SKCCC Protocol #: J1548

ClinicalTrials.gov Identifier: NCT02491411

TITLE: A Pilot Study of Dexamethasone Therapy Prior to Rechallenge with Enzalutamide in Men with Metastatic Castration-Resistant Prostate Cancer

Dex **EXT**ends **E**nza **R**esponse (The **DEXTER** Trial)

8/24/2016

Statistical Analysis Plan

The treatment regimen would be considered of insufficient activity for further study in these population if PSA response rate is 5% or less, and the minimum required level of efficacy that would warrant further study with the proposed regimen is a 25% PSA response rate. The sample size is calculated to detect an improved PSA response rate from 5% to 25%. A minimax Simon two-stage design is planned. A total of 13 patients will be entered in the first stage. If none of them show PSA response after Enza, the treatment regimen will be terminated and we will conclude the regimen is ineffective. If >=1 subjects has PSA response, then additional 7 patients will be studied. If a total of 2 or fewer subjects achieve PSA response in stage one and two combined, we consider this regimen ineffective. If a total of 3 or more respond, we conclude the regimen is promising and warrant further study. The trial could be terminated early also as soon as 3 PSA responses with the post-Dex Enza treatment are confirmed.

The maximum sample size will be 20. Patients who receive at least one dose of Dex will be evaluable for the primary endpoint of PSA response. Those who do not start Enza subsequent to Dex will be considered as non-responders in the analysis. This design provides 90% power to reject a 5% PSA response in favor of 25% response rate, with a type I error of 0.1. The chance of early stopping is 0.51 when the response rate is less than 5%.

We will determine the PSA response rate with the re-challenge of Enza following Dex as the proportion of subjects with a ≥50% PSA decline from baseline level when starting Enza and maintained for ≥4 weeks at any time-point after receiving Enza, and its corresponding 95% confidence interval. For the secondary endpoints, we will estimate objective response rate to Enza in patients with measurable disease on CT scan and its 95% confidence interval. Time to PSA progression and Radiographic Progression for treatment with Dex will be summarized using Kaplan-Meier 29 approach. Quality of life will be assessed via FACIT-Fatigue Scale and RANDSF-36 questionnaires. Summary statistics of the scores will be reported at baseline before starting Dex and each follow-up time during the treatment of Dex and Enza. Changes in quality of life scores over the course of the study will be computed and their significance will be evaluated by paired-sample t-tests. Response rate to Dex and Enza will also be reported by AR-V7 status at baseline of study entry.