MULTI-OMIC PROFILING OF METASTATIC LESIONS TO GUIDING TREATMENT SELECTION: THE SIDE OUT 2 TRIAL EXPERIENCE

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The aim of this prospective pilot study was to explore if treatment selection based on Multi-omic Profiling (MoP) provides clinical benefits superior to empiric treatment selection in progressive metastatic breast cancers (MBC).

Methods

Study Primary Objective

Trial design: The Side Out 2 trial (clinicaltrials.gov ID NCT01919749) was an open-label, multicenter pilot study which used the molecular profile of target lesions to guide treatment selection. Therapeutic regimens were selected only from FDA approved compounds.

Patient population: Between 2014 and 2016, 4 US sites enrolled 32 previously treated MBC patients.

Key Eligibility Criteria:

- Age ≥ 18 years;
- ECOG of 0–1;
- Absence of symptomatic CNS metastasis;
- Adequate organ and bone marrow function;
- Documented diagnosis of metastatic breast cancer with measurable disease accessible to biopsy;
- Progression of disease ≥ 1 prior chemotherapy and/or hormonal regimen(s) for advanced disease within 6 months of treatment initiation.

Response Rate Criteria: Growth Modulation Index (GMI) was used to assess patients' response to treatment based on tumor response by RECIST 1.1.

Consenting/Screening/Enrollment: MBC patient with disease progression, clear documentation of time between treatments, and documented progression on the most recent treatment.

Tissue Collection and Multi-omic Analysis: Multi-omic analysis of the metastatic lesion - RNA-Seq and Exome Sequencing - Immunohistochemistry of 7 predictive markers* - LCM-RPMA based protein singling network analysis of 12 FDA approved drug targets and downstream substrates**.

Study workflow

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Results

Enrollment overview

Patients with GMI <1.3 (n=11; 44%) Patients with GMI ≥1.3 (n=14; 56%)

Patient outcome based on GMI score

- Of the 25 patients, 14 (56%) met or exceeded a GMI of 1.3.
- The most frequently selected treatments were: Imitinib-based on TOP01 expression (n = 12; single agent n = 5) and Capecitabine based on TS expression (n = 10; single agent n = 3).
- Seven patients received endocrine therapy, 3 of whom were treated with Everolimus and Exemestane.
- Based on HER2 amplification/pathway activation, HER2 targeted agents were given to 5 patients.

Conclusions

This study confirmed the unique role of MoP in selecting effective treatments for MBC.

This approach provided clinical benefits for 56% of previously treated MBC patients, which met the primary objective of the study.

This study also suggests that irinotecan may be an under-developed drug for MBC patients.

As such, this approach merits further investigation.