Clinical Utility of Encyclopedic Tumor Analysis to Treat Breast Cancer Patients who have Failed Standard of Care Treatments

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BACKGROUND

Advanced refractory breast cancers (Br-Ca) pose formidable management challenges. Post failure of multiple lines of therapy, patients may be considered for palliation or clinical trials.

RATIONAL

Advanced refractory Br-Ca have latent vulnerabilities which can be identified by deep multi-analyte interrogation of the tumor interactome. We developed an Encyclopedic Tumor Analysis (ETA) which evaluates gene mutations, copy number variations, fusions, gene expression (mRNA and lncRNA) and in vitro chemoresistance profile of viable tumor cells. ETA findings were used to assign patient-specific drug-priority lists with optimum chemoresistance profile of viable tumor cells.

APPROACH

We retrospectively evaluated 27 patients with advanced refractory Br-Ca where the cancer had previously progressed following failure of ≥2 prior systemic lines. These patients received ETA-guided treatments. Treatment response was determined from follow-up radiological scans and used to calculate Response Rates, Progression Free Survival.

ENCYCLOPEDIC TUMOR ANALYSIS

ETA findings were integrated and harmonized to generate patient-specific drug-priority lists with optimum chemoresistance profile of viable tumor cells. ETA findings were used to assign patient-specific label- and tumor interactome. We developed an Encyclopedic Tumor Analysis (ETA) which evaluates gene mutations, copy number variations, fusions, gene expression (mRNA and lncRNA) and in vitro chemoresistance profile of viable tumor cells. ETA findings were used to assign patient-specific label- and organ-agnostic combination treatment regimens.

REPRESENTATIVE CASE

39 year old female patient.
Presented with lump in breast in 2016.
TruCut Bx: Grade III IDC ER+, PR-, HER2+.
Received #24 Paclitaxel + Trastuzumab.
2017: PET-CT showed progression.
• TruCut Bx: Grade III IDC ER+, PR-, HER2+.
• Received #24 Paclitaxel + Trastuzumab.
2017: PET-CT: recurrence + metastases.
• Received #24 Paclitaxel + Trastuzumab.
• 39 year old female patient.
• 2017: PET-CT showed progression.
• TruCut Bx: Grade III IDC ER+, PR-, HER2+.
• Received #24 Paclitaxel + Trastuzumab.

TREATMENT RESPONSE

Response to ETA-guided treatments assessed radiologically.
Chances to tumor dimensions (SLD: Sum of Longest Diameters) calculated as per RECIST v1.1 criteria.
Complete Response (CR) was seen in 1 patient.
Partial Response (PR) was seen in 14 patients.
Stable Disease (SD ≤45 days) was seen in 12 patients.
Objective Response Rate (ORR) = 55.6%.
Disease Control Rate (DCR) = 96.3%.
Kaplan Meier Curve shows robust PFS.
Median PFS was ~4 months at the most recent follow-up.
90-day PFS rate was 96.3%.
Patients being followed up further for PFS and OS (data not mature).
There were no Grade IV Therapy Related Adverse Events.
There were no related deaths.

CONCLUSION

Multi-analyte tumor profiling (ETA) can reveal latent actionable vulnerabilities in refractory cancers. ETA-guided treatments were safe and offered meaningful survival benefits in this heavily pretreated cohort of advanced refractory breast cancers.

Fig 1. Analytes and Analyses in ETA.
- Freshly biopsied tumor tissue and 15 mL blood was obtained from all patients for ETA.
- ETA evaluated gene alterations (SNV, CNA, Indels) in DNA, and in vitro chemoresistance profile of viable tumor cells.
- ETA findings were integrated and harmonized to generate patient-specific drug-priority lists with optimum chemoresistance profile of viable tumor cells.

Fig 2. Actionable Indications.
- 2017: PET-CT showed progression.
- There we no therapy related deaths.
- There were no Grade IV Therapy Related Adverse Events.
- Median PFS was ~4 months at the most recent follow-up.
- 90-day PFS rate was 96.3%.
- Patients being followed up further for PFS and OS (data not mature).
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Fig 3. Types of Combination Regimens.
- Stable Disease (SD ≥45 days) was seen in 12 patients.
- Patients being followed up further for PFS and OS (data not mature).
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Fig 4. Targeted and Endocrine Agents.
- Partial Response (PR) was seen in 14 patients.
- Objective Response Rate (ORR) = 55.6%.
- Disease Control Rate (DCR) = 96.3%.
- Kaplan Meier Curve shows robust PFS.
- Median PFS was ~4 months at the most recent follow-up.
- 90-day PFS rate was 96.3%.
- Patients being followed up further for PFS and OS (data not mature).
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Fig 5. Cytotoxic Agents.
- Complete Response (CR) was seen in 1 patient.
- Changes to tumor dimensions (SLD: Sum of Longest Diameters) calculated as per RECIST v1.1 criteria.
- Complete Response (CR) was seen in 1 patient.
- Partial Response (PR) was seen in 14 patients.
- Stable Disease (SD ≤45 days) was seen in 12 patients.
- Objective Response Rate (ORR) = 55.6%.
- Disease Control Rate (DCR) = 96.3%.
- Kaplan Meier Curve shows robust PFS.
- Median PFS was ~4 months at the most recent follow-up.
- 90-day PFS rate was 96.3%.
- Patients being followed up further for PFS and OS (data not mature).
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Key ETA Findings
- DNA Mutations
- RNA Mutations
- Gene Expression
- VEGF

Therapy Recommendation

- DNA Mutations
- RNA Mutations
- Gene Expression
- VEGF

Fig 6. Response to ETA Guided Treatments.
- Disease Control Rate (DCR) = 100%.
- Stable Disease (SD ≥45 days) was seen in 12 patients.
- Patients being followed up further for PFS and OS (data not mature).
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Fig 7. Kaplan Meier Curve and Progression Free Survival.
- There we no therapy related deaths.
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Fig 8. Treatment Outcome.
- Significant regression of hepatic metastases.
- 90-day PFS rate was 96.3%.
- Patients being followed up further for PFS and OS (data not mature).
- There were no Grade IV Therapy Related Adverse Events.
- There were no related deaths.

Table 1. Subtype

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<th>Subtype</th>
<th>Grade</th>
<th>Metastatic Sites</th>
<th>Therapy Treatments</th>
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Table 2. Grade

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Table 3. Metastatic Sites

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Table 5. Therapy related AEs

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