

FINAL REPORT

PATIENT	SPECIMEN INFORMATION	ORDERED BY
Name: Patient, Test Date of Birth: XX-Mon-1940 Sex: Female Case Number: TN15-111111 Diagnosis: Carcinosarcoma, NOS	Primary Tumor Site: Uterus, NOS Specimen Site: Small bowel, NOS Specimen ID: ABC-12345-YZ Specimen Collected: XX-Mon-2015 Completion of Testing: XX-Mon-2015	Ordering Physician, MD The Cancer Center 123 Main Street Springfield, XY 12345 (123) 456-7890

Bold Therapies = On NCCN Compendium® Therapies

✓ THERAPIES WITH POTENTIAL BENEFIT (PAGE 4)					
docetaxel, paclitaxel	TUBB3, TLE3*, PGP	topotecan	TOPO1	irinotecan	TOPO1
doxorubicin, liposomal-doxorubicin	PGP, TOP2A, Her2/Neu	epirubicin	PGP, TOP2A, Her2/Neu	nab-paclitaxel	TUBB3, TLE3*, PGP

★ Indicates Clinical Trial Opportunity • 52 Chemotherapy Trials • 26 Targeted Therapy Trials (See Clinical Trials Connector™ on page 7 for details.)

✗ THERAPIES WITH POTENTIAL LACK OF BENEFIT (PAGE 5)					
anastrozole, exemestane, letrozole, megestrol acetate, tamoxifen	PR, ER	capecitabine, fluorouracil, pemetrexed	TS	fulvestrant, toremifene	PR, ER
abarelix, degarelix, goserelin, leuprolide, triptorelin	Androgen Receptor, ER, PR	dabrafenib, vemurafenib	BRAF	gemcitabine	RRM1
abiraterone, bicalutamide, enzalutamide, flutamide	Androgen Receptor	dacarbazine, temozolomide	MGMT	lapatinib	Her2/Neu
ado-trastuzumab emtansine (T-DM1), pertuzumab, trastuzumab	Her2/Neu				

? THERAPIES WITH INDETERMINATE BENEFIT (PAGE 6)		
carboplatin, cisplatin	everolimus	oxaliplatin

Results continued on the next page. >

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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THERAPIES WITH **INDETERMINATE BENEFIT** (PAGE 6)

tensirolimus

imatinib

vandetanib

SAMPLE REPORT. FOR ILLUSTRATIVE PURPOSES ONLY. NOT FOR CLINICAL USE

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SUMMARY OF BIOMARKER RESULTS (SEE APPENDIX FOR FULL DETAILS)

Biomarker	Method	Result	Biomarker	Method	Result
ABL1	NGS	Mutation Not Detected	IDH1	NGS	Mutation Not Detected
AKT1	NGS	Mutation Not Detected	JAK2	NGS	Mutation Not Detected
ALK	NGS	Mutation Not Detected	KDR (VEGFR2)	NGS	Mutation Not Detected
Androgen Receptor	IHC	Negative	KRAS	NGS	Mutation Not Detected
APC	NGS	Mutation Not Detected	MGMT	IHC	Positive
ATM	NGS	Mutation Not Detected	MPL	NGS	Mutation Not Detected
BRAF	NGS	Mutation Not Detected	NOTCH1	NGS	Mutation Not Detected
BRCA1	NGS	Mutation Not Detected	NRAS	NGS	Mutation Not Detected
BRCA2	NGS	Mutation Not Detected	PD-1	IHC	Positive
c-KIT	NGS	Mutation Not Detected	PDGFRA	NGS	Mutation Not Detected
cMET	IHC	Negative	PD-L1	IHC	Negative
cMET	NGS	Mutation Not Detected	PGP	IHC	Negative
cMET	CISH	Not Amplified	PIK3CA	NGS	Mutation Not Detected
CSF1R	NGS	Mutation Not Detected	PR	IHC	Negative
CTNNB1	NGS	Mutation Not Detected	PTEN	IHC	Positive
EGFR	IHC	Positive	PTEN	NGS	Mutation Not Detected
EGFR	NGS	Mutation Not Detected	RET	NGS	Mutation Not Detected
ER	IHC	Negative	RRM1	IHC	Positive
FGFR1	NGS	Mutation Not Detected	SMO	NGS	Quantity Not Sufficient
FGFR2	NGS	Mutation Not Detected	SPARC Polyclonal	IHC	Negative
FLT3	NGS	Mutation Not Detected	TLE3	IHC	Positive
GNA11	NGS	Mutation Not Detected	TOP2A	IHC	Positive
GNAQ	NGS	Mutation Not Detected	TOPO1	IHC	Positive
GNAS	NGS	Mutation Not Detected	TP53	NGS	Mutation Not Detected
Her2/Neu	IHC	Negative	TS	IHC	Positive
Her2/Neu	CISH	Not Amplified	TUBB3	IHC	Positive
Her2/Neu (ERBB2)	NGS	Mutation Not Detected	VHL	NGS	Quantity Not Sufficient
HRAS	NGS	Mutation 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. Genes tested: 35 | Genes with actionable mutations: 0 | Genes with unclassified mutations: 0 | Genes with no mutations detected: 33

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

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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	PGP	IHC	Negative	0+ 100%	✓			II-3 / Fair	42, 43
	TLE3	IHC	Positive	2+ 80%	✓			II-2 / Good	41
	TUBB3	IHC	Positive	3+ 35%		✓		I / Good	37, 38, 39, 40
doxorubicin, epirubicin, liposomal-doxorubicin	Her2/Neu	CISH	Not Amplified	1.21		✓		I / Good	48, 49
	PGP	IHC	Negative	0+ 100%	✓			II-1 / Fair	44, 45
	TOP2A	IHC	Positive	1+ 35%	✓			I / Good	46, 47
irinotecan, topotecan	TOPO1	IHC	Positive	2+ 70%	✓			II-1 / Good	59, 60, 61

* 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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X 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
abarelix, degarelix, goserelin, leuprolide, triptorelin	Androgen Receptor	IHC	Negative	0+ 100%			✓	II-3 / Good	1
	ER	IHC	Negative	0+ 100%			✓	I / Good	2
	PR	IHC	Negative	0+ 100%			✓	I / Good	2
abiraterone, bicalutamide, enzalutamide, flutamide	Androgen Receptor	IHC	Negative	0+ 100%			✓	I / Good	1, 3, 4, 5
ado-trastuzumab emtansine (T-DM1), pertuzumab, trastuzumab	Her2/Neu	CISH	Not Amplified	1.21			✓	I / Good	6, 7, 8, 9, 10, 11, 12, 13
	Her2/Neu	IHC	Negative	0+ 100%			✓	I / Good	6, 7, 8, 9, 10, 12, 13
anastrozole, exemestane, fulvestrant, letrozole, megestrol acetate, tamoxifen, toremifene	ER	IHC	Negative	0+ 100%			✓	I / Good	14, 17, 18, 19, 20, 21, 22, 23
	PR	IHC	Negative	0+ 100%			✓	I / Good	14, 15, 16, 17, 18, 19, 20, 21
capecitabine, fluorouracil, pemetrexed	TS	IHC	Positive	1+ 25%			✓	I / Good	24, 25, 26
dabrafenib, vemurafenib	BRAF	Next Gen SEQ	Mutation Not Detected				✓	I / Good	31, 32, 33, 34
dacarbazine, temozolomide	MGMT	IHC	Positive	1+ 40%			✓	II-2 / Good	35, 36
gemcitabine	RRM1	IHC	Positive	2+ 60%			✓	I / Good	53
lapatinib	Her2/Neu	CISH	Not Amplified	1.21			✓	I / Good	11, 62, 63, 64
	Her2/Neu	IHC	Negative	0+ 100%			✓	I / Good	62, 63, 64

* 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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? 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
<u>carboplatin, cisplatin, oxaliplatin</u>	<u>BRCA1</u>	Next Gen SEQ	Mutation Not Detected				✓	II-2 / Good	27, 28, 29, 30
	<u>BRCA2</u>	Next Gen SEQ	Mutation Not Detected				✓	II-2 / Good	27, 29, 30
<u>everolimus, temsirolimus</u>	<u>PIK3CA</u>	Next Gen SEQ	Mutation Not Detected			✓		II-2 / Good	50 [#] , 51 [#] , 52 [#]
<u>imatinib</u>	<u>c-KIT</u>	Next Gen SEQ	Mutation Not Detected				✓	II-2 / Good	54, 55
	<u>PDGFRA</u>	Next Gen SEQ	Mutation Not Detected				✓	II-3 / Good	56, 57, 58
<u>vandetanib</u>	<u>RET</u>	Next Gen SEQ	Mutation Not Detected					I / Good	65

* 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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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 (52)			
Drug Class	Biomarker	Method	Investigational Agent(s)
Taxanes (52)	TLE3	IHC	docetaxel, paclitaxel

TARGETED THERAPY CLINICAL TRIALS (26)			
Drug Class	Biomarker	Method	Investigational Agent(s)
EGFR monoclonal antibody (13)	EGFR	IHC	cetuximab
Immunomodulatory agents (10)	PD-1	IHC	MK-3475, MPDL3280A, lambrolizumab, lambrolizumab (MK-3475), nivolumab
MDM2 inhibitors (3)	TP53	Next Gen SEQ	CGM097, DS-3032, Kevetrin (thioureidobutyronitrile)

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

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SOURCE	LEVEL OF EVIDENCE*
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2. Cuzick J, LHRH-agonists in Early Breast Cancer Overview group. (2007). "Use of luteinising-hormone-releasing hormone agonists as adjuvant treatment in premenopausal patients with hormone-receptor-positive breast cancer: a meta-analysis of individual patient data from randomised adjuvant trials." <i>The Lancet</i> 369: 1711-1723. View Citation Online	I / Good
3. Jaspers, H.C., C.M. van Herpen, et. al. (2011). "Androgen-receptor-positive salivary duct carcinoma: a disease entity with promising new treatment options". <i>J Clin Oncol</i> . 29(16):e473-476. View Citation Online	II-3 / Fair
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7. Baselga, J., S.M. Swain, et. al. (2012). "Pertuzumab plus trastumab plus docetaxel for metastatic breast cancer". <i>N. Engl. J. Med</i> . 36:109-119. View Citation Online	I / Good
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* See Appendix page 6 for Level of Evidence description.

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PHYSICIAN: Ordering Physician, MD

REFERENCES

SOURCE	LEVEL OF EVIDENCE*
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22. Anderson, H., M. Dowsett, et al. (2011). "Relationship between estrogen receptor, progesterone receptor, HER-2 and Ki67 expression and efficacy of aromatase inhibitors in advanced breast cancer. <i>Annals of Oncology</i> . 22:1770-1776. View Citation Online	II-3 / Good
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26. Lee, S.J., Y.H. Im, et al. (2010). "Thymidylate synthase and thymidine phosphorylase as predictive markers of capecitabine monotherapy in patients with anthracycline- and taxane-pretreated metastatic breast cancer." <i>Cancer Chemother. Pharmacol.</i> DOI 10.1007/s00280-010-1545-0. View Citation Online	II-3 / Good
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SOURCE	LEVEL OF EVIDENCE*
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REFERENCES

SOURCE	LEVEL OF EVIDENCE*
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* See Appendix page 6 for Level of Evidence description.

PATIENT: Patient, Test (XX-Mon-1940)

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PHYSICIAN: Ordering Physician, MD

SPECIMEN(S) RECEIVED (GROSS DESCRIPTION)

Specimen ID: ABC-12345-YZ

Specimen Collected: XX-Mon-2015

The specimen(s) consist of: 1 (A) Paraffin Block - Client ID(ABC-12345-YZ) with the corresponding surgical pathology report labeled "ABC-12345-YZ".

Clinical History: Per the submitted documents, the patient is a 74 year-old female with metastatic carcinosarcoma.

Pathologic Diagnosis: Small bowel resection: Metastatic high grade malignant neoplasm consistent with patient's known history of carcinosarcoma (MMMT).

Disclaimer

All of the individual assays that are available through Caris Molecular Intelligence™ were developed and validated by Caris MPI, Inc. d/b/a Caris Life Sciences® and their test performance characteristics were determined and validated by Caris Life Sciences pursuant to the Clinical Laboratory Improvements Amendments and accompanying regulations ("CLIA"). Some of the assays that are part of Caris Molecular Intelligence have been approved by the U.S. Food and Drug Administration (FDA). For any remaining assays, Caris MPI, Inc. is certified under CLIA to perform high complexity testing, including all of the assays that comprise the Caris Molecular Intelligence.

The CLIA certification number of Caris MPI, Inc. laboratory performing testing in connection with Caris Molecular Intelligence can be found at the bottom of each page. This report includes information about therapies that appear to be associated with clinical benefit based on NCCN Compendium® guidelines, relevance of tumor lineage, level of published evidence and strength of biomarker results. This report, neither ranks biomarkers listed nor therapies associated with such biomarkers, in order of potential or predicted efficacy, and such therapies may or may not be suitable for administration to a particular patient. A determination of biomarker results do not necessarily indicate pharmacologic effectiveness or lack thereof. This report does not guarantee or suggest that any particular agent will be effective with the treatment of any particular condition. Caris Life Sciences expressly disclaims and makes no representation or warranty whatsoever relating, directly or indirectly, to review of identified scientific literature, the conclusions drawn from such review or any of the information set forth in this report that is derived from such review, including information and conclusions relating to therapies that are included or omitted from this report.

Decisions regarding care and treatment should not be based on a single test such as this test or the information contained in this report. The decision to select any, all or none of the listed therapies resides solely within 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 applicable information concerning the patient's condition, including but not limited to, patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the applicable standard of care.

The information presented in the Clinical Trials Connector™ section of this report (if applicable) is compiled from sources believed to be reliable and current. We have used our best efforts to make this information as accurate as possible. However, the accuracy and completeness of this information cannot be guaranteed. The contents are to be used for clinical trial guidance and may not include all relevant trials. Current enrollment status for these trials is unknown. The clinical trials information present in the biomarker description was compiled from www.clinicaltrials.gov. The contents are to be used only as a guide, and health care providers should employ their judgment in interpreting this information for a particular patient. Specific eligibility criteria for each clinical trial should be reviewed as additional inclusion criteria may apply. Caris Life Sciences makes no promises or guarantees that a healthcare provider, insurer or other third party private or government payor, will provide reimbursement for any of the tests performed.

The next-generation sequencing assay performed by Caris Life Sciences examines nucleic acids obtained from tumor tissue only and does not examine normal tissue such as tumor adjacent tissue or whole or peripheral blood. As such, the origin of any mutation detected may be a somatic mutation (not inherited) or a germline mutation (inherited) and will not be distinguishable by this assay. It is recommended that results be considered within the patient's clinical and health history. If a germline inheritance pattern is suspected then counseling by a board certified genetic counselor is recommended.



MUTATIONAL ANALYSIS BY **NEXT-GENERATION SEQUENCING (NGS)**

GENES TESTED WITH NO MUTATIONS DETECTED

ABL1	c-KIT	FGFR1	HRAS	NOTCH1	TP53
AKT1	cMET	FGFR2	IDH1	NRAS	
ALK	CSF1R	FLT3	JAK2	PDGFRA	
APC	CTNNB1	GNA11	KDR	PIK3CA	
ATM	EGFR	GNAQ	KRAS	PTEN	
BRAF	ERBB2	GNAS	MPL	RET	

GENES TESTED WITH QNS RESULTS (QUANTITY NOT SUFFICIENT)

SMO VHL

For Next-Generation Sequencing, a total of 35 genes were analyzed. The results above include genes most commonly associated with cancer and any additional mutations identified. No alterations were identified in 33 genes. For a complete list of genes tested, visit www.CarisMolecularIntelligence.com/profilemenu.

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Comments on NGS Analysis

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.

NGS Methods

Direct sequence analysis was performed on genomic DNA isolated from a formalin-fixed paraffin-embedded tumor sample using the Illumina MiSeq platform. Specific regions of the genome were amplified using the Illumina TruSeq Amplicon Cancer Hotspot panel. This panel only sequences selected regions of 44 genes and the amino acids sequenced by this assay can be found at www.carislifesciences.com. All variants reported by this are detected with >99% confidence based on the frequency of the mutation present and the amplicon coverage. This test is not designed to distinguish between germ line inheritance of a variant or acquired somatic mutation. This test has a sensitivity to detect as low as approximately 10% population of cells containing a mutation in a sequenced amplicon. This test has not been cleared or approved by the United States Food and Drug Administration (FDA) as such approval is not necessary. All performance characteristics were determined by Caris Life Sciences. Insertions or deletions larger than 27 bp will not be detected by this assay. Benign and non-coding variants are not included in this report but are available upon request.

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PHYSICIAN: Ordering Physician, MD

MUTATIONAL ANALYSIS BY **NEXT-GENERATION SEQUENCING (NGS)**

GENES TESTED WITH NO MUTATIONS DETECTED

BRCA1

BRCA2

Electronic Signature

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BRCA1 Sequencing Methods

Direct sequence analysis was performed on genomic DNA isolated from a formalin-fixed paraffin-embedded tumor sample using the Illumina MiSeq platform. Specific regions of BRCA1 were amplified using primers flanking coding regions of this gene. All variants reported by this are detected with >99% confidence based on the frequency of the mutation present and the amplicon coverage. This test is not designed to distinguish between germ line inheritance of a variant or acquired somatic mutation. This test has a sensitivity to detect as low as approximately 20% population of cells containing a mutation a sequenced amplicon. This test has not been cleared or approved by the United States Food and Drug Administration (FDA) as such approval is not necessary. All performance characteristics were determined by Caris Life Sciences. Insertions or deletions larger than 27 bp will not be detected by this assay. Benign and non-coding variants are not included in this report but are available upon request.

BRCA2 Sequencing Methods

Direct sequence analysis was performed on genomic DNA isolated from a formalin-fixed paraffin-embedded tumor sample using the Illumina MiSeq platform. Specific regions of BRCA2 were amplified using primers flanking coding regions of this gene. All variants reported by this are detected with >99% confidence based on the frequency of the mutation present and the amplicon coverage. This test is not designed to distinguish between germ line inheritance of a variant or acquired somatic mutation. This test has a sensitivity to detect as low as approximately 20% population of cells containing a mutation a sequenced amplicon. This test has not been cleared or approved by the United States Food and Drug Administration (FDA) as such approval is not necessary. All performance characteristics were determined by Caris Life Sciences. Insertions or deletions larger than 27 bp will not be detected by this assay. Benign and non-coding variants are not included in this report but are available upon request.

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PROTEIN EXPRESSION BY **IMMUNOHISTOCHEMISTRY (IHC)**

Biomarker	Patient Tumor			Threshold * Biomarker Intensity/Percentage
	Staining Intensity	Percent Staining	Result	
SPARC Polyclonal	1	100	Negative	<30% or <2+ or ≥2+ and ≥30%
ER	0	100	Negative	=0+ or <10% or ≥1+ and ≥10%
PR	0	100	Negative	=0+ or <10% or ≥1+ and ≥10%
Androgen Receptor	0	100	Negative	=0+ or <10% or ≥1+ and ≥10%
TOPO1	2	70	Positive	=0+ or <30% or <2+ or ≥2+ and ≥30%
TOP2A	1	35	Positive	=0+ or <10% or ≥1+ and ≥10%
TLE3	2	80	Positive	<30% or <2+ or ≥2+ and ≥30%
TUBB3	3	35	Positive	<30% or <2+ or ≥2+ and ≥30%
PGP	0	100	Negative	=0+ or <10% or ≥1+ and ≥10%
EGFR	2	30	Positive	=0+ or <10% or ≥1+ and ≥10%
Her2/Neu	0	100	Negative	≤1+ or =2+ and ≤10% or ≥3+ and >10%
cMET	2	20	Negative	<50% or <2+ or ≥2+ and ≥50%
MGMT	1	40	Positive	=0+ or ≤35% or ≥1+ and >35%
PD-L1	2	3	Negative	<5% or <2+ or ≥2+ and ≥5%
PTEN	1	55	Positive	=0+ or ≤50% or ≥1+ and >50%
RRM1	2	60	Positive	=0+ or <50% or <2+ or ≥2+ and ≥50%
TS	1	25	Positive	=0+ or ≤3+ and <10% or ≥1+ and ≥10%

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IHC Methods

These tests were developed and their performance characteristics determined by Caris MPI, Inc. d/b/a Caris Life Sciences®

* Caris Life Sciences has defined threshold levels of reactivity of IHC to establish cutoff points based on published evidence. Polymer detection systems are used for each IHC.

* Please note that PD-L1 staining is read from the cytoplasmic or membrane staining of cancer cells.

Clones used: SPARC Polyclonal (Polyclonal), ER(SP1), PR(1E2), Androgen Receptor (AR27), TOPO1(1D6), TOP2A(3F6), TLE3 (Polyclonal), TUBB3 (Polyclonal), PGP(C494), EGFR(31G7), Her2/Neu(4B5), cMET(SP44), MGMT(MT23.2), PD-L1 (SP142), PTEN(6H2.1), RRM1 (Polyclonal), TS(TS106/4H4B1).

Additional IHC results continued on the next page. >

PATIENT: Patient, Test (XX-Mon-1940)

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PHYSICIAN: Ordering Physician, MD

PROTEIN EXPRESSION BY **IMMUNOHISTOCHEMISTRY (IHC)**

Biomarker	TIL Count/HPF w/40X Objective	Result	Threshold *
PD-1	2-5/HPF	Positive	=0+ or ≥1+

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IHC Methods

These tests were developed and their performance characteristics determined by Caris MPI, Inc. d/b/a Caris Life Sciences®

* Please note that PD1 staining is read from the tumor infiltrating lymphocytes (TIL). Clones used: PD-1 (MRQ-22).

Clones used: PD-1 (MRQ-22).

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PATIENT: Patient, Test (XX-Mon-1940)

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PHYSICIAN: Ordering Physician, MD

AMPLIFICATION BY **CHROMOGENIC IN SITU HYBRIDIZATION (CISH)**

Gene / ISCN	Cells Counted	Result	Total/Avg Gene Copy Number	Total/Avg Control Copy Number	Cells with ≥4 Copies	Cells with ≥15 Copies	Ratio Calculation	Ratio
Her2/Neu nuc ish (D17Z1x1-2,HER2x1-2)[/30]	20	Not Amplified	2.30	1.90	N/A	N/A	Her2/neu/ Chromosome 17	1.21
<i>Reference Range:</i> Her2/Neu:CEP 17 signal ratio of ≥ 2.0 ; and non-amplification as < 2.0 per Ventana INFORM HER2 CISH Package insert.								
cMET nuc ish (D7Z1x1-2,cMETx1-2)[100/100]	20	Not Amplified	2.50	3.50	N/A	N/A		0.71
<i>Reference Range:</i> Positivity for increased gene copy number for cMET CISH has been defined as ≥ 5 copies of mean MET gene copy number per cell in NSCLC based on cMET FISH evidence (Cappuzzo et al 2009). The gene copy number threshold for other tumor types has not been determined.								

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CISH Methods

HER2 CISH test was carried out using the INFORM DUAL HER2 ISH Assay (Ventana Medical Systems, Inc.), which has been cleared by the US Food and Drug Administration (FDA) for enumerating the ratio of HER2/Chr 17 in Breast Cancer samples. The HER2 CISH testing for cancer lineages other than breast has been developed and their performance characteristics determined by Caris MPI, Inc. (d/b/a Caris Life Sciences), and have not been cleared or approved by the FDA.

cMET CISH was carried out using a probe specific for cMET and a probe for the pericentromeric region of chromosome 7 (Ventana). The cMET CISH testing for cancer lineages has been developed and its performance characteristics determined by Caris MPI, Inc. (d/b/a Caris Life Sciences), and has not been cleared or approved by the FDA.

TOP2A CISH was carried out using a probe specific for TOP2 and a probe for the pericentromeric region of chromosome 17 (Ventana). The TOP2A CISH testing for cancer lineages has been developed and its performance characteristics determined by Caris MPI, Inc. (d/b/a Caris Life Sciences), and has not been cleared or approved by the FDA.

The FDA has determined that such clearance or approval is not currently necessary. These tests should not be regarded as investigational or research as they are used for clinical purpose and determined to be medically necessary by the ordering physician, who is not employed by Caris MPI, Inc. or its affiliates. This laboratory is certified under Clinical Laboratory Improvement Amendment of 1988 (CLIA-88) and is qualified to perform high complexity testing. CLIA 03D1019490

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