Patient

Name:
Date of Birth:
Sex: Female
Case Number: TN22-
Diagnosis: Ductal carcinoma, NOS

Specimen Information

Primary Tumor Site: Upper-outer quadrant of breast
Specimen Site: Breast, NOS
Specimen ID:
Specimen Collected:
Test Report Date:

Ordered By

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
PD-L1 (22c3)	**IHC**	**Protein**	**Positive, CPS: 10**	**BENEFIT**	**pembrolizumab + chemotherapy**	**Level 1**
ER/PR/Her2/Neu	**IHC**	**Protein**	**Triple Negative**	**BENEFIT**	**sacituzumab govitecan**	**Level 2**
TMB	**Seq**	**DNA-Tumor**	**High, 10 mut/Mb**	**BENEFIT**	**pembrolizumab**	**Level 2**
ERBB2 (Her2/Neu)	IHC	Protein	Negative | 1+, 20%	LACK OF BENEFIT	trastuzumab ado-trastuzumab emtansine (T-DM1)	Level 1
					pertuzumab, margetuximab fam-trastuzumab deruxtecan-nxki lapatinib, neratinib, tucatinib	Level 2
ER	IHC	Protein	Negative | 0	LACK OF BENEFIT	endocrine therapy	Level 2
PR	IHC	Protein	Negative | 0			
AR	IHC	Protein	Negative | 1+, 1%	LACK OF BENEFIT	bicalutamide, enzalutamide	Level 3
BRCA1	Seq	DNA-Tumor	Pathogenic Variant Exon 7 | p.Q169*	carboplatin, cisplatin A pathogenic or likely pathogenic BRCA1 mutation, and/or deletion, was detected in this tumor for which germline status is negative or unavailable. Per NCCN, platinum agents are options for advanced triple negative breast cancer patients harboring germline BRCA1/2 mutations based on studies demonstrating a pronounced clinical benefit in these patients (Isakoff, et al. 2015; Tutt, et al. 2018). The benefit of platinum agents in the context of somatic-only mutations (including deletions) remains to be determined.		
				olaparib, talazoparib A pathogenic or likely pathogenic BRCA1 mutation, and/or deletion, was detected in this tumor for which germline status is negative or unavailable. In breast cancer, the strongest evidence for PARP inhibitors comes from predominantly germline studies and, therefore, drug labels and guidelines for PARP inhibitors state a requirement for germline mutations. The benefit of these therapies in the context of somatic-only mutations (including deletions) remains to be determined.		

* Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines; Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically significant findings.

4610 South 44th Place, Suite 100 • Phoenix, AZ 85040 • (888) 979-8669 • Fax: (866) 479-4925
CLIA 03D1019490 • CAP 7195577 • ISO 15189:2012 • Matthew Oberley, MD, PhD, Medical Director •

Important Note

A pathogenic nonsense mutation was detected in BRCA1. Pathogenic germline mutations in this gene are causal for hereditary cancers of the breast, ovaries, pancreas and prostate. Confirmation of the patient's carrier status should be considered.

The chemotherapy regimens for the KEYNOTE-355 trial (pembrolizumab + chemotherapy in TNBC) included paclitaxel, nab-paclitaxel, and gemcitabine + carboplatin.

TMB-High status should only be used to guide pembrolizumab treatment when no satisfactory alternative treatment options are available.

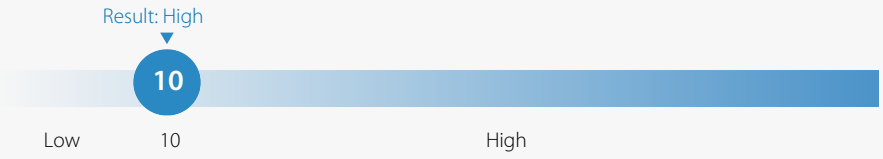
MI GPSai was performed on this case. Please see *Page 5* for results.

Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result
Genomic LOH	**Seq**	**DNA-Tumor**	**High**
MSI	Seq	DNA-Tumor	Stable
Mismatch Repair Status	IHC	Protein	Proficient
NTRK1/2/3	Seq	RNA-Tumor	Fusion Not Detected
AKT1	Seq	DNA-Tumor	Mutation Not Detected
BRCA1	CNA-Seq	DNA-Tumor	Deletion Not Detected
BRCA2	CNA-Seq	DNA-Tumor	Deletion Not Detected
	Seq	DNA-Tumor	Mutation Not Detected
ERBB2 (Her2/Neu)	CNA-Seq	DNA-Tumor	Amplification Not Detected
	Seq	DNA-Tumor	Mutation Not Detected

Biomarker	Method	Analyte	Result
ESR1	Seq	RNA-Tumor	Fusion Not Detected
		DNA-Tumor	Mutation Not Detected
MTAP	CNA-Seq	DNA-Tumor	Deletion Not Detected
NF1	CNA-Seq	DNA-Tumor	Deletion Not Detected
	Seq	DNA-Tumor	Mutation Not Detected
PIK3CA	Seq	DNA-Tumor	Mutation Not Detected
PTEN	IHC	Protein	Positive | 1+, 1%
	CNA-Seq	DNA-Tumor	Deletion Not Detected
	Seq	DNA-Tumor	Mutation Not Detected

Genomic Signatures

Biomarker	Method	Analyte	Result
Microsatellite Instability (MSI)	Seq	DNA-Tumor	Stable
Tumor Mutational Burden (TMB)	Seq	DNA-Tumor	
Genomic Loss of Heterozygosity (LOH)	Seq	DNA-Tumor	High - 29% of tested genomic segments exhibited LOH (assay threshold is ≥ 16%)

PATIENT: **TN22-** **PHYSICIAN:**

Genes Tested with Pathogenic or Likely Pathogenic Alterations

Gene	Method	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency %
BRCA1	Seq	DNA-Tumor	Pathogenic Variant	p.Q169*	7	c.505C>T	28
STK11	Seq	DNA-Tumor	Pathogenic Variant	p.K48fs	1	c.141delC	30
TP53	Seq	DNA-Tumor	Pathogenic Variant	p.R342*	10	c.1024C>T	29

Unclassified alterations for DNA and RNA sequencing can be found in the MI Portal.
Formal nucleotide nomenclature and gene reference sequences can be found in the Appendix of this report.
Variants of Uncertain Significance can be found in the MI Portal.

Human Leukocyte Antigen (HLA) Genotype Results

The impact of HLA genotypes on drug response and prognosis is an active area of research. These results can help direct patients to clinical trials recruiting for specific genotypes. Please see www.clinicaltrials.gov for more information.

Gene	Method	Analyte	Genotype
MHC CLASS I			
HLA-A	Seq	DNA-Tumor	A*02:01, A*24:02
HLA-B	Seq	DNA-Tumor	B*44:03, B*51:09
HLA-C	Seq	DNA-Tumor	C*01:02, C*04:01

HLA genotypes with only one allele are either homozygous or have loss-of-heterozygosity at that position.

Immunohistochemistry Results

Biomarker	Result	Biomarker	Result
AR	Negative | 1+, 1%	MSH6	Positive | 3+, 90%
ER	Negative | 0	PD-L1 (22c3)	Positive, CPS: 10
ERBB2 (Her2/Neu)	Negative | 1+, 20%	PMS2	Positive | 3+, 100%
MLH1	Positive | 3+, 90%	PR	Negative | 0
MSH2	Positive | 3+, 100%	PTEN	Positive | 1+, 1%

Genes Tested with Indeterminate Results by Tumor DNA Sequencing

AXIN2	COL2A1	NPM1	PIK3CB	PIK3R2	PTPN11	PTPRD	RAC1	RASA1	TRAF7	XRCC1

Genes in this table were ruled indeterminate due to low coverage for some or all exons.

4610 South 44th Place, Suite 100 • Phoenix, AZ 85040 • (888) 979-8669 • Fax: (866) 479-4925
CLIA 03D1019490 • CAP 7195577 • ISO 15189:2012 • Matthew Oberley, MD, PhD, Medical Director •

To view the rest of the report, contact a Caris Life Sciences® representative today.

(888) 979- 8669
CustomerSupport@carisls.com

4610 South 44th Place, Suite 100 • Phoenix, AZ 85040 • (888) 979-8669 • Fax: (866) 479-4925
CLIA 03D1019490 • CAP 7195577 • ISO 15189:2012 • Matthew Oberley, MD, PhD, Medical Director