Phenotypic circulating tumor cell (CTC) classifier of genomic instability (GI) associates with improved overall survival (OS) for metastatic castration-resistant prostate cancer (mCRPC) patients (pts) receiving platinum agents in addition to taxanes

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Background: The presence of GI has been associated with DNA Damage Response (DDR) genomics. mCRPC pts with DDR(+) can have treatment (Tx) efficacy with poly ADP ribose polymerase inhibitors (PARPi). Similar Tx benefit for DDR(-) pts has been observed with alkylating agents such as platinum Tx in small cohorts. However, obtaining and sequencing metastatic biopsies is currently not scalable for routine use in the clinic due to accessibility, cost and time to result. We previously developed an imaging-based phenotypic classifier to predict presence of GI from individual CTC morphology and demonstrated that these pts had statistically worse OS when receiving androgen receptor signaling inhibitors (ARSi) or Taxanes. In a separate cohort, the same classifier predicted improved PSA response when pts were treated with a PARPi + ARSi vs. ARSi alone. Here, we examined if GI (+) mCRPC pts can have improved OS when receiving a commonly available and inexpensive platinum chemotherapy.

Methods: 89 blood samples were collected from mCRPC pts prior to taxane Tx (n = 62) or a combination of taxane + platinum (T+P) (n = 27), and processed utilizing the Epic Sciences platform. Choice of therapy was at the discretion of attending physician without knowledge of CTC results. The percent of predicted GI cells per pt sample (%pGI) was calculated after single-cell characterization. Pts were followed for OS.

Results: Pts receiving a T+P combination had higher CTC burdens and lower PSA levels but otherwise showed similar pre-Tx characteristics to taxane-only pts. In a multivariate model containing %pGI, therapy class, and total CTC burden (to help correct for disease burden and severity), a significant interaction between the T+P combination and increasing %pGI, and increased OS (HR: 0.14, CI: 0.026 to 0.72, p = 0.018) was observed.

Conclusions: The results of this study suggest that in a prospective setting with a balanced cohort, pts with high %pGI might have improved OS on taxanes with the addition of platinum agents. Prospective validation of the signature is planned.

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