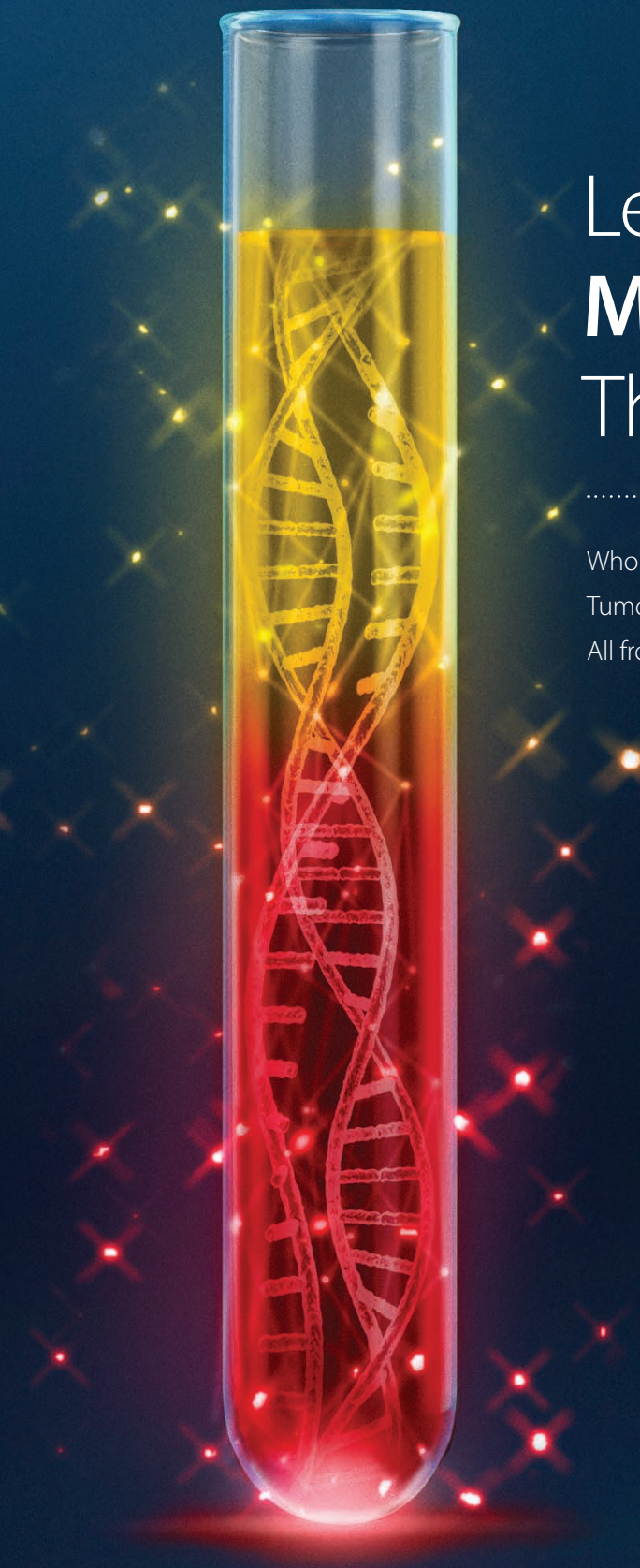


Less Invasive, **More Intelligent** Than Ever

Whole Exome and Whole Transcriptome Sequencing

Tumor-Derived, Incidental Germline*, and Incidental CH Variant Detection

All from a Blood Sample

CARIS® ASSURE

THERAPY SELECTION

The Most Powerful Liquid Biopsy Assay Ever Developed

Caris Assure™ sets the new standard for liquid biopsy profiling and is the first pan-cancer, comprehensive assay that uses a novel circulating Nucleic Acids Sequencing (cNAS) approach. With deep molecular insights from a simple blood sample, Caris Assure offers a minimally invasive option for biomarker analysis for cancer patients when tissue samples are not available. Caris' flexible, multi-faceted molecular profiling platforms deliver uncompromising reliability and performance to guide personalized treatment decisions and help improve patient outcomes.

Whole Exome and Whole Transcriptome Sequencing from Blood

Technology
Circulating Nucleic Acids Sequencing (cNAS)

Application
Biomarker Analysis (including resistance mutations)

Biological Coverage
Plasma: cfDNA, cfRNA
White Blood Cells: gDNA, mRNA

Variant Coverage (pathogenic and likely pathogenic)
Tumor-Derived Incidental Germline* Incidental CH

Genes & Depth
23,000+ 8,000x (raw average for clinically relevant genes)

Next-Generation Sequencing
Whole Exome
Whole Transcriptome

Alterations
SNV INDEL CNA Fusions

Genomic Signatures/Other
bTMB HLA Genotype MSI

Sample Quantity
2 Tubes Whole Blood

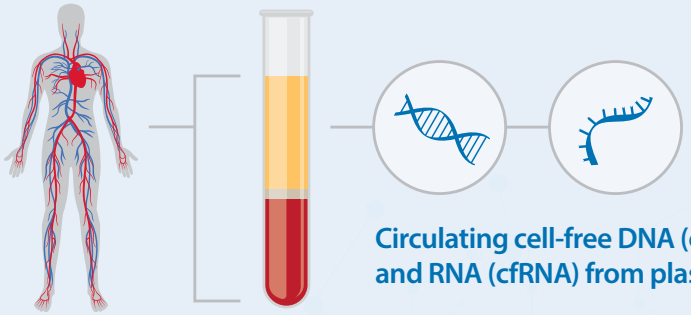
Performance in Advanced/Metastatic Patients
Compared to matched tissue collected within 30 days; based on ≥5 ng of cNAS input. Minimum reportable allele frequency is 0.1%.

Clinically Actionable SNV and INDEL:
Sensitivity 93.8% PPV 96.8%
Specificity >99.9%

Incidental Germline*:
Sensitivity >99% PPV >99%
Specificity >99%

**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.*

Caris Assure™ is intended for patients with previously diagnosed solid malignant neoplasms when tissue is not feasible and is to be used by qualified healthcare professionals. RNA results are intended for investigational purposes only. Not available in all locations.



Circulating cell-free DNA (cfDNA) and RNA (cfRNA) from plasma

Circulating Nucleic

cNAS is a novel liquid biopsy mole
Caris Assure distinguishes tumor-d

Tumor-Derived, Incidental Germline* and Incidental CH Detection in a Single Assay

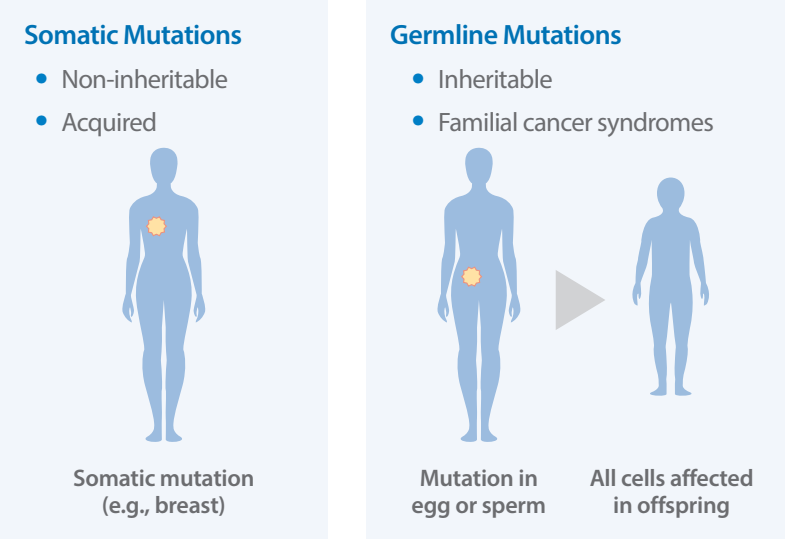
Caris molecular profiling leverages a multi-faceted approach to personalized cancer treatment. By identifying tumor-derived somatic variants, plus incidental germline* and incidental CH variants, Caris Assure provides clinicians with the comprehensive molecular intelligence needed to develop treatment plans that may help improve patient outcomes.

Tumor-Derived Somatic Testing

Somatic (acquired) variants are genetic alterations that are not present in egg or sperm cells but occur after conception, and therefore cannot be inherited by following generations. Somatic variants are classified by the level of clinical actionability in the Caris Assure report and can be tumor-specific.

Incidental Germline Characterization

Germline (hereditary) variants are genetic alterations that are present in egg or sperm cells. Such variants will be present in every cell of the body when inherited by offspring. Recognizing germline mutations in predisposed individuals can assist in risk reduction and cancer prevention. Caris Assure analyzes genomic DNA from circulating white blood cells and can distinguish incidental germline* mutations from somatic mutations.



Incidental CH Analysis

Clonal hematopoiesis (CH) mutations are common age-related somatic mutations that accumulate in the cells of blood or bone marrow. CH mutations create biological "noise" that may cause false positive results.[1] Caris Assure distinguishes somatic CH mutations from somatic tumor mutations to reduce false positives and improve specificity.

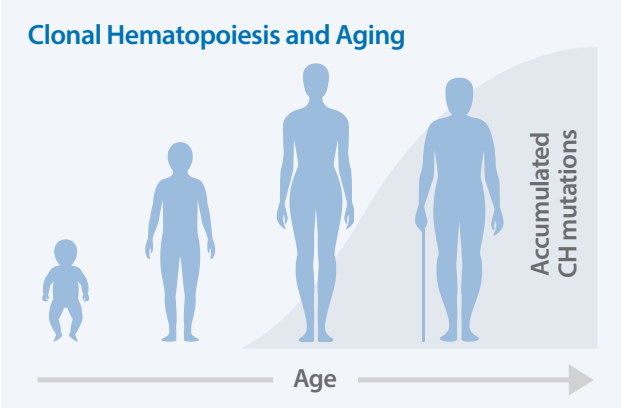
Acids Sequencing (cNAS)

cular profiling approach that analyzes cell-free DNA and RNA from plasma, plus genomic DNA and
erived somatic variants from incidental germline and/or incidental CH mutations to reduce false po

Improved Assay Performance with CH Subtraction

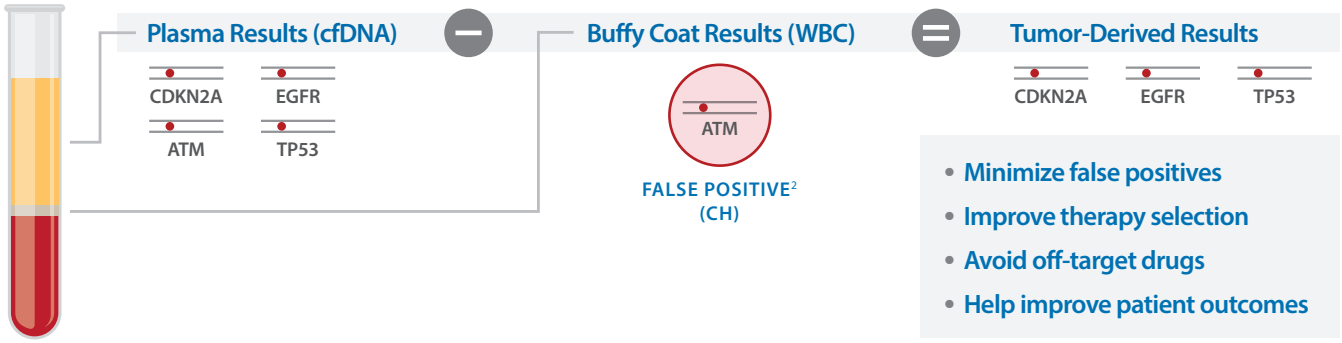
Clonal Hematopoiesis (CH) mutations are age-related somatic mutations that accumulate in blood cells. While such mutations may be precursors to disease, their presence does not necessarily indicate hematologic cancer. When CH mutations occur in genes that are common onco-drivers for solid tumors, detection of such sequences may cause false positive results in blood-based nucleic acid tests.[1]

Caris Assure analyzes and subtracts these incidental CH mutations from somatic tumor mutation results to reduce false positives and improve assay specificity. CH mutations are confirmed by sequencing genomic DNA from white blood cells in the buffy coat, distinguishing both incidental CH and incidental germline mutations.



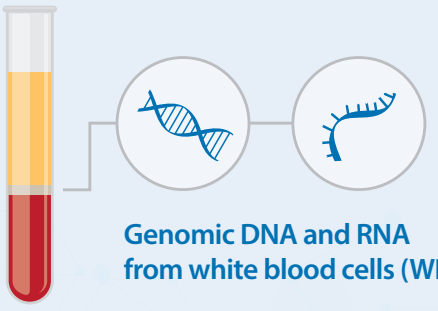
CH mutations accumulate in blood cells of aging patients and may create false positives in blood-based tests.

CH Analysis and Subtraction Yields More Accurate Results



- Minimize false positives
- Improve therapy selection
- Avoid off-target drugs
- Help improve patient outcomes

RNA from circulating WBCs.
ositives and improve specificity.



Genomic DNA and RNA from white blood cells (WBC)

Easy-to-Interpret Results for Clarity in Treatment Planning

The Caris Assure report maximizes clinical utility in an easy-to-interpret format.

Clinical Utility:

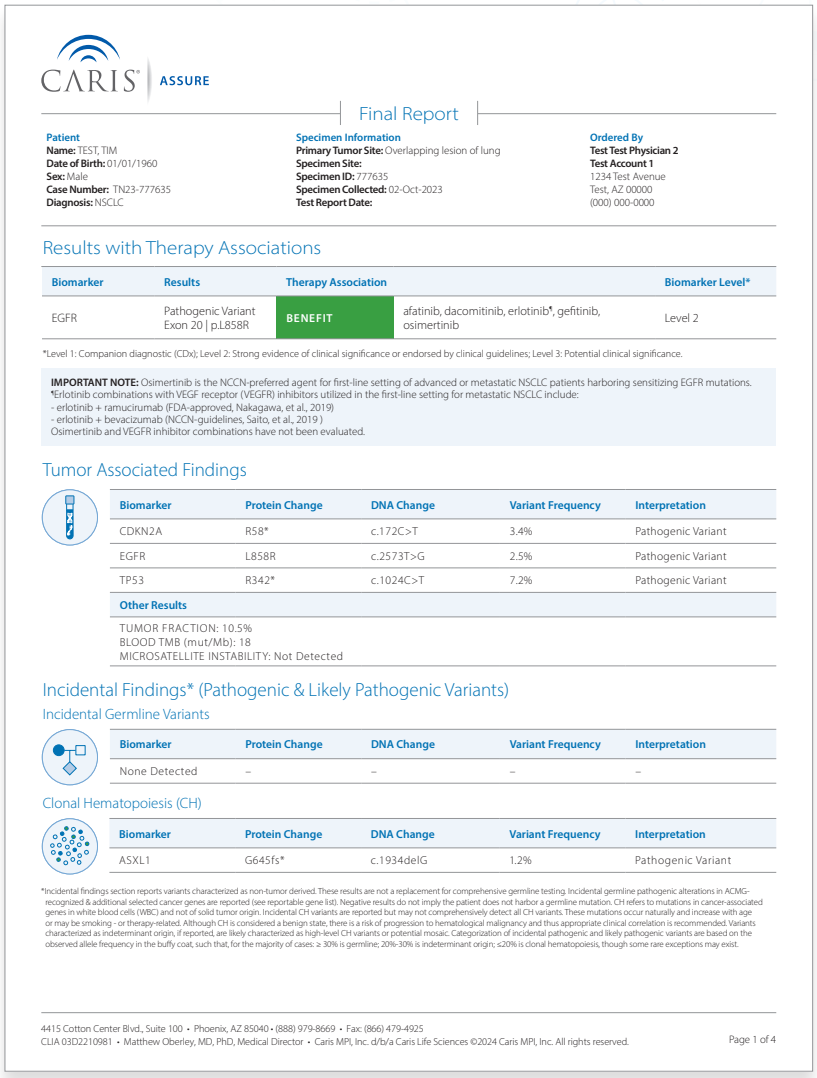
- Navigate among therapies with potential benefit or lack of benefit
- Identify therapies that may not have been considered
- Match patient to clinical trials based on tumor biology

Evidence-guided:

- Drug associations based on peer-reviewed literature
- Testing methodologies consistent with industry guidelines

EHR Compatible:

- HIPAA compliant
- Easy installation
- Secure encryption
- Real-time sync



CARIS® ASSURE

Final Report

Patient
Name: TEST, TIM
Date of Birth: 01/01/1960
Sex: Male
Case Number: TN23-777635
Diagnosis: NSCLC

Specimen Information
Primary Tumor Site: Overlapping lesion of lung
Specimen Site:
Specimen ID: 777635
Specimen Collected: 02-Oct-2023
Test Report Date:

Ordered By
Test Test Physician 2
Test Account 1
1234 Test Avenue
Test, AZ 00000
(000) 000-0000

Results with Therapy Associations

Biomarker	Results	Therapy Association		Biomarker Level*
EGFR	Pathogenic Variant Exon 20 | p.L858R	BENEFIT	afatinib, dacomitinib, erlotinib¶, gefitinib, osimertinib	Level 2

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

IMPORTANT NOTE: Osimertinib is the NCCN-preferred agent for first-line setting of advanced or metastatic NSCLC patients harboring sensitizing EGFR mutations.
¶Erlotinib combinations with VEGF receptor (VEGFR) inhibitors utilized in the first-line setting for metastatic NSCLC include:
- erlotinib + ramucirumab (FDA-approved, Nakagawa, et al, 2019)
- erlotinib + bevacizumab (NCCN-guidelines, Saito, et al., 2019)
Osimertinib and VEGFR inhibitor combinations have not been evaluated.

Tumor Associated Findings

Biomarker	Protein Change	DNA Change	Variant Frequency	Interpretation
CDKN2A	R58*	c.172C>T	3.4%	Pathogenic Variant
EGFR	L858R	c.2573T>G	2.5%	Pathogenic Variant
TP53	R342*	c.1024C>T	7.2%	Pathogenic Variant

Other Results

TUMOR FRACTION: 10.5%
BLOOD TMB (mut/Mb): 18
MICROSATELLITE INSTABILITY: Not Detected

Incidental Findings* (Pathogenic & Likely Pathogenic Variants)

Incidental Germline Variants

Biomarker	Protein Change	DNA Change	Variant Frequency	Interpretation
None Detected	–	–	–	–

Clonal Hematopoiesis (CH)

Biomarker	Protein Change	DNA Change	Variant Frequency	Interpretation
ASXL1	G645fs*	c.1934delG	1.2%	Pathogenic Variant

*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 ACMG-recognized & additional selected cancer genes are reported (see reportable gene list). 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 state, there is a risk of progression to hematological malignancy and thus appropriate clinical correlation is recommended. Variants characterized as indeterminant origin, if reported, are likely characterized as high-level CH variants or potential mosaic. 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 indeterminant origin; ≤20% is clonal hematopoiesis, though some rare exceptions may exist.

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1 Abbosh, C., *et al.* (2019). Clonal haematopoiesis: a source of biological noise in cell-free DNA analyses. *Ann Oncol 30*, 358-359.
2 Razavi P., *et al.* (2019). High-intensity sequencing reveals the sources of plasma circulating cell-free DNA variants. *Nat Med 25*, 1928-1937.

The Most Powerful Liquid Biopsy Assay Ever Developed

Tumor-Derived, Incidental Germline and Incidental CH Detection*

CARIS® ASSURE
THERAPY SELECTION

Comprehensive analysis of 23,000+ genes

Biomarker analysis (including resistance mutations)

Less invasive alternative to tissue biopsy

Reports tumor-derived, incidental germline* and incidental CH variants

Reduces false positives from incidental CH mutations

Be Sure with Caris Assure.

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

Caris Assure™ is intended for patients with previously diagnosed solid malignant neoplasms when tissue is not feasible and is to be used by qualified healthcare professionals. RNA results are intended for investigational purposes only. Not available in all locations.

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Where Molecular Science Meets Artificial Intelligence.