Clonal Concordance and Genomic Heterogeneity in Single CTC Copy Number Alterations vs. Paired IMPACT Metastatic Tissue Sequencing from mCRC Patient Samples

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Background
High CTC phenotypic heterogeneity is associated with nonresponse to ARSs but not taxane chemotherapy assessed using a non-invasive rapid blood test. The MSK-IMPACT™ NGS assay is FDA approved for tumor tissue profiling to guide treatment selection. The frequency of directly actionable alterations in prostate cancer (PC) is ~5%. 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 concordance in isolation vs. tumor, the relationship to CTC phenotypic heterogeneity and response.

Methods

CTC and Matched Tissue Demonstrate Concordant and Discordant Genomic Profiles

Example 1: Similar Clonal Genomic Profile Tissue re-segmented CTC

Example 2: Dissimilar Clonal Genomic Profile Tissue re-segmented CTC

Areas of Clonal Concordance Areas of Clonal Discordance

Prevalence of Multiple Unique Genomic Clones Observed in CTCs

CTC and Matched Tissue Demonstrate Concordant and Discordant Genomic Profiles

High Occurrence of Resistant Genomics Identified 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

Patient Demographics & Study Design

Conclusions

• Single CTC sequencing is often discordant to metastatic tissue, but unique CTC clones highlight the prevalence of sub-clonal disease in mCRC 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.
• Known genomic alterations of progressive mCRC are frequently observed in CTCs from patients with shortOS.