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Caris Life Sciences Publishes Landmark Study Demonstrating the Superiority of Caris Assure™

A large, blood-based profiling study accurately identified clonal hematopoiesis (CH) variants, effectively decreasing clinical false positives missed by other plasma only approaches

IRVING, Texas, February 11, 2025 – [Caris Life Sciences](#)® (Caris), a leading next-generation AI TechBio company and precision medicine pioneer, today announced the publication of "[Characterization of plasma cell-free DNA variants as of tumor- or clonal hematopoiesis-origin in 16,812 advanced cancer patients](#)," in *Clinical Cancer Research*. Utilizing [Caris Assure](#)™ blood-based profiling, the study shows how CH-associated variants, which are highly prevalent in cancer patients, can often overlap with therapeutic targets. The findings underscore the importance of distinguishing CH- from tumor-derived mutations to improve diagnostic accuracy and guide appropriate cancer therapy.

The study characterized plasma cell-free DNA (cfDNA) variants of tumor, CH or germline origin in 16,812 patients with advanced cancer using Caris Assure, which sequences both the plasma and buffy coat using a proprietary whole exome and whole transcriptome assay. CH occurs when a mutation-carrying hematopoietic stem cell produces blood cells with the same mutation. As people age, these mutations build up in the blood and can be confused with cancer cells during blood tests, leading to false positives that complicate treatment decisions.

Key findings include:

- **CH prevalence:** CH variants were detected in 42.3% of patients, with 76% of *CHEK2*, 66.5% of *BRCA2*, and 58.6% of *BRCA1* somatic-derived variants arising from CH.
- **Age correlations:** CH rates increased with age from 20% in patients ages 65-69 years to 50% in patients ages 80 and older.
- **Clinical impact:** High CH rates were found in otherwise actionable genetic variants associated with PARP inhibitor (PARPi) therapies in breast, ovarian, pancreatic, prostate and endometrial cancer, with nearly 6% of prostate cancer patients having a CH mutation in a PARPi-associated gene. Without accurate CH classification, these patients could be inappropriately directed toward PARPi therapy.

"Without accurate CH classification, oncologists risk recommending therapies based on mutations that do not come from the tumor," said [George W. Sledge, Jr., MD](#), EVP and Chief Medical Officer of Caris and study author. "Caris Assure is the only blood profiling assay on the market that uses sequencing rather than algorithmic estimations to accurately determine the mutational origin, to our knowledge."

"This study, the largest of CH in cfDNA to date, sets a new benchmark for liquid biopsy accuracy and cancer care," said Caris President and study author [David Spetzler, MS, PhD, MBA](#). "By leveraging

paired plasma and buffy coat analysis, Caris Assure accurately identifies CH variants, providing clinicians with precise insights into tumor biology and ensuring that every treatment decision is based on the most reliable information available.”

Detailed Scientific Information

At least one CH variant was identified within reportable clinical genes in 42.3% of the 16,812 patients. A total of 41,380 reportable somatic mutations were detected in the plasma, of which 11,639 (27.8%) were classified as CH. More than three-quarters of *CHEK2* variants were of CH origin, as were 66.5% of *BRCA2*, 58.6% of *BRCA1*, 46.2% of *ATM*, 7.8% of *NRAS*, 6.1% of *BRAF*, 2.6% of *EGFR* and 2.1% of *KRAS* variants. For patients ages 65-69 years, the median proportion of CH classification was 20%, whereas it was 33% for patients ages 70-74, 33% for ages 75-79 and 50% for ages 80 and older. Prevalence of CH also varied by cancer type, from 13.6% in uveal melanoma to 61.5% in uterine serous carcinoma.

High rates of CH variants were detected in what would be otherwise druggable targets in many cancer types typically treated with PARPi therapy, including breast, ovarian, pancreatic, prostate and endometrial cancers. These findings point to CH as a critical source of false positive variants for biomarker-directed PARPi therapy, highlighting the need for thorough CH classification during liquid biopsy to recommend therapies appropriately. Clinicians should carefully interpret liquid biopsy results used to determine PARPi eligibility and avoid relying on these results unless the assay specifically identifies and subtracts CH variants.

The study was performed in collaboration with members of the [Caris Precision Oncology Alliance](#)[™] (Caris POA), which includes 96 cancer centers, academic institutions, research consortia and healthcare systems, including 47 NCI-designated cancer centers, collaborating to advance precision oncology and biomarker-driven research. Caris and POA members work together to establish and optimize standards of care for molecular testing through innovative research focused on predictive and prognostic markers that can improve clinical outcomes for cancer patients.

About Caris Life Sciences

Caris Life Sciences® (Caris) is a leading next-generation AI TechBio company and precision medicine pioneer that is actively developing and delivering innovative solutions to revolutionize healthcare and improve the human condition. Through comprehensive molecular profiling (Whole Exome and Whole Transcriptome Sequencing) and the application of advanced AI and machine learning algorithms, Caris has created the large-scale, multimodal database and computing capability needed to analyze and further unravel the molecular complexity of disease. This convergence of sequencing power, big data and AI technologies provides a differentiated platform to deliver the next generation of precision medicine tools for early detection, diagnosis, monitoring, therapy selection and drug development.

Caris was founded with a vision to realize the potential of precision medicine in order to improve the human condition. Headquartered in Irving, Texas, Caris has offices in Phoenix, New York, Cambridge (MA), Tokyo, Japan and Basel, Switzerland. Caris or its distributor partners provide services in the U.S. and other international markets. To learn more, please visit [CarisLifeSciences.com](#).

Caris Life Sciences Media:
Corporate Communications
CorpComm@CarisLS.com
214.294.5606