RESPONSE TO BY DR GANDAGLIA (16TL0226)

We thank Dr Gandaglia for the comments. Radiotherapy was encouraged for N0M0 patients from the start of the trial, but was only mandated after the results of the MRC PR07/NCIC PR.3 and SPCG-7 trials demonstrated a survival advantage with radiotherapy.(1, 2) The planned use of radiotherapy was a stratifying factor at randomisation. The planned use of radiotherapy was in N0M0 patients, who are at the better end of the risk spectrum in the STAMPEDE trial. Use of radiotherapy thus reflects relevant contemporary practice during recruitment. There are no randomized trials supporting the use of radiotherapy in node-positive prostate cancer, hence the pattern of use reflects this ongoing uncertainty and cannot be described as undertreatment. There was no evidence in multivariate analysis that the treatment effects from docetaxel on failure-free survival or overall survival was affected by planned use or non-use of radiotherapy.

No patients were planned for radical prostatectomy as part of their treatment within the trial, hence this was not described in the protocol. Increasingly, surgery is becoming a treatment option to be considered for patients at the higher end of the risk spectrum. There is no direct evidence from randomised controlled trials in this setting at the moment of any benefit to surgery over radiotherapy. Patients with high-risk relapse after previous prostatectomy and/or radiotherapy now starting long-term hormone therapy were eligible for the trial.

We were deliberately measured in the conclusion of our manuscript: “Standard of care should be updated to include docetaxel chemotherapy in suitable patients with metastatic disease, and docetaxel may be considered for men with high-risk non-metastatic prostate cancer with or without radiotherapy.”(3) The NHS guidelines in England were rapidly changed following our publication and support the use of docetaxel in metastatic patients. We would agree that for patients with non-metastatic disease better treatment of the primary site may dilute any effect of any systemic treatment on overall survival in a ceiling effect by reducing risk of death from prostate cancer.

We will report updated findings in the coming years when there will be more events from patients who were initially non-metastatic and we will see whether the substantial advantage in failure-free survival translates to an advantage in survival they way it has for patients who were metastatic when joining the trial.

373 words (target <400)

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