



Bversity LifeSciences

Comprehensive Genomic Profiling Report

Clinical Next-Generation Sequencing Analysis

PATIENT DEMOGRAPHICS

PATIENT ID: #45992

AGE: 43 Years

SEX: Female

DIAGNOSIS: Triple Negative Breast Cancer (TNBC)

SPECIMEN ID: TNBC-2024-001

DATE: August 02, 2024

PHYSICIAN DETAILS

ORDERING PHYSICIAN: Dr. S. Batra

FACILITY: Max Super Speciality Hospital

Genomic Executive Summary

Actionable Biomarker

**Tumor Mutational
Burden (TMB)**

High (16 Muts/Mb)

Associated with potential response to Immune Checkpoint Inhibitors.

Prognostic Variant

TP53 p.Arg175His Tier 2C

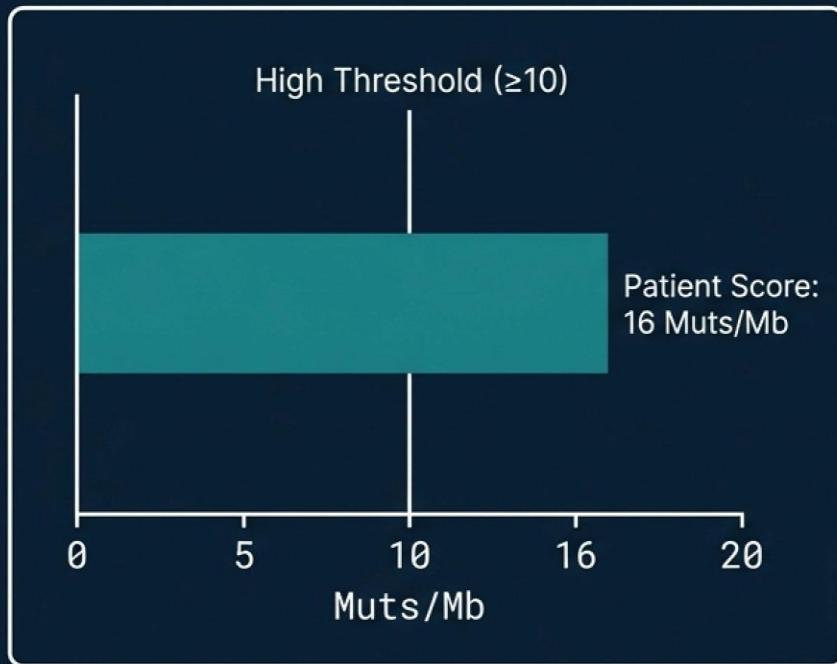
Prognostic Significance / Potential Clinical Utility.

Variants of Uncertain Significance (VUS)

4 Variants Detected

ABL2, BRCA2, ARID1B, AKAP9

Biomarker Analysis: Tumor Mutational Burden (TMB)



This sample harbors a TMB level (16 Muts/Mb) associated with improved Objective Response Rate (ORR) and Disease Control Rate (DCR) in pan-solid tumors. Evidence indicates that High TMB is associated with greater sensitivity to immunotherapeutic agents, including anti-PD-L1 and anti-PD-1 therapies.

Source: Prospective Phase 2 MyPathway trial data regarding TMB thresholds.

Therapeutic Implications: Immunotherapy

FDA Agnostic Approval

Pembrolizumab (Keytruda)

Unresectable or metastatic solid tumors with TMB-High (≥ 10 mut/Mb) that have progressed following prior treatment.



Combination Therapy Evidence

Nivolumab + Ipilimumab

Associated with improved responses in high TMB cohorts across various solid tumor studies.

Genomic Findings: TP53

Variant Data

Gene: **TP53**

Gene: Roboto Mono

Alteration: **p.Arg175His**

Roboton: p.Arg175His

Classification: **Tier 2C (Prognostic)**

Variant Allele Frequency: **56.0%**

Roboto Mono: 56.0%

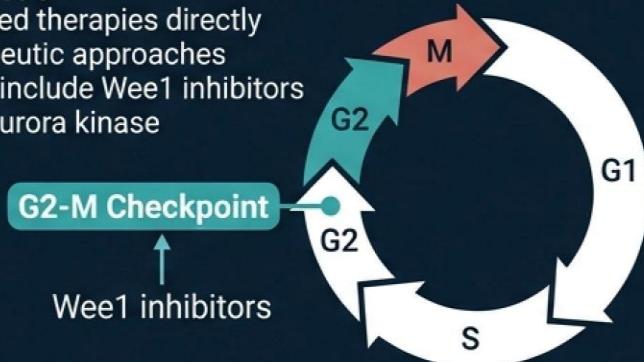
Functional Impact

Biological Impact

TP53 encodes the p53 tumor suppressor protein. The p.Arg175His alteration is a hotspot mutation associated with gain of oncogenic function, loss of tumor suppression, and genomic instability.

Clinical Relevance

Currently no approved therapies directly target TP53. Therapeutic approaches under investigation include Wee1 inhibitors (adavosertib) and Aurora kinase inhibitors.



Variants of Uncertain Significance (VUS)

The following variants were detected but their clinical significance is currently unresolved.



Gene	Alteration	Pathway/Function
ABL2	p.Thr753Ala	Tyrosine Kinase / Cytoskeletal Rearrangement
BRCA2	p.Glu1593Ter	Homologous Recombination / DNA Repair
ARID1B	p.Gly897Ala	Chromatin Remodeling (SWI/SNF)
AKAP9	p.Asp2313His	Protein Kinase A Signaling Scaffold

VUS Profile: BRCA2 & ABL2

BRCA2 p.Glu1593Ter	ABL2 p.Thr753Ala
<p>Context: BRCA2 is a critical component of the homologous recombination DNA repair pathway. While BRCA2 loss is a known driver in breast cancer and a sensitizer to PARP inhibitors, this specific termination variant is currently classified as a VUS in this specific analysis context. Clinical correlation is recommended.</p>	<p>Context: Encodes a non-receptor tyrosine kinase involved in cytoskeletal rearrangement. The specific p.Thr753Ala variant has not been fully characterized in scientific literature regarding drug sensitivity in TNBC.</p>

VUS Profile: ARID1B & AKAP9

ARID1B p.Gly897Ala	AKAP9 p.Asp2313His
<p>Context: Member of the SWI/SNF chromatin remodeling complex. Mutation or loss of SWI/SNF members is considered a tumor suppressor event in various cancers.</p>	<p>Context: A-kinase anchor protein; coordinates signaling pathways by binding to Protein Kinase A (PKA). The significance of the Asp2313His change is currently unknown.</p>

Pertinent Negatives & Pathway Analysis

Negative Findings



ERBB2 (HER2): Negative

No amplification or pathogenic mutation detected. Absence of ERBB2 amplification confirms lack of eligibility for anti-HER2 therapies (Trastuzumab, Pertuzumab) based on this assay.



PIK3CA: Negative (Wildtype)

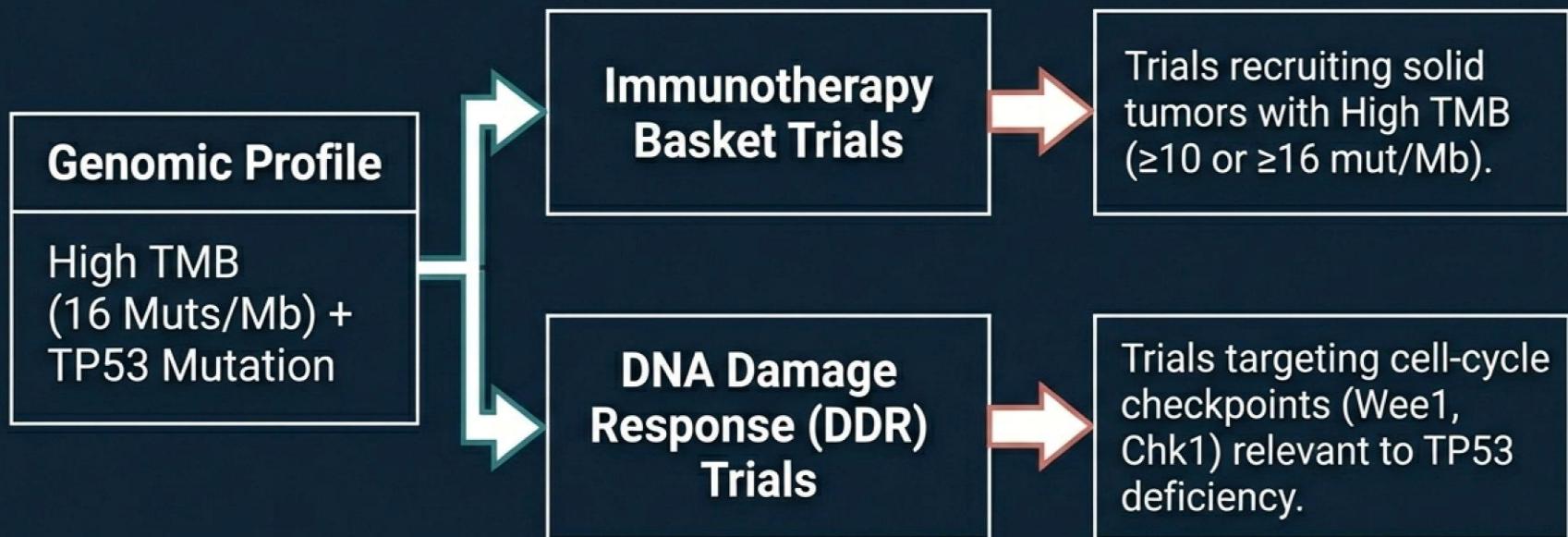
No pathogenic mutations detected.



RAS Pathway (HRAS/ KRAS/NRAS): Negative

No pathogenic mutations detected.

Clinical Trial Considerations



*Inhibition of DNA damage checkpoints may enhance activity of DNA-damaging agents in p53-deficient tumors.

Methodology & Test Specifications

Assay

Next-Generation Sequencing (NGS) based assay identifying genomic findings within hundreds of cancer-related genes.

Sequencing

Platform: Illumina® Sequencing (HiSeq/NovaSeq). Hybrid capture-selected libraries sequenced to high uniform depth (targeting >500X median coverage).

Analysis

Sequence data processed to detect base substitutions, indels, copy number alterations, and genomic signatures (TMB, MSI).

Technical Definitions

Tumor Mutational Burden (TMB)

A measure of the number of somatic protein-coding base substitutions and indels per megabase of genome tested. TMB calculation excludes known germline variants and synonymous mutations.

Variant Allele Frequency (VAF)

Represents the fraction of sequencing reads in which the variant is observed. Caution is recommended in interpreting VAF to indicate potential germline vs. somatic origin.

*Inhibition of DNA damage checkpoints may enhance activity of DNA-damaging agents in p53-deficient tumors.

Appendix: Gene List (DNA)

Entire coding sequence for detection of base substitutions, indels, and copy number alterations.

ABL1	ABL2	AKT1	AKT2	ALK	APC	ARID1A	ARID1B
ATM	ATR	BRAF	BRCA1	BRCA2	CDH1	CDK4	CDKN2A
EGFR	CDK4	CDKN2A	CTNNB1	EGFR	ERBB2	ERBB3	ESR1
FGFR1	FGFR2	FGFR3	HRAS	IDH1	IDH1	IDH2	IDH2
JAK1	JAK2	KIT	KRAS	MAP2K1	MET	MLH1	MSH2
MSH6	MTOR	MYC	NF1	NOTCH1	NRAS	NRAS	PALB2
PIK3CA	PMS2	PTEN	RAF1	RB1	RET	ROS1	SMAD4
SMO	SRC	STK11	TP53	TSC1	TSC2	VHL	WT1

Review & Approval

The content in this report is an aid to diagnosis and should not substitute for independent medical judgment. Treatment decisions are the responsibility of the treating physician.

Electronically Signed By:

Medical Director, Bversity LifeSciences

Date: 02 Aug 2024

Clinical Summary

This TNBC profile is characterized by **High Tumor Mutational Burden (16 Muts/Mb)** and a prognostic **TP53** alteration.

Next Steps

1. Evaluate eligibility for **Immune Checkpoint Inhibitor** therapy (Pembrolizumab).
2. Consider **Clinical Trials** targeting DNA damage response pathways.
3. Monitor **VUS** findings for future reclassification.