Non-invasive interrogation of oligometastatic castration-resistant prostate cancer and the benefit of metastasis directed therapy in the phase II FORCE randomized clinical trial

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Metastasis Directed Therapy (MDT) is the focus of recently completed and ongoing clinical trials in prostate cancer. In castration-resistant prostate cancer (CRPC), there has been a paucity of investigation as to the benefit of MDT. The potential of MDT may be greater in oligometastatic CRPC (omCRPC) as CRPC metastasis seed new metastasis, and minimizing viable burden of disease may delay systemic therapy resistance. Thus, concurrent treatment with first line CRPC therapy (e.g. enzalutamide or abiraterone) and MDT, may significantly increase time on first line treatment, potentially improving survival or the quality of life of patients (as first-line therapies typically have less side effects then chemotherapies used later). The clinical benefit of this approach is being tested in the ongoing randomized phase II FORCE trial (FOcal Radiation for oligometastatic Castration-rEsistant prostate cancer) of first line systemic therapy with or without MDT by radiotherapy. Within this trial, the impact of radiation on circulating aspects of disease (e.g. circulating tumor cells) and the natural history of untreated PSMA positive lesions (found on a research scan) are being explored. To improve recruitment efforts, several changes were made in 2018-2019. First, the supervision of the trial was re-organized. This created the Rogel Cancer Center as a multi-site coordinating center, thus allowing the study to open at the Ann Arbor Veterans Administration Hospital (where it is currently undergoing regulatory review). Second, as PSMA based diagnostics are being used in the non-metastatic castration resistant setting, molecular omCRPC patients are being identified. Anticipating this to be a future clinical entity, the study allows these patients to participate, but they are stratified equally between arms (to maintain patient balance). Third, the visit schedule was minimized to avoid burden on patients. This trial design, combined with circulating correlative analysis (circulating tumor cells), will allow us to investigate the safety and efficacy of MDT in omCRPC (Aim 1), the potential impact of PSMA positive, conventional imaging negative metastases in patients treated with first line systemic therapy (Aim 2), and to assess non-invasively resistance patterns gain or loss and the potential elimination of circulating disease (Aim 3). Too few failure events have happened to correlate circulating analyte changes with outcomes between arms. The research PSMA scans are also sequestered until that patient progresses to avoid clinician bias, thus cannot be reported yet. Overall recruitment should improve with the new site and changes.

Conflicts of Interest:

Z.R.R.: No conflicts of interest to report

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