ABSTRACT

TISSUE SEQUENCING (Foundation Medicine, Inc.)

NGS-based cancer genomic profiling test

CONCORDANCE BETWEEN MULTIPLE TISSUE SAMPLES

Discordance Between Multiple Tissue Samples

METHODS & RESULTS

BACKGROUND: Success of targeted therapy requires expression of the protein. Tumor tissue source can include diagnostic biopsy, surgical sample from initial or follow-up surgeries, fluids e.g., pleural or ascites and circulating tumor cells (CTCs). The goal of using CTCs was 1. To determine whether CTCs can be used as a "liquid" tumor biopsy and enable gene sequence information at the single cell level 2. To determine the heterogeneity represented in the circulation compared to that seen in solid tumor by examining single cells (or a small cluster of cells) for the presence of a specific mutation which was detected in tissue tumor source.

METHODS: We performed sequencing for mutational analysis on formalin-fixed paraffin embedded (FFPE) tissue samples from patients with inflammatory breast cancer (IBC). Tumor sources varied from mastectomy tissue, metastatic site (s) e.g. liver or skin from chest wall disease, pleural fluid and CTC isolated into pure single cell populations (or groups) using CellSearch technology. All gene amplifications were noted including AKT, RPTOR, MLC1, MYC, CCND1, AURKA, MDM2, FGFR1 and ERBB2. For one patient’s chest wall biopsy compared to two single CTCs and a cluster of 10 CTCs the same TP53C229fs*10 mutation was detected revealing the same 2bp deletion. No 2bp deletion was found in single white blood cells. Whereas, another patient which showed a TP53 R110fs*13 mutation in her skin biopsy of chest wall disease, only amplifications of AURKA, CCND1, IGFR1, MDM2 and SRC in pleural tumor cells were detected and no mutations in single CTC; two single pleural tumor cells and in single white blood cells were seen. Primary tumor tissue is being sent for both of these patients. Mutational data reviewed to date suggest that IBC is not one disease but a multiplicity of diseases, revealing a variety of targets. Alterations were not consistent across tissue source.

CONCLUSIONS: Successful treatment outcomes using standard of care chemotherapy combined with targeted therapies will require not one, but a panel, of tissue source for sequencing to guide the selection of appropriate targeted therapies.

OBJECTIVES

- To detect genomic abnormalities with potential for therapeutic targeting.
- To compare mutations/amplifications in tissue from various disease sites and compare to circulating tumor cells (CTCs).
- To improve the understanding of the molecular drivers of metastasis in IBC and metastatic breast cancer.

RESULTS

To date 35 patients have had mutational data performed, of tissue sources for sequencing to guide the selection of appropriate treatments.

What is the appropriate sample(s) on which to perform sequencing for mutational analysis to guide the selection of targeted therapy?

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