Molecular Characterization of Metastatic Inflammatory Breast Cancer (IBC) with Next generation Sequencing (NGS) Identifies Actionable Genomic Abnormalities for treatment selection.

Background

- Breast Cancer is the second leading cause of death in women in the US.
- Inflammatory breast cancer (IBC) is the most aggressive form of breast cancer and it is associated with aggressive features and poor outcomes.
- Standard breast cancer treatments have minimal impact on IBC outcome and more effective and individualized treatments are needed.
- The availability of comprehensive cancer genomic testing using Next-Generation Sequencing (NGS) technology can be used to optimize selection of treatment regimens.
- We evaluated metastatic IBC patients by molecular analysis of plasma and/or tissue biopsy before starting new systemic treatment.

Research Objectives

- The aim of this study is to Describe clinical and molecular characteristics of a large cohort of metastatic IBC cases.
- Demonstrate the feasibility of NGS analysis in tissue or plasma of patients with advanced IBC.

Methods

- Forty five patients with IBC were included in this analysis. All patients were included in a prospective registry study and signed ICF. We retrospective reviewed clinical and molecular information.
- All patients underwent plasma sampling analysis of circulating tumor DNA (ctDNA) using Guardant test (Guardant Health, CA).
- Tissue analysis was performed using commercial tests, TEMPUS, Foundation medicine Northwestern, in-house assessing the following tissue specimens: mastectomy (11 patients), skin (1 patient), chest wall (1 patient), pleural fluid (2 patients), lymph nodes (6 patients), brain (1 patient), and liver (2 patients).

Fig. 1 Landscape of Genomic alterations

Results

- The most common procedure was unilateral radical mastectomy (42%), followed by bilateral mastectomy (32%). Thirteen patients (26%) had no surgery. No patients underwent lumpectomy. 42% of the patients were estrogen or progesterone receptor positive, 30% were Her-2 neu positive, and 28% of the patients had no tissue receptors (triple negative breast cancer).
- Tissue and blood NGS was performed in all patients demonstrating at least 1 genomic variant (Figure 1).
- CTDNA detected mutations in 100% of cases. The most common plasma mutations/amplifications detected by NGS were TP53 (51%), PIK3CA (26%), MYC (22%), BRAF (15%), FGFR1 (15%), ERBB2 (11%), PTEN (11%).
- Among tissue sampling TP53 was the most common mutation present in breast tissue (54%) and in 100% of the skin and the chest wall samples. ESR1 and FGFR1 were noted in 100% of the liver tissue biopsies and in 100% of the pleural fluid samples.

Limitations

- This analysis was retrospective with a limited sample of patients. Not all patients with IBC were seen initially at Northwestern Memorial Hospital (NMH) and their prior treatment and responses were not always verified or supported by source documents.
- Patients frequently continued treatments in outside Institutions after NGS and patients outcome could not be measured. Data was limited to the information available in the charts from Northwestern Memorial Hospital.

Conclusions

- This study demonstrated that NGS analysis of plasma or tissue of patients with advanced IBC is feasible and improves our understanding of this complex, aggressive and deadly form of breast cancer.
- Future studies should evaluate the impact of genomic testing on treatment selection and outcome.