




**FINAL REPORT**

PATIENT	SPECIMEN INFORMATION	ORDERED BY
<b>Name:</b> Patient, Test <b>Date of Birth:</b> XX-Mon-19XX <b>Sex:</b> Female <b>Case Number:</b> TN16-XXXXXX <b>Diagnosis:</b> Adenocarcinoma, NOS	<b>Primary Tumor Site:</b> Sigmoid colon <b>Specimen Site:</b> Sigmoid colon <b>Specimen ID:</b> ABC-1234-XY <b>Specimen Collected:</b> XX-Mon-2016 <b>Testing Completed:</b> XX-Mon-2016	<b>Ordering Physician, MD</b> <b>The Cancer Center</b> 123 Main Street Springfield, XY 12345 (123) 456-7890

 THERAPIES WITH <b>POTENTIAL BENEFIT</b> (PAGE 5)					
Anti-EGFR combination strategies (e.g. cetuximab/panitumumab +/- vemurafenib/dabrafenib +/- trametinib)	BRAF <sup>★</sup>	cetuximab, panitumumab	NRAS, PIK3CA, KRAS	doxorubicin, epirubicin, liposomal-doxorubicin	TOP2A
capecitabine, fluorouracil, pemetrexed	TS <sup>★</sup>	dacarbazine, temozolomide	MGMT <sup>★</sup>	gemcitabine	RRM1 <sup>★</sup>
carboplatin, cisplatin, oxaliplatin	ERCC1	docetaxel, nab-paclitaxel, paclitaxel	TUBB3 <sup>★</sup>		

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

 THERAPIES WITH <b>POTENTIAL LACK OF BENEFIT</b> (PAGE 7)	
vemurafenib/dabrafenib monotherapy	BRAF

 THERAPIES WITH <b>INDETERMINATE BENEFIT</b> (PAGE 8)		
ado-trastuzumab emtansine (T-DM1) <sup>†</sup> , pertuzumab <sup>†</sup> , trastuzumab <sup>†</sup>  imatinib	irinotecan <sup>†</sup>	lapatinib <sup>†</sup>

†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.

**SUMMARY OF RESULTS** (SEE APPENDIX FOR FULL DETAILS)

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

Biomarker	Method	Result	Biomarker	Method	Result
ABL1	NGS	Mutation Not Detected	CHEK1	NGS	Mutation Not Detected
AKT1	NGS	Mutation Not Detected	CHEK2	NGS	Mutation Not Detected
AKT2	NGS	Amplification Not Detected	cMET	NGS	Mutation Not Detected
ALK	NGS	Mutation Not Detected		NGS	Amplification Not Detected
	NGS	Amplification Not Detected	CREBBP	NGS	Amplification Not Detected
APC	NGS	Mutation Not Detected	CRKL	NGS	Amplification Not Detected
AR	IHC	Negative   0, 100%	CSF1R	NGS	Mutation Not Detected
ARAF	NGS	Mutation Not Detected	CTNNB1	NGS	Mutation Not Detected
ARID1A	NGS	Amplification Not Detected	DDR2	NGS	Mutation Not Detected
ATM	NGS	Mutation Not Detected	DICER1	NGS	Mutation Not Detected
AURKB	NGS	Amplification Not Detected	EGFR	NGS	Mutation Not Detected
BAP1	NGS	Mutation Not Detected		NGS	Amplification Not Detected
BMPR1A	NGS	Mutation Not Detected	EP300	NGS	Amplification Not Detected
BRAF	NGS	Mutated, Pathogenic	ER	IHC	Negative   0, 100%
		Exon 15   V600E	ERBB3	NGS	Mutation Not Detected
BRCA1	NGS	Mutation Not Detected	ERBB4	NGS	Mutation Not Detected
BRCA2	NGS	Mutation Not Detected	ERCC1	IHC	Negative   1+, 2%
c-KIT	NGS	Mutation Not Detected	ESR1	NGS	Mutation Not Detected
CCND1	NGS	Amplification Not Detected	EZH2	NGS	Amplification Not Detected
CCND3	NGS	Amplification Not Detected	FBXW7	NGS	Mutation Not Detected
CCNE1	NGS	Amplification Not Detected	FGF10	NGS	Amplification Not Detected
CDC73	NGS	Mutation Not Detected	FGF3	NGS	Amplification Not Detected
CDH1	NGS	Mutation Not Detected	FGF4	NGS	Amplification Not Detected
CDK4	NGS	Mutation Not Detected	FGFR1	NGS	Mutation Not Detected
	NGS	Amplification Not Detected		NGS	Amplification Not Detected
CDK6	NGS	Amplification Not Detected	FGFR2	NGS	Mutation Not Detected
CDK8	NGS	Amplification Not Detected		NGS	Amplification Not Detected
CDKN1B	NGS	Mutation Not Detected	FGFR3	NGS	Mutation Not Detected
CDKN2A	NGS	Mutation Not Detected		NGS	Amplification 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. >

**PATIENT:** Patient, Test (XX-Mon-19XX)

**TN16-XXXXXX**

**PHYSICIAN:** Ordering Physician, MD

**SUMMARY OF RESULTS** (SEE APPENDIX FOR FULL DETAILS)

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

**IHC:** Immunohistochemistry

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

Biomarker Results continued on the next page. >

**PATIENT:** Patient, Test (XX-Mon-19XX)

**TN16-XXXXXX**

**PHYSICIAN:** Ordering Physician, MD

**SUMMARY OF RESULTS** (SEE APPENDIX FOR FULL DETAILS)

Biomarker	Method	Result	Biomarker	Method	Result
RRM1	IHC	Negative   2+, 40%	SUFU	NGS	Mutation Not Detected
SDHAF2	NGS	Mutation Not Detected	TERT	NGS	Mutation Not Detected
SDHB	NGS	Mutation Not Detected	TOP1	NGS	Amplification Not Detected
SDHC	NGS	Mutation Not Detected	TOP2A	IHC	Positive   1+, 30%
SDHD	NGS	Mutation Not Detected	TOPO1	IHC	Test Not Performed
SMAD4	NGS	Mutation Not Detected	TP53	NGS	Mutated, Pathogenic Exon 6   L206fs
SMARCA4	NGS	Mutation Not Detected	TS	IHC	Negative   0, 100%
SMARCB1	NGS	Mutation Not Detected	TSC1	NGS	Mutation Not Detected
SMARCE1	NGS	Mutation Not Detected	TUBB3	IHC	Negative   2+, 20%
SMO	NGS	Mutated, Presumed Benign Exon 1   L23dup	VHL	NGS	Mutation Not Detected
SRC	NGS	Mutation Not Detected	WT1	NGS	Mutation Not Detected
STK11	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.

**PATIENT:** Patient, Test (XX-Mon-19XX)

**TN16-XXXXXX**

**PHYSICIAN:** Ordering Physician, MD

✓ THERAPIES WITH **POTENTIAL BENEFIT**

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

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

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**TN16-XXXXXX**

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✓ THERAPIES WITH **POTENTIAL BENEFIT**

Therapies	Test	Method	Result	Value <sup>†</sup>	Clinical Association				
					Potential Benefit	Decreased Potential Benefit	Lack of Potential Benefit	Highest Level of Evidence*	Reference
<a href="#">docetaxel, nab-paclitaxel, paclitaxel</a>	<a href="#">TUBB3</a>	IHC	Negative	2+ 20%	✓			I / Good	42, 43, 44, 45
<a href="#">doxorubicin, epirubicin, liposomal-doxorubicin</a>	<a href="#">TOP2A</a>	IHC	Positive	1+ 30%	✓			I / Good	46, 47
<a href="#">gemcitabine</a>	<a href="#">RRM1</a>	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.

**PATIENT:** Patient, Test (XX-Mon-19XX)

**TN16-XXXXXX**

**PHYSICIAN:** Ordering Physician, MD

**X THERAPIES WITH POTENTIAL LACK OF BENEFIT**

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

\* 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 <sup>†</sup>	Clinical Association				
					Potential Benefit	Decreased Potential Benefit	Lack of Potential Benefit	Highest Level of Evidence*	Reference
<b>ado-trastuzumab emtansine (T-DM1), pertuzumab, trastuzumab</b>	<b>Her2/Neu</b>	CISH	Other						
	<b>Her2/Neu</b>	IHC	Negative	2+ 10%			✓	I / Good	3, 4, 5, 6, 7, 8, 9
	<b>Her2/Neu</b>	NGS	Amplification Not Detected						
<b>imatinib</b>	<b>c-KIT</b>	NGS	Mutation Not Detected				✓	II-2 / Good	49, 50
	<b>PDGFRA</b>	NGS	Mutation Not Detected				✓	II-3 / Good	51, 52, 53
<b>irinotecan</b>	<b>TOPO1</b>	IHC	Technical Issues	Technical Issues					
<b>lapatinib</b>	<b>Her2/Neu</b>	CISH	Other						
	<b>Her2/Neu</b>	IHC	Negative	2+ 10%			✓	I / Good	54, 55
	<b>Her2/Neu</b>	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](http://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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**To view the rest of the report, contact a  
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