A phase 1/2 study investigating the safety and efficacy of autologous TAC T cells in subjects with unresectable, locally advanced or metastatic claudin18.2+ solid tumors

SCAN ME

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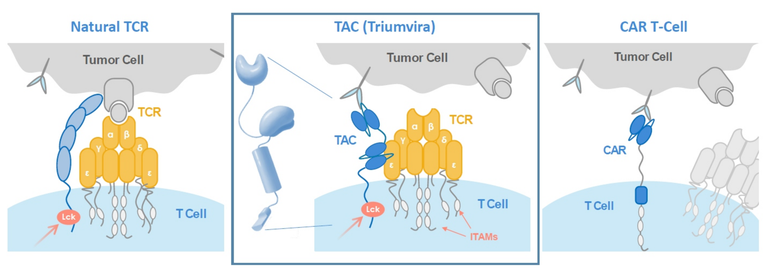
INTRODUCTION

- The T cell antigen coupler (TAC) is a novel, proprietary chimeric receptor that facilitates the re-direction of T cells to tumor cells and activates T cells by co-opting the endogenous T cell receptor complex, with the goal to elicit a safe and durable anti-tumor response. In preclinical models, TAC-engineered T cells effectively eradicate tumor cells in vitro and in vivo without toxicities typically associated with engineered T cell products. TAC01-CLDN18.2 is an autologous T cell product comprising T cells expressing the CLDN18.2 TAC, which specifically recognize CLDN18.2+ cells.
- TACTIC-3 (NCT05862324) is an open-label, multicenter phase I/II study that aims to establish safety, maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), pharmacokinetic profile, and efficacy of TAC01-CLDN18.2 in patients with CLDN18.2 positive, HER2-negative solid tumors by immunohistochemistry (i.e. gastric, GEJ, esophageal adenocarcinoma, PDAC, colorectal cancer, cholangiocarcinoma, ovarian mucinous cancer, gallbladder cancer and NSCLC) who have measurable disease after at least 2 prior anti-cancer therapies.

TAC SCIENCE



TAC achieves TCR activation via a CD3 binding domain while tightly binding the target of interest, CLDN18.2. TAC thus co-opts natural TCR function and provides intracellular co-receptor signaling via Lymphocyte-Specific Protein Tyrosine Kinase (LCK), mimicking physiologic TCR activation.

Watch a short animation to understand the TAC mechanism

Key Inclusion Citeria

- Age: 18 years or older
- Tumor tissue samples positive for CLDN18.2 expression and negative for HER2 expression.
- Histologically confirmed advanced, metastatic, unresectable solid tumors after at least 2 lines of therapy (LOT), or 1 for PDAC.
- Solid tumors with genetic alterations must have been previously treated with approved therapies (if available), or refused such approved targeted therapy for their cancers, prior to enrollment, or in the opinion of the Investigator would be unlikely to tolerate or derive clinically meaningful benefit from these standard-of-care therapies.
- Measurable disease per RECIST 1.1 at time of enrollment. Lesions situated in a previously irradiated area, are considered measurable if progression has been demonstrated in such lesions.
- ECOG 0 or 1, life expectancy of at least 12 weeks.
- Adequate organ and bone marrow reserve function prior to leukapheresis (laboratory parameters).
- Adequate vascular access for leukapheresis as per institutional standards.

Key Exclusion Citeria

- Prior treatment with adoptive cell transfer of any kind (including CAR T) and gene therapy.
- Prior treatment with a CLDN18.2 targeted agent (Phase 2 only).
- Known active CNS metastases and/or carcinomatous meningitis; or inflammatory neurological disorder.
- Receipt of a live or live-attenuated vaccine within 30 days prior to the first dose of study intervention. Note: Administration of killed vaccines are allowed.
- Colony stimulating factors, including granulocyte-colony stimulating factor (G-CSF), granulocytemacrophage colony-stimulating factor (GM-CSF), erythropoietin, and other hematopoietic cytokines, within 14 days prior to leukapheresis.

TRIAL DESIGN

Phase I (Dose Escalation)

The classic 3+3 dose escalation design will be employed to efficiently determine the maximum tolerated dose (MTD) and RP2D using well-defined DLT criteria.

N = 9-24 subjects

Phase II (Dose Expansion)

Groups A and C:
Approach: Simon 2-stage design.
Objective: Assess efficacy (ORR).
Group B:
Initial Approach: Evaluate experimental ORR after 10 PDAC treatments.
Future: Adopt Simon 2-stage based on outcomes.

Preferred Lymphodepleting Chemotherapy (LDC):
3 consecutive days of fludarabine (Flu) IV (30 mg/m^2) and cyclophosphamide (Cy) IV (300 mg/m^2) +/- Mesna IV, and a single dose of nab-paclitaxel (100mg/m^2) on the second day of LDC.

Outcome Measures

Ph1 **Safety and Tolerability:**
Documenting incidence of dose limiting toxicities (DLTs), adverse events (AEs),and clinically significant lab abnormalitties.

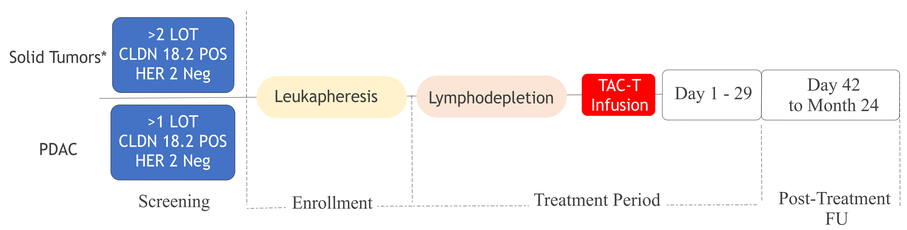
Ph1 **Determine MTD or RP2D for TAC01-CLDN18.2:**
Document incidence of DLTs up to 29 days post-infusion.

Ph2 **ORR** (Overall Response Rate); **DoR** (Duration of Response); **OS** (Overall Survival)
DCR (Disease Control Rate); **PFS** (Progression-Free Survival); **TTP** (Time to Progression)

Ph2 **Safety and Tolerability:**
To document type, frequency, and severity of AEs over 24 months, including clinically significant lab abnormalities

PHASE I Overview

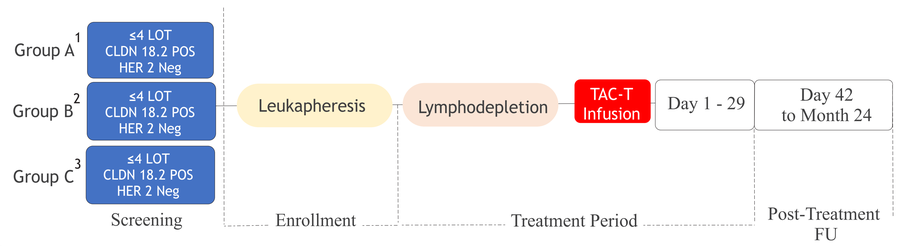
Patients with advanced, metastatic, unresectable solid tumors which express CLDN18.2, HER2 negative, after at least 2 lines of therapy (LOT), at least 1 measurable lesion per RECIST version 1.1, ECOG performance score 0-1, grade 1 or baseline for any prior treatment related toxicities.



Gastric, GEJ, esophageal adenocarcinoma, PDAC, colorectal, cholangiocarcinoma, ovarian mucinous, gallbladder and NSCLC.

PHASE II Overview

Patients with advanced, metastatic, unresectable solid tumors which express CLDN 18.2 after at least 2 lines of therapy and no more than 4, at least 1 measurable lesion per RECIST version 1.1, ECOG performance score 0-1, grade 1 or baseline for any prior treatment related toxicities.



[1]*Group A (Gastric, esophageal).*
[2]*Group B (PDAC).*
[3]*Group C (ovarian mucinous and NSCLC).*

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