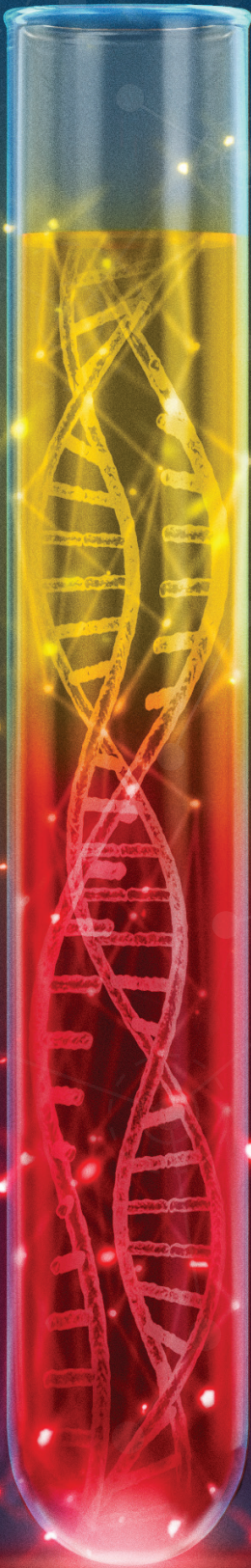


NEW

RNA-Based Fusion Detection



Caris Assure[®]

Therapy Selection

A New Standard in Liquid Biopsy

- Whole Exome Sequencing
- Whole Transcriptome Sequencing
- Whole Blood Analysis (plasma + white blood cells)
- Tiered Molecular Depth

SEE THE COMPLETE MOLECULAR PICTURE

THE COMPLETE PICTURE STARTS WITH CONFIDENT VARIANT DETECTION

Built to Deliver Accuracy You Can Trust for Confidence in Every Result

Variant detection in liquid biopsy is often limited by low amounts of circulating tumor DNA—increasing the likelihood of false negatives



Breadth and depth - Not one at the expense of the other

Caris Assure® is built differently—pairing a broad WES-backbone with deep, targeted sequencing of therapy-relevant biomarkers



23,000+ genes

Delivers broad WES coverage while supporting emerging biomarkers and clinical trial opportunities



Up to
40,000x Depth¹

Improves detection of low-frequency variants in therapy-relevant biomarkers



96.9% Sensitivity^{*1}

Finds more opportunities to act with testing built to maximize detection

Ultra Low Variant Detection You Can Count On

Limit of Detection (LOD) – minimum and median by variant category¹

● Minimum LoD95 ● Median LoD95

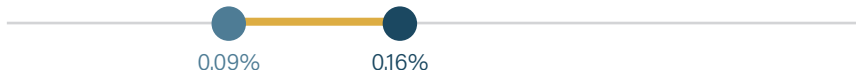
SNVs



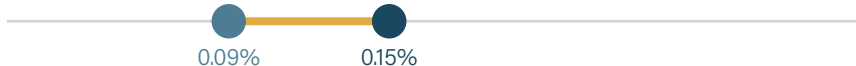
DNA Rearrangements



NSCLC Variants^{**}



CRC Variants[‡]



Accurate Decisions Depend on Reliable Answers

^{*}For drug-rule variants

^{**}Across seven therapy-relevant NSCLC driver variants

[‡]Across five CRC-relevant RAS/RAF variants

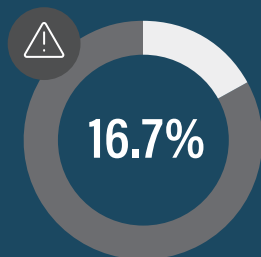
Reported performance is based on ≥30 ng of cfDNA input using a composite tissue-liquid comparator that incorporates the FDA-approved MI Cancer Seek[®] tissue assay and the original Caris Assure assay to account for the biology of tumor-derived signals in blood.

Limit of detection is defined here as the minimum observed VF at the lowest target VF level with a ≥95% hit rate across replicates.

THE COMPLETE PICTURE GOES BEYOND DNA TO INCLUDE RNA-BASED FUSION DETECTION

Built to See What DNA-Only Approaches May Miss

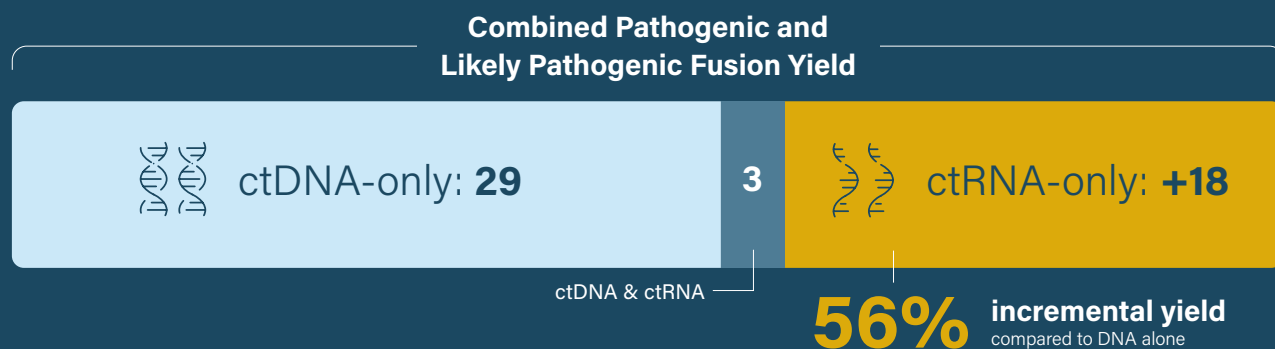
Fusion breakpoints are structurally difficult for DNA-based assays to capture



tissue-confirmed fusions detected by ctDNA testing alone²

A NEW WAY OF SEEING

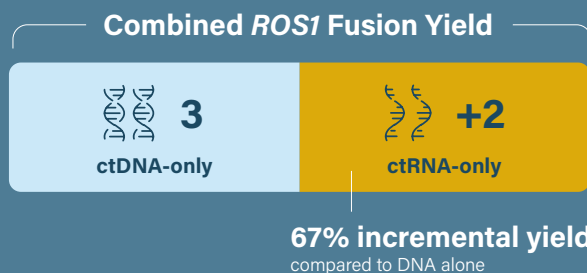
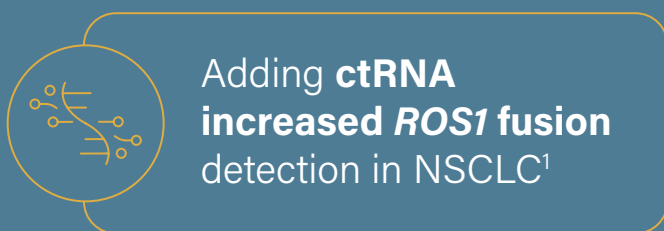
Complementary ctDNA and ctRNA increases fusion detection beyond DNA^{*1}



In Advanced Disease, a Missed Fusion Can Be a Missed Line of Therapy

Fusion detection matters in NSCLC

- Tissue is often insufficient for comprehensive molecular analysis
- 6.1% of NSCLC patients are eligible for an FDA-approved fusion therapy³



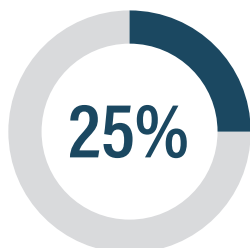
Caris Assure® reveals additional RNA-based findings for accurate therapy selection by detecting and reporting clinically actionable fusions

^{*}Among tissue-confirmed fusion samples

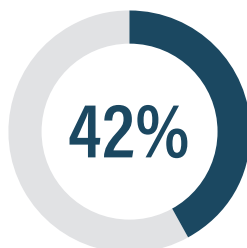
THE COMPLETE PICTURE REQUIRES INTERPRETATION, NOT JUST DETECTION

Built to See What Plasma-Only Approaches May Misinterpret

Not Every Variant Found in Blood Comes from the Tumor



mutations of
non-tumor origin⁴



patient prevalence with
non-tumor mutations⁵

in genes including *BRCA1*, *BRCA2*, *ATM* and *CHEK2*

Clonal Hematopoiesis (CH) mutations are non-tumor mutations from blood cells that increase with age, smoking and previous chemotherapy and create “biological noise” in plasma, potentially leading to false positive results and off-target therapy

Real-World Consequence of Variant Misinterpretation*

High CH rates are found in genes associated with PARP inhibitor therapy in almost **2% of breast cancer** patients and in over **3% of prostate cancer cases**⁵

PLASMA ONLY

BRCA2 variant appears actionable

- ✗ Receives ineffective olaparib (~\$15k/mo)⁶
- ✗ Suffers anemia, nausea and fatigue
- ✗ Loses time while the tumor continues to grow

COST

SIDE EFFECTS

TIME

WHOLE BLOOD ANALYSIS

Plasma + White Blood Cells

BRCA2 variant is confirmed as CH-derived

- ✓ Spared cost of ineffective therapy
- ✓ Avoids side effects
- ✓ Moves faster to a therapy option that can help

Caris Assure Delivers Trusted Interpretation for Confident Therapy Decisions



Somatic Tumor



Incidental Germline^{‡}**



Clonal Hematopoiesis

* Hypothetical case for illustrative purposes

** Confirmatory germline testing is not required if positive.

‡ Not a replacement for comprehensive germline testing. Incidental pathogenic alterations are reported, including ACMG recognized cancer genes. Negative results do not imply the patient does not harbor a germline mutation.

A New Standard in Liquid Biopsy

Look beyond detection to confidently interpret what is found

Caris Assure*

Therapy Selection



PATIENT

Name:
DOB:
Sex: Male | MRN: 123
Case Number:
Diagnosis: Adenocarcinoma, metastatic,
NGS

SPECIMEN INFORMATION

Primary Tumor Site: Upper lobe, lung
Specimen Site: Blood
Specimen ID:
Specimen Collected:
Test Report Date:

ORDERED BY

FINAL REPORT

Results with Therapy Associations

BIOMARKER	ANALYTE	ORIGIN	RESULTS	THERAPY ASSOCIATION
EGFR	ctDNA	Somatic Tumor	Pathogenic Variant Exon 21 p.L858R	BENEFIT afatinib, dacomitinib, erlotinib, erlotinib + ramucicamab, gefitinib, icotinib + amivantamab, osimertinib, dacomitinib, neratinib
EML4:ALK	ctDNA	Somatic Tumor	Fusion Detected	BENEFIT alectinib, brigatinib, ceritinib, crizotinib, ensartinib, lorlatinib
UGT1A1	gDNA	Germline	Poor Metabolizer c.215G>A	SERIOUS ADVERSE EVENT irinotecan

*Level 1: Companion diagnosis (CDx); Level 2: Strong evidence of clinical significance or endorsed by clinical guidelines; Level 3: Potential clinical significance.

IMPORTANT NOTE (S): An EML4:ALK fusion was identified with an EGFR exon 21 p.L858R mutation. Depending on clinical context and treatment history, either alteration may represent a primary driver or a resistance mechanism; combined or sequential EGFR- and ALK-targeted therapies have been described (PMIDs: 29883818, 30957057, 30880506, 32024070, 30257958).

Tumor Associated Findings

BIOMARKER	ALTERATION PROTEIN CHANGE * DNA CHANGE	VF (%)	INTERPRETATION	CLINICAL TRIAL MATCHES (page 6)
EGFR	L858R c.2573T>G	27.3%	Pathogenic	YES
EML4:ALK	Fusion / Rearrangement	-	Pathogenic	YES
CCNE1	Amplification	-	Pathogenic	YES
PTEN	Deletion	-	Pathogenic	YES
PTEN	E436 c.1274delG	37.0%	Pathogenic	YES
BRAF	G469A c.1406G>C	0.2%	Pathogenic	YES
FBXW7	G517R c.1549G>A	0.3%	Likely Pathogenic	NO
RBI	- c.2325+2T>G	24.5%	Pathogenic	NO
TP53	- c.959+1G>A	0.2%	Pathogenic	NO
TP53	V203L c.607G>T	28.5%	Likely Pathogenic	NO
CEBPA	S150P c.558T>C	1.4%	VUS	-
EGFR	Q703L c.2102A>T	28.9%	VUS	-

OTHER RESULTS

BLOOD TMB (mut/Mb): 5	MICROSATELLITE INSTABILITY: NOT DETECTED	TUMOR FRACTION: 37%
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Analysis included these guideline-recommended biomarkers: ALK, BRAF, EGFR (T790M, etc.), ERBB2 (HER2), KRAS, MET, NTRK1/2/3, RET, ROS1

Incidental* Germline Variants

BIOMARKER	ALTERATION PROTEIN CHANGE * DNA CHANGE	VF (%)	ZYGOSITY	INTERPRETATION
NONE DETECTED				

Clonal Hematopoiesis (CH)

BIOMARKER	ALTERATION PROTEIN CHANGE * DNA CHANGE	VF (%)	INTERPRETATION
DNMT3A	S663* c.1585C>A	0.2%	PATHOGENIC

*Incidental findings section reports variants characterized as non-tumor derived. These results are not a replacement for comprehensive germline testing. Incidental germline pathogenic alterations in ACM-seq recognized. Substantial selected cancer genes are reported low penetrance genes. Not negative results do not imply the patient does not harbor a germline mutation. CH refers to mutations in cancer-associated genes in white blood cells (WBC) and not of solid tumor origin. Incidental CH variants are reported but may not comprehensively detect all CH variants. These mutations occur naturally and increase with age or may be smoking- or therapy-related. Although CH is considered a benign finding, there is a risk of progression to hematological malignancy and thus appropriate clinical correlation is recommended. Variants characterized as unknown origin, if reported, are likely characterized as high-level CH variants, potential mosaic or germline origin. Categorization of incidental pathogenic and likely pathogenic variants are based on the observed allele frequency in the buffy coat, such that, for the majority of cases: > 30% is germline, 20%-30% is unknown origin, <20% is clonal hematopoiesis, though there are exceptions may exist.

Pharmacogenomics (PGx) - Variants associated with response to anticancer therapies

GENE	ALTERATION PROTEIN CHANGE * DNA CHANGE	ZYGOSITY	CYPIC DEFINED PHENOTYPE	VARIANT ACTIVITY SCORE (or annotated)	TOTAL ACTIVITY SCORE (or annotated)	METABOLIZER PHENOTYPE
DPYD	No Variants Detected	-	-	-	-	NORMAL
UGT1A1	c.215G>A	G71R	Homozygous	Decreased Function	-	POOR

DPYD **Guiding Recommendation:** Huo, W, et al. 2024 | Mol Diagn 24(2):1851-1853. CYPIC Guideline for Fluoropyrimidines and DPYD: cyp450.org/guidelines/guideline-for-fluoropyrimidines-and-dpyd. DPYD, Dihydropyrimidine Dehydrogenase, encoded by the gene DPYD, is involved in metabolic reduction of uracil and thymine as well as the chemotherapeutic drug 5-fluorouracil (5-FU). Individuals with decreased DPYD activity are less able to break down 5-fluorouracil to inactive metabolites, thereby increasing exposure to active drug molecules. Compromised DPYD activity increases an individual's risk of experiencing potentially life-threatening 5-FU-related toxicity, including bone marrow suppression, gastrointestinal toxicity, and neurotoxicity. DPYD Phenotypes are defined as: (1) normal metabolizer, total activity score of 2; (2) intermediate metabolizer, total activity score of 1-2; (3) poor metabolizer, total activity score 0-1.

UGT1A1 **Guiding Recommendation:** Huo, W, et al. 2023 | Eur J Hum Genet. 31(9):1089-1098. DPYD Guideline for Irinotecan and UGT1A1: Pharmacogenetics guideline for UGT1A1: UGT1A1, UDP-glucuronosyltransferase 1A1, mediates glucuronidation of bilirubin and drugs including irinotecan. Decreased UGT1A1 activity may increase the risk of irinotecan-related toxicity, including severe neutropenia and diarrhea. UGT1A1 phenotypes are defined as: (1) normal metabolizer, two normal function alleles; (2) normal function and one decreased-function allele; and (3) poor metabolizer, two decreased-function alleles. For UGT1A1, poor metabolizers receiving irinotecan, genotype-guided dosing, with subsequent dose modification based on clinical tolerance.

Therapy Response and Clonal Kinetics (TRACK)

BIOMARKER + ALTERATION	TISSUE 01/13/2025	WHOLE BLOOD 1 02/13/2025	WHOLE BLOOD 2 12/16/2025
BRAF G469A	Not Detected	Not Detected	0.2%
EGFR L858R	Detected	39.9%	27.3%
FBXW7 G517R	Not Detected	Not Detected	0.3%
PTEN E436	Detected	61.2%	37.0%
RBI c.2325+2T>G	Detected	50.3%	24.5%
TP53 V203L	Detected	51.9%	28.5%
TP53 c.959+1G>A	Not Detected	Not Detected	0.2%
CCNE1 Amplification	Not Detected	Detected	Detected
EML4:ALK	Detected	Not Detected	Detected
TMB	5 MUT/MB	3 MUT/MB	4 MUT/MB
MSI	Not Detected	Not Detected	Not Detected
TUMOR FRACTION	Not Assessed	61.2%	37.0%

A Find Actionable Targets



Tumor Alterations

RNA and DNA Fusion Detection

Resistance Mutations (additional insights in TRACK table)

B Act with Confidence



Incidental Germline

Clonal Hematopoiesis (CH)

C Receive Additional Clinical Insights



Pharmacogenomics (DPYD Tier 1/2 & UGT1A1)

Genomic Signatures (bTMB, MSI)

Predicted HLA Genotype

Predicted Human Leukocyte Antigen (HLA) Genotype Results

GENE	METHOD	ANALYTE	ORIGIN	GENOTYPE
HLA-A	SEQ	gDNA	GERMLINE	A*11:01, A*30:01
HLA-B	SEQ	gDNA	GERMLINE	B*45:01, B*35:01
HLA-C	SEQ	gDNA	GERMLINE	C*06:02, C*04:01

The predicted HLA genotype results are summarized in the table below. Please note that this assay is not a substitute for histocompatibility testing. It is recommended to confirm the patient's HLA type with an appropriate assay. HLA genotypes with only one allele are either homozygous or have loss-of-heterozygosity at that position.

EXPECT MORE FROM YOUR LIQUID BIOPSY

See the Complete Molecular Picture



Whole Exome Sequencing

Broad WES backbone + therapy-focused depth

23,000+ Genes

- Up to 40,000x depth¹
- 96.9% sensitivity¹



Whole Transcriptome Sequencing

Complementary ctDNA + ctRNA fusion detection
ALK, BRAF, ERG, FGFR1/2/3, NRG1, NTRK1/2/3, RET, ROS1

+56%

Fusion findings vs ctDNA alone¹



Whole Blood Analysis (plasma + white blood cells)

Accurate molecular interpretation

Somatic Tumor • CH • Incidental Germline[‡]

Greater clarity in variant origin to reduce false positives⁴



7-Day Median TAT

Fast answers when
decisions matter most



Patient Insurance Coverage

95% of patients have \$0
out-of-pocket costs



A New Standard in Liquid Biopsy

To order or learn more, visit www.CarisLifeSciences.com/Assure

[‡] Not a replacement for comprehensive germline testing. Incidental pathogenic alterations are reported, including ACMG recognized cancer genes. Negative results do not imply the patient does not harbor a germline mutation.

¹. Caris Assure Internal Validation Data. ². Hasegawa N. et al. (2021) *Cancer Sci.* 112(10), 4393-4403. ³. McDonnell K., et. al. (2023) *Ann Oncol.* Oct, 34S254. ⁴. Lockwood, Christina M. et al. (2023) *J Mol Diagn.* 25, 876-897. ⁵. Magee D, et al. (2025) *Clin Cancer Res.* 31, 2710-2718. ⁶. Based on the method in Roskoski R, Jr. (2024) *Pharmacol Res.* 199, 107036, olaparib price per pill from pharmacychecker.com (in zip code 75039, Irving, TX) was combined with dosage from the FDA label to yield drug price per 30-day period.

Caris Assure[®] is intended for patients with previously diagnosed solid malignant neoplasms when tissue profiling is not feasible and is to be used by qualified healthcare professionals. Not available in all locations.



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