Title: PIONEER's systematic review of outcomes in RCTs of men with non-metastatic castration resistant prostate cancer: Is there a need for a core outcome set?

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Introduction & objectives: Standardising outcome measurements promotes data homogeneity in audits and trials thereby facilitating critical review, synthesis and Big Data projects. Our aim was to determine if there is a need for a non-metastatic castration resistant prostate cancer (nmCRPC) core outcome set (COS) over and above a separate COS for metastatic disease, based on the results of a separate review investigating that topic. This research is part of PIONEER – an international Big Data Consortium led by the European Association of Urology (EAU) to answer key questions for patients with prostate cancer, funded through the IMI2 Joint Undertaking under grant agreement No.777492.

Methods & materials: We systematically reviewed RCTs of any intervention for men with nmCRPC published between 1.01.2014 and 21.12.2018. The search criteria were extended to include metastatic castration resistant prostate cancer (mCRPC), hormone resistant prostate cancer (HRPC), metastatic prostate cancer (mPC) to ensure we capture all relevant literature. Verbatim outcome names, definitions and reported data were extracted, coded and categorised according to a predefined protocol.

Results: Literature searches identified 1,136 citations for men with nmCRPC, mCRPC, HRPC, mPC. 1,262 references were identified, from which five RCTs met the inclusion criteria. Reported outcomes for nmCRPC, which differ from the already identified outcomes in the PIONEER metastatic outcome set, are: Time to initiation of subsequent antineoplastic therapy, time to metastasis (time from randomization to the first detection of distant metastasis involving the bone or soft tissue on imaging), time to symptomatic progression (time from randomization to a skeleton-related event, pain progression, or worsening of disease-related symptoms leading to the initiation of a new systemic anticancer therapy or the time to the development of clinically significant symptoms due to local or regional tumor progression leading to surgery or radiation therapy) and second progression–free survival (time from randomization to investigator-assessed disease progression (PSA progression, detection of metastatic disease on imaging, symptomatic progression, or any combination).

Conclusions: Very few new outcomes were identified for nmCRPC as compared with the metastatic setting. Therefore, PIONEER currently does not recommend a specific COS for nmCRPC. However, if in future further treatment options warrant new RCTs and different outcome measurements, this recommendation may change.

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