MI PROFILE™
MOLECULAR INTELLIGENCE TUMOR REPORT

CARIS® LIFE SCIENCES

FINAL REPORT

PATIENT

Name: Patient, Test
Date of Birth: XX-Mon-19XX
Sex: Female
Case Number: TN17-XXXXXX
Diagnosis: Carcinoma, metastatic, NOS

SPECIMEN INFORMATION

Primary Tumor Site: Breast, NOS
Specimen Site: Liver
Specimen ID: ABC-1234-XX
Specimen Collected: XX-Mon-2017
Completion of Testing: XX-Mon-2017

ORDERED BY

Ordering Physician, MD
Cancer Center
123 Main Street
Springfield, XY 12345 USA
1 (123) 456-7890

BIOMARKER HIGHLIGHTS (SEE PAGE 2 AND APPENDIX FOR MORE DETAILS)

Biomarker	Method	Result
Lineage Relevant Biomarkers		
ER	IHC	Positive | 2+, 30%
PR	IHC	Negative | 0, 100%
Her2/Neu (ERBB2)	IHC	Negative | 0, 100%
AR	IHC	Negative | 0, 100%
PIK3CA	NGS	Mutation Not Detected
PTEN	IHC	Negative | 0, 100%
ESR1	NGS	Mutation Not Detected
BRCA1	NGS	Mutation Not Detected

Biomarker	Method	Result
Lineage Relevant Biomarkers (cont)		
BRCA2	NGS	Mutation Not Detected
Other Notable Biomarker Results		
Total Mutational Load		High | 17 Mutations/Mb
MSI	NGS	Stable
TP53	NGS	Mutated, Pathogenic
		Exon 6 | H193R
PD-L1	IHC	Negative | 0, 100%

The therapies listed below are FDA-approved, on-NCCN Compendium® for the tested lineage or deemed relevant for this lineage by a panel of internal and external oncology experts. Complete therapy association information and Off-NCCN Compendium therapies are listed on pages (5-8).

THERAPIES WITH POTENTIAL BENEFIT

anastrozole★, exemestane★, fulvestrant★, letrozole★, megestrol acetate, tamoxifen★, toremifene★	**ER**
everolimus★	**ER**
palbociclib★, ribociclib	**ER, Her2/Neu (ERBB2)**
carboplatin, cisplatin	ERCC1
goserelin, leuprolide	ER

See page 5 for off-NCCN compendium therapies.

★ Drug/biomarker association(s) supported by the highest level of clinical evidence.

THERAPIES WITH UNCERTAIN BENEFIT

capecitabine, fluorouracil	TS

Drugs are placed in the Uncertain benefit category when a result suggests only a decreased likelihood of response (vs. little to no likelihood of response) or if there is insufficient evidence to associate the drug with either benefit or lack of benefit.

THERAPIES WITH POTENTIAL LACK OF BENEFIT

ado-trastuzumab emtansine (T-DM1), lapatinib, pertuzumab	Her2/Neu (ERBB2)
trastuzumab	Her2/Neu (ERBB2)

Therapies associated with potential benefit or lack of benefit are based on biomarker results and published medical evidence derived from multiple tumor types. The selection of any, all, or none of the matched therapies resides solely with the discretion of the treating physician. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all available information concerning the patient's condition in accordance with the applicable standard of care.

CE

BIOMARKER RESULTS

This summary includes biomarkers most commonly associated with cancer. Complete details of all biomarkers tested can be found in the Appendix.

TOTAL MUTATIONAL LOAD

Mutations / Megabase: 17	Result: High

MICROSATELLITE INSTABILITY (MSI) BY NEXT-GENERATION SEQUENCING

MSI by NGS	Result: Stable

GENES TESTED WITH MUTATIONS/ALTERATIONS

Gene	Method	Result	Alteration	Frequency (%)	Exon
TP53	NGS	Mutated, Pathogenic	H193R	67	6

Unclassified alterations can be found in the Appendix

IMMUNOHISTOCHEMISTRY (IHC)

Biomarker	Result	Biomarker	Result	Biomarker	Result
AR	Negative | 0, 100%	Her2/Neu (ERBB2)	Negative | 0, 100%	PTEN	Negative | 0, 100%
ER	Positive | 2+, 30%	PD-L1	Negative | 0, 100%	TOPO1	Positive | 2+, 100%
ERCC1	Negative | 2+, 10%	PR	Negative | 0, 100%	TS	Positive | 1+, 10%

GENES TESTED WITH INDETERMINATE* SEQUENCING RESULTS BY NGS

ARID1A	ATRX	KDM5C	PIK3R1	PTEN	SMARCE1						

* Genes in this table were ruled indeterminate due to low coverage for some or all exons. Please see Appendix for a complete list of indeterminate genes.

GENES TESTED WITHOUT POINT MUTATIONS OR INDELS BY NGS

ABL1	AKT1	ALK	AMER1	APC	AR	ARAF	ARID2	ATM	BAP1	BMPR1A	BRAF
BRCA1	BRCA2	c-KIT	CDC73	CDH1	CDK4	CDKN1B	CDKN2A	CHEK1	CHEK2	cMET	CSF1R
CTNNB1	DDR2	DICER1	EGFR	ERBB3	ERBB4	ESR1	FGFR1	FGFR2	FGFR3	FGFR4	FH
FLCN	FLT3	FOXL2	FUBP1	GATA3	GNA11	GNAQ	GNAS	Her2/Neu (ERBB2)	HNF1A	IDH1	IDH2
JAK2	JAK3	KDM6A	KDR (VEGFR2)	KMT2A	KMT2D	KRAS	MAX	MEK1	MEK2	MEN1	MITF
MLH1	MPL	MSH2	MSH6	MTOR	MUTYH	NF1	NF2	NPM1	NRAS	NTRK1	PALB2
PBRM1	PDGFRA	PHOX2B	PIK3CA	PMS2	POLE	POT1	PPARG	PPP2R1A	PRKAR1A	PTCH1	PTPN11
RAF1	RB1	RET	RNF43	ROS1	SDHAF2	SDHB	SDHC	SDHD	SETD2	SF3B1	SMARCA4
SMARCB1	SMO	SPOP	SRC	SUFU	TERT	TSC1	TSC2	VHL	WT1		

Additional results continued on the next page. >

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GENES TESTED WITHOUT COPY NUMBER VARIATIONS (AMPLIFICATIONS) BY NGS											
AKT2	ALK	ARID1A	AURKB	CCND1	CCND3	CCNE1	CDK4	CDK6	CDK8	CDKN2A	cMET
CREBBP	CRKL	EGFR	EP300	EZH2	FGF10	FGF3	FGF4	FGFR1	FGFR2	FGFR3	GATA3
Her2/Neu (ERBB2)	KDR (VEGFR2)	MCL1	MDM2	MEK1	MYC	NF2	NFKBIA	NTRK1	RB1	RICTOR	ROS1
TOP1	WT1										

IN SITU HYBRIDIZATION
Not Amplified
TOP2A

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NOTES OF SIGNIFICANCE

SEE APPENDIX FOR FULL DETAILS

Clinical Trials Connector™ opportunities based on biomarker expression: 211 Chemotherapy Trials | 226 Targeted Therapy Trials. See page 9 for details.

SPECIMEN INFORMATION

Specimen ID: ABC-1234-XX

Specimen Collected: XX-Mon-2017

Specimen Received: XX-Mon-2017

Testing Initiated: XX-Mon-2017

Gross description: 1 (A) Paraffin Block - Client ID (ABC-123-XY) from XYZ Medical Center, Springfield, XY, with the corresponding cytology report labeled "ABC-123-XY".

Pathologic Diagnosis: Liver, biopsy: Metastatic carcinoma.

Dissection Information: Molecular testing of this specimen was performed after harvesting of targeted tissues with an approved manual microdissection technique. Candidate slides were examined under a microscope and areas containing tumor cells (and separately normal cells, when necessary for testing) were circled. A laboratory technician harvested targeted tissues for extraction from the marked areas using a dissection microscope. The areas marked and extracted were microscopically reexamined on post-microdissected slides and adequacy of microdissection was verified by a board certified Pathologist.

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THERAPIES WITH **POTENTIAL BENEFIT**

Refer to the Appendix for detailed Result and Value information for each biomarker, including appropriate cutoffs, unit of measure, etc.

Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
anastrozole★, exemestane★, fulvestrant★, letrozole★, megestrol acetate, tamoxifen★, toremifene★	ER	IHC	Positive	2+ 30%	Yes	I / Good	9#, 10#, 11#, 12#, 13#, 14#, 15#, 16#, 17#
	ESR1	NGS	Mutation Not Detected	-	No	-	-
	PR	IHC	Negative	0+ 100%	No	-	-
everolimus★	ER	IHC	Positive	2+ 30%	Yes	I / Good	24#, 25#, 26#
	ESR1	NGS	Mutation Not Detected	-	No	-	-
	PIK3CA	NGS	Mutation Not Detected	-	No	-	-
palbociclib★, ribociclib	ER	IHC	Positive	2+ 30%	Yes	I / Good	30#, 31#, 32#, 33#
	ESR1	NGS	Mutation Not Detected	-	No	-	-
	Her2/Neu (ERBB2)	IHC	Negative	0+ 100%	Yes	I / Good	2#, 30#, 31#, 32#, 33#
	PR	IHC	Negative	0+ 100%	No	-	-
carboplatin, cisplatin	ATM	NGS	Mutation Not Detected	-	No	-	-
	BRCA1	NGS	Mutation Not Detected	-	No	-	-
	BRCA2	NGS	Mutation Not Detected	-	No	-	-
	ERCC1	IHC	Negative	2+ 10%	Yes	II-3 / Good	21, 22#, 23

Additional Therapies with Potential Benefit continued on the next page. >

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THERAPIES WITH **POTENTIAL BENEFIT**

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Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
goserelin, leuprolide	AR	IHC	Negative	0+ 100%	No	-	-
	ER	IHC	Positive	2+ 30%	Yes	I / Good	17#
	PR	IHC	Negative	0+ 100%	No	-	-
OFF-NCCN COMPENDIUM®							
irinotecan	TOPO1	IHC	Positive	2+ 100%	Yes	II-1 / Good	27, 28, 29

★ Drug/biomarker association(s) supported by the highest level of clinical evidence.

* The level of evidence for all references is assigned according to the Literature Level of Evidence Framework consistent with the US Preventive Services Task Force described further in the Appendix of this report. The data level of each biomarker-drug interaction is the highest level of evidence based on the body of evidence, overall clinical utility, competing biomarker interactions and tumor type from which the evidence was gathered.

Evidence reference includes data from the same lineage as the tested specimen.

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THERAPIES WITH **UNCERTAIN BENEFIT**

Drugs are placed in the Uncertain benefit category when a result suggests only a decreased likelihood of response (vs. little to no likelihood of response) or if there is insufficient evidence to associate the drug with either benefit or lack of benefit. Refer to the Appendix for detailed Result and Value information for each biomarker, including appropriate cutoffs, unit of measure, etc.

Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
capecitabine, fluorouracil	TS	IHC	Positive	1+ 10%	Yes	II-1 / Good	18, 19#, 20#

* The level of evidence for all references is assigned according to the Literature Level of Evidence Framework consistent with the US Preventive Services Task Force described further in the Appendix of this report. The data level of each biomarker-drug interaction is the highest level of evidence based on the body of evidence, overall clinical utility, competing biomarker interactions and tumor type from which the evidence was gathered.

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THERAPIES WITH **POTENTIAL LACK OF BENEFIT**

Refer to the Appendix for detailed Result and Value information for each biomarker, including appropriate cutoffs, unit of measure, etc.

Therapies	Test	Method	Result	Value	Drug Association Details		
					Does Result Support Drug Association?	Highest Level of Evidence*	Reference
FDA-APPROVED/ON-NCCN COMPENDIUM®							
ado-trastuzumab emtansine (T-DM1), lapatinib, pertuzumab	Her2/Neu (ERBB2)	IHC	Negative	0+ 100%	Yes	I / Good	1#, 2#, 3#, 4#, 5#, 6#, 7#, 8#
trastuzumab	Her2/Neu (ERBB2)	IHC	Negative	0+ 100%	Yes	I / Good	2#, 5#, 34#, 35#
	PIK3CA	NGS	Mutation Not Detected	-	No	-	-
	PTEN	IHC	Negative	0+ 100%	No	-	-

* The level of evidence for all references is assigned according to the Literature Level of Evidence Framework consistent with the US Preventive Services Task Force described further in the Appendix of this report. The data level of each biomarker-drug interaction is the highest level of evidence based on the body of evidence, overall clinical utility, competing biomarker interactions and tumor type from which the evidence was gathered.

Evidence reference includes data from the same lineage as the tested specimen.

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CLINICAL TRIALS CONNECTOR™

For a complete list of open, enrolling clinical trials visit MI Portal to access the **Clinical Trials Connector**. This personalized, real-time web-based service provides additional clinical trial information and enhanced searching capabilities, including, but not limited to:

- Location: filter by geographic area
- Biomarker(s): identify specific biomarkers associated with open clinical trials to choose from
- Drug(s): search for specific therapies
- Trial Sponsor: locate trials based on the organization supporting the trial(s)

Visit www.CarisMolecularIntelligence.com to view all matched trials.

CHEMOTHERAPY CLINICAL TRIALS (211)

Drug Class	Biomarker	Method	Investigational Agent(s)
Anti-hormonal therapy (111)	ER	IHC	anastrozole, exemestane, fulvestrant, goserelin, letrozole, leuprolide, tamoxifen, toremifene
Platinum compounds (85)	ERCC1	IHC	carboplatin, cisplatin, oxaliplatin
TOPO1 inhibitors (15)	TOPO1	IHC	irinotecan , topotecan

TARGETED THERAPY CLINICAL TRIALS (226)

Drug Class	Biomarker	Method	Investigational Agent(s)
Cell cycle inhibitors (5)	TP53	NGS	LY2606368, MK-1775
Immunomodulatory agents (120)	T.M.L.	NGS	MEDI4736, MK-3475, MPDL3280A, MSB0010718C, atezolizumab, avelumab, durvalumab, nivolumab, pembrolizumab
p53-targeted biological agents (2)	TP53	NGS	Ad5CMV-p53, modified vaccinia virus ankara vaccine expressing p53
PARP inhibitors (27)	PTEN	IHC	BMN-673, MK4827, niraparib, olaparib, rucaparib, talazoparib, veliparib
PI3K/Akt/mTor inhibitors (72)	PTEN	IHC	ARQ092, AZD2014, AZD5363, BAY80-6946, BKM120, BYL719, GDC-0068, GDC0941, LY2780301, MK2206, MLN0128, PF-05212384, buparlisib, everolimus, ipatasertib, sirolimus, temsirolimus, triciribine

( ) = represents the total number of clinical trials identified by the Clinical Trials Connector for the provided drug class or table.

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