

# The Benefits of comprehensive NGS Panels using Liquid Biopsy in Breast Cancer

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## INTRODUCTION

The approval of targeted therapies for breast cancer has increased the clinical relevance of Next-Generation Sequencing (NGS) liquid biopsy analysis, particularly in the metastatic setting. Smaller targeted panels provide rapid and cost-effective results, while comprehensive panels offer broader genomic insights, including Tumor Mutational Burden (TMB) and Microsatellite Instability (MSI). This study compares a 12-gene targeted panel with a 1021-gene comprehensive panel to evaluate their clinical impact.

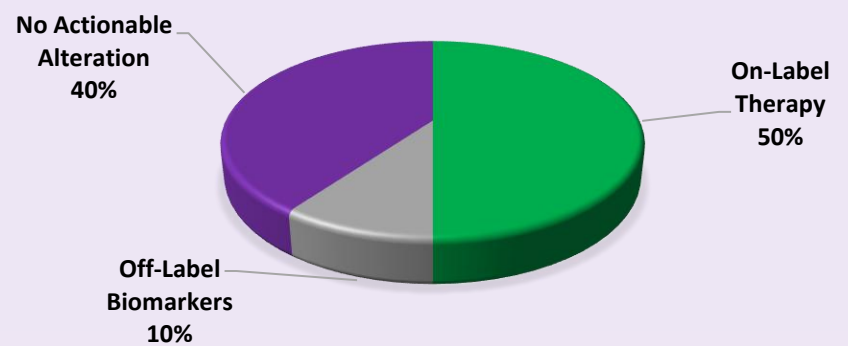
## MATERIAL & METHODS

Plasma samples from 1011 metastatic breast cancer patients were analyzed using a 12-gene targeted panel (Oncomine™ Breast cfDNA Research Assay v2 - Thermo Fisher Scientific). A subset of 104 patients underwent testing with a 1021-gene comprehensive panel (Gene Plus), which also included bTMB and MSI assessment, as well as paired white blood cell sequencing to filter out CHIP (Clonal Hematopoiesis of Indeterminate Potential) mutations. The study assessed mutation detection rates, on-label treatment eligibility, and potential therapeutic implications.

## RESULTS

In the smaller gene targeted panel cohort 56% of patients had a positive finding, while the prevalence of on-label treatment was 47%, limited to *ESR1*, *PIK3CA* and *AKT1* genes. In contrast, the comprehensive cfDNA analysis revealed a positive gene finding in 80% of the patients.

### 1021-GENE PANEL THERAPY ELIGIBILITY



### 12-GENE PANEL THERAPY ELIGIBILITY

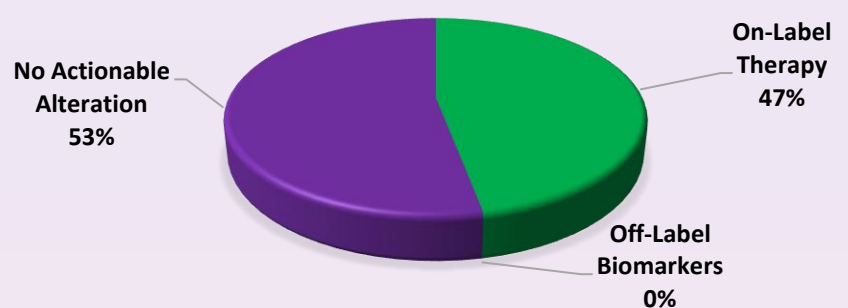


Chart 2. Comparison of patients' therapy eligibility between the two panels.

The inclusion of paired blood analysis revealed a pathogenic/likely pathogenic germline variant in homologous recombination genes (*BRCA1/2*, *CHEK2*, *PALB2*) in almost 9% of the cases. Finally, approximately 11% of the patients were TMB-High (>16mut/mb) and potentially eligible for immunotherapy.

### bTMB & MSI STATUS IN 1021-GENE PANEL

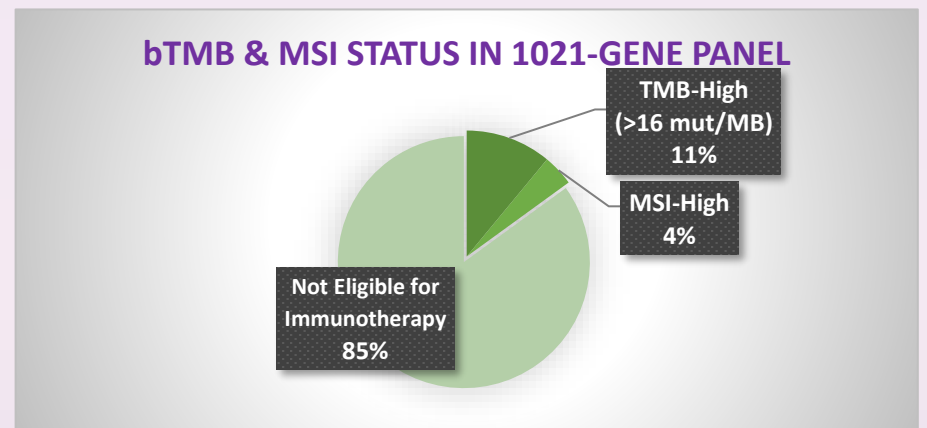


Chart 3. Immunotherapy eligibility according to bTMB & MSI status.

### ALTERED GENES ELIGIBLE FOR THERAPY PER PANEL

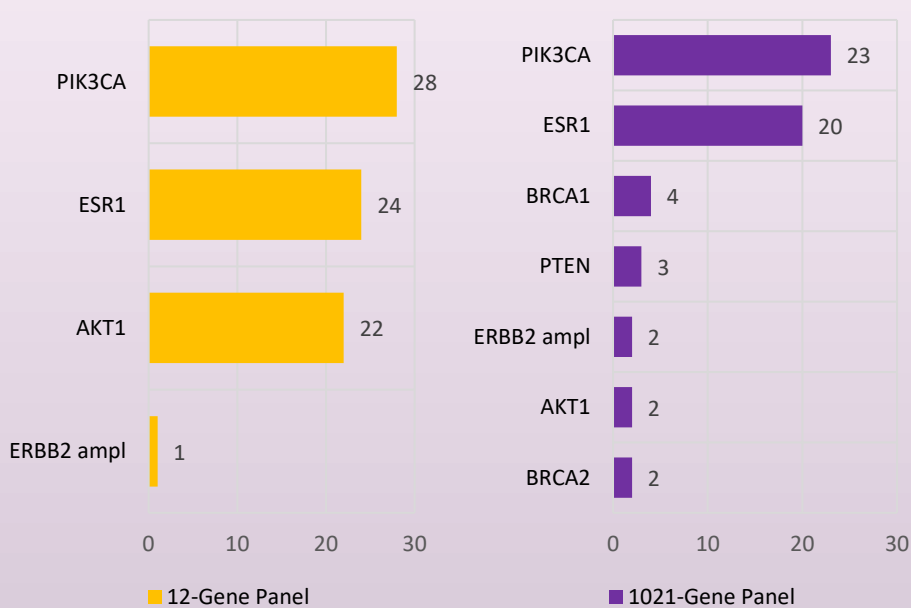


Chart 3. Genes associated with on label therapy in each panel.

Over 50% of the findings were associated with on-label treatments, while 10% of them would have been missed if the 12-gene panel had been implemented. *PIK3CA* (41%), *ESR1* (36%), *BRCA1/2* (11%), *PTEN* (5%), *AKT1* (4%), *ERBB2* amplification (4%) and *NTRK3* (1%) were the targetable on-label alterations detected. At least one off-label biomarker was identified in 10% of the cases.

## REFERENCES

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Table 1. Overall comparison of the two panels.

Parameter	12-Gene Panel	1021-Gene Panel
Mutation Detection Rate	56%	80%
On-Label Therapy Eligibility	47%	50%
Turnaround Time (days)	10	15
Cost-Effectiveness	High	Lower
TMB/MSI Information	Not Available	Available
Resistance Detection	Limited	Comprehensive

## DISCUSSION-CONCLUSIONS

Comprehensive liquid biopsy panels provide at least 20% more actionable information compared to targeted panels, enabling broader therapeutic options, including PARP inhibitors and immunotherapy. The inclusion of concurrent ctDNA and germline analysis enhances clinical decision-making, particularly for complex or refractory cases. While targeted panels are more cost-effective for routine clinical use, comprehensive panels offer greater clinical value in guiding advanced treatment strategies.