TSC-101 eliminates recipient hematopoietic cells and demonstrates potential for improved relapse-free survival in patients with AML, ALL, or MDS undergoing allogeneic HCT: Updated results from the Phase 1 (ALLOHA) trial

Monzr Al Malki[1], Yi-Bin Chen[2], Tania Jain[3], Alla Keyzner[4], Melhem Solh[5], Uday Popat[6], Michele Donato[7], Luis Pineiro[8], Hugo Fernandez[9], Saar Gill[10], Anson Snow[11], Joseph Uberti[12], Timothy White[13], Yun Wang[13], Cuong Nguyen[14], Chrystal U Louis[13], Shrikanta Chattopadhyay[13], Michelle Matzko[13], Ran Reshef[15]

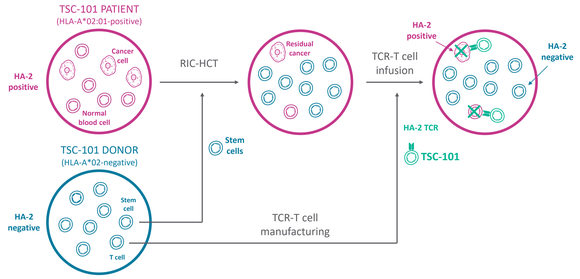
[1]City of Hope National Medical Center, Duarte, CA, United States, [2]Massachusetts General Hospital /Harvard Medical School, Boston, MA, United States, [3]Johns Hopkins University, Baltimore, MD, United States, [4]Mount Sinai Tisch Cancer Center, New York, NY, United States, [5]Northside Hospital Cancer Institute, Atlanta, GA, United States, [6]The University of Texas MD Anderson Cancer Center, Houston, TX, United States, [7]Hackensack University Medical Center, Hackensack, NJ, United States, [8]Baylor University College of Medicine, Houston, TX, United States, [9]Memorial Cancer Institute, Pembroke Pines, FL, United States, [10]Abramson Cancer Center and Hospital of the University of Pennsylvania, Philadelphia, PA, United States, [11]University of Carolina at Chapel Hill, Chapel Hill, NC, United States, [12]Karmanos Cancer Institute, Detroit, MI, United States, [13]TScan Therapeutics, Waltham, MA, United States, [14]Biostatistical Consulting, Lexington, MA, United States, [15]Columbia University Irving Medical Center, New York, NY, United States

Abstract #12098

RELAPSE AFTER HCT REMAINS AN UNMET NEED

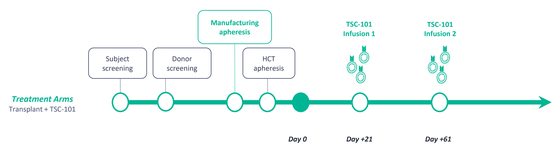
- Allogeneic hematopoietic cell transplantation (HCT) is currently the only curative option for patients with AML, ALL, or MDS
- Advances in reduced intensity conditioning (RIC) HCT regimens as well as GvHD prophylaxis with post-transplant cyclophosphamide (PTCy) have expanded patient access to HCT by markedly improving treatment-related morbidity and mortality
- However, a significant unmet medical need remains as **~ 40% of patients will relapse and subsequently die from their disease**
- TSC-101 is a donor-derived, engineered TCR-T cell product designed to treat relapse by targeting the HA-2 antigen presented by HLA-A*02:01 and selectively eliminating residual patient-derived hematopoietic cells after HCT
- The ALLOHA Study (TSCAN-001, NCT05473910) is a Phase 1, multi-center, open-label, biologically controlled study evaluating TSC-101 in HA-2-positive patients with AML, ALL, or MDS undergoing RIC-HCT

TSC-101 TCR-T CELLS ARE DESIGNED TO TARGET RESIDUAL PATIENT-DERIVED CELLS AND PREVENT RELAPSE FOLLOWING HCT



- TSC-101 is engineered to recognize HA-2 in an HLA-A*02:01-restricted manner
- This design allows TSC-101 to selectively target residual patient hematopoietic cells (malignant and non-malignant), prevent relapse, and maximize the chance of cure post allogeneic HCT

PHASE 1 TRIAL FOR TSC-101 IN SUBJECTS WITH AML, ALL, AND MDS



Key eligibility criteria

- Age ≥18 years
- Undergoing first allo-HCT for ALL, AML, MDS
- Subject positive for HLA-A*02:01 with an HLA-A*02 negative donor
- Eligible for RIC-HCT followed by PTCy for GvHD prophylaxis

Key endpoints

- Safety: dose limiting toxicities, adverse events
- Efficacy: probability of relapse, RFS, OS
- Exploratory: donor chimerism, minimal residual disease

ABBREVIATIONS

ALL, Acute Lymphoblastic Leukemia; AML, Acute Myeloid Leukemia; CR, complete remission; CRS, Cytokine Release Syndrome; DLT, Dose Limiting Toxicity; GvHD, Graft vs. Host Disease; HCT, Hematopoietic Cell Transplantation; HLA, Human Leukocyte Antigen; ICANS, Immune Effector Cell Associated Neurotoxicity Syndrome; MDS, Myelodysplastic Syndrome; MLFS, morphologic leukemia-free state; MRD, minimal residual disease; OS, Overall Survival; PR, partial remission; PTCy, Post-Transplant Cyclophosphamide; RIC, Reduced Intensity Conditioning; RFS, Relapse Free Survival; TCR, T-cell Receptor

MAJORITY OF SUBJECTS IN THE TREATMENT AND CONTROL ARMS ARE AT HIGH RISK FOR RELAPSE

		TSC-101	Control
Enrolled Subjects		23	19
Evaluable Subjects*		19 (100%)	18 (100%)
Median Time from HCT, months		13.4 (4-33)	16.1 (1-36)
Age, Median (Range)		65 (52-74)	66 (23-77)
Sex, Male %)		13 (68%)	9 (50%)
Underlying Disease	ALL	2 (11%)	1 (6%)
	AML	13 (68%)	11 (61%)
	MDS	4 (21%)	6 (33%)
Genetics/ cytogenetics	**TP53 mutated**	**6 (32%)**	**2 (11%)**
	Adverse Risk**	13 (68%)	11 (61%)
Pre-HCT MRD Positive		13 (68%)	8 (44%)
MRD positive or adverse risk genetics		15 (79%)	13 (72%)
Clinical Status at time of HCT			
CR1		9 (47%)	12 (67%)
CR2		2 (11%)	1 (6%)
MLFS		5 (27%)	0 (0%)
Hematologic improvement		1 (5%)	0 (0%)
PR		1 (5%)	1 (6%)
Untreated		1 (5%)	1 (6%)
Other status		0 (0%)	3 (17%)

Data as of 19 September 2025

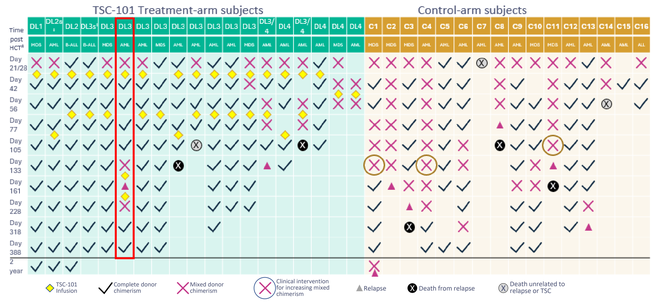
*Subjects on the treatment arm who received ≥1 infusion of TSC-101 and on the control arm who reached Day 21 were considered evaluable for safety and efficacy
**Adverse risk is defined as having either an IPSS-M mutation if the subject has MDS or European Leukemia Network (ELN) high risk genetics or cytogenetics for AML

ADVERSE EVENTS OF SPECIAL INTEREST WERE LOW GRADE AND MANAGEABLE

- No DLTs reported
- Low rates of Grade III – IV acute GvHD (aGVHD) across both arms
- No moderate or severe chronic GvHD (cGVHD) with TSC-101
  - 1 case of mild cGVHD seen in both arms
- Three cases of CRS reported after TSC-101 infusions
  - Two Grade 1 events and one Grade 2 event; all resolved
- One case of ICANS reported after a TSC-101 infusion
  - Depressed consciousness (Grade 2) reported following infusion #2 in a patient with relapsing disease. Treated with tocilizumab and steroids; resolved within 24 hours

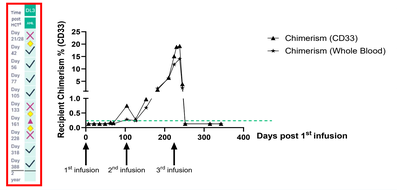
	TSC-101 n=19	Control n=18
Treatment- emergent aGvHD (MAGIC)	12 (63%)	10 (56%)
Grade I	8 (42%)	5 (28%)
Grade II	3 (16%)	4 (22%)
Grade III	1 (5%)	1 (6%)
Grade IV	0 (0%)	0 (0%)
Any Treatment-emergent cGvHD (NIH)	1 (5%)	2 (11%)
Mild	1 (5%)	1 (6%)
Moderate	0 (0%)	1 (6%)
Severe	0 (0%)	0 (0%)
Any CRS	14 (74%)	7 (39%)
Grade 1 - 2	14 (74%)	6 (33%)
Grade 3 - 4	0 (0%)	1 (6%)
Treatment-emergent CRS	3 (16%)	0 (0%)
Grade 1 - 2	3 (16%)	0 (0%)
Grade 3 - 4	0 (0%)	0 (0%)
Any ICANS	1 (5%)	0 (0%)

MORE SUBJECTS IN COMPLETE DONOR CHIMERISM AT ALL TIMEPOINTS POST TSC-101 INFUSION COMPARED TO CONTROL



#Donor chimerism results using investigational NGS assay (Alloheme) with LOD of 0.2% or the short tandem repeat (STR) with LOD of 1-2% at indicated days post-HCT (± 3 days, y-axis) in patients at least 60 days post-HCT as of 19 Sept 2025 datacut; ‡Dose did not meet target dose criteria in supplemental cohorts

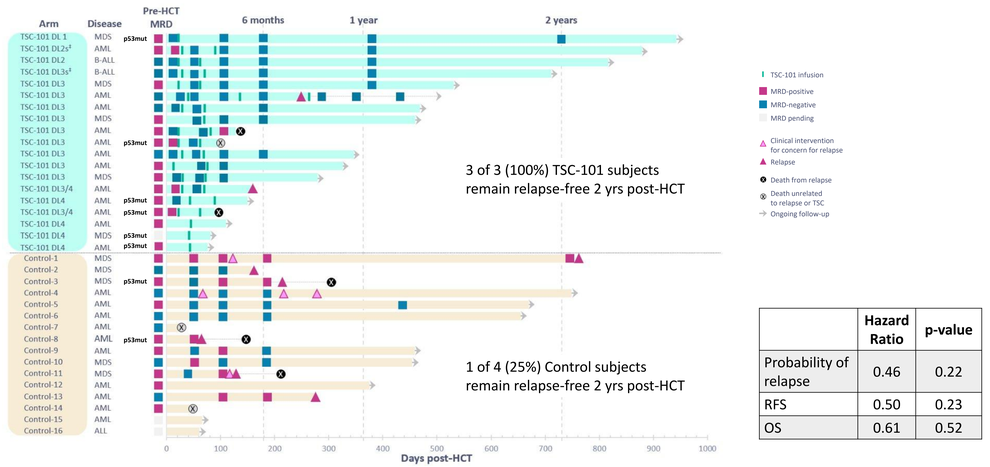
CASE STUDY: TSC-101 INFUSION POST-RELAPSE CONVERTED SUBJECT TO FULL DONOR CHIMERISM AND INTO COMPLETE REMISSION



- 74 yo male with AML in CR1 received 2 infusions of TSC-101 per DL 3
- 2nd infusion was delayed by 36 days due to treatment of aGvHD
- At time of relapse, received 370m cells without lymphodepletion or additional chemotherapy
- No evidence of disease at next evaluation and remained in complete remission for 5 months

TSC-101 IS ASSOCIATED WITH FEWER RELAPSES, MORE DURABLE REMISSIONS, AND LONGER SURVIVAL

- All subjects who were MRD-positive post-HCT became MRD-negative following their first infusion of TSC-101
- Subjects treated with TSC-101 demonstrated a longer duration of response vs. control
- Preliminary efficacy data trends support a reduced risk of relapse and increased survival (RFS & OS) with TSC-101 relative to subjects that did not receive TSC-101 TCR-T cell therapy

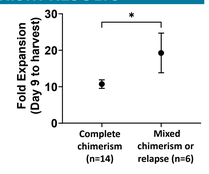


	Hazard Ratio	p-value
Probability of relapse	0.46	0.22
RFS	0.50	0.23
OS	0.61	0.52

MRD measured by flow cytometry (lower limit of detection 0.1-1%) or NGS (lower limit of detection 0.05-0.1% in myeloid and 0.001-0.01% in lymphoid malignancies).
‡Dose did not meet target dose criteria in supplemental cohorts

EXTENT OF *EX-VIVO* EXPANSION IN PHASE 1 MANUFACTURING PROCESS MAY BE ASSOCIATED WITH CHIMERISM RESULTS

- Previous Phase 1 process required 17 days (range 14-20 days) to manufacture TSC-101
- Mixed chimerism, as determined by the high-sensitivity chimerism assay, and relapse in the TSC-101 arm appear associated with higher *ex-vivo* expansion of TCR-T cells
- New commercial-ready process reduces manufacturing time by 5 days (12 days vs. 17 days) and shows a significant reduction in *ex-vivo* expansion (from mean 13-fold to 5-fold expansion, p=0.007, data not shown)



Symbols: mean +/- standard error; *p<0.05

CONCLUSIONS

- TSC-101 is well-tolerated with no DLTs
- Longer-term follow-up demonstrates TSC-101 treated subjects remain in durable remission post infusion (3 subjects > 2 years; 7 subjects > 1 year)
- Direct evidence of anti-tumor activity in subjects treated with TSC-101 post-relapse converting to complete remission with no other anti-cancer therapy
- Ongoing trend toward improved relapse-free survival in TSC-101 treated subjects relative to controls
- These data support the continued evaluation of TSC-101 to eliminate residual disease and prevent relapse in subjects with hematological malignancies post allogeneic HCT
  - Pivotal trial to commence in Q2 2026

ACKNOWLEDGEMENTS & REFERENCES

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