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Researchers provide rationale for use of targeted immunotherapy in sarcomatoid lung carcinomas

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Sarcomatoid carcinomas of the lung include rare subtypes of poorly differentiated non–small-cell lung carcinomas of high grade and aggressive behavior. The biology of these neoplasms is poorly understood and these tumors are aggressive and resistant to chemotherapy and radiotherapy. The identification of actionable molecular targets for such infrequent and aggressive diseases is critical for design of new clinical trials. Programmed death-1 (PD-1) is a co-inhibitory inducible receptor present on T-cells and macrophages. Tumor cells with increased programmed death ligand-1 (PD-L1) are believed to escape immunity through activation of PD-1/PD-L1 pathway and suppression of effector-immune responses.

Researchers at the Yale School of Medicine measured the levels of the PD-L1 protein in sarcomatoid carcinomas. In a recent study published in the *Journal of Thoracic Oncology* (*JTO*), the results show that SCs show higher PD-L1 levels than other NSCLC, supporting a potential for the use of anti-PD-1/PD-L1 targeted therapies.

The study says, "despite the presence of rich inflammatory infiltrates patients with SCs have worse outcomes compared with other histologic subtypes of NSCLC. Elevated expression of PD-L1 by SC cells might account for this apparent contradiction because local inactivation of effector-immune cells through PD-1 receptor signaling could ultimately enhance the disease progression." The researchers, "suggest the

possibility of using novel immunotherapy approaches such as PD-1/PD-L1 blockers in this otherwise difficult to treat disease."

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