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New Research from Caris Life Sciences Finds Immunotherapy Resistance in Leiomyosarcoma

Study reveals subtypes may benefit from more personalized treatments

IRVING, Texas, June 4, 2021 – Caris Life Sciences®, a leading innovator in molecular science and artificial intelligence focused on fulfilling the promise of precision medicine, to present findings that provide a deeper understanding of how immunotherapies (IO) affect leiomyosarcoma (LMS), a rare cancer that affects smooth muscle tissue, through the use of whole exome and whole transcriptome sequencing. These results will be presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting on June 4, and show that traditional predictive biomarkers of response to immunotherapies (IO) are unlikely to be useful in LMS and suggest future trials should focus on combination therapies instead.

The [presentation](#), “Large Scale Multiomic Analysis Suggests Mechanisms of Resistance to Immunotherapy in Leiomyosarcoma,” will be presented at the *Emerging Trends in Sarcoma Precision Medicine Clinical Science Symposium* by researchers from Columbia University Medical Center. The study was led by Dr. Roman Groisberg of Rutgers Cancer Institute, a member of [Caris’ Precision Oncology Alliance](#), and examined 1,115 LMS specimens, a mix of uterine and soft tissue site samples to explore mechanisms of IO resistance. Historically, LMS has been reported to have immunohistochemical (IHC) and gene expression signatures that suggest an immune-responsive tumor microenvironment. Despite this, immune checkpoint inhibitors have demonstrated minimal activity in LMS.

The study found only a small proportion of LMS specimens were identified as high tumor mutational burden (TMB-H) or high microsatellite instability (MSI-H). TMB-H was observed in 3.8% of LMS specimens, deficient mismatch repair/MSI-H was rarely detected (1.5%), whereas 8.2% (n = 88) were positive for PD-L1 expression. This suggests that the neoantigen burden in LMS may not be sufficient to promote a robust anti-tumor response, even in the presence of PD-L1 positive tumor cells. Additionally, LMS has an immune microenvironment characterized by a high fibroblast and low T cell abundance associated with melanoma. The use of combination therapies may reverse T-cell exclusion/desmoplastic phenotype.

“This study helps us understand why immune checkpoint inhibitors have demonstrated minimal activity in LMS in the past,” said Roman Groisberg, M.D., Medical Oncologist at Rutgers Cancer

Institute. “With these findings, future therapies for LMS can become more personalized for patients and ultimately improve care.”

“For many rare cancers, the treatment path can be unclear, and these findings reinforce the impact whole exome and transcriptome sequencing and collaboration across renowned institutions have on finding effective treatment approaches,” said [David Spetzler](#), M.S., Ph.D., MBA, President and Chief Scientific Officer of Caris Life Sciences. “Measuring all of the genes and all of the transcripts can increase our understanding of specific cancer subtypes and provide clarity as to why certain therapies may not generate the response expected. This technology continues to improve approaches to treating all types of cancers – from the most common to the rarest.”

A complete list of [Caris’ ASCO 2021 poster presentations](#) are available on the Company’s website.

About Caris Life Sciences

Caris Life Sciences® is a leading innovator in molecular science and artificial intelligence focused on fulfilling the promise of precision medicine through quality and innovation. The company’s suite of market-leading molecular profiling offerings assesses DNA, RNA and proteins to reveal a molecular blueprint that helps physicians and cancer patients make more precise and personalized treatment decisions. MI Exome™ whole exome sequencing with 22,000 DNA genes, and MI Transcriptome™ whole transcriptome sequencing with 22,000 RNA genes along with cancer-related pathogens, bacteria, viruses and fungi analysis run on every patient provides the most comprehensive and clinically relevant DNA and RNA profiling available on the market.

Caris is also advancing precision medicine with Caris MAI™ (Molecular Artificial Intelligence) that combines its innovative service offerings, Caris Molecular Intelligence® with its proprietary artificial intelligence analytics engine, DEAN™, to analyze the whole exome, whole transcriptome and complete cancer proteome. This information, coupled with mature clinical outcomes on thousands of patients, provides unmatched molecular solutions for patients, physicians, payers and biopharmaceutical organizations.

Caris Pharmatech is changing the paradigm and streamlines the clinical trial process by assisting biopharma companies with accessing research-ready oncology sites for clinical trials. With over 420 research sites within the Caris Pharmatech Just-In-Time (JIT) Oncology Network, biopharma companies can identify and enroll more patients, faster. Caris Pharmatech Just-In-Time Clinical Trial Solutions focus on rapid site activation and patient enrollment to streamline the drug development process. By implementing Caris’ Just-In-Time Trial-Matching System, Caris will automatically match patients to clinical trials and sites can be activated and eligible to enroll patients within one week.

Headquartered in Irving, Texas, Caris Life Sciences has offices in Phoenix, Denver, New York, and Basel, Switzerland. Caris provides services throughout the U.S., Europe, Asia and other

international markets. To learn more, please visit www.CarisLifeSciences.com or follow us on Twitter ([@CarisLS](https://twitter.com/CarisLS)).

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