

PHASE 1/2 STUDY OF AN ANTI-GALECTIN-9 ANTIBODY, LYT-200, IN PATIENTS WITH METASTATIC SOLID TUMORS

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Background Galectin-9 (gal-9) acts as a pivotal immuno-suppressor that disables immune mediated activity through modulation of T cells, macrophages and other immune functions. As such it has emerged as a powerful biological target for cancer immunotherapy and a potential biomarker of response and/or prognosis. Patients exhibiting high gal-9 expression in tumors and blood often have poor prognosis and tumors with aggressive and immunosuppressed molecular features (Chen L. et al, AACR 2020-LB-350). LYT-200 is a fully human IgG4 monoclonal antibody targeting gal-9. LYT-200 has high affinity, high specificity, stability, and blocks galectin-9 interactions with its binding partners in biochemical and human cell-based assays. In murine models of melanoma and pancreatic cancer, LYT-200 significantly reduced tumor growth, extended survival and modulated the intra-tumoral immune microenvironment. LYT-200 treated patient derived tumor organoids showed an increase in T cell activation (Chen L. et al, SITC 2019-P765).

Methods LYT-200 is now being evaluated in the USA, in the first part of an adaptive Phase 1/2 trial (NCT04666688) in relapsed/refractory solid tumors. Patients with solid tumor malignancy that is metastatic or unresectable and refractory to prior therapy are included. Patients are treated with LYT-200 by IV infusion, every 2 weeks (Q2W), until disease progression or toxicity. Phase 1 of the study uses the continuous reassessment design (CRM), and entails recruiting two patients per dosing level. Starting dose level was 0.2mg/kg Q2W. Additionally, the protocol stipulates six patients must be treated at the dose level intended to be declared recommended phase 2 dose (RP2D), for more robust assessment of safety/tolerability. RP2D may be the maximum tolerated dose or the optimal biological dose. The primary objective of the ongoing Phase 1 is to assess the safety and tolerability of LYT-200 and to identify the RP2D. The Phase 1 is also assessing LYT-200's pharmacokinetics, immunogenicity and pharmacodynamics (measuring circulating gal-9 and cytokine levels, immunophenotyping peripheral blood mononuclear cells and tumor tissue). Preliminary efficacy is captured as an exploratory endpoint in Phase 1. Phase 2 expansion cohorts would implement the Simon's two-stage design to further assess LYT-200 as a single agent and/or in combination with chemotherapy and tislelizumab. Phase 2 is currently planned in pancreatic cancer and other/different tumor types for Phase 2 may be guided by results of the Phase 1.

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