



“
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New results from the STAMPEDE trial strengthen existing evidence that addition of docetaxel chemotherapy to long-term hormone treatment at the initiation of therapy improves survival in men with hormone-sensitive metastatic prostate cancer.

The STAMPEDE trial is an ongoing multicentre randomized controlled trial with an adaptive multiarm and multistage design, enrolling men diagnosed with high-risk localized, metastatic or node-positive, or relapsing disease who have not previously received systemic therapy. With the aim to determine whether the addition of certain treatments to current standard of care (SOC) is beneficial, patients are randomized to the control arm (currently, hormone therapy only or additional radiotherapy in localized disease) or experimental arms. The adaptive study design enables experimental arms to be initiated as novel agents that are worthy of study become available.

The most recent paper to emerge from STAMPEDE reports the comparison of survival and safety data at a median follow-up duration of 43 months from 2,962 men randomized 2:1:1 to receive SOC only or SOC plus zoledronic acid, docetaxel or both. Most men were enrolled with newly diagnosed

disease (94%) of whom 62% had metastasis. Gleason score was ≥ 8 in 71% of patients. Across groups, radiotherapy was used as part of SOC in 25–27% of men.

In the SOC only arm, 35.1% of patients died and 5-year survival (5YS) was 55%. In the experimental arms, for SOC plus zoledronic acid 33.9% died (5YS 57%), for SOC plus docetaxel 29.6% died (5YS 63%) and for SOC plus both zoledronic acid and docetaxel 31.5% died (5YS 60%). Statistical analysis demonstrated that men receiving docetaxel in addition to SOC had a significant survival advantage in comparison with SOC only (HR 0.78 and 10-month increase in median survival); however, the addition of zoledronic acid to SOC alone or SOC plus docetaxel did not result in a survival advantage.

Owing to data gathered in the CHAARTED and GETUG-15 trials, which investigated the addition of docetaxel only to hormone therapy in men with metastatic disease, a preplanned analysis of data from this patient subgroup was also performed and corroborated results found in the whole patient population. Data specific for patients without metastasis, however, were still underpowered at the point of manuscript write up, according to the authors.

Safety data across all groups show that a higher proportion of patients in the groups receiving docetaxel experienced adverse events of grade 3 or higher (52%) in comparison with those receiving SOC or SOC plus zoledronic acid only (32%). Most of this additional toxicity seemed to be caused by docetaxel and the investigators suggest that early growth factor treatment could be considered.

The report of these STAMPEDE data in *The Lancet* is accompanied by the publication in *The Lancet Oncology* of a systematic analysis of trials investigating the same treatments in comparable patient populations, such as CHAARTED and GETUG-15. The authors conclude that addition of docetaxel to hormone therapy as the standard of care for men with treatment-naive metastatic prostate cancer is supported by robust evidence, but that data to enable a recommendation for men with nonmetastatic disease are still lacking. In addition, their analysis did not show evidence that the addition of zoledronic acid treatment to SOC would result in a clinically meaningful benefit in either patient population.

The STAMPEDE trial continues, currently recruiting to two experimental arms. One investigates potential benefits of radiotherapy in men with metastatic disease and the other of combination treatment with enzalutamide and abiraterone regardless of metastatic status, in addition to SOC.

Clemens Thoma

ORIGINAL ARTICLES James, N. D. 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* [http://dx.doi.org/10.1016/S0140-6736\(15\)01037-5](http://dx.doi.org/10.1016/S0140-6736(15)01037-5) (2015) | Vale, C. L. et al. Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: a systematic review and meta-analyses of aggregate data. *Lancet Oncol.* [http://dx.doi.org/10.1016/S1470-2045\(15\)00489-1](http://dx.doi.org/10.1016/S1470-2045(15)00489-1) (2015)
FURTHER READING Higano, C. S. Prostate cancer: Mapping the course after CHAARTED. *Nat. Rev. Urol.* **12**, 656–658 (2015)