Overall, tumor material for profiling was obtained in 91% cases, 77% by biopsy, 67% by CTC, and difficult approved from (28%). CTC genomic profiling provides a clinical alternative to characterize patient’s disease in real time. A total of 148 samples (139 Unique Pts) were collected and analyzed, with a median number of 4.1 (2.6, 4.8) CTCs detected per sample, which was determined automatically using IMPACT™, a high-throughput, targeted-DNA-sequencing panel for somatic mutations created by the Department of Pathology at Memorial Sloan Kettering Cancer Center (MSK) that is FDA approved for tumor tissue profiling to guide treatment selection.

Recognizing access to tumor material for profiling in many cancers is difficult and may harbor inter- & intra-tumoral heterogeneity, we evaluated:

1) The ability to obtain tumor material for profiling from patients with metastatic castration resistant prostate cancer who underwent a biopsy of a metastatic lesion and who had a blood sample drawn to profile CTC.
2) The concordance of sequencing single CTCs vs. paired biopsy analyzed by MSK-IMPACT, to assess differences in the alterations identified, clonality, and their relationship to outcomes.

DESCRIPTION OF PATIENTS

78 samples, each bar represents a sample. Overall Survival was reviewed by three genomics bioinformatician and scientists.

METHODS

Epic Sciences CTC Detection

- BIOMARKERS.
- Epithelial cell from patient blood samples in a hard agar plate; 3 (biopsy) samples obtained.
- CTCs isolated and captured by Enzyme-linked immunosorbent assay (ELISA) or CTC-ID:
- CTCs identification based on (ELISA) OR (DHS), or A
- CTCs identification using a multi-parametric digital pathology algorithm.

Genomics Processing & Methodology

- 1) IDENTIFIED CTC
- 2) CTC RELOCATION
- 3) SINGLE CTC ISOLATION
- 4) SINGLE CELL WGA & LIBRARY PREP

MAL-IMPACT™ PROCESS

- Single CTC Sequencing
- 1) Identified CTCs were relocated and captured individually. 4-5) Each captured cell was lysis, whole genome amplified (WGA).
- RNAseq dual index MSI-library prepared and low pass whole genome sequenced using Illumina NextSeq 500. CN analysis was performed as previously described (Greene et al., J Clin Onc 2016).
- MSK-IMPACT™ Sequencing

Dna derived from matched fresh biopsy was sequenced as previously described by the MSK-IMPACT tumor sequencing. For purposes of comparison, CNAs were called from across the panel using the same ONP algorithm and for single cells.

Overall Concordance Between CTC and Matched Tissue

Overall concordance was assessed for all patients. Concordance rates were assessed using 2 different definitions:

- Overall concordance: 
  - Similar: CTC profile with ≤ 2 copy number changes
  - Different: CTC profile with ≥ 3 copy number changes

- Discordant: CTC profile with ≥ 3 copy number changes

Concordance rates were 28% (20/71) and 20% (14/71) for LN biopsy and CTC, respectively. The overall concordance rate was 33% (24/71) for CTC and matched tissue.

Cancer Driver Gene Alterations Detected in CTCs Improve Prognostication vs Tissue

Case Study: CTC Sequencing Can Provide Actionable Information When Tissue is Not Informative

CONCLUSIONS

- Overall tumor material for profiling was obtained in 89/113 cases, 77% by biopsy, 6% by CTC, and 53% by both.
- Single CTC sequencing is concordant to metastatic tissue in about ~50% pts, and unique CTC clones highlight the prevalence of sub-clonal disease in mCRPC patients under-ampled by tissue biopsy.
- CTC genomic profiling provides a clinical alternative to characterize patient’s disease in real time when tumor biopsy material is insufficient/inadequate.
- We don’t know which profile is most predictive of treatment success if an actionable molecular alteration is identified.
- Known genomic alterations of progressive mCRPC are frequently observed in CTCs from patients with short OS.

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