TRoMbone: Testing Radical prostatectomy in men with oligoMetastatic prostate cancer that has spread to the bone; a randomized controlled feasibility trial

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Background

Recent observational studies suggest an oncologic benefit from treating the primary tumor in men with oligo-metastatic prostate cancer. European Trials like STAMPEDE and HORRAD examine management of the primary lesion in men with metastatic disease using radiation therapy. The American SWOG trial investigates synchronous metastatic patients of all metastatic tumor burdens. But there remains an unmet need to examine locally-directed therapy in the oligo-metastatic setting specifically. The German-led RAMPP Trial is doing this but is finding recruitment challenging and is currently accruing below target.

Aim

TRoMbone is a multi-center UK Trial to assess the feasibility and safety of a randomized controlled trial (RCT) comparing radical prostatectomy surgery plus systemic therapy versus systemic therapy alone, for men with synchronous oligo-metastatic prostate cancer. The trial aimed to recruit 50 men over a 12-month period and was co-ordinated by the Surgical Intervention Trials Unit at the University of Oxford.

Methods

The initial Protocol randomized men with synchronous oligo-metastatic prostate cancer (1-3 skeletal metastases on conventional imaging) who were <75 years old and ECOG PS 0-1, to radical prostatectomy and extended pelvic lymphadenectomy within 3 months of starting standard care systemic therapy (Intervention) versus standard care systemic therapy alone (Control).

The Trial opened to Recruitment in February 2017. A Quintet Recruitment Investigation (QRI) was integrated into the feasibility RCT to identify and address recruitment challenges and assess feasibility for a full RCT.

Results

As a result of STAMPEDE, practice changed as the Trial opened to include docetaxel for most UK centers. Hence, there was no recruitment in the first 3 months of the Trial. The QRI identified that delay to docetaxel and fewer eligible patients than predicted were the 2 major barriers to recruitment. The Protocol was amended to: (1) extend period of systemic therapy before surgery to 12 months in the Intervention Arm; (2) increase numbers of centres to 9; (3) increase accrual period to 18 months.
A rapid improvement in recruitment occurred with the final patient randomized within 12-months of the first recruit, 4 months ahead of the revised schedule. Lessons learnt from the QRI included: (1) how to optimize Urology-Oncology referral pathways; (2) the importance of clarifying the role of novel imaging regarding eligibility; (3) overcoming challenges with treatment sequencing in the Intervention arm; (4) how to overcome problems with clinician equipoise especially regarding technical safety/operability in the Intervention arm.

The Data Lock for the Trial has occurred and the Statistical Descriptive Analyses and the QRI Report are awaited.

Conclusions

It is feasible to randomize UK men with synchronous oligo-metastatic prostate cancer to standard care systemic therapy versus that plus locally-directed surgery. Safety outcomes are awaited, and consideration of a Full Trial will follow.