TPS2697 Poster Session

A phase 1 trial of APX-343A, NOX inhibitor targeting CAF-mediated immunosuppression, as monotherapy or in combination with pembrolizumab in patients with advanced solid tumors.

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Background: Cancer-associated fibroblasts (CAFs), a key component of tumor stroma, promote tumor growth and resistance to anticancer therapy. They contribute to immune suppression within the tumor microenvironment (TME), with evidence linking CAFs to immune checkpoint inhibitor (ICI) resistance and T-cell exclusion. Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX), which is clinically upregulated by CAF in many human cancers, has been reported to be a critical effector of myofibroblast transformation during fibrosis. Inhibiting NADPH oxidases, NOX2 and NOX4, restored cluster of differentiation 8 + T-cell proliferation by reducing reactive oxygen species (ROS) generation in CAF-induced myeloidderived suppressor cells (MDSCs). A pivotal role of CAFs in regulating monocyte recruitment and differentiation demonstrated that CC-chemokine receptor 2 inhibition and ROS scavenging abrogate the CAF-MDSC axis, illuminating a potential therapeutic path to reversing the CAF-mediated immunosuppressive microenvironment. APX-343A, a selective NOX1, NOX2, and NOX4 inhibitor, has been shown to ameliorate the fibrotic and immunosuppressive properties of CAFs. In CAF-rich tumor mouse models that do not respond to ICIs, APX-343A demonstrated significant anticancer efficacy by modulating both fibrosis and immunosuppression via NOX inhibition. **Methods:** This is a Phase 1, open-label, dose-escalation study designed to assess the safety, tolerability, PK, and preliminary efficacy of APX-343A as monotherapy (Part A) and in combination with pembrolizumab (Part B) in patients with advanced solid tumors. The trial aims to determine the MTD and/or RP2D. Part A is a dose-escalation study of APX-343A monotherapy, starting at a dose of 100 mg BID (Cohort 1) and escalating up to 600 mg BID (Cohort 6) until dose-limiting toxicity (DLT) is identified. APX-343A will be administered on a continuous daily dosing schedule in 21-day cycles. Part B is a dose-escalation study of APX-343A in combination with pembrolizumab (200mg IV, Q3W). Using the BOIN design, the dose level of APX-343A will escalate from 200 up to 600 mg BID without exceeding the MTD. The BOIN design will guide dose escalation based on safety, with decisions made by the Safety Review Committee (SRC). Dose finding will be conducted independently for Parts A and B. APX-343A selective NOX inhibitor has the potential to become an effective treatment option in combination with ICIs for patients with CAF-rich solid tumors that are unresponsive to current immunotherapies. By inhibiting CAF activity in the TME and resensitizing tumors to cancer immunotherapy, APX-343A offers a promising therapeutic approach. Phase 1 results are anticipated in Q1 2026. Research Sponsor: Aptabio Therapeutics Inc.