Abstract #888

Tumor Genomic Profiling Results in Breast Cancer Patients: A Comprehensive Analysis from a Laboratory Research Registry

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Background

- Precision oncology has transformed breast cancer care, with comprehensive genomic profiling (CGP) playing a key role in identifying tumor (somatic) alterations and biomarkers that guide personalized treatment.
- Additionally, germline testing helps uncover inherited pathogenic variants relevant to therapy and hereditary risk.
- Despite the growing use of CGP and germline testing, real-world data on the distribution and clinical relevance of results across diverse breast cancer populations is limited.
- To better understand the molecular landscape of breast cancer in a real-world setting, we analyzed CGP results from a clinical laboratory research registry, including tumor variant classifications, biomarker profiles, and germline findings.

Methods

- A retrospective analysis was conducted on 279 breast cancer patients who underwent CGP utilizing a clinical laboratory research registry.
- Variables assessed included age at diagnosis, sex at birth, histological subtype, ancestry, microsatellite instability (MSI), tumor mutational burden (TMB), PD-L1 expression, tumor variant classifications based on their clinical significance (IA, IB, IIC, IID), and gene-specific alterations.
- Germline testing rates and pathogenic variant (PV) findings were also assessed. Ordering provider specialties and family history were reviewed to contextualize clinical decision-making.

Table 1. Gender Distribution

Gender	Count	Percentage
Female	273	98%
Male	6	2%

Table 2. Tumor Genomic Variant Classification Definitions

IA	IB	IIC	IID
Variant of strong clinical significance, Level A evidence (FDA approved therapy or practice guideline in patient's tumor type)	Variant of strong clinical significance, Level B evidence (consensus in the field based on well-powered studies in patient's tumor type)	Variant of potential clinical significance, Level C evidence (FDA approved therapy or practice guideline in other tumor type(s), evidence from multiple small published studies, or based on availability of investigational therapies)	Variant of potential clinical significance, Level D evidence (case reports or preclinical studies)

Figure 1. Histological types

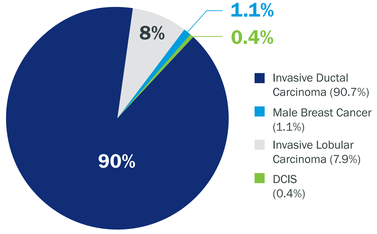
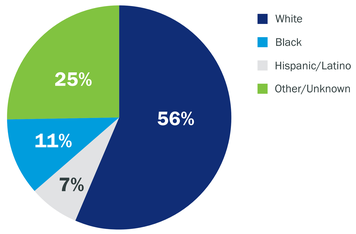


Figure 2. Race Distribution



Results

- The majority of patients, 253/279 (90.4%), had invasive ductal carcinoma, followed by 22 (7.9%) with invasive lobular carcinoma, 3 (1.1%) with male breast cancer, and 1 (0.36%) with ductal carcinoma in situ (DCIS) (**Figure 1**).
- The median age at diagnosis was 61 years (range 24 - ≥90).
- Most patients were female (273, 98%) (**Table 1**).
- This cohort was predominantly White (156, 53.6%), with Black (32, 11.5%) and Hispanic/Latino (20, 6.9%) individuals comprising smaller proportions (**Figure 2**).
- Tumor variant classification showed that 96.8% (270) of patients had at least one classified tumor variant in categories IA, IB, IIC, or IID (**Table 2**). IA variants, defined as alterations with an FDA-approved therapy for the patient's tumor type, were present in 126 patients (45.0%), where 16 patients harbored 2 variants (**Figure 3**).
- The most frequently altered IA genes were *PIK3CA* (75), *ERBB2* (27), *ESR1* (10), *PTEN* (7), *AKT1* (6), *BRCA1* (5), *BRCA2* (4), and gene fusions (4) (**Figure 4**).

Figure 3. CGP Summary Biomarkers

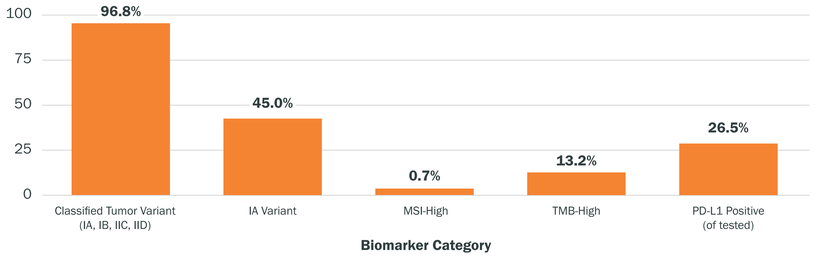
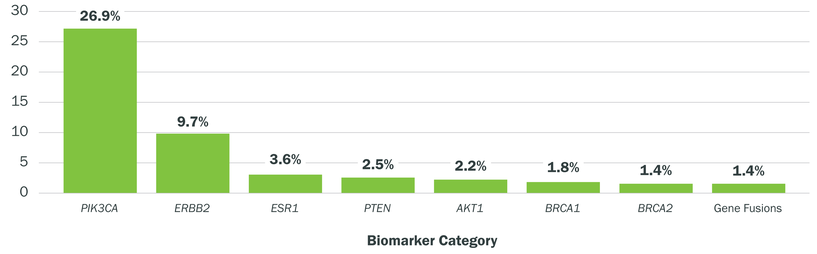


Figure 4. CGP IA Gene Alterations



- Immunological Biomarkers: Microsatellite instability (MSI) was high in only 2 (0.7%) patients. High tumor mutational burden (TMB) was observed in 37 (13.2%) cases. PD-L1 analysis was performed in 204 (73.1%) patients, with 54 (26.5%) having positive PD-L1 expression (**Figure 3**).
- Germline testing was conducted in 163 (58%) patients (**Figure 5**).
- 14 germline pathogenic variants were identified, including in *MUTYH* (5), *CHEK2* (2), and one each of *BRCA1*, *BRCA2*, *RAD51C*, *TP53*, *PALB2*, *APC*, and *MSH3*. 13 of these variants (93%) were detected in tumor profiling (**Figure 6**).
- Most genomic tests were ordered by medical oncologists (218, 76.8%), followed by genetics providers (51, 18%).
- There were 499 relatives with reported cancer. 111 (22.2%) had a history of female breast cancer.
- Half of the patients reported no family history of cancer.

Figure 5. Frequency of Combined Germline and CGP testing

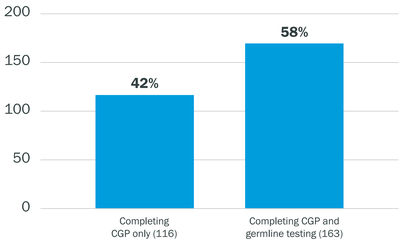
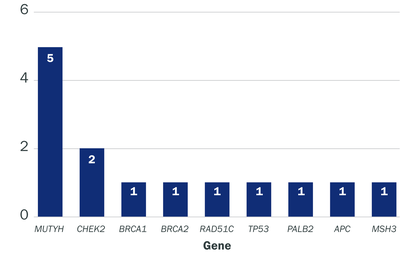


Figure 6. Germline Pathogenic Variants identified



Conclusions

- This analysis highlights the genomic complexity and heterogeneity of breast cancer.
- The high prevalence of actionable tumor variants, particularly in *PIK3CA* and *ERBB2*, demonstrates the clinical utility of CGP.
- Importantly, 93% of germline PVs were also detected in tumor profiling; however, one PV was missed, consistent with prior data showing that 8–10% of germline PVs may be missed by tumor-only testing.
- Despite guideline recommendations, only 58% of patients underwent germline testing, and just half reported a family history of cancer.
- The results suggest that using both germline and somatic testing may contribute to more comprehensive genomic assessment and inform patient care.

Female = sex at birth

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