A Phase I/II Trial Investigating Safety and Efficacy of Autologous TAC01-HER2 in Relapsed or Refractory Solid Tumors (TACTIC-2)

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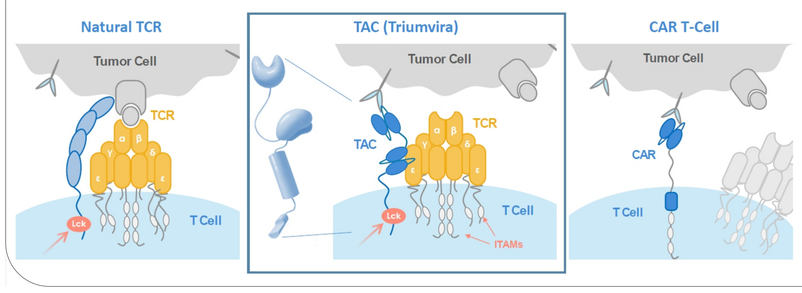
SCAN ME

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-HER2 is an autologous T-cell product comprising T cells expressing the HER2 TAC, which specifically recognize HER2+ cells.
- 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 by immunohistochemistry that are 1+, 2+, or 3+ (i.e. breast, lung, pancreatic, colorectal, gastric, endometrial, ovarian, and others) whom have progressed on prior anti-cancer therapies.
- We present updated preliminary data from Cohorts 1-4 (20 participants) that highlights safety and efficacy data; the study further elucidates potential therapeutic impact to patients with HER2 overexpressed solid tumors.

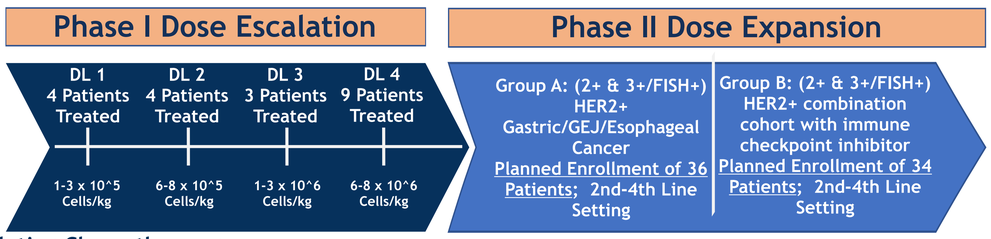
TAC SCIENCE



TAC achieves TCR activation via a CD3 binding domain while tightly binding the target of interest, HER2. TAC thus co-opts natural TCR function and provides intracellular co-receptor signaling via LCK, mimicking physiologic TCR activation.

Watch a short animation to understand the TAC mechanism

TRIAL DESIGN



Lymphodepleting Chemotherapy:
3 consecutive days of fludarabine (Flu)* IV (30 mg/m^2) and cyclophosphamide (Cy) IV (300 mg/m^2) +/- Mesna IV
***due to national shortage of fludarabine, modified LDC given per institutional standard**

PHASE I TRIAL PROGRESS

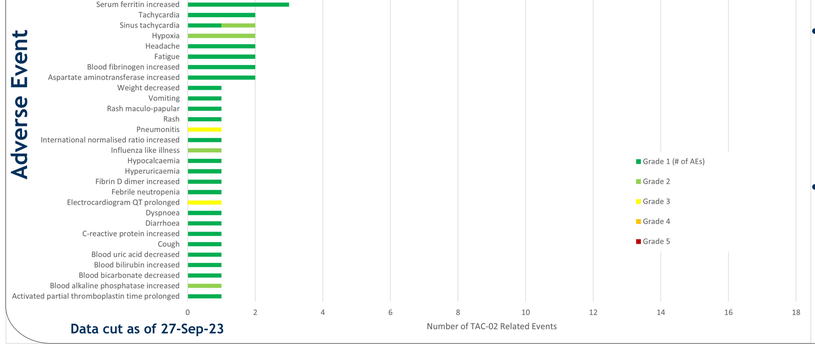
Primary Endpoints	Secondary Endpoints
Safety: DLTs, AEs	Efficacy (ORR, DoR, OS); RP2D; PK

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.

Demographics and Tumor Intrinsic Characteristics (all cohorts, n=20)				
Median Age (Range), by Year		59 (40-70)	Tumor Type, n (%)	Gastroesophageal Junction 5 (25)
Sex: Male/Female, n (%)	M	12 (60)		Gastric 3 (15)
	F	8 (40)		Esophageal 2 (10)
Race, n (%)	White	18 (90)		Breast 3 (15)
	Other	2 (10)		Colorectal 4 (20)
ECOG PS, n (%)	0	11 (55)		Gall Bladder 1 (5)
	1	9 (45)		NSCLC 1 (5)
HER2 Expression, n (%)	3+	11 (55)		Ovarian 1 (5)
	2+/FISH+	6 (30)	Previous HER2 Therapy Types, n (%)	Trastuzumab 16 (80)
	2+/FISH-	1 (5)		Trastuzumab Deruxtecan 8 (40)
	1+	2 (10)		Investigative 6 (30)
Previous Anti-Cancer Therapy, Median (Range)		4 (2-12)		Pertuzumab 4 (20)
				Tucatanib 1 (5)
Previous Lines of HER2 Therapy, Median (Range)		2 (0-9)		Trastuzumab Emtansine 1 (5)
				Lapatinib 1 (5)

PHASE I SAFETY DATA



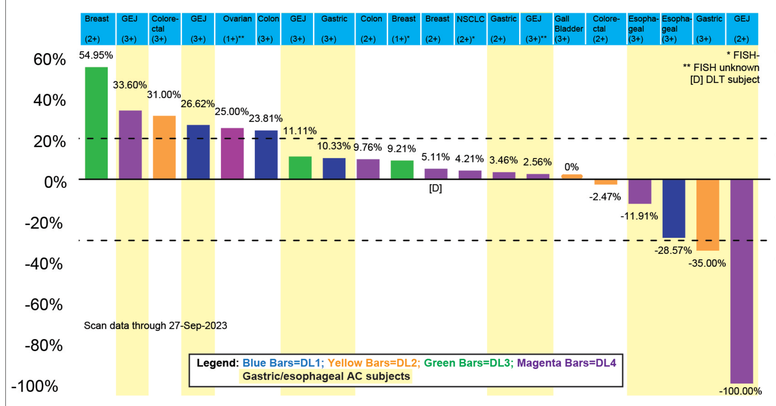
Data cut as of 27-Sep-23

Safety Summary

- 1 patient experienced a DLT (grade 3 pneumonitis) that resolved with standard of care intervention
- 11 patients experienced 14 CRS events which resolved with standard of care intervention:
  - Grade 1, n=7
  - Grade 2, n=6
  - Grade 3, n=1
- No Observed Immune Effector Cell-Associated Neurotoxicity (ICANS)

Most grade ≥2 events were expected and related to LD chemotherapy.

CHANGES IN TUMOR MEASUREMENTS ACROSS ALL DOSE LEVELS



Cohort 1
- Entry DL, however 1st signal of clinical activity, showing 1 pt. with mixed response (SoD reduction but new lesion development)

Cohort 2
- Original DL1
- 1 pt. with PR (for 3 months after treatment) and 2 pts. with SD (minimal change from baseline)

Cohort 3
- 2 pts. with SD and 1 pt. with PD

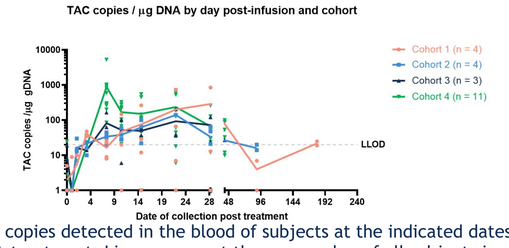
Cohort 4
- 1 pt. with PR (for 3 months after treatment), 5 pts. with SD and 3 pts. with PD

Follow-Up

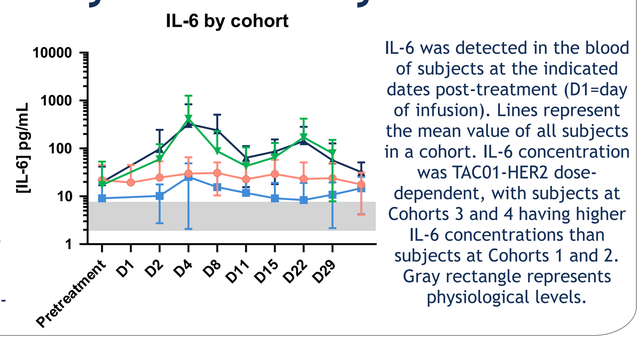
All patients are still in 2-year follow-up per protocol, except for nine patients who died due to PD, two who withdrew consent and one who was lost to follow-up.

Disease control rate of 69% at DL2-4, in heavily pretreated pts. with aggressive malignancies
ORR of 29% and DCR of 86% in gastric/esophageal AC pts at DL2-4.

TAC01-HER2 PK and Cytokine Analysis



TAC copies detected in the blood of subjects at the indicated dates post-treatment. Lines represent the mean value of all subjects in a cohort. Cohort 4 subjects (highest dose level) show the highest concentration of TAC transgene, with detectable levels 48 days post-treatment in most subjects.



IL-6 was detected in the blood of subjects at the indicated dates post-treatment (D1=day of infusion). Lines represent the mean value of all subjects in a cohort. IL-6 concentration was TAC01-HER2 dose-dependent, with subjects at Cohorts 3 and 4 having higher IL-6 concentrations than subjects at Cohorts 1 and 2. Gray rectangle represents physiological levels.

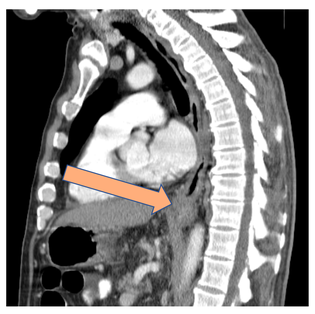
TUMOR ASSESSMENT: PATIENT RESPONSES

Patient 0105-0033

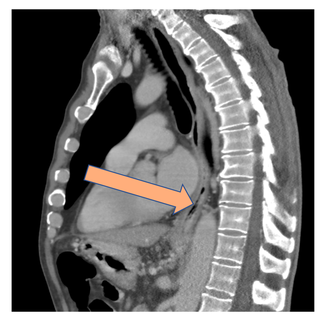
59 year old male with HER2+ (IHC 2+/FISH+) stage IV metastatic GEJ.
Previously treated with 3 lines of HER2-directed therapy (including Trastuzumab Deruxtecan) + chemotherapy.
The patient also received bridging therapy with HER2-directed therapy.
The subject progressed 3 months after treatment.

RECIST 1.1 Tumor Response Assessments (Measurable Disease)		
Baseline	Day 29	% change
30 mm	0 mm	-100%

Baseline Day 0 (3.00 cm)



Day 29 (0 cm)



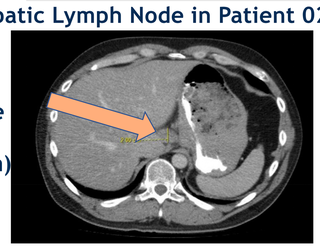
Patient 0203-0021

42 year old male with HER2+ (IHC 3+) stage IVb metastatic gastric adenocarcinoma.
Previously treated with 2 lines of HER2-directed therapy, chemotherapy & radiation therapy. The patient also received bridging chemotherapy.
The subject progressed 3 months after treatment.

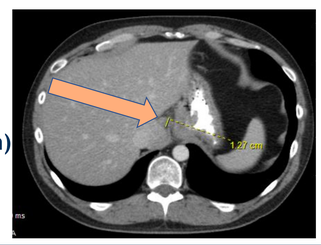
RECIST 1.1 Tumor Response Assessments (Measurable Disease)		
Baseline	Day 29	% change
20 mm	13 mm	-35%

Gastrohepatic Lymph Node in Patient 0203-0021*

Baseline Day 0 (2.00 cm)

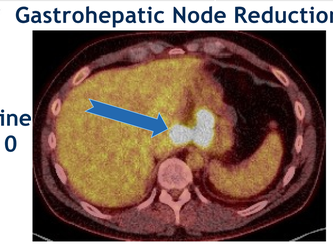


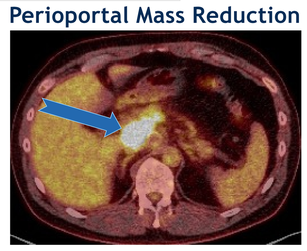
Day 28 (1.30 cm)



Gastrohepatic Node Reduction

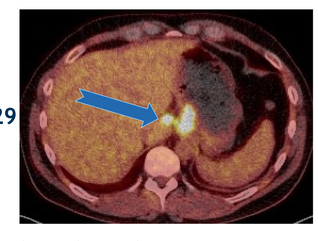
Baseline Day 0

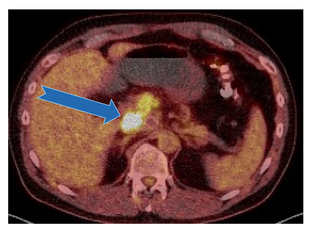




Perioportal Mass Reduction

Day 29





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 manageable safety for TAC-01 HER2 treatment. One DLT of G3 pneumonitis and one G3 CRS were observed, which resolved with standard of care measures. No ICANs reported to date across all cohorts.

TRIAL PROGRESS: Phase I trial completed. Phase II enrollment begins in Q4 2023.

EFFICACY

Demonstrated early signals of clinical activity, highlighting two partial responses (in a stage IVb gastric cancer patient and a stage IV GEJ patient, at DL 2 and 4, respectively) and a disease control rate 69% at 1st scan across DL2-4. In gastric/GEJ/esophageal patients, the DCR is 86%, while the ORR is 29% across DL 2-4.

Sponsorship: This Phase I/II Clinical Trial has been fully funded by Triumvira Immunologics Inc.
DOI: Dr. Olson has received consulting fees from GLG Consulting, Alphasights Consulting, Iovance and Novartis.
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Acknowledgments: Clinical Trial Sites and Apheresis Unit staff: Princess Margaret Cancer Centre, The University of Chicago Medical Center, Dana Farber Cancer Institute, MD Anderson Cancer Center, Rutgers Cancer Institute as well as the patients and their families.