Background
The reliable and accurate pretreatment prediction of a patient’s response to AR Tx or Taxane chemotherapy is an unmet medical need, as some patients may respond to both classes of drugs, some to one but not the other, and others are resistant to both. Molecular profiling studies of mCRPCs suggest an association between high genomic instability (GIs) and lack of response to either class of drugs.

Our overarching objectives are:
1) To develop blood-based assays of circulating tumor cells (CTCs) to predict GI using phenotypic features from individual CTCs with next generation sequencing (NGS). And,
2) To evaluate the performance of the assay for the context of use for identifying patients for whom alternative approaches can be explored early avoiding the toxicity of ineffective standard of care therapies.

Methods for CTC Detection; Phenotypic, Genomic Characterization

CTC phenotype classifier identifies mCRPC patients with high genomic instability CTCs and predicts failure of Androjen Receptor Signaling (AR Tx) and taxane systemic therapies

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Conclusions

• An algorithm was developed that identifies CTCs with high genomic instability from their phenotypic features alone. Accuracy: 80%.
• A cut point of high genomic instability CTC/mL was found to maximize prognostication on SOC drugs. The overall prevalence of patients this biomarker+ classification was 30% (59/196), and was associated with inferior OS times on AR Tx (HR=7.69, p<0.0001) and taxane therapy (HR=2.79, p<0.005).
• High Phenotypic Genomic Instability helps identify patients who are resistant to the approved AR Tx and taxanes, for whom alternative approaches should be considered.
• This rapid blood imaging analysis will also help to screen patients for HRD directed therapies and to improve patient outcomes.

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