

PRESS RELEASE

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**Local radiotherapy improves survival in metastatic prostate cancer with low disease burden**

Munich, Germany, 21 October 2018 - Radiotherapy to the prostate improves overall survival in men newly diagnosed with metastatic prostate cancer who have a low metastatic disease burden but not in those with higher burden of disease, according to results from a pre-planned analysis of a large comparison study reported at ESMO 2018 (1).

“Standard treatment for men newly diagnosed with metastatic prostate cancer is currently drug treatment alone,” explained the lead author Dr Chris Parker, Clinical Oncologist, The Royal Marsden NHS Foundation Trust, Sutton, UK. “Although outcomes have improved, men still typically die from metastatic prostate cancer within around five years, so there is a need for more effective treatment. We wanted to know if radiotherapy to the prostate might not only improve local control but also slow progression of metastatic disease.”



The multi-arm, multi-stage STAMPEDE study included a randomised phase III comparison to test whether radiotherapy to the prostate improves overall survival in men with newly diagnosed metastatic prostate cancer. This was based on the hypothesis that primary tumours, which are the original or first tumours occurring in a patient with cancer, could contribute to overall disease progression and shorter survival in men with metastatic prostate cancer.

The study included 2061 patients (median age 68 years) from the UK and Switzerland who were newly diagnosed with metastatic prostate cancer. They were randomly allocated to standard of care (SOC) treatment consisting of lifelong androgen deprivation therapy plus early docetaxel from 2016 or to SOC plus radiotherapy to the prostate. The radiotherapy schedule was 55Gy/20f daily over 4 weeks or 36Gy/6f weekly over 6 weeks.

Results showed that prostate radiotherapy improved failure-free survival (hazard ratio [HR] 0.68, 95% confidence interval 0.68, 0.84) but not overall survival (HR 0.92, 95% CI 0.80, 1.06) in the whole group of patients.

Prespecified subgroup analysis showed that radiotherapy to the prostate improved overall survival by just over one-third (32%) in the 819 men with a low burden of metastatic disease (HR=0.68, 95% CI 0.52, 0.90). In contrast, overall survival was not improved with radiotherapy in the 1120 men with higher metastatic burden. Higher burden of disease in prostate cancer is defined as four or more bone metastases with at least one outside the axial skeleton and/or visceral metastases (2).

Radiotherapy to the prostate was well tolerated with 5% of patients having grade 3-4 adverse events during treatment and 4% following treatment. “There was a small increase in risk of bladder and bowel side-effects but these were modest. The side-effects are certainly outweighed by the survival benefit,” said Parker.

“Prostate radiotherapy improves the survival of men with metastatic prostate cancer who have a low disease burden,” reported Parker. He recommended: “Prostate radiotherapy, in addition to drug treatment, should now be a standard treatment option for men with oligometastatic disease.”

Parker noted that prostate radiotherapy is a simple technique that is widely available and relatively cheap, so he considered that it can be implemented easily. He added that the study results are also relevant to men with pelvic node positive but non-metastatic disease (N1M0) where addition of radiotherapy to drug treatment could be curative.

Commenting on the findings for ESMO, Prof. Karim Fizazi, from the Gustave Roussy Institute, University of Paris Sud, France, said: “For the first time, this study provides evidence that treating the local primary tumor is associated with improvement in overall survival in men with metastatic prostate cancer and minimal disseminated disease.” He added that the finding that there was no significant increase in overall survival in men with higher burden of disease was in line with the previously reported HORRAD trial (3).

Considering the implications for clinical practice, Fizazi suggested: “For men with newly diagnosed oligometastatic prostate cancer, it is quite likely that this data is practice changing.” Looking to the future, he said: “For men with higher burden of disease more data are needed regarding whether upfront local treatment improves or prevents local symptoms, which, by itself, may justify its use in the absence of an overall survival benefit.”

In terms of limitations, Fizazi noted that although the study was a large, randomised phase 3 trial only 18% of the patients had received early docetaxel and none had received early abiraterone, although these treatments are now part of standard treatment in fit men.

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## References

1 Abstract LBA5\_PR 'Radiotherapy (RT) to the primary tumour for men with newly-diagnosed metastatic prostate cancer (PCA): survival results from STAMPEDE (NCT00268476)' will be presented by Chris Parker during Presidential Symposium 2 on Sunday 21 October, 16:30 to 18:10 (CEST) in Room 18 - Hall A2. *Annals of Oncology*, Volume 29 Supplement 8 October 2018

2 Sweeney CJ, Chen Y-H, Carducci M et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. *NEJM* 2015; 373: 737-746.

3 Boevé L, Hulshof M, Vis A et al. PD10-10 a prospective, randomized controlled trial evaluating overall survival in patients with primary bone metastatic prostate cancer (MPCA) receiving either androgen deprivation therapy (ADT) or ADT combined with concurrent radiation therapy to the prostate, final data from the HORRAD trial. *The Journal of Urology* 2018; 199: e231-e232.

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## **LBA5\_PR - Radiotherapy (RT) to the primary tumour for men with newly-diagnosed metastatic prostate cancer (PCa): Survival results from STAMPEDE (NCT00268476)**

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**Background:** Local treatment of the prostate might not only improve local control but also slow progression of metastatic disease. We hypothesised that RT to the prostate would improve overall survival in men presenting with metastatic PCa & that survival benefit would be greater in men with lower metastatic burden.

**Methods:** STAMPEDE, a multi-arm multi-stage platform protocol, included a randomised phase III comparison to test this hypothesis. Standard-of-care (SOC) was lifelong androgen deprivation therapy (ADT), with early docetaxel permitted from 2016. Stratified randomisation within 12 wk on ADT allocated pts 1:1 to SOC or SOC+RT. Men allocated to RT had daily (55Gy/20f/4wk) or weekly (36Gy/6f/6wk) schedules, started  $\leq$ 8wk after randomisation or docetaxel. The primary outcome measure (OM) was death from any cause; secondary OMs included failure-free survival (FFS). 90% power & 2.5% 1 sided  $\alpha$  for hazard ratio (HR) 0.75 required  $\sim$ 267 control arm deaths. Analyses used Cox proportional hazards & flexible parametric models. Directionally pre-specified subgroup analysis tested effects by metastatic burden at entry.

**Results:** 2061 men with newly-diagnosed M1 PCa were randomised Jan 2013 - Sep 2016. Randomised groups were well balanced: median age 68 yr; median PSA 97ng/ml; 18% early docetaxel; metastatic burden: 40% lower, 54% higher, 6% unknown. Prostate RT improved FFS (HR=0.76, 95%CI 0.68, 0.84) but not overall survival (HR=0.92, 95%CI 0.80, 1.06). Subgroup analysis showed improved overall survival for prostate RT in 819 men with lower metastatic burden (HR=0.68, 95%CI 0.52, 0.90) but not in 1120 men with higher metastatic burden (HR=1.07, 95%CI 0.90, 1.28). RT was well-tolerated during (5% Grd3-4 SOC+ RT) & after treatment (Grd3-4 <1% SOC, 4% SOC+RT).

**Conclusions:** Radiotherapy to the prostate did not improve survival for unselected patients with newly-diagnosed metastatic prostate cancer, but, in a pre-planned analysis, did improve survival in men with a lower metastatic burden. Therefore, prostate radiotherapy should be a standard treatment option for men with oligometastatic disease.

**Clinical trial identification:** NCT00268476

**Legal entity responsible for the study:** Medical Research Council Clinical Trials Unit at UCL (MRC CTU at UCL)

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