Patients with high risk prostate cancer may benefit 'equally' from two new treatments

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Patients with high risk prostate cancer starting long-term hormone therapy may benefit from two new treatments, according to late-breaking results from the STAMPEDE trial presented at the ESMO 2017 Congress in Madrid. (1)

Long-term hormone therapy alone has been the standard of care for patients with high risk locally advanced or metastatic prostate cancer since the 1940s.

STAMPEDE is a platform protocol using a multi-arm, multi-stage design to efficiently investigate a number of new treatments versus standard of care in patients with high risk prostate cancer. It included men who were starting long-term hormonal therapy for the first time. The trial previously found that docetaxel improved survival compared to standard of care (hazard ratio [HR], 0.78), (2) and that abiraterone acetate with prednisolone also improved survival compared to the same standard of care (HR, 0.63). (3)

First author Matthew Sydes, statistician, MRC Clinical Trials Unit, University College London, UK, said: "Right now, oncologists and urologists want to know which combination is preferable, which is why we conducted this analysis."

The analysis presented today uses prospectively collected data from the STAMPEDE trial to directly compare patients randomised to the docetaxel and abiraterone acetate plus prednisolone (AAP) research

arms while both arms of the trial were recruiting. The randomisations overlapped between November 2011 and March 2013. This comparison included 566 patients, of whom 189 were randomised to receive docetaxel and 377 were randomised to receive AAP, both on top of standard of care androgen-deprivation therapy (with radiotherapy for some patients).

The estimate for the primary outcome of overall survival was a HR of 1.16, and the difference between the two treatments was not statistically significant, with confidence intervals capturing estimates favouring both AAP and docetaxel. (4)

For the early outcome measures of failure-free survival and progression-free survival, estimates of treatment effect clearly favoured AAP with HRs of 0.51 and 0.65, respectively. The estimates of treatment effect for late outcome measures of freedom from metastatic progression and freedom from symptomatic skeletal events favoured AAP but the differences between treatment groups were not statistically significant.

Sydes said: "This comparison was of course underpowered, but it is the only data we have to directly compare docetaxel and abiraterone in this setting."

Professor Nicholas D. James, Chief Investigator of STAMPEDE and Consultant Oncologist at University of Birmingham and Queen Elizabeth Hospital, Birmingham, UK, said: "The individual trials suggested that abiraterone may have a larger effect on survival than docetaxel, but this did not translate into a clear advantage in this study. Both drugs provide a survival advantage over standard of care alone in men with high risk prostate cancer beginning long-term hormone therapy. This study suggests that starting with either drug is acceptable and choice may depend on availability."

Sydes said: "We could only make this head-to-head comparison because of the platform nature of this protocol."

Commenting for ESMO, professor Cora N.Sternberg, Chief, Department of Medical Oncology, San Camillo Forlanini Hospital, Rome, Italy, said: "The STAMPEDE trial has a unique design and has prospectively studied more than 9,000 patients with high risk or metastatic hormone sensitive prostate cancer compared to the standard of care. By 2025 it will have reported the results of ten randomised clinical trials."

"This comparison offers strong evidence for the combination of standard of care plus AAP versus standard of care alone in terms of failure-free survival and progression-free survival and less strong evidence in terms of metastases-free survival and skeletal related events," she continued. "There was no difference in survival with standard of care plus docetaxel, as compared to standard of care plus AAP."

Sternberg pointed out that the toxicity profiles were quite different in the two trials. The AAP results are consistent with the LATITUDE trial, which also favoured AAP over standard of care in high risk patients. (5)

She said: "Both STAMPEDE randomised trials support starting hormonal therapy plus either AAP or six cycles of docetaxel. At one and two years, the percentage of patients with grade 3 or 4 (severe) toxicities was low and similar among the two groups. Toxicities associated with chemotherapy for six cycles will dominate decisions about upfront docetaxel. Toxicities associated with AAP are also likely to influence decisions. Physicians will base their choice of therapy on availability and patient characteristics and preferences."

Regarding the need for further studies, Sternberg said: "Cardiovascular follow-up will be important in patients taking AAP. In the future, we

will get data on whether patients could start with both docetaxel and novel hormonal therapy such as AAP. Ongoing randomised trials in metastatic hormone sensitive prostate cancer will evaluate the combination of novel hormonal therapy and chemotherapy upfront (ARASENS; NCT02799602) as will data from the PEACE 1 trial (NCT01957436) in which two-thirds of patients will receive AAP plus docetaxel chemotherapy for hormone sensitive high risk prostate cancer."

Further research on abiraterone in patients with high risk prostate cancer will be presented on Friday, 8 September. (6) STAMPEDE contributes substantially to the network meta-analysis presented on Sunday, 10 September by Dr CL Vale. (7)

More information: References:

1 Abstract LBA31_PR 'Adding abiraterone acetate plus prednisolone (AAP) or docetaxel for patients (pts) with high-risk prostate cancer (PCa) starting long-term androgen deprivation therapy (ADT): directly randomised data from STAMPEDE (NCT00268476)' will be presented by Mr Matthew Sydes during Proffered Paper Session 'Genitourinary tumours, prostate' on Friday, 8 September 2017, 14:00 to 15:30 (CEST) in the Sevilla Auditorium.

2 James ND, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. Lancet. 2016;387:1163-1177. DOI: 10.1016/S0140-6736(15)01037-5. Epub 2015 Dec 21.

3 James ND, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. N Engl J Med. 2017;377:338-351. DOI: 10.1056/NEJMoa1702900. Epub 2017 Jun 3.

4 HR1 favours docetaxel

5 Fizazi K, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med. 2017;377(4):352-360. DOI: 10.1056/NEJMoa1704174.

6 Abstract 783O 'Benefits of Abiraterone Acetate Plus Prednisone (AA+P) When Added to Androgen Deprivation Therapy (ADT) in LATITUDE on Patient (Pt) Reported Outcomes (PRO)' will be presented by Dr Kim Chi during Proffered Paper Session 'Genitourinary tumours, prostate' on Friday, 8 September 2017, 14:00 to 15:30 (CEST) in the Sevilla Auditorium.

7 Abstract LBA33 'What are the optimal systemic treatments for men with metastatic, hormone-sensitive prostate cancer? A STOPCaP systematic review and network meta-analysis' will be presented by Dr CL Vale during Poster Discussion Session 'Genitourinary tumours, prostate' on Sunday, 10 September 2017, 09:15 to 10:30 (CEST) in the Bilbao Auditorium.

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