CARIS MI®
MOLECULAR INTELLIGENCE

MI Profile
Comprehensive Tumor Profiling

The Caris Molecular Intelligence® comprehensive tumor profiling approach to assess DNA, RNA and proteins reveals a molecular blueprint to guide more precise and individualized treatment decisions from among 60+ FDA-approved therapies.

DNA
Whole Exome Sequencing
(Mutations, Indels & Copy Number Alterations)

RNA
Whole Transcriptome Sequencing
(Fusions & Variant Transcripts)

Protein
Immunohistochemistry

Technical Specifications

Sufficient tumor content (>20% tumor nuclei) must be present to complete all analysis. If you have any questions, please contact Customer Support at (888) 979-8669.

Technical Information	IHC	CISH	FISH
Sample Requirements *(see requisition for full details)*	1 unstained slide at 4µm thickness from FFPE block, with evaluable tumor present, per IHC test	1 unstained slide at 4µm thickness from FFPE block, with at least 100 evaluable tumor cells present, per CISH test	2 unstained slides at 4µm thickness from FFPE block, with at least 100 evaluable cells present and 10% tumor, per FISH test
Sensitivity/Specificity	>95%	>95%	>95%

Technical Information	NGS (Whole Exome - DNA)	NGS (Whole Transcriptome - RNA)
Sample Requirements	FFPE block or 10 unstained slides with a minimum of 20% malignant origin for DNA and 10% malignant origin for RNA. Needle biopsy is also acceptable (4-6 cores).	
Tumor Enrichment (when necessary)	Microdissection to isolate and increase the number of cancer cells to improve test performance and increase the chance for successful testing from small tumor samples	
Number of Genes	~22,000 genes	
Average Depth of Coverage (DNA) Average Read Count (RNA)	500x for 700+ clinical and research genes and 200x for all other genes	60 million
Positive Percent Agreement (PPA)	> 95% for base substitutions at ≥ 5% mutant allele frequency; > 99% for indels at ≥ 5% mutant allele frequency; >95% for copy number alterations (amplifications ≥ 6 copies)	>97%
Negative Percent Agreement (NPA)	>99%	>99%
Genomic Signatures	Microsatellite Instability (MSI) Tumor Mutational Burden (TMB)* Loss of Heterozygosity (LOH)* MI FOLFOXai™* – AI predictor of FOLFOX response in metastatic colorectal adenocarcinoma	–
	MI GPSai™* Genomic Prevalence Score – CUP, atypical presentation or clinical ambiguity cases	

Caris Molecular Intelligence® Associations List

The list below details the biomarkers assessed, technology platforms utilized and associated therapies or clinical trials. **Biomarkers and therapy associations may vary by the tumor type submitted.** *Individual assay results are always included with the final report.*

Biomarker	Technology/Alteration	Agent
ALK	IHC, RNA Fusion	crizotinib, ceritinib, alectinib, brigatinib (NSCLC only), lorlatinib (NSCLC only)
	DNA Mutation	resistance to crizotinib, alectinib
AR	IHC	bicalutamide, leuprolide (salivary gland tumors only)
		enzalutamide, bicalutamide (TNBC only)
BRAF	DNA Mutation	vemurafenib, dabrafenib, cobimetinib, trametinib
		encorafenib + binimetinib (melanoma only)
		dabrafenib+trametinib (anaplastic thyroid and NSCLC only)
		atezolizumab + cobimetinib + vemurafenib (melanoma only)
		cetuximab + encorafenib (CRC only)
BRCA1/2	DNA Mutation	carboplatin, cisplatin, oxaliplatin
		niraparib (ovarian, prostate), olaparib (breast, cholangiocarcinoma, ovarian, pancreatic, prostate), rucaparib (ovarian, pancreatic, prostate), talazoparib (breast only), veliparib combination (pancreatic only)
		resistance to olaparib, niraparib, rucaparib with reversion mutation
EGFR	DNA Mutation	afatinib (NSCLC only)
		afatinib + cetuximab (T790M; NSCLC only)
		erlotinib, gefitinib (NSCLC and CUP only)
		osimertinib, dacomitinib (NSCLC only)
ER	IHC	endocrine therapies
		everolimus (breast only)
		palbociclib, ribociclib, abemaciclib (breast only)
ERBB2 (HER2)	IHC, CISH, DNA Mutation, CNA	trastuzumab, lapatinib, neratinib (breast only), pertuzumab, T-DM1, fam-trastuzumab deruxtecan-nxki, tucatinib
	DNA Mutation	T-DM1 (NSCLC only)
ER/PR/ERBB2 (HER2)	IHC, CISH	sacituzumab govitecan (TNBC only)
ESR1	DNA Mutation	exemestane + everolimus, fulvestrant, palbociclib combination therapy (breast only)
		resistance to aromatase inhibitors (breast only)
FGFR2/3	DNA Mutation, RNA Fusion	erdafitinib (urothelial bladder only), pemigatinib (cholangiocarcinoma only)
HRR	DNA Mutation	olaparib (prostate only)
IDH1	DNA Mutation	temozolomide (high grade glioma only)
		ivosidenib (cholangiocarcinoma and EBDA only)
KIT	DNA Mutation	imatinib
		regorafenib, sunitinib (both GIST only)
KRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to erlotinib/gefitinib (NSCLC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC only)
MET	RNA Exon Skipping, DNA Exon Skipping, CNA	capmatinib, crizotinib (both NSCLC only)
MGMT	Pyrosequencing (Methylation)	temozolomide (high grade glioma only)
MMR Deficiency	IHC, DNA Mutation	pembrolizumab
MSI		pembrolizumab, nivolumab (CRC, small bowel adenocarcinoma), nivolumab+ipilimumab (CRC, small bowel adenocarcinoma)
MMR Proficiency	IHC, DNA Mutation	pembrolizumab + lenvatinib (endometrial only)
MSS		
NRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC only)
NTRK1/2/3	RNA Fusion	entrectinib, larotrectinib
	DNA Mutation	resistance to larotrectinib, entrectinib
PALB2	DNA Mutation	olaparib (pancreatic and prostate), veliparib combination (pancreatic only)
PDGFRA	DNA Mutation	imatinib, avapritinib (GIST only), sunitinib
PD-L1	IHC	pembrolizumab (22c3 TPS in NSCLC; 22c3 CPS in cervical, esophageal, GEJ/gastric, head & neck, urothelial and non-urothelial bladder, vulvar)
		atezolizumab (SP142 IC urothelial bladder cancer and SP142 IC & TC NSCLC)
		pembrolizumab + chemotherapy (22c3 CPS in TNBC only)
		atezolizumab + nab-paclitaxel (SP142 IC in TNBC only)
		nivolumab/ipilimumab combination (28-8 NSCLC only)
PIK3CA	DNA Mutation	alpelisib + fulvestrant (breast only)
POLE	DNA Mutation	pembrolizumab (endometrial and CRC only)
PR	IHC	endocrine therapies
RET	RNA Fusion	cabozantinib, vandetanib, selpercatinib, pralsetinib (NSCLC only)
	DNA Mutation	vandetanib, cabozantinib, selpercatinib (thyroid only); resistance to vandetanib, cabozantinib
ROS1	IHC, RNA Fusion	crizotinib, ceritinib, entrectinib, lorlatinib (NSCLC only)
TMB	DNA Mutation	pembrolizumab

IHC: Immunohistochemistry **CISH:** Chromogenic *in situ* Hybridization **CNA:** Copy Number Alteration (DNA)

HRR (Homologous Recombination Repair) genes: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L

Note: in certain instances, some biomarkers included in MI Profile or genes ordered individually will not associate with commercially available cancer therapies or clinical trials.

Biomarker Analysis by Tumor Type

The information below details the biomarkers analyzed by technology for the tumor type submitted. Before ordering testing services, please refer to the profile menu online (www.CarisMolecularIntelligence.com/profiling-menu) to view the most up-to-date listing of biomarkers that will be performed. Tests may vary if insufficient tumor samples are submitted.

MI Profile™					
Tumor Type	Immunohistochemistry (IHC)	Whole Exome Sequencing (WES)		Whole Transcriptome Sequencing (WTS)	Other
		DNA Alterations	Genomic Signatures	RNA Alterations	
Bladder	MMR, PD-L1 (SP142 and 22c3)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Breast	AR, ER, Her2/Neu, MMR, PD-L1 (SP142, 22c3), PR, PTEN	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Cancer of Unknown Primary - Female	AR, ER, Her2/Neu, MMR, PD-L1(SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Cancer of Unknown Primary - Male	AR, Her2/Neu, MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Cervical	ER, MMR, PD-L1 (22c3), PR	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Cholangiocarcinoma/ Hepatobiliary	Her2/Neu, MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	Her2 *(Chromogenic in situ Hybridization)*
Colorectal and Small Intestinal	Her2/Neu, MMR, PD-L1 (SP142), PTEN	Mutations, Indels, CNA	MSI, TMB, MI FOLFOXai™ *(CRC only)*	Fusions, Variant Transcripts	
Endometrial	ER, MMR, PD-L1 (SP142), PR, PTEN	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Esophageal Cancer	Her2/Neu, MMR, PD-L1 (22c3)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	EBER *(Chromogenic in situ Hybridization)*
Gastric/GEJ	Her2/Neu, MMR, PD-L1 (22c3)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	EBER, Her2 *(Chromogenic in situ Hybridization)*
GIST	MMR, PD-L1 (SP142), PTEN	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Glioma	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	MGMT Methylation *(Pyrosequencing)*
Head & Neck	MMR, p16, PD-L1 (22c3)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	EBER, HPV *(Chromogenic in situ Hybridization)*, HPV reflex to confirm p16 result
Kidney	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Melanoma	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Merkel Cell	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Neuroendocrine	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Non-Small Cell Lung	ALK, MMR, PD-L1 (22c3, 28-8 and SP142), PTEN	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Ovarian	ER, MMR, PD-L1 (22c3), PR	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Pancreatic	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Prostate	AR, MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Salivary Gland	AR, Her2/Neu, MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Sarcoma	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Small Cell Lung	MMR, PD-L1(22c3)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Thyroid	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Uterine Serous	ER, Her2/Neu, MMR, PD-L1 (SP142), PR, PTEN	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	Her2 *(Chromogenic in situ Hybridization)*
Vulvar Cancer (SCC)	ER, MMR, PD-L1 (22c3), PR	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	
Other Tumors	MMR, PD-L1 (SP142)	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	

MI FOLFOXai™: AI predictor of FOLFOX response in metastatic colorectal adenocarcinoma.
MMR = Mismatch Repair proteins: MLH1, MSH2, MSH6, PMS2

Next-Generation Sequencing Gene List

Whole Exome Sequencing – Genomic Stability Testing (DNA)		
Microsatellite Instability (MSI)	Tumor Mutational Burden (TMB)*	Loss of Heterozygosity (LOH)*

Whole Exome Sequencing – Genes most commonly associated with cancer below.								
Point Mutations and Indels (DNA)								
ABL1	BCOR	FANCF	HIST1H3B	LZTR1	NBN	PPP2R1A	RHOA	TMEM127
AIP	BTK	FANCI	HIST1H3C	MAPK1	NOTCH1	PPP2R2A	SDHA	VHL
AKT1	CD79B	FANCM	HNF1A	MAPK3	NRAS	PRKACA	SDHAF2	XRCC1
AMER1	CDH1	FAT1	HOXB13	MAX	NTHL1	PRKDC	SETD2	YES1
AR	CDK12	FOXL2	HRAS	MED12	PARP1	RABL3	SMARCA4	
ARAF	CXCR4	FYN	KDM5C	MPL	PHOX2B	RAD51B	SOCS1	
ATRX	DNMT3A	GLI2	KDM6A	MSH3	PIK3CB	RAD51C	SPOP	
B2M	EPHA2	GNA11	KDR	MST1R	PMS1	RAD51D	SRC	
BCL2	FANCB	HDAC	LYN	MUTYH	POLD1	RAD54L	TERT	

Point Mutations, Indels and Copy Number Alterations* (DNA)									
ALK	BRIP1	CSF1R	FANCC	FLT4	KIT	MRE11	PALB2	PTPN11	SMARCE1
APC	CARD11	CTNNA1	FANCD2	FUBP1	KMT2A	MSH2	PBRM1	RAD50	SMO
ARID1A	CBFB	CTNNB1	FANCE	GATA3	KMT2C	MSH6	PDGFRA	RAF1	SPEN
ARID2	CCND1	CYLD	FANCG	GNA13	KMT2D	MTOR	PDGFRB	RB1	STAT3
ASXL1	CCND2	DDR2	FANCL	GNAQ	KRAS	MYCN	PIK3CA	RET	STK11
ATM	CCND3	DICER1	FAS	GNAS	LCK	MYD88	PIK3R1	RNF43	SUFU
ATR	CDC73	EGFR	FBXW7	H3F3A	MAP2K1	NF1	PIM1	ROS1	TNFAIP3
BAP1	CDK4	EP300	FGFR1	H3F3B	MAP2K2	NF2	PMS2	RUNX1	TNFRSF14
BARD1	CDK6	ERBB2	FGFR2	IDH1	MAP2K4	NFE2L2	POLE	SDHB	TP53
BCL9	CDKN1B	ERBB3	FGFR3	IDH2	MAP3K1	NFKBIA	POT1	SDHC	TSC1
BLM	CDKN2A	ERBB4	FGFR4	IRF4	MEF2B	NPM1	PPARG	SDHD	TSC2
BMPR1A	CHEK1	ERCC2	FH	JAK1	MEN1	NSD1	PRDM1	SF3B1	U2AF1
BRAF	CHEK2	ESR1	FLCN	JAK2	MET	NTRK1	PRKAR1A	SMAD2	WRN
BRCA1	CIC	EZH2	FLT1	JAK3	MITF	NTRK2	PTCH1	SMAD4	WT1
BRCA2	CREBBP	FANCA	FLT3	KEAP1	MLH1	NTRK3	PTEN	SMARCB1	

Whole Transcriptome Sequencing – Genes most commonly associated with cancer listed below.								
Fusions (RNA)								**Variant Transcripts (RNA)**
ABL	BRD3	FGFR3	INSR	MYB	NUMBL	PRKCA	RSPO3	AR-V7
AKT3	BRD4	ERG	MAML2	NOTCH1	NUTM1	PRKCB	TERT	
ALK	EGFR	ESR1	MAST1	NOTCH2	PDGFRA	RAF1	TFE3	EGFR vIII
ARHGAP26	EWSR1	ETV1	MAST2	NRG1	PDGFRB	RELA	TFEB	
AXL	FGR	ETV4	MET	NTRK1	PIK3CA	RET	THADA	MET Exon 14 Skipping
BCR	FGFR1	ETV5	MSMB	NTRK2	PKN1	ROS1	TMPRSS2	
BRAF	FGFR2	ETV6	MUSK	NTRK3	PPARG	RSPO2		

** Not available in New York State.*

To order or learn more, visit **www.CarisMolecularIntelligence.com.**
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