Background
High CTC phenotypic heterogeneity is associated with nonresponse to ARs but not taxane chemotherapy assessed using a noninvasive rapid blood test. The MSK-IMPACT™ NGS assay is FDA approved for tumor profiling to guide treatment selection. The frequency of directly actionable alterations in prostate cancer (PC) is ~35%. Recognizing many cancers harbor intra- and intercellular heterogeneity, we sought to evaluate concordance of sequencing single-CTCs vs. paired biopsy analyzed by MSK-IMPACT, to assess CTC clonality in correlation vs. tumor, the relationship of CTC phenotypic heterogeneity and response.

Methods
CTC and Matched Tissue Demonstrate Concordant and Discordant Genomic Profiles

Example 1: Similar Clonal Genomic Profile

Example 2: Dissimilar Clonal Genomic Profile

Prevalence of Multiple Unique Genomic Clones Observed in CTCs

CTC vs. Bone/Visceral Biopsy Patients

CTC vs. Lymph Node Biopsy Patients

Genomic Alterations Identified in CTCs & Tissue

Associate with Survival

Case Study: CTC Genomic Profile in Aggressive Disease

High Clonal Concordance in Bone/Visceral; Low Concordance with LN Metastatic

Conclusions
• Single CTC sequencing is often concordant to metastatic tissue, but unique CTC clones highlight the prevalence of sub-clonal disease in mCRPC patients under-sampled by tissue biopsy.
• Lymph node biopsy may under-represent the cancer cells circulating in the blood, leading to lower utility of genomic calls in these patients.