Radiotherapy (RT) to the primary tumour for men with newly-diagnosed metastatic prostate cancer (PCa): Survival results from STAMPEDE


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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 & 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) or weekly (36Gy/6f) schedules, started ≤8wk after randomisation or docetaxel. The primary outcome measure (OM) was death from any cause; secondary OMs included failure-free survival (FFS). 99% power & 2.5% 1 sided z score hazard ratio (HR) 0.75 required ~267 control arm deaths. Analyses used Cox proportional hazards & flexible parametric models. Directionally pre-specified subgroup analyses 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 0.96, 1.28). RT was well-tolerated during (3% Grd3–4 SOC+ RT) and after treatment (Grd4–5 <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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Long-term safety and health-related quality of life: A phase III trial of radium-223 (Ra-223) in combination with abiraterone acetate and prednisone/prednisolone for the treatment of asymptomatic or mildly symptomatic chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) led to a higher fracture rate. Based on these results, we do not recommend Ra-223 in combination with abiraterone acetate and prednisone/prednisolone.

Fractures occurred in 29% and 11% of pts in the Ra-223 and control arms, respectively. The trial was unblinded early after more fractures and deaths were observed in the Ra-223 arm. All pts had completed study-specified Ra-223/PBO treatment, with no additional treatment during the study.

Additional secondary endpoints are shown in the Table. Fractures occurred in 29% and 11% of pts in the Ra-223 and control arms, respectively. The trial was unblinded early after more fractures and deaths were observed in the Ra-223 arm. All pts had completed study-specified Ra-223/PBO treatment, with no additional treatment during the study.

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Overall confirmed ALP response, n/N (%) 218/398 (55) 104/402 (26) –

Overall confirmed PSA response, n/N (%) 287/396 (72) 267/401 (67) –

Time to deterioration in health-related quality of life*, median (95% CI), months 9.5 (6.9–12.0) 10.5 (8.3–13.0) 1.079 (0.865–1.345)

Time to ALP progression, median (95% CI), months 7.4 (7.1–7.9) 6.8 (5.3–8.4) 1.083 (0.918–1.276)

Time to opiate use for cancer pain, median (95% CI), months 19.0 (14.4–23.2) 22.6 (18.0–25.7) 1.126 (0.921–1.378)

Time to cytotoxic chemotherapy, median (95% CI), months 29.5 (26.5–35.7) 28.5 (23.7–NE) 1.033 (0.816–1.308)

Disclosure: M.R. Sydes: Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis; Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE. Educational grant plus drug from Astellas, Janssen, Novartis, Pfizer, Sanofi-Aventis for STAMPEDE.