A Phase I/II Trial Investigating Safety and Efficacy of Autologous T Cell Antigen-Coupler (TAC) T Cells Targeting HER2 in Relapsed or Refractory Solid Tumors (TACTIC-2).

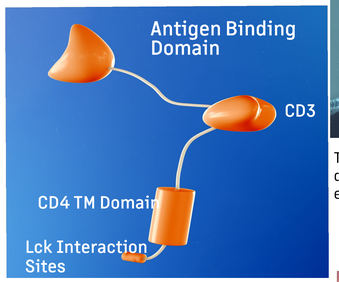
Ecaterina E. Dumbrava[1], Daniel Olson[2], Benjamin L. Schlechter[3], Samuel Saibil[4], Donna Rilf[5], Andreas G. Bader[5], Deyaa Adib[5] , Michael Bishop[2]

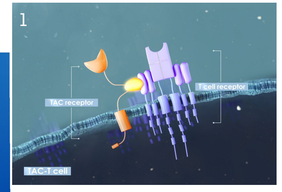
[1]The University of Texas MD Anderson Cancer Center; [2]University of Chicago; [3]Dana Farber Cancer Center; [4]University Health Network Princess Margaret; [5]Triumvira Immunologics, Inc.

BACKGROUND:

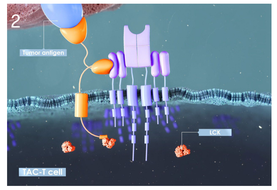
Despite recent therapeutic advances for patients with breast, colorectal and gastroesophageal cancers with HER2 overexpression, there is still a significant unmet medical need for better treatment options for HER2-positive solid tumors, especially those with low or intermediate HER2 expression (1+ and 2+ by immunohistochemistry (IHC)). The T Cell Antigen-Coupler (TAC) technology is a novel way to genetically modify T cells and to redirect these T cells to target cancer antigens and to activate T cells naturally by co-opting the natural T cell Receptor (TCR).

TAC SCIENCE





The TAC receptor interacts directly with the TCR-CD3 epsilon domain (1).



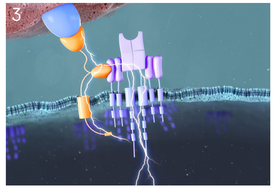
The TAC receptor also binds directly to the tumor antigen. Initiating the first step in T cell activation (2) which then leads to the clustering of TAC-TCR complexes required for full T cell activation.

Key features of TAC Technology:

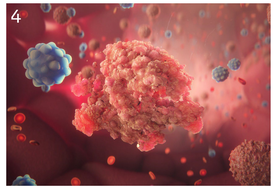
- **TAC** functions independently of MHC

- **TAC** requires endogenous TCR for T cell activation

- **TAC** incorporates the CD4 co-receptor and recruits the TCR complex, mimicking natural TCR activation

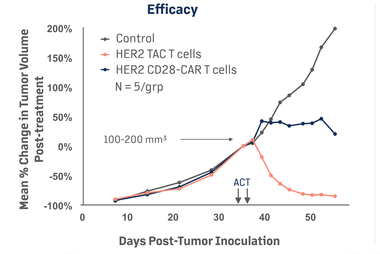


The TAC receptor then signals through the CD3-TCR complex (3).



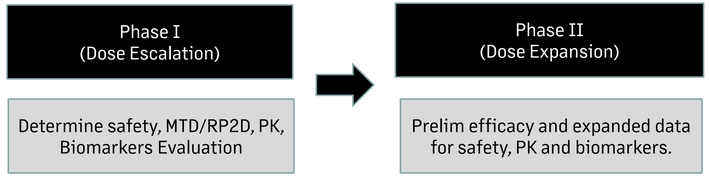
This ultimately results in tumor cell lysis (4).

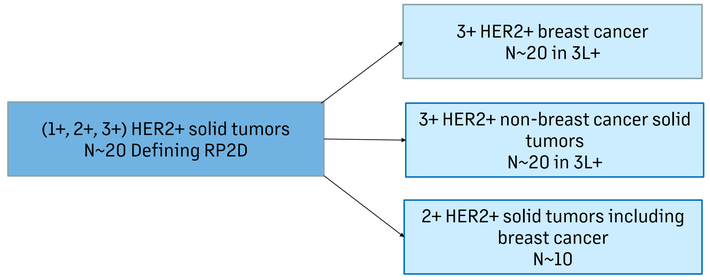
PRECLINICAL DATA



NRG mice (N=5) were subcutaneously inoculated with 2.5x10^6 OVCAR3 tumor cells. Tumors were allowed to engraft and grow to an average size of 100-200mm^3. Mice were then treated (2 doses 48hr apart) via tail vain injection, using a split dose of 1 million transduced HER2-TAC, HER2-CAR or control T cells per dose

TACTIC-2 Study Design





OBJECTIVES	ENDPOINTS
PRIMARY: To Evaluate the safety of TACO1-HER2 in subjects with HER2+ solid tumors	Incidence of Dose Limiting Toxicities (DLTs); Adverse events (AEs) and laboratory abnormalities
SECONDARY: To determine the MT and RP2D for TACO1-HER2	Incidence of DLTs
SECONDARY: To characterize the pharmacokinetic (PK) profile of TACO1-HER2	Cmax, Tmax, and AUC of TACO1-HER2 cells Duration of persistence of TACO1-HER2 cells
SECONDARY: To evaluate the efficacy of TACO1-HER2	Response Evaluation Criteria in Solid Tumors (RECIST) Criteria Version 1.1 Overall Response Rate (ORR) Duration of Response (DOR) Overall Survival (OS)
EXPLORATORY: Biomarker Studies to characterize T-cells and clinical outcomes (safety and efficacy)	

Key Inclusion:

- Eligible pts are ≥ 18 years with **HER2-positive solid tumors (1+, 2+ or 3+ by IHC, regardless of amplification status)** who progressed after at least two lines of systemic therapy.
- ECOG of 0/1 at screening
- Life expectancy of at least 12 weeks
- Adequate vascular access for leukapheresis
- Absolute Leukocyte Count (ALC) of ≥ 450/mcL

Key Exclusion:

- Prior treatment with adoptive cell transfer of any kind including CAR-T cells and Gene Therapy,
- Receipt of a live vaccine, monoclonal antibody or radiation within 28 days of leukapheresis
- Chemotherapy or targeted small molecule therapy within 14 days prior to leukapheresis

Study Assessments:

- Upon enrollment, patients will undergo leukapheresis to obtain T-cells for manufacture, some patients may receive bridging therapy prior to lymphodepletion chemotherapy (LDC).
- LDC will be administered and completed at least 24-48 hrs. prior to TACO1-HER2
  - Flu = 3 consecutive days at 30 mg/m^2
  - Cy = 3 consecutive days at 300mg/m^2
- Tumor response assessments are performed at 4 weeks, then at months 3, 6, 9, 12, 18 and 24.
- After study completion, subjects are followed for survival and long-term safety for up to 15 years.

Study Progress:

The TACTIC-2 study has completed enrollment of cohort #1. The study is registered with Clinicaltrials.gov (NCT04727151).

The study is currently recruiting patients with HER2 positive tumors at the following clinical sites:

- MD Anderson Cancer Center – Dr. Ecaterina E. Dumbrava
- Dana Farber Cancer institute – Dr. Benjamin Schlechter
- The University of Chicago – Dr. Michael Bishop and Dr. Daniel Olson
- Princess Margaret, Toronto - Dr. Samuel Saibil

AACR American Association for Cancer Research

AACR 2022 Abstract #: CT247

triumvira