#778TiP A PHASE I/II TRIAL INVESTIGATING SAFETY AND EFFICACY OF AUTOLOGOUS TAC T CELLS TARGETING HER2 IN RELAPSED OR REFRACTORY SOLID TUMORS (TACTIC-2)

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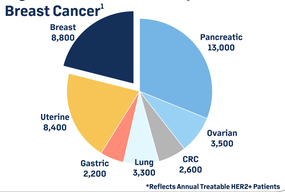
INTRODUCTION

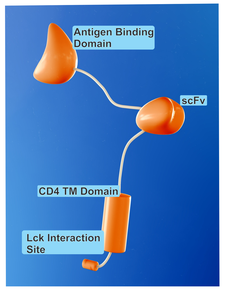
- The T cell antigen coupler (TAC) is a novel, proprietary chimeric receptor that facilitates the re-direction of T cells to tumor cells and activates T cells by co-opting the endogenous T cell receptor complex, with the goal to elicit a safe and durable anti-tumor response. In preclinical models of cancer, TAC-engineered T cells effectively eradicate tumor cells in vitro and in vivo without TAC-related toxicities.
- TACTIC-2 (NCT04727151) 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-HER2 in patients with HER2-positive solid tumors (i.e. breast, lung, pancreatic, colorectal, gastric, endometrial, ovarian, and others) whom have progressed on prior anti-cancer therapies.
- We present a clinical update from Cohorts 1 & 2 (8 participants) that highlights safety and efficacy data; the study further elucidates potential therapeutic impact to patients with HER2 overexpressed solid tumors.

Significant Unmet Need Beyond HER2+ Breast Cancer[1]



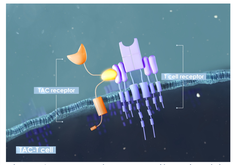
*Reflects Annual Treatable HER2+ Patients

TAC01-HER2 SCIENCE

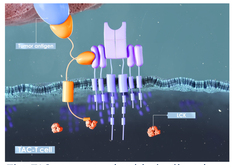


Key features of TAC01-HER2 technology:

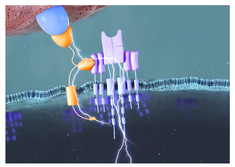
- TAC01-HER2 functions independently of MHC
- TAC01-HER2 requires endogenous TCR for T cell activation
- TAC01-HER2 incorporates the co-receptor and recruits the TCR complex, mimicking natural TCR activation



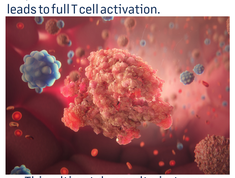
The TAC receptor interacts directly with the TCR-CD3 epsilon domain.



The TAC receptor also binds directly to the tumor antigen. Initiating the first step in T cell activation, which then leads to full T cell activation.



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



This ultimately results in tumor cell lysis.

TRIAL DESIGN & MANUFACTURING

Phase I Dose Escalation

DL 1: 4 Patients Treated — 1-3 x 10^5 Cells/kg
DL 2: 4 Patients Treated — 6-8 x 10^5 Cells/kg
DL 3: Patients Enrolled — 1-3 x 10^6 Cells/kg
DL 4: Enrolling — 6-8 x 10^6 Cells/kg

Phase II Dose Expansion

(1+, 2+ & 3+) HER2 Positive Breast Cancer
Planned Enrollment of 23 Patients; 2nd Line + Setting

(1+, 2+ & 3+) HER2 Positive non-Breast Cancer
Planned Enrollment of 35 Patients; 2nd Line + Setting

Lonza Cocoon Eliminates Several Manufacturing Steps

Sample Collection | Sample Preparation | Selection (Optional) | Activation | Transduction | Expansion | Formulation & Release | Patient Administration

Fully Automated Manufacturing & Vein-Vein Timeline: 21-24 Days

Lymphodepleting Chemotherapy: 3 consecutive days of fludarabine (Flu) IV (30 mg/m2) and cyclophosphamide (Cy) IV (300 mg/m2) with/without Mesna IV

Planned Combination Cohort
TAC-01 HER2 + Immune Checkpoint Inhibitors

Planned Enrollment for Combination Cohort
(1+, 2+, 3+) HER2+ cancers in the Second Line and Beyond

PHASE I TRIAL ENROLLMENT

Primary Endpoints	Secondary Endpoints
Safety: DLTs, MTD	Efficacy: ORR, DOR, PFS, OS, RP2D, AEs

Eligibility Criteria

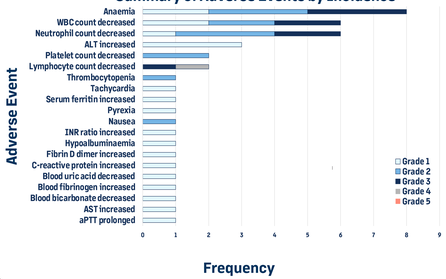
Patients with advanced, metastatic, unresectable solid tumors which express HER2 after at least 2 lines of therapy, at least 1 measurable lesion per RECIST version 1.1, ECOG performance score 0-1, grade 1 or baseline for any prior treatment related toxicities.

Cohorts 1 & 2: Demographic & Tumor-Intrinsic Characteristics

Median Age (Range), by Year	65.5 (42-70)	Tumor Type (%)	Gastric	2 (25.0%)
			Colorectal	2 (25.0%)
			Gastroesophogeal Junction	1 (12.5%)
			Gall Bladder	1 (12.5%)
Sex: Male/Female (%)	M 5 (62.5%)		Esophageal	1 (12.5%)
	F 3 (37.5%)		Rectosigmoid	1 (12.5%)
Race (%)	White 7 (87.5%)	Previous Anti-Cancer Therapy Median (Range)		4.5 (2-12)
	Other 1 (12.5%)			
ECOG PS (%)	0 4 (50.0%)	Previous Lines of HER2 Therapy Median (Range)		2 (0-9)
	1 4 (50.0%)			
HER2 Expression (%)	3+ 7 (87.5%)	Previous HER2 Therapy Types (%)	Trastuzumab	5 (62.5%)
	2+/ISH+ 1 (12.5%)		Trastuzumab Deruxtecan	3 (37.5%)
			Investigative	5 (62.5%)

PHASE I SAFETY DATA

Summary of Adverse Events by Incidence



Safety Summary

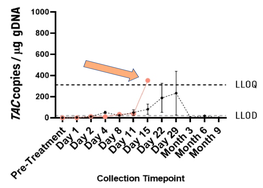
No Observed Cytokine Release Syndrome (CRS) in Cohorts 1 & 2

No Observed Immune Effector Cell-Associated Neurotoxicity (ICANS) in Cohorts 1 & 2

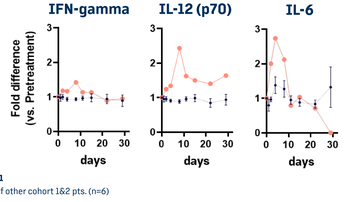
All Serious Adverse Events are Confirmed to be Unrelated to TAC-01 HER2 Infusions

BIOMARKER DATA: FIRST PATIENT RESPONSE

Blood Pharmacokinetics



IFN-gamma | IL-12 (p70) | IL-6



Blood PK Data from Patient 0203-0021

Low but definitive presence TAC01-HER2 cells indicated by elevated TAC copies at day 15 marker. Compared against average (+/- SEM) of other cohort 1 & 2 patients (n=6).

Cytokine Data from Patient 0203-0021

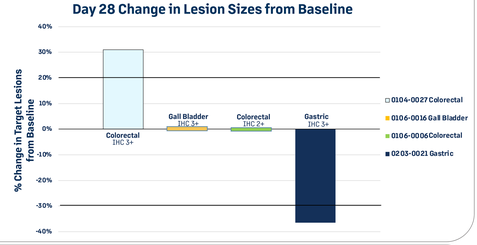
Serum cytokine analysis indicates slightly elevated levels in patient 0203-0021 vs others. Absence of IL-6 confirms lack of CRS. This is subtle, but intriguing biomarker data that corroborates safe response in patient 0203-0021.

EFFICACY: DOSE LEVEL 2 RESPONSE

Partial Response Observed in Patient 0203-0021

42 year old male with **IHC 3+**, HER2+ stage IVb metastatic gastric adenocarcinoma.
Previously treated with 2 lines of HER2-directed targeted + chemotherapy & palliative radiation.
Stable Disease noted in both, patients 0106-0016 and **0106-0006 with IHC 2+**. Remarkably, a **0.0%** change in tumor volume from baseline was observed in both patients.

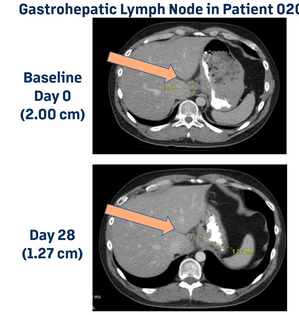
Dose Level 2 (6-8 x 10^5 cells/kg)
Day 28 Change in Lesion Sizes from Baseline



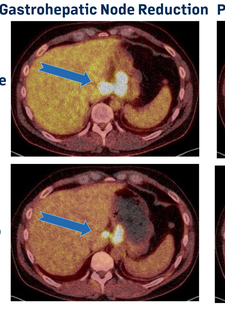
RECIST 1.1 Tumor Response Assessments (Measurable Disease)		
Baseline	Day 29	% change
20 mm	12.7mm	-36.5%

TUMOR REGRESSION: FIRST PATIENT RESPONSE

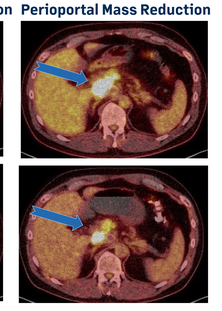
Gastrohepatic Lymph Node in Patient 0203-0021*



Gastrohepatic Node Reduction



Perioportal Mass Reduction



PET Scan Results (Evaluable disease)				
Tumor	Size Pre	Size Post	SUVmax pre TAC-T	SUVmax post TAC-T
Right lower paraoesophageal node at the level of T10	-	-	6.5	3.2
Gastrohepatic ligament lymph nodes	2.4 x 2.3 cm	1.9 x 1.2 cm	20.5	15
Portacaval nodal mass*	5.1 x 4.0 cm	4.8 x 3.4 cm	22.1	29
Left common iliac lymph node	No gross interval change per radiologist		19.3	23.1

Lymph Node Reduction

There has been overall interval decreased size of previously noted metabolically active lymph nodes associated with the mass, however with persistent intense metabolic activity in most of them.
*Despite SUVmax increase the lesions shows more extensive photopenic areas, representing cystic/necrotic change cancer cell death.
** There was also a stable cystic/necrotic node cancer cell death.

SUMMARY & CONCLUSIONS

SAFETY

Interim results from the Phase I TACTIC-02 study suggest that TAC-01 HER2 is safe and well tolerated, supported by the absence of DLTs and events of special interest such as CRS & ICANS.

EFFICACY

Demonstrated early signals of clinical activity, highlighting a **partial response in a stage IVb gastric cancer patient** and a disease control rate of 75% in cohort 2.

TRIAL PROGRESS

This study is ongoing with further investigation of TAC-01 HER2 in the remaining phase I trial, with enrollment in dose level 3 & patients consented for dose level 4. Phase II enrollment begins in 2023.

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Sources: 1. Siegel R, et. al. Cancer Statistics 2022. A Cancer Journal for Clinicians. 2022;72(1):7-33 & Triumvira Internal Analysis and Assumptions
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