2023-5274 Additional Information

Statin use will be handled as a binary variable, (Statin yes/no). However, it will be more complicated than that at the time of statistical analysis. We will calculate a propensity score for statin use using a logistic regression model. We will match for each statin user,  two non-statin users and adjust for potential confounders (Age, Gleason Score, ECOG, Baseline PSA, Alkaline Phosphatase, LDH, Opiate use, Geographic region, Metastasis stage at initial diagnosis (TITAN, ACIS), Visceral disease and bone metastasis at baseline (TITAN, ACIS), docetaxel status (TITAN, ACIS).

We will split our matched cohort in three groups:

1. Statin use (reference group = non-users)

2. Statin use + treatment arm (reference group = placebo arm)

3. Statin use + treatment arm + statin x treatment interaction

Analyses will be done by statin type and dose/duration if that information is available.  For statin type, depending on the distribution of statins used the analysis will be bivariate (hydrophilic vs. hydrophobic) or will be done by specific type (e.g.

atorvastatin vs. simvastatin vs. Rosuvastatin, etc.). For statin dose we have recently submitted our manuscript "Statin concentration in prostatic tissue is subtype- and dose-dependent" in which we analyzed if statin concentration in the serum and the prostate was dose-dependent and divided the groups in high-dose and low-dose.  We will use our same dose subgroups definition: High-dose atorvastatin defined as 40-80 mg daily and low-dose as 10-20 mg daily. High-dose rosuvastatin defined as 20-40 mg daily, and low-dose (RSV-LD) as 5-10 mg daily. We will adjust this definition to other statin types, if this information is available.