT + Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>21%</td>
<td>13%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>33%</td>
<td>9%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6%</td>
<td>9%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Extrahematologic toxicity**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>ADT alone</th>
<th>ADT + Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>22%</td>
<td>9%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Constipation</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Evaluation delay due to toxicity (%):**

- ADT alone: 20%
- ADT + Docetaxel: 16%

**Patient’s characteristics:**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ADT alone</th>
<th>ADT + Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>73</td>
<td>75</td>
</tr>
<tr>
<td>Median age (years) (range)</td>
<td>46-79</td>
<td>46-79</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>180</td>
<td>100</td>
</tr>
<tr>
<td>PSA &lt; 65 (ng/ml)</td>
<td>82/45</td>
<td>88/38</td>
</tr>
<tr>
<td>Gleason score &lt; 8</td>
<td>20/5</td>
<td>5/1</td>
</tr>
<tr>
<td>Gleason score ≥ 8</td>
<td>42/19</td>
<td>26/11</td>
</tr>
<tr>
<td>Biochemical progression</td>
<td>28%</td>
<td>22%</td>
</tr>
<tr>
<td>Biochemical progression ≤ 20%</td>
<td>99% (ADT alone)</td>
<td>99% (ADT + Docetaxel)</td>
</tr>
<tr>
<td>Biochemical progression &gt; 20%</td>
<td>1% (ADT alone)</td>
<td>1% (ADT + Docetaxel)</td>
</tr>
</tbody>
</table>

**Safety results of a phase III trial evaluating androgen deprivation therapy (ADT) + Docetaxel in hormone-naïve metastatic prostate cancer.**

**Inclusion criteria:**

- Patients with androgen naïve metastatic prostate cancer who are categorized into risk groups as good (48%), intermediate (29%), and poor prognosis (22%).

**Exclusion criteria:**

- Patients with advanced cancer or advanced cancer not controlled with androgen deprivation therapy.

**Conclusion:**

Relative to ADT alone Docetaxel is associated with higher rates of toxicity.

Apart from a higher incidence of febrile neutropenia, overall toxicity was comparable to toxicity rates observed in previous studies in metastatic castration resistant prostate cancer patients.

Systematic use of G-CSF is recommended in this setting.