FIRST IN HUMAN STUDY OF AUTO4, A TRBC1-TARGETING CAR T-CELL THERAPY IN R/R TRBC1-POSITIVE PERIPHERAL T-CELL LYMPHOMA

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INTRODUCTION

- Relapse/refractory (r/r) peripheral T cell lymphomas (PTLC) are highly aggressive tumors associated with poor prognosis: median PFS ~ 3 months; median OS <6 months [1,2,3].
- Brentuximab survival benefit restricted to CD30 positive ALCL subtype[4] approx. 12% of total PTCL patient population[4,5].
- PTCL has not benefited from advances in immunotherapy to date: Pan T-cell depletion highly toxic.

AIM

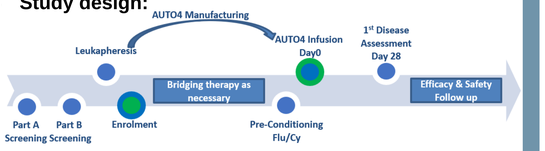
- Mature T cells express either T cell receptor β-chain constant domains 1 or 2 (TRBC1 or TRBC2).
- T cell lymphomas are clonal and either express TRBC1 or TRBC2: targeting strategy based on mutually exclusive expression of TRBC domains can spare a proportion of the normal T cell compartment[6].
- Here we present first in human clinical findings of AUTO4, a TRBC1 directed autologous CAR T cell therapy, tested against relapsed/refractory (r/r) TRBC1+ PTCL.

METHOD

NCT03590574 is a multi-centre, single-arm study of AUTO4 with a phase I dose escalation and a phase II expansion cohort.

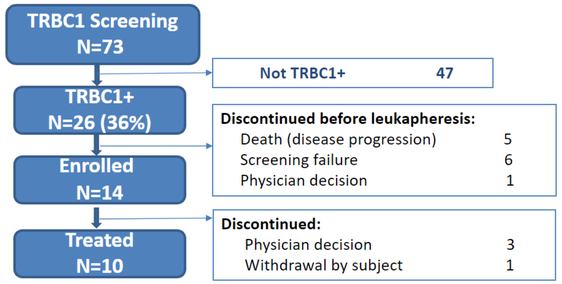
- Biopsies from patients were screened for TRBC1-positive PTCL using NGS.
- Initial Phase I data are reported here.
- **Phase I dose escalation:**

- **Study design:**



RESULTS

Patient Disposition



Baseline Characteristics

	Total (N=10)
Age, median (range)	55 (34 – 63)
Median prior lines of treatment (range)	3 (1 – 5)
Stage of Lymphoma at screening	
I/II	2 (20%)
III/IV	8 (80%)
Lymphoma Subtype, n (%)	
Peripheral T-cell lymphoma NOS	5 (50%)
Anaplastic large cell lymphoma, ALK-negative	1 (10%)
Angioimmunoblastic T cell lymphoma (AITL)	4 (40%)
Prior Autologous Stem Cell Transplant, n (%)	3 (30%)
CD30+ Immunophenotype for T-Cell NHL, n (%)	5 (50%)*
ECOG 0/1, n (%)	3 (30%), 7 (70%)
Bridging therapy YES, n (%)	7 (70%)

*3/5 received Brentuximab as bridging therapy or prior line treatment; 1/5 ALCL

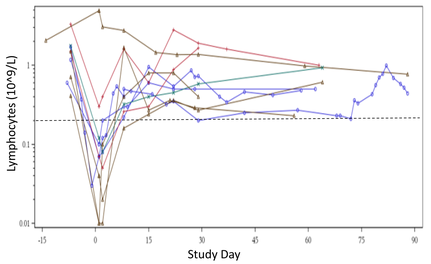
Data cutoff: 7thNov22

Key Safety Data

	Cohort 1 25x106 cells (N = 3)	Cohort 2 75x106 cells (N = 2)	Cohort 3 225x106 cells (N = 1)	Cohort 4 450x106 cells (N = 4)	Total (N = 10)
Dose Limiting Toxicity (DLT)	0	0	0	0	0
Grade 3 or 4 TEAE within 60 days	3 (100%)	2 (100%)	1 (100%)	4 (100%)	10 (100%)
Neutropenia/Netrophil counts decreased	3 (100%)	2 (100%)	0	3 (75%)	8 (80%)
Infections and Infestations	0	0	0	0	0
Serious TEAE	2 (67%)	0	0	2 (50%)	4 (40%)
Any grade CRS	0	0	0	4 (100%)	4 (40%)
Grade 3 CRS	0	0	0	1 (25%)	1 (10%)
Any grade ICANS	0	0	0	0	0

TEAE, Treatment-emergent adverse events; CRS, cytokine release syndrome; ICANS, Immune Effect Cell-Associated Neurotoxicity Syndrome

Transient lymphopaenia was observed after Flu/Cy and AUTO4

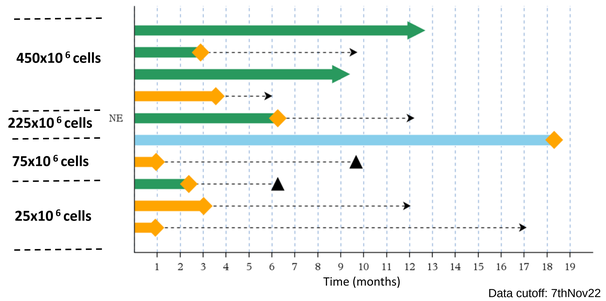


- The most common treatment-emergent adverse events were cytopenias.
- Any grade CRS was observed in 4/10 patients (all occurred in Cohort 4), one patient developed Grade 3 CRS which resolved within 3 days.
- No patients experienced ICANS.
- No prolonged lymphopenias were observed with lymphocyte numbers recovering in all patients after effects of pre-conditioning.
- No Grade 3 or higher infections and infestations.

Cohort1 (25x10⁶ cells) Cohort2 (75x10⁶ cells) Cohort3 (225x10⁶ cells) Cohort4 (450x10⁶ cells)

Data cutoff: 7thNov22

Efficacy

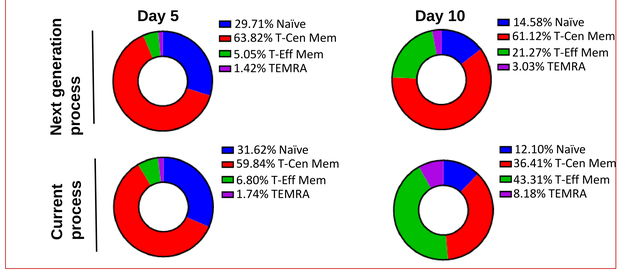


Data cutoff: 7thNov22

PD (Progressive Disease) CR (Complete Response) PR (Partial Response) Death due to underlying cancer

NE = Non-evaluable PET at baseline

AUTO4 Next generation manufacturing process results in less differentiated CAR T cells



CONCLUSIONS

- AUTO4 treatment was well tolerated with no DLT.
- Ongoing responses at 9 and 12 months post-dosing at the highest dose tested (450x10⁶) are encouraging.
- No CAR T cell expansion was seen in peripheral blood but CAR T cells were detected in an on-treatment lymph node biopsy.
- Optimization of the AUTO4 manufacturing process has been performed, resulting in a product with a more naïve and central memory phenotype.
- The study is ongoing, with additional patients due to be treated to define the recommended phase II dose.

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CONTACT INFORMATION

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