Background

• The integration of next-generation sequencing (NGS) into clinical practice has significantly advanced personalized medicine for patients with breast cancer.

• NGS enables the precise identification of clinically relevant genomic aberrations, allowing physicians to select appropriate targeted therapies for their patients.

• NGS has also highlighted the heterogeneity of breast cancer, and there remains the challenge of understanding how and why tumor heterogeneity confounds molecular analysis and treatment decisions.

• The NanoOmics Cancer Study (OMICS) enrolled patients with metastatic triple negative breast cancer (mTNBC) who are platinum-naive and planned to receive cisplatin.

• Primary objective: to establish the safety and feasibility of collecting, analyzing, and storing panomic and other data from serially monitored tumor tissues.

Methods and Patients

Study Design

• Eligibility: mTNBC, platinum-naive, scheduled to receive cisplatin, ECOG performance status 0-1.

• Between 10 and 100 tissue samples/biopsy specimens were obtained from each patient once or twice.

• A subset of tumor specimens is chosen for DNA sequencing, RNA sequencing, and quantitative proteomics.

Genomic Analysis

• Between 100 and 133 tissue samples/biopsy specimens were obtained from each patient once or twice.

• Blood samples were collected for matched tumor-normal genomic analysis.

• DNA sequencing data were processed using ContraScan® and MutTect.

Proteomics Analysis

• Proteomics analysis was done using a quantitative, multiplexed, selected reaction monitoring-mass spectrometry assay comprising a panel of 500 proteins.

• A subset of FFPE tumor samples (for which sufficient material was available) were laser-microdissected, solubilized, and enzymatically digested.

• Absolute quantitation of proteins was accomplished through the simultaneous detection of endogenous targets and identical, synthetic, labeled heavy peptides; protein levels were normalized to total protein digested.

• Four patients showed progressive disease when treated with crizotinib, enzalutamide, cyclophosphamide, or pembrolizumab expressed GPNMB treated with glembatumumab vedotin.

Omics Analysis

45-year-old woman diagnosed with TNBC early 2011, with response to neoadjuvant chemotherapy after left mastectomy. Subsequently presented with right breast, radical mastectomy late 2012, then metastases involving the liver, lung, and lymph nodes. Before enrollment, progressed despite treatment with radiation, nab-paclitaxel, and doxorubicin.

DNA Sequencing

2 Exome-sequencing mutations of FGFR2 (D1298N) and WSCD2 (Y376C) after neoadjuvant chemotherapy; mutation in FGFR2 (D1298N); 7-fold amplification of FGFR2.

Quantitative Proteomics

Autophagy assay: FGFR2; not detected. EMT 6 not reportable.

Results

45-year-old woman diagnosed with Stage 3B breast cancer in 2009. Developed mTNBC in 2013, despite hormonal therapy, with involvement of the liver, lung, and lymph nodes. Before enrollment, progressed despite treatment with radiation, nab-paclitaxel, and doxorubicin.

DNA Sequencing

PIK3CA (activating mutation) at all time points; 3-fold amplification of PIK3CA.

Quantitative Proteomics

Autophagy assay: HSP27; EMT 6 not detectable.

Studies

45-year-old woman diagnosed with Stage 3B breast cancer in 2009. Developed mTNBC in 2013, despite hormonal therapy, with involvement of the liver, lung, and lymph nodes. Before enrollment, progressed despite treatment with radiation, nab-paclitaxel, and doxorubicin.