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: Colon, NOS
Specimen Site: Inguinal lymph node
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		
KRAS	NGS	Mutation Not Detected
NRAS	NGS	Mutation Not Detected
BRAF	NGS	Mutation Not Detected
PIK3CA	NGS	Mutation Not Detected
Her2/Neu (ERBB2)	NGS	Amplification Not Detected
MSI	FA	High
	NGS	Stable
MLH1	IHC	Negative | 0, 100%
MSH2	IHC	Positive | 2+, 90%

Biomarker	Method	Result
Lineage Relevant Biomarkers (cont)		
MSH6	IHC	Positive | 2+, 90%
PMS2	IHC	Negative | 0, 100%
PTEN	IHC	Positive | 1+, 100%
TS	IHC	Positive | 1+, 20%
TOPO1	IHC	Positive | 2+, 90%
ERCC1	IHC	Negative | 1+, 5%
Other Notable Biomarker Results		
Total Mutational Load		Low | 6 Mutations/Mb
PD-L1	IHC	Negative | 1+, 2%

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 (5-7).

THERAPIES WITH **POTENTIAL BENEFIT**

cetuximab★, panitumumab★	**BRAF, KRAS, NRAS, PIK3CA, PTEN**
nivolumab★, pembrolizumab★	**MLH1, MSI, PMS2**
irinotecan	TOPO1
oxaliplatin	ERCC1

★ 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 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: 6	Result: Low

MICROSATELLITE INSTABILITY (MSI) BY FRAGMENT ANALYSIS

MSI by Fragment analysis	Result: High

MICROSATELLITE INSTABILITY (MSI) BY NEXT-GENERATION SEQUENCING

MSI by NGS	Result: Stable

IMMUNOHISTOCHEMISTRY (IHC)

Biomarker	Result	Biomarker	Result	Biomarker	Result
ERCC1	Negative | 1+, 5%	MSH6	Positive | 2+, 90%	PTEN	Positive | 1+, 100%
MLH1	Negative | 0, 100%	PD-L1	Negative | 1+, 2%	TOPO1	Positive | 2+, 90%
MSH2	Positive | 2+, 90%	PMS2	Negative | 0, 100%	TS	Positive | 1+, 20%

GENES TESTED WITH INDETERMINATE* SEQUENCING RESULTS BY NGS

ATRX	KMT2C	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	CIC	cMET
CSF1R	CTNNB1	DDR2	EGFR	ERBB3	ERBB4	ESR1	FBXW7	FGFR1	FGFR2	FGFR3	FGFR4
FH	FLCN	FLT3	FOXL2	FUBP1	GATA3	GNA11	GNAQ	GNAS	Her2/Neu (ERBB2)	HNF1A	HRAS
IDH1	JAK2	JAK3	KDM5C	KDM6A	KDR (VEGFR2)	KMT2A	KMT2D	KRAS	MAX	MEK1	MEK2
MEN1	MITF	MLH1	MPL	MSH2	MSH6	MTOR	MUTYH	NF2	NOTCH1	NPM1	NRAS
NTRK1	PALB2	PBRM1	PDGFRA	PDGFRB	PHOX2B	PIK3CA	PIK3R1	PMS2	POLE	POT1	PPARG
PPP2R1A	PRKAR1A	PTCH1	PTEN	PTPN11	RAF1	RB1	RET	RNF43	ROS1	SDHAF2	SDHB
SDHC	SDHD	SETD2	SF3B1	SMAD4	SMARCA4	SMARCB1	SMO	SPOP	SRC	STK11	SUFU
TERT	TP53	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										

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NOTES OF SIGNIFICANCE

SEE APPENDIX FOR FULL DETAILS

Clinical Trials Connector™ opportunities based on biomarker expression: 144 Chemotherapy Trials | 109 Targeted Therapy Trials. See page 8 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: Left inguinal lymph node needle 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®							
cetuximab★, panitumumab★	BRAF	NGS	Mutation Not Detected	-	Yes	I / Good	4#, 5#, 6#, 7#, 8#, 9#, 10#
	KRAS	NGS	Mutation Not Detected	-	Yes	I / Good	11#, 12#, 13#, 14#, 15#, 16#, 17#, 18#, 19#
	NRAS	NGS	Mutation Not Detected	-	Yes	I / Good	6#, 12#, 20#
	PIK3CA	NGS	Mutation Not Detected	-	Yes	I / Good	6#, 8#, 22#, 24#
	PTEN	IHC	Positive	1+ 100%	Yes	II-2 / Good	8#, 21#, 22#, 23#
nivolumab★, pembrolizumab★	MLH1	IHC	Negative	0+ 100%	Yes	I / Good	5#, 28#, 29#, 30
	MSH2	IHC	Positive	2+ 90%	No	-	-
	MSH6	IHC	Positive	2+ 90%	No	-	-
	MSI	FA	High	High	Yes	I / Good	5#, 28#, 29#, 30
	MSI	NGS	Stable	Stable	No	-	-
	PMS2	IHC	Negative	0+ 100%	Yes	I / Good	5#, 28#, 29#, 30
irinotecan	TOPO1	IHC	Positive	2+ 90%	Yes	II-1 / Good	25#, 26#, 27#

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

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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®							
oxaliplatin	ATM	NGS	Mutation Not Detected	-	No	-	-
	BRCA1	NGS	Mutation Not Detected	-	No	-	-
	BRCA2	NGS	Mutation Not Detected	-	No	-	-
	ERCC1	IHC	Negative	1+ 5%	Yes	II-2 / Good	31#, 32#

★ 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+ 20%	Yes	II-1 / Good	1, 2, 3

* 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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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 (144)

Drug Class	Biomarker	Method	Investigational Agent(s)
Platinum compounds (89)	ERCC1	IHC	carboplatin, cisplatin, oxaliplatin
TOPO1 inhibitors (55)	TOPO1	IHC	irinotecan

TARGETED THERAPY CLINICAL TRIALS (109)

Drug Class	Biomarker	Method	Investigational Agent(s)
Immunomodulatory agents (108)	MLH1	IHC	MEDI4736, MK-3475, MPDL3280A, MSB0010718C, atezolizumab, avelumab, durvalumab, nivolumab, pembrolizumab
	MSI	Fragment Analysis	
MDM2 inhibitors (1)	TP53	NGS	DS-3032

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

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To view the rest of the report, contact a Caris Molecular Intelligence® representative today.

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