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: TN16-XXXXXX
Diagnosis: Adenocarcinoma, NOS

SPECIMEN INFORMATION

Primary Tumor Site: Sigmoid colon
Specimen Site: Sigmoid colon
Specimen ID: ABC-1234-XY
Specimen Collected: XX-Mon-2016
Testing Completed: XX-Mon-2016

ORDERED BY

Ordering Phyician, MD
The Cancer Center
123 Main Street
Springfield, XY 12345
(123) 456-7890

✔ THERAPIES WITH **POTENTIAL BENEFIT** (PAGE 5)

Anti-EGFR combination strategies (e.g. cetuximab/ panitumumab +/- vemurafenib/ dabrafenib +/- trametinib)	BRAF★
capecitabine, fluorouracil, pemetrexed	TS★
carboplatin, cisplatin, oxaliplatin	ERCC1
cetuximab, panitumumab	NRAS, PIK3CA, KRAS
dacarbazine, temozolomide	MGMT★
docetaxel, nab-paclitaxel, paclitaxel	TUBB3★
doxorubicin, epirubicin, liposomal-doxorubicin	TOP2A
gemcitabine	RRM1★

★ **Indicates Clinical Trial Opportunity • 248 Chemotherapy Trials • 205 Targeted Therapy Trials** *(See Clinical Trials Connector™ on page 9 for details.)*

✘ THERAPIES WITH **POTENTIAL LACK OF BENEFIT** (PAGE 7)

vemurafenib/ dabrafenib monotherapy	BRAF

? THERAPIES WITH **INDETERMINATE BENEFIT** (PAGE 8)

ado-trastuzumab emtansine (T-DM1)†, pertuzumab†, trastuzumab†	irinotecan†	lapatinib†
imatinib		

†Association to Benefit was not indicated due to assay failure.

Therapies associated with potential benefit or lack of benefit, as indicated above, are based on biomarker results provided in this report and are based on published medical evidence. This evidence may have been obtained from studies performed in the cancer type present in the tested patient's sample or derived from another tumor type. 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 in addition to this report concerning the patient's condition in accordance with the applicable standard of care.

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CE

SUMMARY OF RESULTS (SEE APPENDIX FOR FULL DETAILS)

Assay	Result
Microsatellite Instability (MSI)	Stable
Total Mutational Load	Low | 3 Mutations / Megabase

Biomarker	Method	Result
ABL1	NGS	Mutation Not Detected
AKT1	NGS	Mutation Not Detected
AKT2	NGS	Amplification Not Detected
ALK	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
APC	NGS	Mutation Not Detected
AR	IHC	Negative | 0, 100%
ARAF	NGS	Mutation Not Detected
ARID1A	NGS	Amplification Not Detected
ATM	NGS	Mutation Not Detected
AURKB	NGS	Amplification Not Detected
BAP1	NGS	Mutation Not Detected
BMPR1A	NGS	Mutation Not Detected
BRAF	NGS	Mutated, Pathogenic
		Exon 15 | V600E
BRCA1	NGS	Mutation Not Detected
BRCA2	NGS	Mutation Not Detected
c-KIT	NGS	Mutation Not Detected
CCND1	NGS	Amplification Not Detected
CCND3	NGS	Amplification Not Detected
CCNE1	NGS	Amplification Not Detected
CDC73	NGS	Mutation Not Detected
CDH1	NGS	Mutation Not Detected
CDK4	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
CDK6	NGS	Amplification Not Detected
CDK8	NGS	Amplification Not Detected
CDKN1B	NGS	Mutation Not Detected
CDKN2A	NGS	Mutation Not Detected
	NGS	Amplification Not Detected

Biomarker	Method	Result
CHEK1	NGS	Mutation Not Detected
CHEK2	NGS	Mutation Not Detected
cMET	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
CREBBP	NGS	Amplification Not Detected
CRKL	NGS	Amplification Not Detected
CSF1R	NGS	Mutation Not Detected
CTNNB1	NGS	Mutation Not Detected
DDR2	NGS	Mutation Not Detected
DICER1	NGS	Mutation Not Detected
EGFR	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
EP300	NGS	Amplification Not Detected
ER	IHC	Negative | 0, 100%
ERBB3	NGS	Mutation Not Detected
ERBB4	NGS	Mutation Not Detected
ERCC1	IHC	Negative | 1+, 2%
ESR1	NGS	Mutation Not Detected
EZH2	NGS	Amplification Not Detected
FBXW7	NGS	Mutation Not Detected
FGF10	NGS	Amplification Not Detected
FGF3	NGS	Amplification Not Detected
FGF4	NGS	Amplification Not Detected
FGFR1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
FGFR2	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
FGFR3	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
FH	NGS	Mutation Not Detected

IHC: Immunohistochemistry **CISH:** Chromogenic *in situ* hybridization **NGS:** Next-Generation Sequencing

Biomarker Results continued on the next page. >

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SUMMARY OF RESULTS (SEE APPENDIX FOR FULL DETAILS)

Biomarker	Method	Result
FLCN	NGS	Mutation Not Detected
FLT3	NGS	Mutation Not Detected
GATA3	NGS	Amplification Not Detected
GNA11	NGS	Mutation Not Detected
GNAQ	NGS	Mutation Not Detected
GNAS	NGS	Mutation Not Detected
Her2/Neu	CISH	See Appendix
	IHC	Negative | 2+, 10%
	NGS	Amplification Not Detected
Her2/Neu (ERBB2)	NGS	Mutation Not Detected
HNF1A	NGS	Mutation Not Detected
HRAS	NGS	Mutation Not Detected
IDH1	NGS	Mutation Not Detected
IDH2	NGS	Mutation Not Detected
JAK2	NGS	Mutation Not Detected
JAK3	NGS	Mutation Not Detected
KDR (VEGFR2)	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
KRAS	NGS	Mutation Not Detected
MAX	NGS	Mutation Not Detected
MCL1	NGS	Amplification Not Detected
MDM2	NGS	Amplification Not Detected
MEK1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
MEK2	NGS	Mutation Not Detected
MEN1	NGS	Mutation Not Detected
MGMT	IHC	Negative | 1+, 5%
MITF	NGS	Mutation Not Detected
MLH1	IHC	Positive | 1+, 80%
	NGS	Mutation Not Detected
MPL	NGS	Mutation Not Detected
MSH2	IHC	Positive | 1+, 90%
	NGS	Mutation Not Detected
MSH6	IHC	Positive | 1+, 60%
	NGS	Mutation Not Detected
MUTYH	NGS	Mutation Not Detected
MYC	NGS	Amplification Not Detected
NF1	NGS	Mutation Not Detected
NF2	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
NFKBIA	NGS	Amplification Not Detected
NOTCH1	NGS	Mutation Not Detected
NPM1	NGS	Mutation Not Detected
NRAS	NGS	Mutation Not Detected
NTRK1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
PALB2	NGS	Mutation Not Detected
PBRM1	NGS	Mutation Not Detected
PD-L1	IHC	Positive | 2+, 10%
PDGFRA	NGS	Mutation Not Detected
PDGFRB	NGS	Mutation Not Detected
PIK3CA	NGS	Mutation Not Detected
PMS2	IHC	Positive | 1+, 70%
	NGS	Indeterminate
POLE	NGS	Mutation Not Detected
POT1	NGS	Mutation Not Detected
PPARG	NGS	Mutation Not Detected
PR	IHC	Negative | 0, 100%
PRKAR1A	NGS	Mutation Not Detected
PTCH1	NGS	Mutation Not Detected
PTEN	IHC	Negative | 0, 100%
	NGS	Mutation Not Detected
PTPN11	NGS	Mutation Not Detected
RAF1	NGS	Mutation Not Detected
RB1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected
RET	NGS	Mutation Not Detected
RICTOR	NGS	Amplification Not Detected
ROS1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected

IHC: Immunohistochemistry **CISH:** Chromogenic *in situ* hybridization **NGS:** Next-Generation Sequencing

Biomarker Results continued on the next page. >

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SUMMARY OF RESULTS (SEE APPENDIX FOR FULL DETAILS)

Biomarker	Method	Result
RRM1	IHC	Negative | 2+, 40%
SDHAF2	NGS	Mutation Not Detected
SDHB	NGS	Mutation Not Detected
SDHC	NGS	Mutation Not Detected
SDHD	NGS	Mutation Not Detected
SMAD4	NGS	Mutation Not Detected
SMARCA4	NGS	Mutation Not Detected
SMARCB1	NGS	Mutation Not Detected
SMARCE1	NGS	Mutation Not Detected
SMO	NGS	Mutated, Presumed Benign
		Exon 1 | L23dup
SRC	NGS	Mutation Not Detected
STK11	NGS	Mutation Not Detected

Biomarker	Method	Result
SUFU	NGS	Mutation Not Detected
TERT	NGS	Mutation Not Detected
TOP1	NGS	Amplification Not Detected
TOP2A	IHC	Positive | 1+, 30%
TOPO1	IHC	Test Not Performed
TP53	NGS	Mutated, Pathogenic
		Exon 6 | L206fs
TS	IHC	Negative | 0, 100%
TSC1	NGS	Mutation Not Detected
TUBB3	IHC	Negative | 2+, 20%
VHL	NGS	Mutation Not Detected
WT1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected

IHC: Immunohistochemistry **CISH:** Chromogenic *in situ* hybridization **NGS:** Next-Generation Sequencing

The Next-Generation Sequencing results above include only the genes most commonly associated with cancer. See summary below and for full Next-Generation Sequencing results, see Appendix page 1.

See the Appendix section for a detailed overview of the biomarker test results for each technology.

NOTES OF SIGNIFICANCE

SEE APPENDIX FOR FULL DETAILS

The tumor does not display evidence of Microsatellite instability or MMR protein deficiency. Patients with MMR proficient or microsatellite stable tumors were associated with decreased overall survival when compared to patients with MMR deficient and/or MSI-H cancers. Ribic, et al. 2003, Sargent, et al. 2010, Funkhouser, et al. 2012, National Comprehensive Cancer Network.Colon Cancer (Version 3.2014).

Next-Generation Sequencing:

Genes tested: 592 | Genes with actionable mutations: 2 | Genes with unclassified mutations: 12 | Genes with no mutations detected: 551

Note: The Caris Molecular Intelligence NGS test is not intended to identify or diagnose a hereditary condition. Mutations detected in this assay may be somatic or germline in origin and are used primarily for theranostic purposes. Appropriate genetic counseling and testing may be considered.

Immunohistochemistry:

Appropriate staining for TOPO1 was not achieved, thus no result is reported for this biomarker.

Chromogenic in situ Hybridization:

HER2 Genetic Heterogeneity is present. Approximately 20% of the tumor shows HER2 gene amplification with a HER2:CEP17 ratio > 2. The amplified cells are present in multifocal scattered clusters of cells.

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✔ THERAPIES WITH **POTENTIAL BENEFIT**

Therapies	Test	Method	Result	Value†	Clinical Association				
					Potential Benefit	Decreased Potential Benefit	Lack of Potential Benefit	Highest Level of Evidence*	Reference
Anti-EGFR combination strategies (e.g. cetuximab/ panitumumab +/- vemurafenib/ dabrafenib +/- trametinib)	BRAF	NGS	Mutated, Pathogenic	V600E	✔			II-1 / Good	1#, 2#
capecitabine, fluorouracil, pemetrexed	TS	IHC	Negative	0+ 100%	✔			II-1 / Good	10, 11, 12
carboplatin, cisplatin, oxaliplatin	ATM	NGS	Mutation Not Detected					II-2 / Good	15, 16, 17
	BRCA1	NGS	Mutation Not Detected					II-2 / Good	18, 19, 20, 21
	BRCA2	NGS	Mutation Not Detected					II-2 / Good	18, 20, 21
	ERCC1	IHC	Negative	1+ 2%	✔			II-2 / Good	13#, 14#
cetuximab, panitumumab	BRAF	NGS	Mutated, Pathogenic	V600E		✔		I / Good	25#, 27#, 38#, 39#
	KRAS	NGS	Mutation Not Detected		✔			I / Good	26#, 30#, 31#, 32#, 33#, 34#, 35#, 36#, 37#
	NRAS	NGS	Mutation Not Detected		✔			I / Good	26#, 27#, 28#
	PIK3CA	NGS	Mutation Not Detected		✔			I / Good	23#, 25#, 27#, 29#
	PTEN	IHC	Negative	0+ 100%		✔		II-2 / Good	22#, 23#, 24#, 25#
dacarbazine, temozolomide	MGMT	IHC	Negative	1+ 5%	✔			II-2 / Good	40, 41

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

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✔ THERAPIES WITH **POTENTIAL BENEFIT**

Therapies	Test	Method	Result	Value†	Clinical Association				
					Potential Benefit	Decreased Potential Benefit	Lack of Potential Benefit	Highest Level of Evidence*	Reference
docetaxel, nab-paclitaxel, paclitaxel	TUBB3	IHC	Negative	2+ 20%	✔			I / Good	42, 43, 44, 45
doxorubicin, epirubicin, liposomal-doxorubicin	TOP2A	IHC	Positive	1+ 30%	✔			I / Good	46, 47
gemcitabine	RRM1	IHC	Negative	2+ 40%	✔			I / Good	48

* 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.

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

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✘ THERAPIES WITH **POTENTIAL LACK OF BENEFIT**

Therapies	Test	Method	Result	Value†	Clinical Association				
					Potential Benefit	Decreased Potential Benefit	Lack of Potential Benefit	Highest Level of Evidence*	Reference
vemurafenib/ dabrafenib monotherapy	BRAF	NGS	Mutated, Pathogenic	V600E			✔	II-3 / Good	56#

* 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.

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

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? THERAPIES WITH **INDETERMINATE BENEFIT**

(Biomarker results do not impact potential benefit or lack of potential benefit)

Therapies	Test	Method	Result	Value†	Clinical Association				
					Potential Benefit	Decreased Potential Benefit	Lack of Potential Benefit	Highest Level of Evidence*	Reference
ado-trastuzumab emtansine (T-DM1), pertuzumab, trastuzumab	Her2/Neu	CISH	Other						
	Her2/Neu	IHC	Negative	2+ 10%			✔	I / Good	3, 4, 5, 6, 7, 8, 9
	Her2/Neu	NGS	Amplification Not Detected						
imatinib	c-KIT	NGS	Mutation Not Detected				✔	II-2 / Good	49, 50
	PDGFRA	NGS	Mutation Not Detected				✔	II-3 / Good	51, 52, 53
irinotecan	TOPO1	IHC	Technical Issues	Technical Issues					
lapatinib	Her2/Neu	CISH	Other						
	Her2/Neu	IHC	Negative	2+ 10%			✔	I / Good	54, 55
	Her2/Neu	NGS	Amplification Not Detected						

* 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.

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

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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 (248)

Drug Class	Biomarker	Method	Investigational Agent(s)
Alkylating agents (5)	MGMT	IHC	dacarbazine, lomustine, temozolomide
Antifolates (12)	TS	IHC	methotrexate, pemetrexed
Nucleoside analog (23)	RRM1	IHC	gemcitabine
Pyrimidine analog (168)	TS	IHC	capecitabine, fluorouracil
Taxanes (40)	TUBB3	IHC	docetaxel, paclitaxel

TARGETED THERAPY CLINICAL TRIALS (205)

Drug Class	Biomarker	Method	Investigational Agent(s)
Cell cycle inhibitors (11)	RB1	NGS	LEE011, LY2606368, MK-1775, palbociclib
	TP53	NGS	
ERK inhibitors (1)	BRAF	NGS	BVD-523
Immunomodulatory agents (87)	PD-L1	IHC	MK-3475, MPDL3280A, atezolizumab, avelumab, nivolumab, pembrolizumab
MEK inhibitors (22)	BRAF	NGS	GDC-0973, PD0325901, XL518, selumetinib, trametinib
Multikinase inhibitors (19)	BRAF	NGS	GSK2118436 (dabrafenib), sorafenib, vemurafenib
p53-targeted biological agents (2)	TP53	NGS	Ad5CMV-p53, modified vaccinia virus ankara vaccine expressing p53
PARP inhibitors (19)	PTEN	IHC	BMN-673, olaparib, rucaparib, veliparib
PI3K/Akt/mTor inhibitors (44)	PTEN	IHC	ARQ092, AZD2014, AZD5363, BAY80-6946, BKM120, BYL719, GDC0941, GSK2110183, GSK2141795, GSK2636771, MLN0128, MLN1117, PF-05212384, ZSTK474, everolimus, sirolimus, temsirolimus

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

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