TPS2678 Poster Session

A phase I study of AFNT-211, autologous CD4$^+$ and CD8$^+$ T cells engineered to express a high avidity HLA-A*11:01-restricted, KRAS G12V-specific transgenic TCR; CD8α/β coreceptor; and FAS-41BB switch receptor in patients with advanced or metastatic solid tumors.

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Background: Activating mutations in KRAS (including KRAS G12V) are well-described oncogenic drivers in solid tumors, conferring poor prognosis to patients due to a lack of effective therapies for cancers with such KRAS driver mutations. T cell receptor (TCR)-T cell therapies targeting mutant KRAS have demonstrated proof of concept in the clinic, but duration of response remains a challenge.[1,2] AFNT-211 represents a novel strategy to address the immunosuppressive tumor microenvironment and improve response rate as well as duration of response in solid tumors. **Methods:** This ongoing Phase 1, first-in-human, multicenter, open-label study of AFNT-211evaluates safety/tolerability, as well as its clinical (antitumor) activity with the goal to identify an optimal biological dose (OBD) and recommended Phase 2 dose (RP2D) in patients with HLA 11:01 who suffer from cancers driven by the KRAS G12V mutation. The initial dose escalation part of the study follows Bayesian optimal interval Phase 1/2 (BOIN12), which quantifies the desirability of a dose in terms of toxicity-efficacy tradeoff and adaptively allocates patients to the dose with the highest estimated desirability. After determination of OBD and RP2D based on the totality of the risk/benefit assessment and the BOIN12, the study is planned to proceed to the dose expansion phase which will consist of cohorts enrolling patients with tumors with high KRAS G12V prevalence (pancreatic cancer, colorectal cancer, non small cell lung cancer) as well as a tumor agnostic arm (any other solid tumor with KRAS G12V). This study has started enrolling patients $\geq$ 18 years old positive for HLA-A*11:01-positivewithadvanced/metastatic solid tumors harboring a KRAS G12V mutation who have proven intolerant of or refractory to at least one prior standard of care systemic therapy. Patients undergo leukapheresis to collect T cells for the manufacturing of AFNT-211, and receive lymphodepleting chemotherapy prior infusion of their autologous AFNT-211 product. Following this, patients proceed into a 28-day dose-limiting toxicity observation period (during dose escalation) followed by a post-treatment follow-up period for 24 months/until disease progression. The study is open for recruitment in the United States (NCT06105021). References: 1. Cook J, Melloni G, Gulhan D, *et al.* The origins and genetic interactions of KRAS mutations are allele- and tissue-specific. *Nat Commun* 2021;12:1808. 2. Hofmann MH, Gerlach D, Misale S, *et al.* Expanding the reach of precision oncology by drugging all KRAS mutants. *Cancer Discov.* 2022;12:924–937. Clinical trial information: NCT06105021. Research Sponsor: Affini-T Therapeutics, Inc.