TScan Therapeutics Tandem Meeting: Promising Phase 1 Clinical Results for the Heme Program

Monday, February 26, 2024

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TSCAN THERAPEUTICS

Presenters

Monzr M. Al Malki, M.D.

- City of Hope
- Associate Professor in the Department of Hematology & Hematopoietic Cell Transplantation
- Director, Unrelated Donor BMT Program and Haploidentical Transplant Program

Dr. Al Malki is the lead PI for the current study

Ran Reshef, M.D., M.Sc.

- Columbia University Irving Medical Center
- Professor of Medicine and Director of the Cellular Immunotherapy Program

Dr. Resehf is a PI for the current study

Gavin MacBeath, Ph.D.
Chief Executive Officer

Debora Barton, M.D.
Chief Medical Officer

Shrikanta Chattopadhyay, M.D.
SVP, Head of Translational Medicine

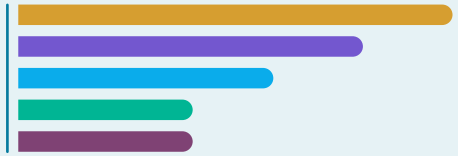
TSCAN THERAPEUTICS

TScan is a fully integrated, next-generation TCR-T cell therapy company

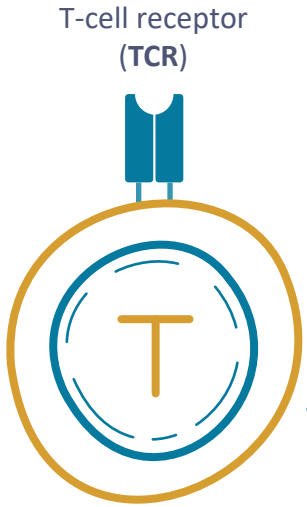
Proprietary discovery platform

Rapid discovery of targets and TCRs

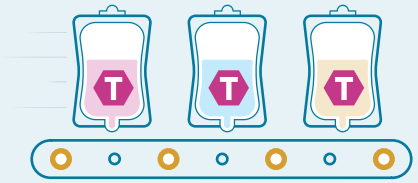
Rapidly-growing oncology pipeline



Clinical-phase programs in heme and solid tumor malignancies

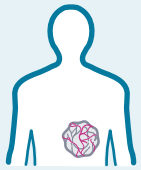


In-house GMP manufacturing

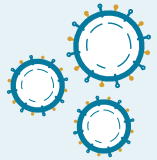


Transposon-based T cell engineering

Broad therapeutic potential



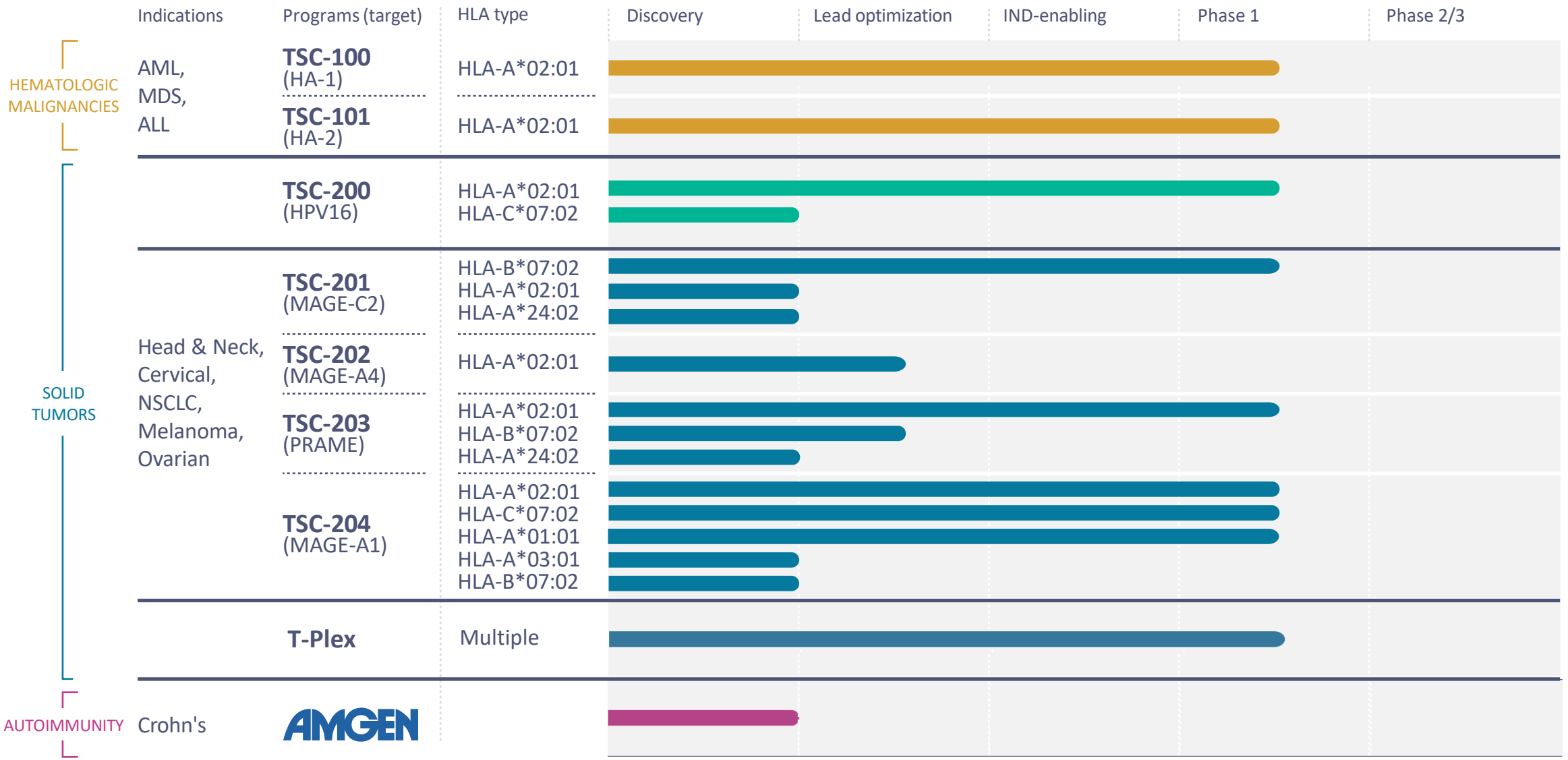
Oncology



Infectious disease

Autoimmune disease

Platform delivers broad proprietary pipeline



Heme malignancies: TCR-T candidates designed to treat residual disease and prevent relapse in patients undergoing allogeneic HCT

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Relapse after hematopoietic cell transplant remains an unmet need

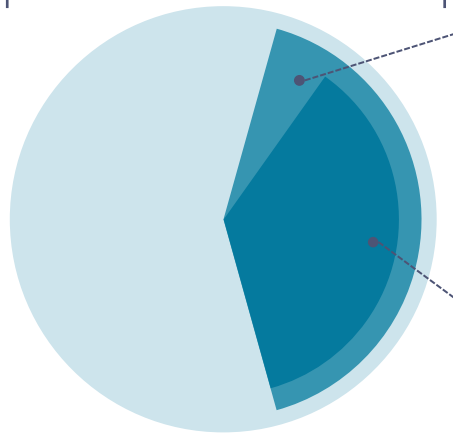
AML, MDS, some ALL not addressed by CAR-T due to shared antigens with normal blood cells

~35,000
cases/year US

Allogeneic hematopoietic cell transplant (HCT) expected to remain standard of care

Allo-HCT creates a unique opportunity to safely target residual cancer cells while sparing normal blood cells

~7,350[1]
undergo transplant



>33% relapse within 2 years[2]
RIC range 38-44%
MAC range 26-30%

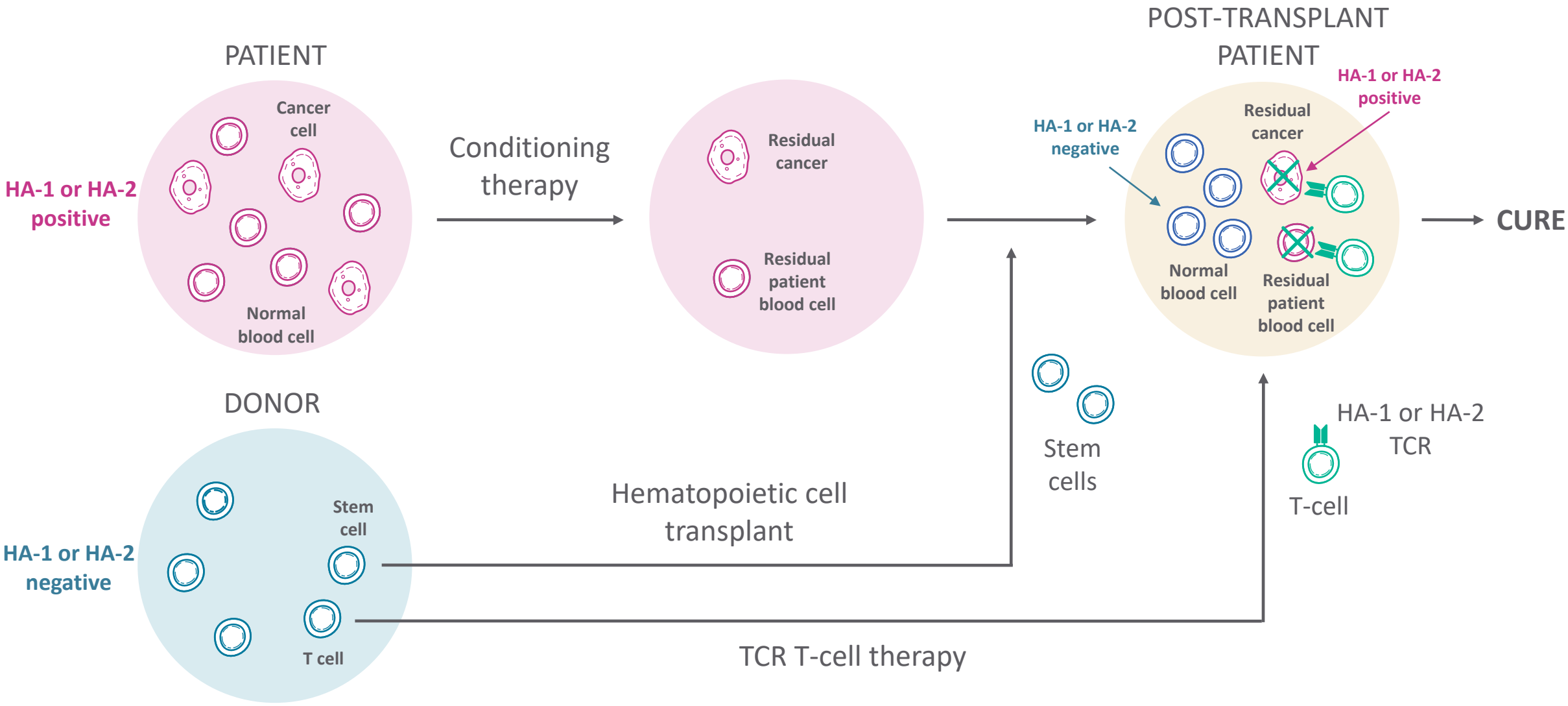
>90% mortality within 1 year[2]

Targeting antigens mismatched between patients and donors can potentially prevent relapse after allo-HCT

1. CIBMTR summary statistics 2022, allogeneic transplants for malignant diseases in 2019 before the COVID-19 pandemic
2. CIBMTR analysis of AML, ALL, MDS allogeneic transplants with myeloablative (MAC) or reduced intensity conditioning (RIC) between 2017-2019 with 2-year follow-up; MAC relapse range 26-30%, RIC relapse range 38-44%

TSCAN THERAPEUTICS

TSC-100 and TSC-101 are engineered TCR-T cells designed to eliminate residual recipient cells and prevent relapse following HCT



Highlights of data presented at the 2024 Tandem meetings of ASTCT and CIBMTR

- TSC-100 and TSC-101 were generally well-tolerated, with no DLTs and no significant differences in safety between treatment and control arms observed to date*
- Treatment arms (8 patients) showed complete donor chimerism and no evidence of residual disease at every reading starting 3 weeks after their first dose, associated with favorable prognosis
  - All eight patients had no evidence of relapse after TSC-100/ TSC-101 treatment, with five patients on study for >6 months and a TP53 mutated MDS patient with >1 year follow-up
- Both TSC-100 and TSC-101 reached dose level 3 and continue to enroll at the anticipated recommended phase 2 dose
- Four out of six control-arm patients showed increased mixed donor chimerism, and/or minimal residual disease, associated with unfavorable prognosis
  - 2 patients relapsed and one other required termination of immune suppression due to worsening chimerism, all before day 180
  - 1 TP53 mutated MDS patient died following relapse

*Data as of Jan. 29, 2024

TSC-100 and TSC-101, TCR-T Cell Therapies That Target Residual Recipient Cells after Reduced Intensity Conditioning Transplantation, Induce Complete Donor Chimerism with Favorable Prognosis: Early Results of a Phase 1 Trial

Monzr M. Al Malki, MD[1], Alla Keyzner MD[2], Hyung C. Suh MD[3], Uday R. Popat, MD[4], Nishant Dwivedi, MD, PhD[5], Ashish S Kothari, MD, MS[5], Erica Buonomo, PhD[6], Yun Wang, PhD[6], Nina Abelowitz, NP[6], Jim Murray[6], Gavin MacBeath, PhD[6], Debora Barton, MD[6], Shrikanta Chattopadhyay, MD[6] and Ran Reshef, MD[7]

(1)Hematology and HCT, City of Hope, Duarte, CA, (2)Division of Hematology & Medical Oncology, Cellular Therapy and Bone Marrow Transplant, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, (3)John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ, (4)Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX, (5)Clinical Development, CareDx, Brisbane, CA, (6)TScan Therapeutics, Waltham, MA, (7) Columbia University Herbert Irving Comprehensive Cancer Center, New York, NY

Multi-arm Phase 1 trial for TSC-100 & TSC-101 has reached highest dose level

Dose Level	Day 21	Day 61
1	5×10^6/kg	
2	5×10^6/kg	5×10^6/kg
3	5×10^6/kg	2×10^7/kg

AML, MDS, ALL undergoing haploidentical donor transplant with reduced intensity conditioning

Control Arm
(HLA-A*02:01 negative)

Transplant Alone

Treatment Arms
(HLA-A*02:01 positive: 42%)

Transplant + TSC-100 (HA-1 positive‡)

Transplant + TSC-101 (HA-2 positive‡)

Key endpoints

- Safety: adverse event profiles, GvHD rates/ grades
- Relapse rates: 6m, 1y, 2y
- Exploratory endpoints: donor chimerism, MRD

Expected relapse rates for HCT alone	
6 months	22%
1 year	33%
2 years	42%

CIBMTR analysis of RIC-haplo transplants from 2017-2019

‡ >99% patients are either HA-1 or HA-2 positive

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Patient risk factors well-balanced between 6 control and 8 treatment arm patients

	Control Arm						TSC-100				TSC-101			
Patient ID	Control 1	Control 2	Control 3	Control 4	Control 5	Control 6	TSC-100 DL1	TSC-100 DL2	TSC-100 DL3	TSC-100 DL3	TSC-101 DL1	TSC-101 DL2-supp	TSC-101 DL2	TSC-101 DL3-supp
Diagnosis	MDS	MDS	MDS	AML	AML	AML	T-ALL	AML	AML	MDS	MDS	AML	B-ALL	B-ALL
Molecular Markers	Trisomy 8, SRSF2 ASXL1	None	Del5q Mono 7 mTP53	Mono 7, RUNX1, EZH2	SETB1, WT1, DNMT3A	FLT3-ITD NPM1 WT1	ATM <2%	FLT3-ITD	Trisomy 8 IDH2, NRAS, ASXL1	SRSF2 ASXL1 STAG2	Del5q, mTP53	IDH2, SRSF2, ASXL1 CUX1	n/a	n/a
Pre-HCT MRD	**Positive**	Negative	**Positive**	Negative	**Positive**	Negative	**Positive**	Negative	**Positive**	**Positive**	**Positive**	**Positive**	Negative	Negative
RIC regimen	Flu/ Cy/ TBI	Flu/ Cy/ TBI	Flu/Mel/ Thio	Flu/ Cy/ TBI	Flu/Mel/ TBI	Flu/ Mel/ TBI	Flu/ Cy/ TBI	Thio/ Bu/ Flu	Flu/Mel/ TBI	Flu/Cy/ TBI	Flu/ Mel/ TBI	Flu/Mel/ TBI	Flu/Mel/ TBI	Flu/Mel/ TBI
Dose Level	N/A						DL1	DL2	DL3	DL3	DL1	sDL2‡	DL2	sDL3‡
TCR-T treatment day	N/A						Day 29	Day 25 Day 76	Day 34 Day 75	Day 27 Day 69	Day 21	Day 27 Day 82	Day 21 Day 62	Day 27 Day 70

‡ Dose did not meet target dose criteria

Data cutoff Jan 29, 2024

Donor chimerism serves as surrogate of efficacy

Donor Chimerism

High sensitivity

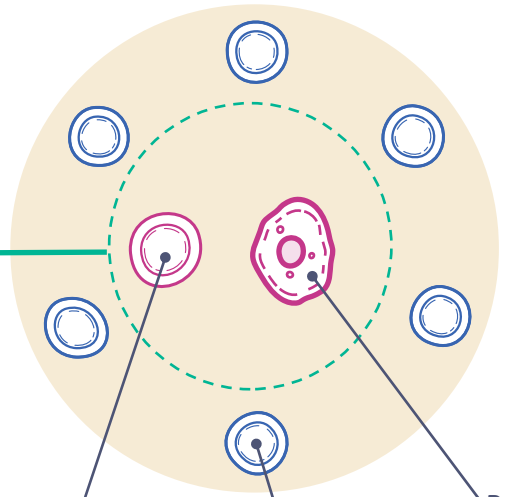
- NGS-based assay (~400 SNPs)
- Sensitivity ~0.13%

Standard

- STR-based assay (16 genetic loci)
- Sensitivity 1-5%

Early complete donor chimerism is a favorable indicator of success[a,b].

Post-transplant Patient



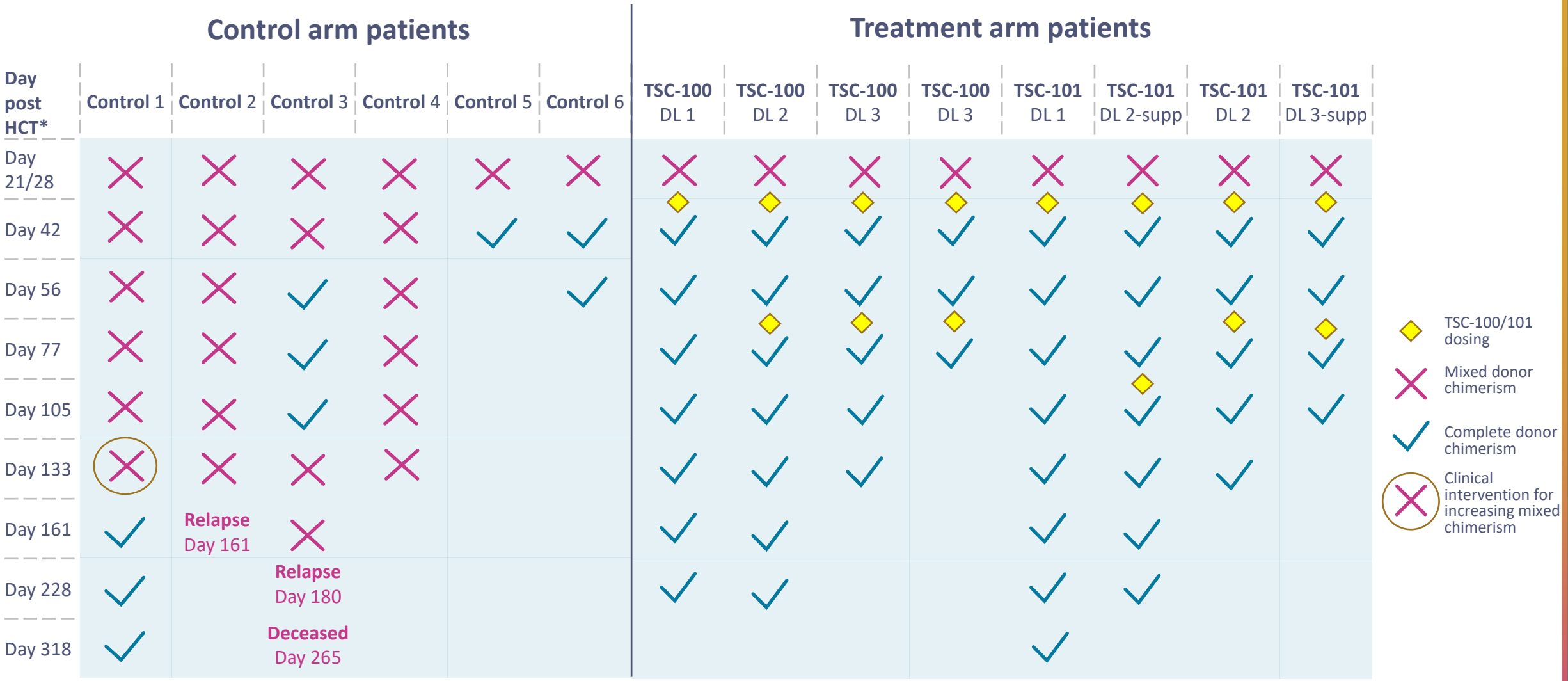
Residual blood cells (HA-1 or HA-2 positive)

Residual Leukemia (HA-1 or HA-2 positive)

Donor blood cells (HA-1 or HA-2 negative)

a. Lindhal, Bone Marrow Transpl, 2022
b. Ciurea, Al Malki, Blood Rev, 2023

Complete donor chimerism achieved and maintained in 8/8 (100%) treated patients



Donor chimerism detected by high-sensitivity next-generation sequencing (NGS) assay (AlloHeme) with limit of detection 0.13%

*Measurements taken at indicated day post HCT ± 3 days

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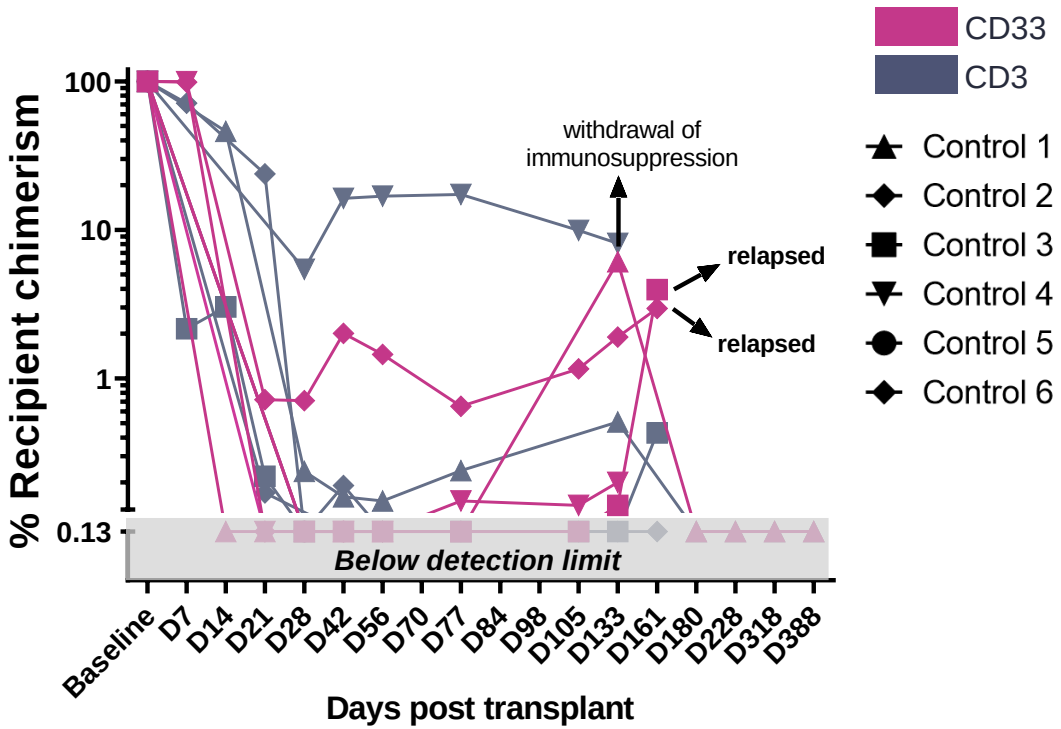
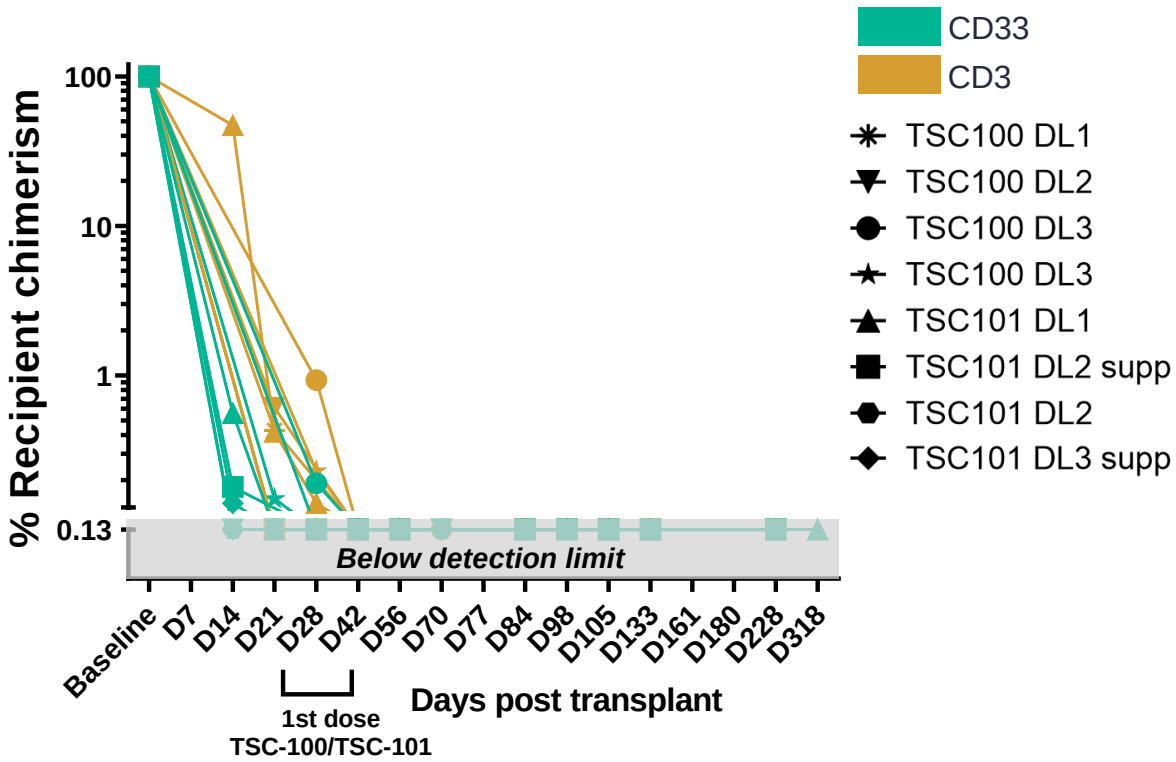
No relapse and complete chimerism in 100% treatment-arm patients
Two relapses and increased mixed chimerism in control-arm patients

Control arm



Treatment arms



All relapses or adverse outcomes occur with mixed chimerism

* Median post-transplant follow-up in treatment arms: 8 months (range 3-12 months); median follow-up in control arm: 7 months (range 2-15 months)

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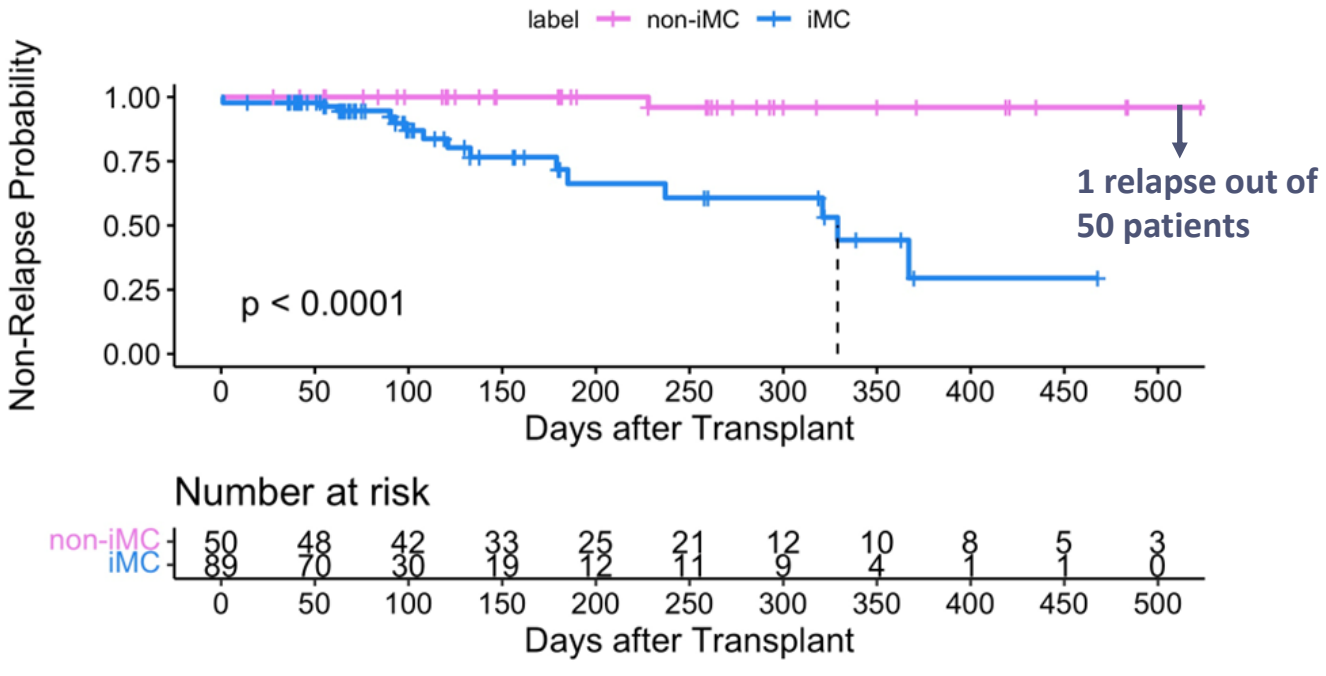
Early data from ACROBAT trial* show relapse risk is very low in patients with maintained complete chimerism by ultra-sensitive NGS assay

Chimerism by ultra-sensitive NGS assay[1]



iMC: ≥0.2% increasing mixed chimerism in CD3+, CD33+ or whole blood
[1] Limit of detection ~0.13% recipient chimerism

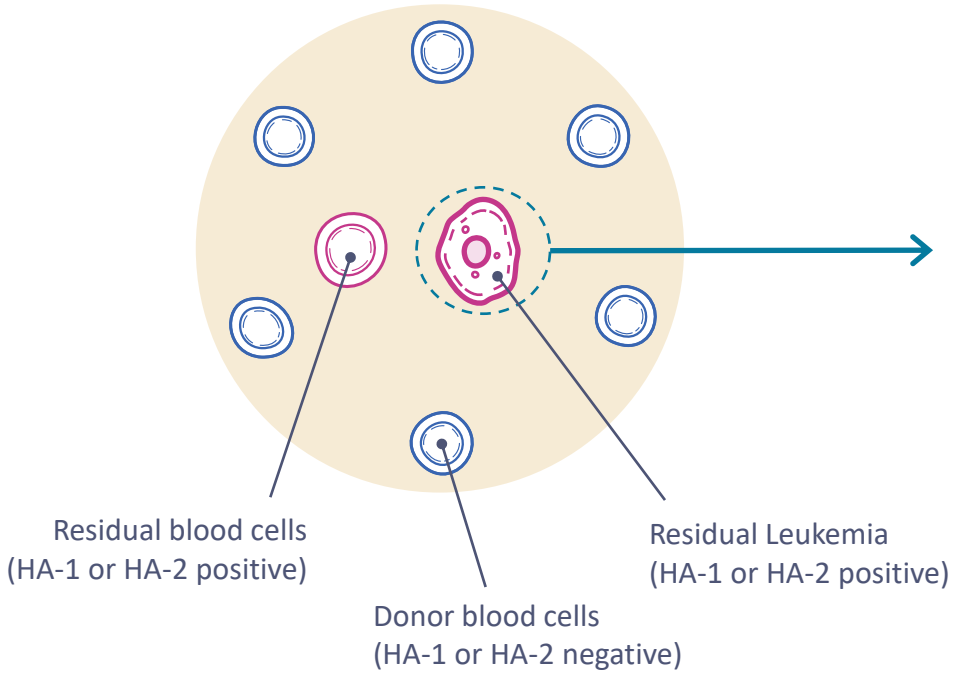
139 patients with complete NGS and STR chimerism testing, median F/U [Q1,Q3] = 365 [270,484] days

- Early data from the ACROBAT trial suggest a favorable prognosis for patients that rapidly achieve and maintain complete chimerism
- All patients treated with TSC-100/ TSC-101 show complete chimerism at every timepoint to date, suggesting a very low risk of relapse

* NCT04635384, Kothari, TCT 2024 abstract # 555

Minimal residual disease serves as a supportive surrogate of efficacy

Post-transplant Patient



Minimal Residual Disease (MRD)

Next-generation sequencing

- Deep sequencing of leukemia-associated genes (centrally)
- Sensitivity 0.05-0.1%

Flow cytometry

- Leukemia-associated immunophenotypes (locally)
- Variable sensitivity

MRD+ patients post-transplant have ~90% chance of relapse[c,d]

c. Craddock, J Clin Oncol, 2021
d. Loke, ASH, 2021

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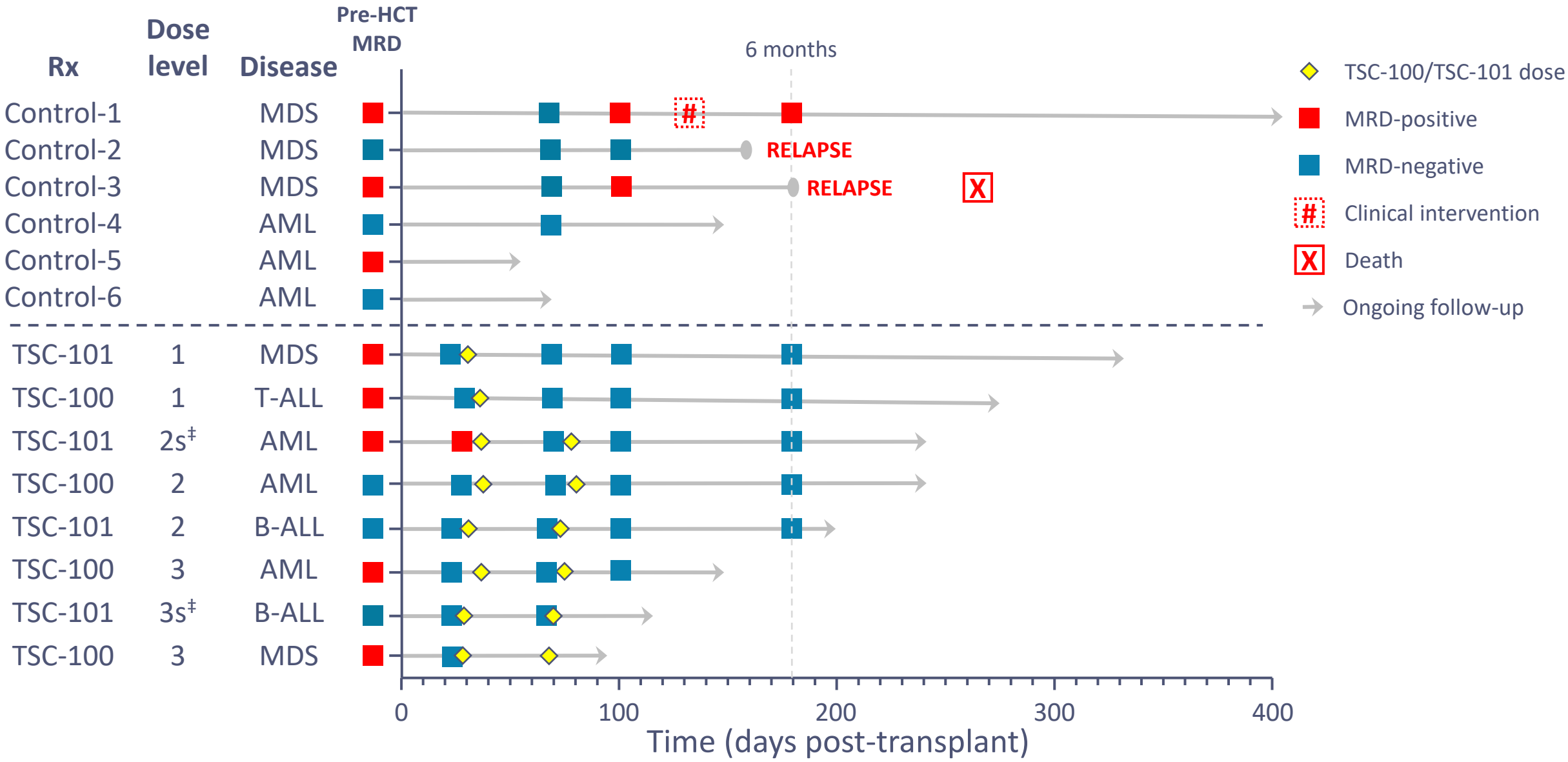
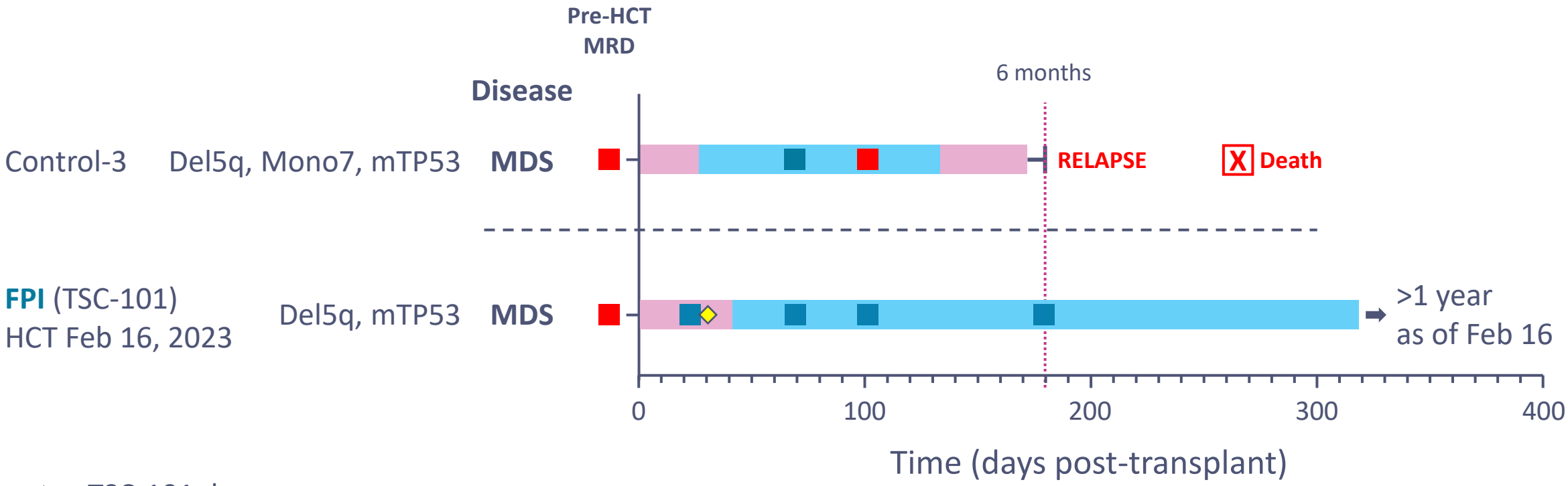
All treated patients achieved MRD negativity



*MRD determined by NGS (lower limit of detection 0.05-0.1%)

‡ Dose did not meet target dose criteria in supplemental cohorts

Very different outcomes observed for two patients with TP53-mutated MDS

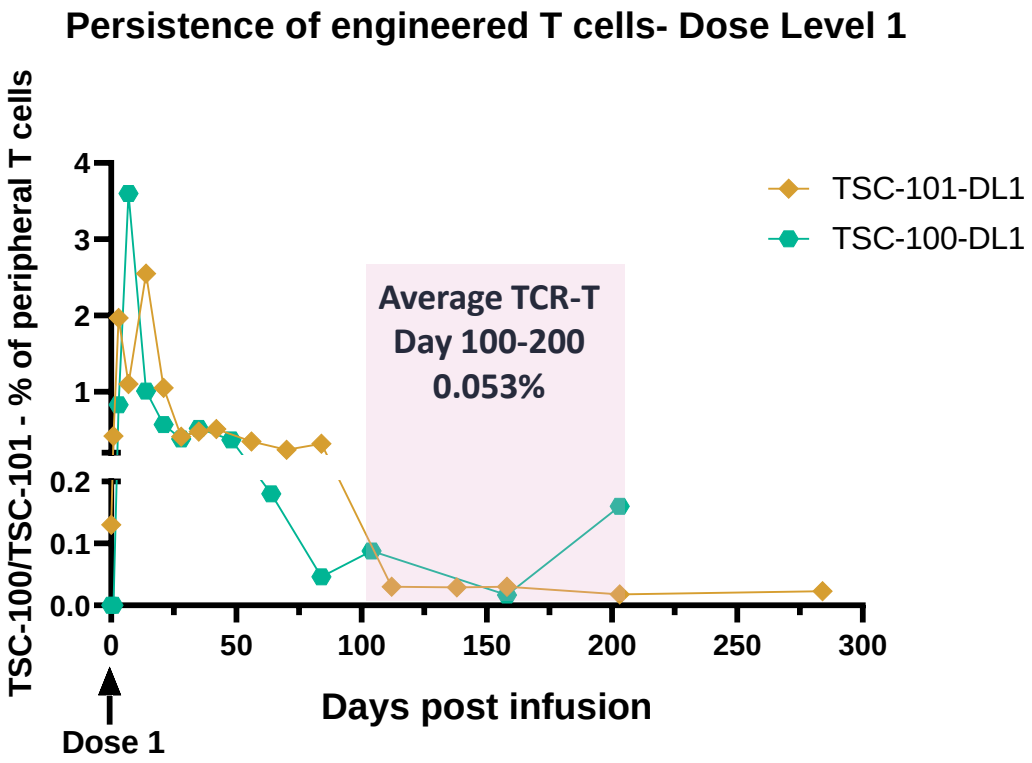


*MRD and chimerism determined by NGS (lower limits of detection 0.1% and 0.13%, respectively)

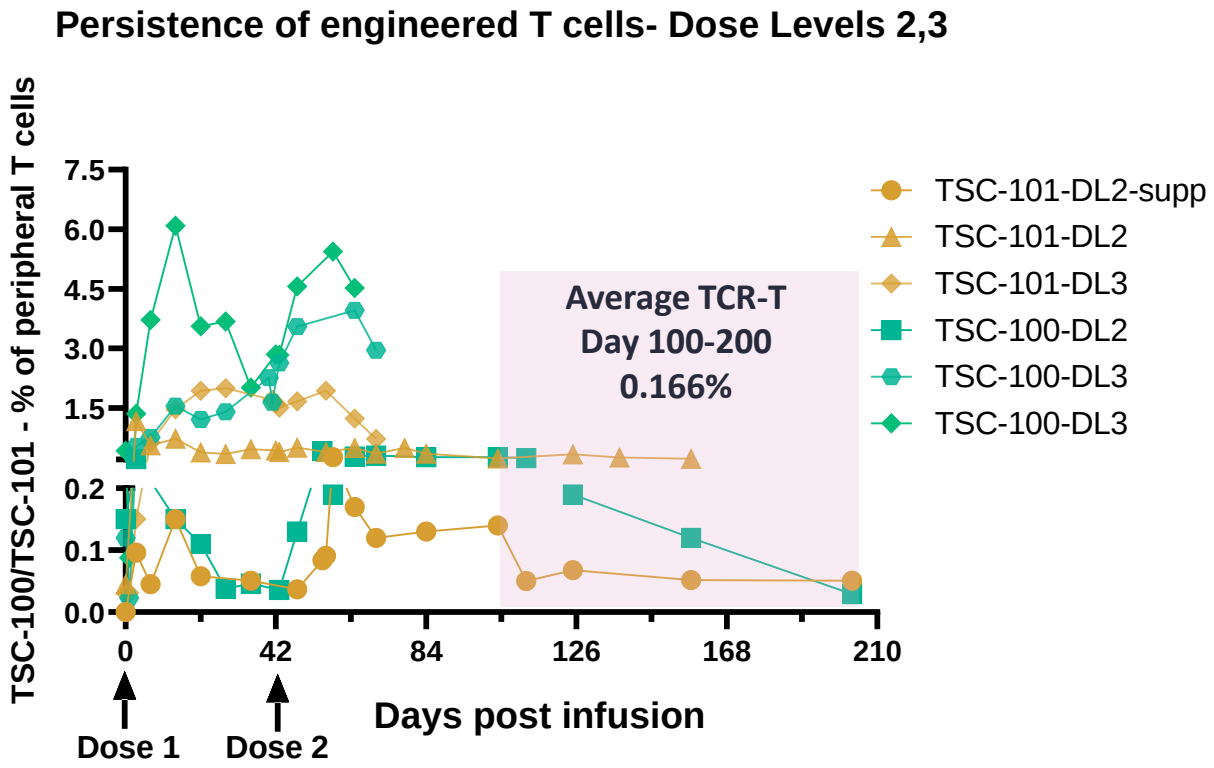
TSC-100 & TSC-101 persisted in peripheral circulation for over 9 months

- TSC-100 and TSC-101 TCR-T cells detected in all patients at all time points to date
- Repeat dosing resulted in increased levels of circulating TCR-T cells

Single dose cohorts



Repeat dose cohorts



Most frequent ≥ grade 2 adverse events* were similar between treatment and control arms

Adverse event ≥ Grade 2	TSC-100/TSC-101 arms Highest grade# N=8	Control arm Highest grade# N=6
Abdominal pain	2	2
ALT/ AST increased	NA	3
Anemia	3	4
Creatinine Increased	2	2
Decreased appetite	2	2
Diarrhea	2	2
Dyspnea	2	2
Fatigue	2	2
Hyperkalaemia	3	2
Hypogammaglobulinemia	2	2
Hypomagnesemia	2	2
Hypophosphatemia	2	2
Hypotension	3	2
Nausea/ vomiting	2	2
Neck pain	2	3
Neutropenia	3	4
Pneumonia	2	3
Pyrexia	2	2

* Events after Day 21 or after TSC-100/TSC-101

Grading by CTCAE v 5.0

TSC-100/TSC-101 arms had median post-HCT follow-up 249 days (90-347 days)
Control arm had median post-HCT follow-up 201 days (59-454 days)

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Serious adverse events were similar between treatment and control arms

Arm	Serious Adverse Event	Highest Grade*	Post Transplant Day	TSC Relatedness
TSC-100-DL3	Sepsis, respiratory failure	4	+9	Not applicable (pre-TSC)
TSC-100-DL2	Pyrexia	1	+136	Not related
TSC-100-DL3	Pericardial effusion#	4	+77	Not related
TSC-101-DL1	Acute graft versus host disease in gastrointestinal tract#, acute kidney injury	3	+49	Possibly related
TSC-101-DL1	Adenovirus viremia, Pneumonia, Clostridium difficile infection	2	+71	Not Related
TSC-101-DL1	Pyrexia	1	+148	Not Related
TSC-101-DL1	Interstitial pneumonitis	2	+182	Not Related
TSC-101-sDL2	HHV-6 reactivation	1	+21	Not applicable (pre-TSC)
TSC-101-sDL2	Influenza viremia, pneumonia, pleural effusion	3	+252	Not Related
TSC-101-sDL3	COVID-19, catheter infection	3	+95	Not Related
Control 3	Cytokine release syndrome	2	+2	Not Applicable
Control 4	Neck pain	3	+53	Not Applicable
Control 2	Acute graft versus host disease in skin	3	+49	Not Applicable
Control 2	Acute graft versus host disease in gastrointestinal tract	3	+53	Not Applicable
Control 2	Pneumonia	3	+56	Not Applicable
Control 5	RSV Pneumonia	3	+28	Not Applicable

*Grading by CTCAE v5.0 or MAGIC consortium grading for GvHD or ASTCT grading for CRS
Research testing by flow cytometry or immunohistochemistry for TSC-100/101 markers did not find evidence of involvement

Adverse events of special interest similar between treatment and control arms

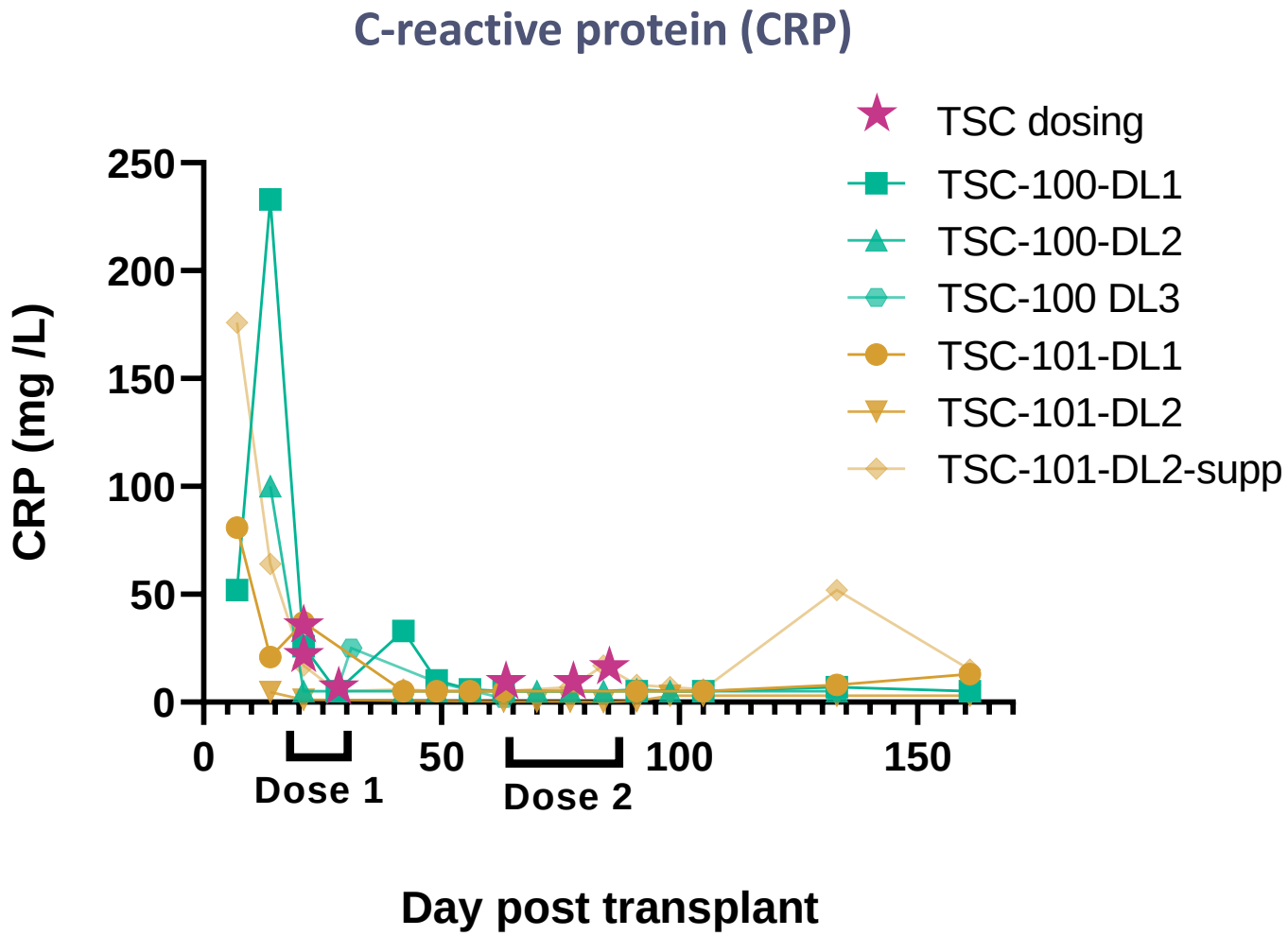
All cytokine release syndrome (CRS) events occurred before TSC-100/ TSC-101 treatment

Arm-Dose Level	Grade*	Adverse Event	HCT Day of Onset	Duration	TSC relatedness
TSC-100-DL2	Grade 1	CRS	+3	2 days	Not applicable (pre-TSC)
TSC-100-DL3	Grade 1	CRS	+3	3 days	Not applicable (pre-TSC)
TSC-101- DL2supp	Grade 2	CRS	+1	3 days	Not applicable (pre-TSC)
TSC-101-DL2	Grade 1	CRS	+1	5 days	Not applicable (pre-TSC)
TSC-101-sDL3	Grade 1	CRS	+1	3 days	Not applicable (pre-TSC)
Control 1	Grade 1	CRS	+2	3 days	Not applicable
Control 2	Grade 1	CRS	+3	2 days	Not applicable
Control 3	Grade 2	CRS	+2	2 days	Not applicable
Control 6	Grade 1	CRS	+1	3 days	Not applicable
TSC-100-DL1	Grade 1	Skin GvHD	+48	8 days	Possibly related
TSC-101-DL1	Grade 3	GI GvHD	+49	8 days	Possibly related
TSC-101-DL2supp	Grade 1	Skin GvHD	+43	3 days	Possibly related
TSC-101-DL2	Grade 1	Skin GvHD	+127	7 days	Possibly related
Control 2	Grade 3	GI GvHD	+53	18 days	Not applicable
Control 2	Grade 3	Skin GvHD	+49	12 days	Not applicable
Control 1	Grade 1	Skin GvHD	+180	pending	Not applicable
Control 3	Grade 1	Skin GvHD	+119	pending	Not applicable

*MAGIC consortium grading for graft-versus host disease (GvHD); ASTCT grading for cytokine release syndrome (CRS)

Lab markers of CRS changed minimally after TSC-100 or TSC-101 administration

No clinical CRS or neurotoxicity reported after TSC-100 or TSC-101 dosing



Summary and next steps

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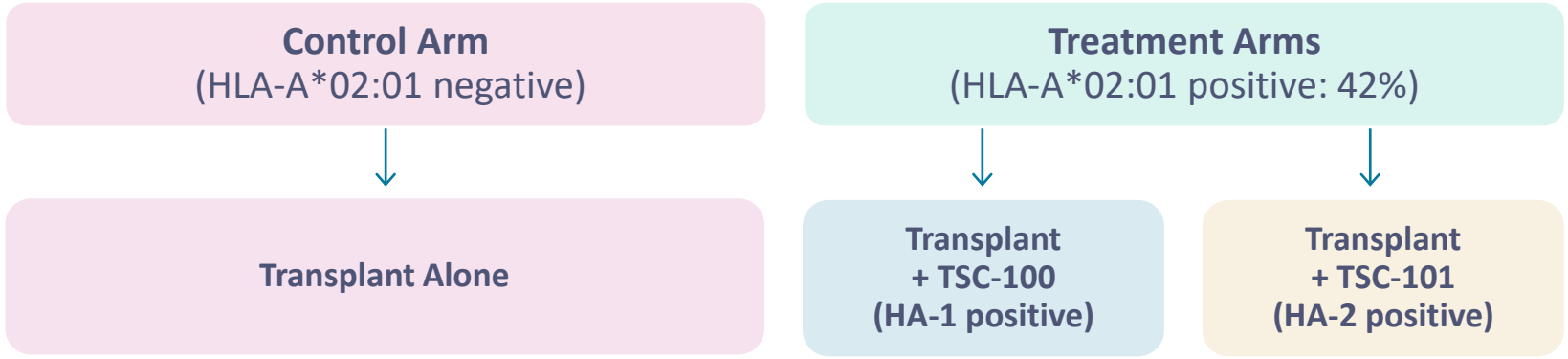
Registrational trial expected to seamlessly transition from Phase 1 design

AML, MDS, ALL undergoing haploidentical donor transplant with reduced intensity conditioning



Endpoints

- **Primary**: relapse-free survival
- **Secondary**: overall survival, complete chimerism rates
- **Exploratory**: MRD rates

Planned regulatory discussions in 2024

- External control data from CIBMTR to reduce sample sizes
- Chimerism data to support early differences of relapse-free survival
- Accelerated approval based on adaptive trial design and sample size re-estimation

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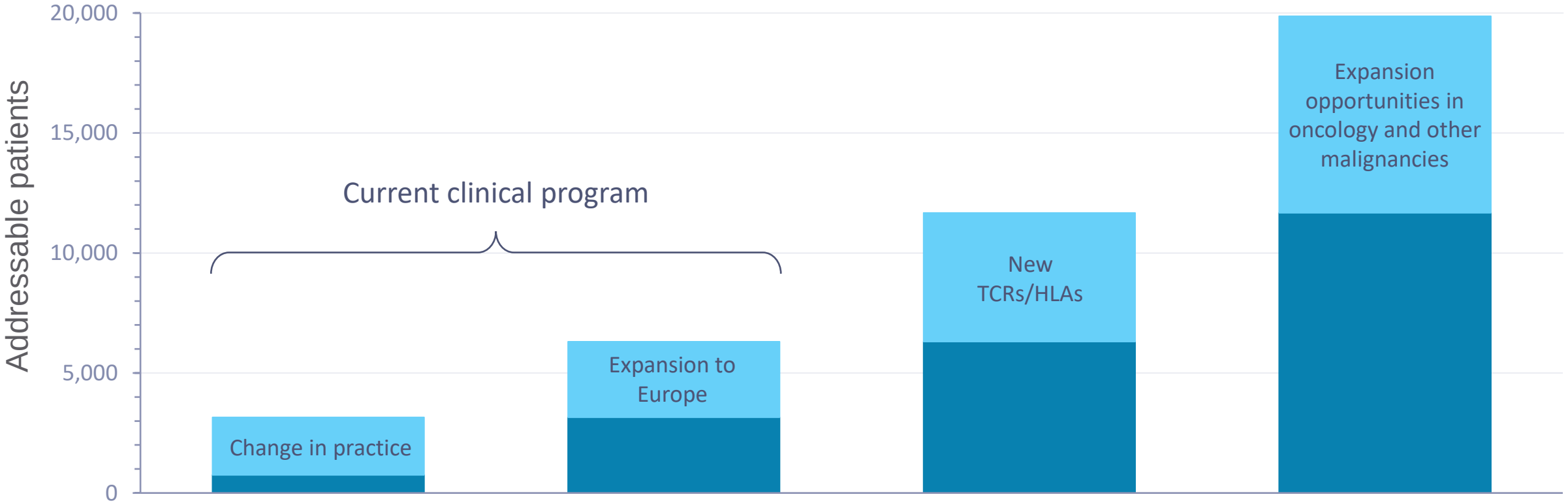
Current program addresses sizable patient population, with several global and lifecycle management opportunities



- Increased adoption of haploidentical donors
- Increased use of more tolerable conditioning

- Increased eligibility of AML, MDS, ALL patients

- Enable transplant for relapsed, refractory heme malignancies
- Use as a conditioning regimen pre-transplant

Source: SEER, CIBMTR, ClearView analysis

TSCAN THERAPEUTICS

Summary

- TSC-100 and TSC-101 were generally well-tolerated, with no DLTs and no significant differences in safety between treatment and control arms observed to date*
- Treatment arms (8 patients) showed complete donor chimerism and no evidence of residual disease at every reading starting 3 weeks after their first dose, associated with favorable prognosis
  - All eight patients had no evidence of relapse after TSC-100/ TSC-101 treatment, with five patients on study for >6 months and a TP53 mutated MDS patient with >1 year follow-up
- Both TSC-100 and TSC-101 reached dose level 3 and continue to enroll at the anticipated recommended phase 2 dose
- Four out of six control-arm patients showed increased mixed donor chimerism, and/or minimal residual disease, associated with unfavorable prognosis
  - 2 patients relapsed and one other required termination of immune suppression due to worsening chimerism, all before day 180
  - 1 TP53 mutated MDS patient died following relapse

*Data as of Jan. 29, 2024

Steady value-generating data flow across clinical programs

Heme Program

- Report updated data at TANDEM ✓
- Open expansion cohorts at RP2D
- Fully enroll clinical study
- One-year data on initial patients
- Launch pivotal study
- Two-year relapse data

Q1 2024 — **Q3 2024** — **YE 2024** — **2025** →

- Dose first patient in clinical study
- Initiate multiplexed dosing
- Initial data for singleplex therapy
- Initial data for multiplexed therapy
- Duration of response data for multiplexed therapy

Solid Tumor Program

TSCAN THERAPEUTICS

Questions and Answers