Background Single agent anti-PD1 therapy has shown limited clinical benefit in liposarcoma, but combination with anti-CTLA-4 demonstrated a higher response rate.1-3 In the MDACC study NCT02815995, combining anti-CTLA4 and anti-PDL1 across multiple soft-tissue sarcomas increased CD73, PD-1, and OX40 expression in T cells early on treatment. The adenosine pathway, which includes CD73 and the A2A receptor, induces immunosuppression4,5 and protects against antitumor responses.6, 7 This pathway is related to immune therapy resistance8-11, metastasis, and poor prognosis.12-15 Conversely, CD73+ T cells have long-lived memory and higher proliferation and survival, suggesting a dual role of the pathway.16-18 We hypothesized that adenosine would negatively correlate with TIL expansion and function.

Methods Surgically resected liposarcoma samples (n=41), are divided for fresh tissue phenotyping by flow cytometry, TIL Metabolic profiles by mitochondrial mass and ROS production and 1.44-87.6%). IFN-g production was related to intrinsic regulation and augments vascular inflammatory response. Circ Res 2004; 95(8):814–21.

Conclusions A heterogeneous adenosine landscape was found in liposarcoma. A2AR but not CD73 correlated with mitochondrial dysfunction and reduced cytotoxicity. Conversely CD73+ TIL were more likely to expand. Our results indicate a dichotomy in two key members in the adenosine pathway in liposarcoma and suggest that CD73 might play a positive role in TIL function.

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