CARIS MI®

MOLECULAR INTELLIGENCE

Comprehensive Tumor Profiling

A better guide for

Molecular Intelligence

Why Caris?

With the promise of precision medicine becoming a reality, molecular profiling has become standard of care for many cancer types – and required for certain therapies (companion dx). More than ever, oncologists need a trusted tumor profiling partner to provide reliable, high-quality molecular information to guide more precise and individualized treatment decisions.

Caris Molecular Intelligence® identifies key molecular features of cancer and provides clinical insights to aid oncologists in personalizing cancer therapies for their solid tumor cancer patients. Caris Molecular Intelligence helps oncologists:

- **navigate among therapies with potential benefit;**
- **identify therapies that may not have been considered;**
- **determine drugs with potential lack of benefit (avoiding unnecessary toxicities and costs); and**
- **match patients to clinical trials.**

The Most Experienced Comprehensive Tumor Profiling Provider

Unmatched Experience

- 2,850,000+ tests completed
- 240,000+ clinical cases performed

Immunotherapy Diagnostics Expertise

- PD-L1 by IHC, including TPS and CPS scoring methods
- Mismatch Repair (MMR) proteins by IHC: MLH1, MSH2, MSH6, PMS2
- Microsatellite Instability (MSI) by NGS
- Tumor Mutational Burden (TMB) by NGS

Rigorous Quality Standards

- CAP, CLIA, NYSDOH, ISO15189 accredited
- 66,000-square-foot clinical laboratory in Phoenix, AZ
- 38,000 square-foot R&D facility in Phoenix, AZ
- 115,000-square-foot blood-based laboratory in Irving, Texas (to open in 2021)
- Staffed by: bioinformaticians, oncologists, molecular geneticists, pathologists and PhD scientists

Limited Tissue Capabilities

- Tumor enrichment via microdissection
- Multiple reflex options to alternative technologies/methods

Rapid Turnaround Time

- 8-14 calendar days

→ www.CarisLifeSciences.com

Tumor Profiling

Comprehensive tumor profiling with Caris Molecular Intelligence® assesses DNA, RNA and Proteins with multiple technologies (NGS DNA-WES & RNA-WTS, PyroSeq, IHC, ISH) to reveal a more complete molecular blueprint to guide precise and individualized treatment decisions.

DNA

Next-Generation Sequencing (Mutations, Indels & Copy Number Alterations)

Whole Exome ~22,000 genes

- 200+ clinically relevant genes
- 700+ genes sequenced at average 500x and balance of exome at average 200x
- ~250,000 exonic/ intronic/ intergenic SNPs

All solid tumors

RNA

Next-Generation Sequencing (Fusions & Variant Transcripts)

Whole Transcriptome ~22,000 genes

- 60 million read counts
- Gene fusions and variant transcripts
- Novel translocation detection independent of intronic breakpoint or fusion partner

All solid tumors

Protein

Immunohistochemistry

Up to 15 Clinically Relevant IHCs (Optimized across ~25 Tumor Types)

- Multiple FDA approved CDx assays for different disease types (per label)
- Controls on every IHC slide
- 4 µm cuts to preserve tissue

All solid tumors

Caris Molecular Intelligence offers two different options for tumor profiling, MI Profile™ and MI Tumor Seek™.

	MI PROFILE™	MI TUMOR Seek™
Whole Genome (NGS-DNA)	✓	✓
MSI	✓	✓
TMB	✓	✓
LOH	✓	✓
HRD	Coming Soon	
Whole Transcriptome (NGS-RNA)	✓	✓
IHC, ISH (Protein)	✓	Not Included
TAT	8-14 days	

Caris MAI™ – Molecular Artificial Intelligence

A revolutionary platform to identify unique "molecular signatures" using artificial intelligence, machine learning and multivariate analysis across the Caris clinical-molecular database to push the boundaries of innovation in precision medicine.

MI GPSai™

Genomic Prevalence Score

- Intended for cancer of unknown primary (CUP), or cases with atypical clinical presentation or clinical ambiguity.
- Provides a cancer type similarity assessment by comparing genomic (DNA) and transcriptomic (RNA) characteristics of the patient's tumor against other tumors in the Caris database.

MI FOLFOXai™

Frontline Therapy Predictor

- Intended as an aid in gauging a patient's likelihood to benefit from FOLFOX chemotherapy (in combination with bevacizumab) as the first-line chemotherapy regimen in metastatic colorectal adenocarcinoma.
- Outcomes data from the MI FOLFOXai validation demonstrated a ~50% improvement of overall survival.

I/O Immunotherapy Diagnostics Expertise

PD-L1
Programmed Cell Death-Ligand 1 by IHC
138,000+
TESTS PERFORMED

MSI
Microsatellite Instability by NGS
97,000+
TESTS PERFORMED

TMB
Tumor Mutational Burden by NGS
105,000+
TESTS PERFORMED

MMR
Mismatch Repair proteins by IHC
81,000+
TESTS PERFORMED

By harnessing the body's immune system to detect and destroy tumor cells, immune checkpoint inhibitors are rapidly ushering in a new era of precision medicine. Identify patients more likely to respond to immunotherapies with reliable molecular information based on validated assays for MMR, MSI, PD-L1 and TMB in our state-of-the-art laboratory.

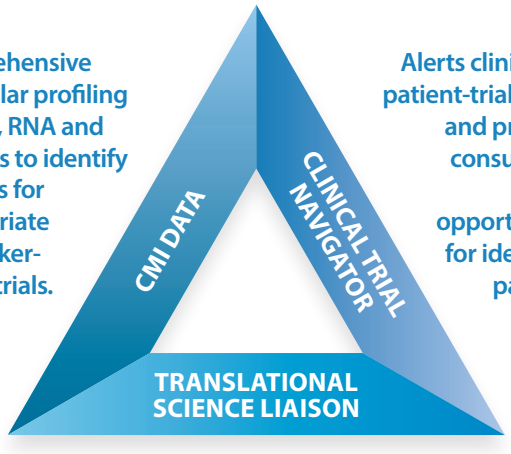
MI Trials

Clinical trials offer patients and physicians access to the latest drugs being developed to improve clinical outcomes. However, awareness of available trials is low and overall participation in oncology trials is less than five percent. Caris helps increase awareness and participation of clinical trials through MI Trials.

MI Trials provides:

- Real-time alerts to clinicians, matching patients with clinical trials in their area,
- Increased patient access to a larger number of potential treatment options, and
- Unsurpassed clinical trial support through a physician consultant team specializing in oncology.

Comprehensive molecular profiling of DNA, RNA and proteins to identify patients for appropriate biomarker-driven trials.



Alerts clinician of patient-trial match and provides consultation on trial opportunities for identified patients.

Provides physician with expertise on CMI results.

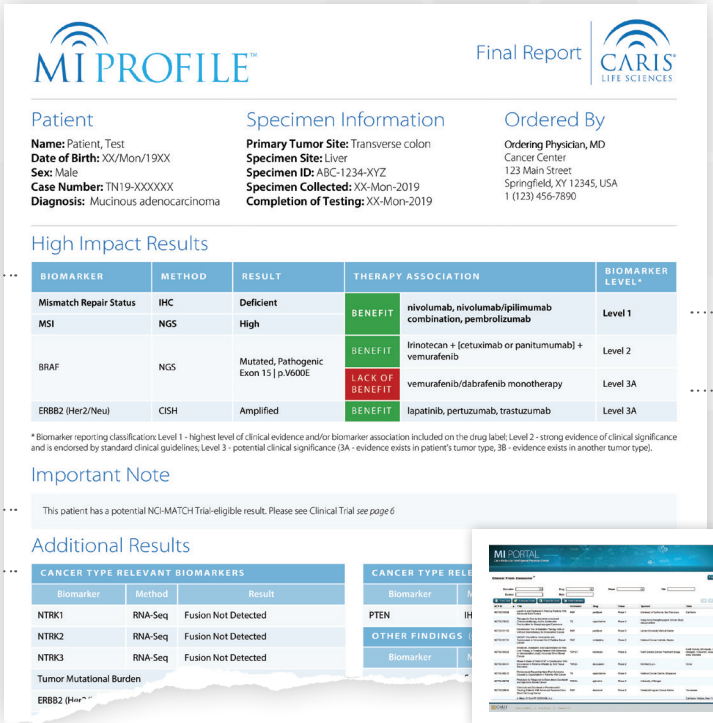
MI Report

Caris Molecular Intelligence reports are built to maximize clinical utility in an easy-to-interpret format. Clinicians need treatment information fast, that's why our report was built by oncologists for oncologists. With results back in 8-14 days, we'll help you find answers when you need them the most.

Contains important biomarker and associated therapy results

Provides important information about drug/ biomarker associations and comments from Caris pathologists and/or molecular geneticists

Lists disease-relevant biomarker information, as well as other altered biomarker results



MI PROFILE™ Final Report — CARIS LIFE SCIENCES

Patient
Name: Patient, Test
Date of Birth: XX/Mon/19XX
Sex: Male
Case Number: TN19-XXXXXX
Diagnosis: Mucinous adenocarcinoma

Specimen Information
Primary Tumor Site: Transverse colon
Specimen Site: Liver
Specimen ID: ABC-1234-XYZ
Specimen Collected: XX-Mon-2019
Completion of Testing: XX-Mon-2019

Ordered By
Ordering Physician, MD
Cancer Center
123 Main Street
Springfield, XY 12345, USA
1 (123) 456-7890

High Impact Results

BIOMARKER	METHOD	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
Mismatch Repair Status	IHC	Deficient	BENEFIT	nivolumab, nivolumab/ipilimumab combination, pembrolizumab	Level 1
MSI	NGS	High			
BRAF	NGS	Mutated, Pathogenic Exon 15 | p.V600E	BENEFIT	Irinotecan + [cetuximab or panitumumab] + vemurafenib	Level 2
			LACK OF BENEFIT	vemurafenib/dabrafenib monotherapy	Level 3A
ERBB2 (Her2/Neu)	CISH	Amplified	BENEFIT	lapatinib, pertuzumab, trastuzumab	Level 3A

* Biomarker reporting classification: Level 1 - highest level of clinical evidence and/or biomarker association included on the drug label; Level 2 - strong evidence of clinical significance and is endorsed by standard clinical guidelines; Level 3 - potential clinical significance (3A - evidence exists in patient's tumor type; 3B - evidence exists in another tumor type).

Important Note

This patient has a potential NCI-MATCH Trial-eligible result. Please see Clinical Trial *see page 6*

Additional Results

CANCER TYPE RELEVANT BIOMARKERS

Biomarker	Method	Result
NTRK1	RNA-Seq	Fusion Not Detected
NTRK2	RNA-Seq	Fusion Not Detected
NTRK3	RNA-Seq	Fusion Not Detected
Tumor Mutational Burden		
ERBB2 (Her2/Neu)		

CANCER TYPE RELE

Biomarker	M
PTEN	IH

OTHER FINDINGS

Biomarker	M

Navigate among therapies with potential benefit (noted in green)

Identify therapies with potential lack of benefit (noted in red)

Utilize the Clinical Trials Connector to match biomarkers with open clinical trials through MI Portal

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