HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) WITH OMIDUBICEL IS ASSOCIATED WITH ENHANCED CIRCULATORY PLASMACYTOID DENDRITIC CELLS (PDC), NK CELLS AND CD4+ T CELLS WITH LOWER RATES OF SEVERE INFECTION COMPARED TO STANDARD UMBILICAL CORD BLOOD TRANSPLANTATION

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DISCLOSURES

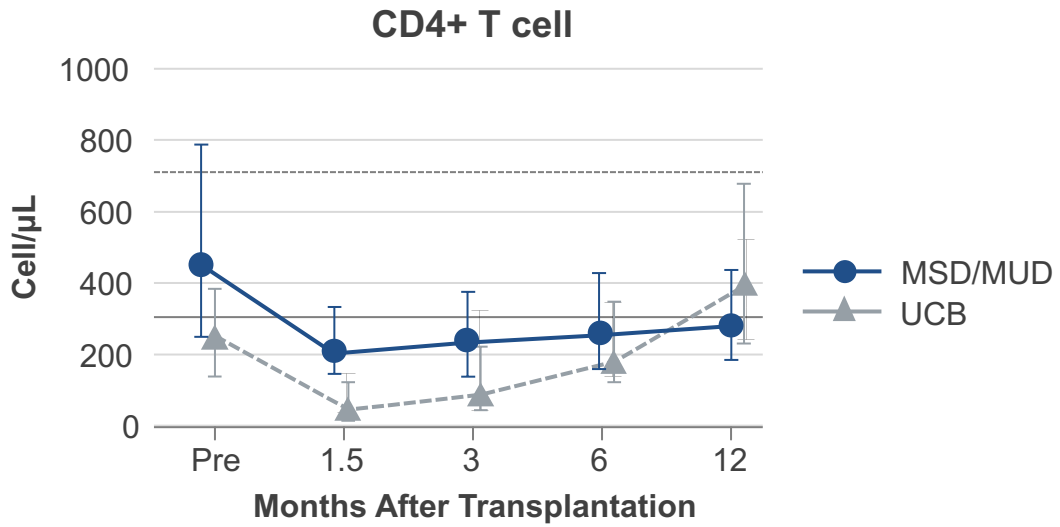
- Forge Therapeutics – Co-inventor/licensee
- Gamida Cell – Consulting, clinical trial participation
- Prevail Therapeutics – Consulting

LIMITATIONS OF CORD BLOOD TRANSPLANTATION

- Delayed hematopoietic recovery
- Delayed immune recovery
- Increased transplant related mortality

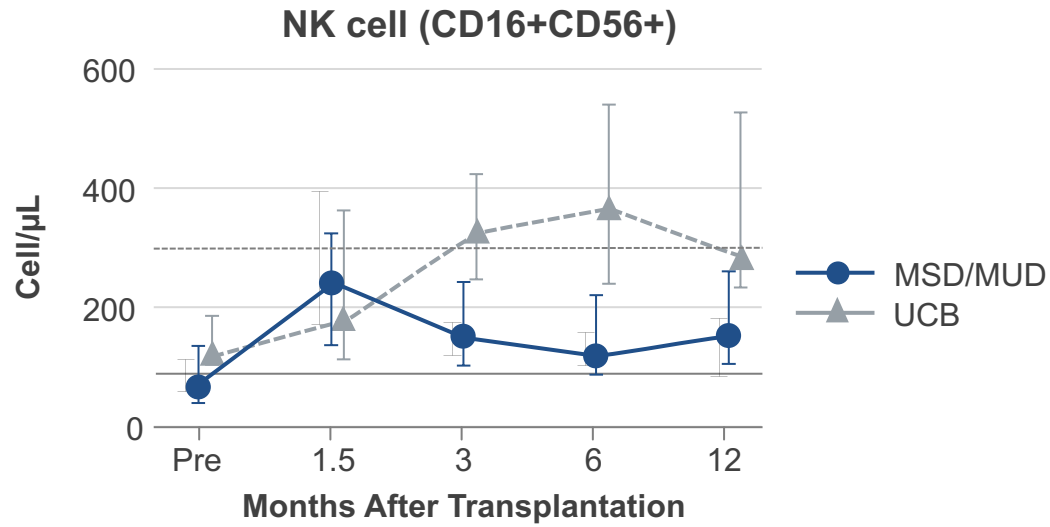
Potential solution: *ex vivo* manipulation of cord blood stem cells (omidubicel)

There is a delay in T cell recovery following cord blood transplants



	Pre	1.5	3	6	12
	P=0.05	*P*<0.01	*P*<0.01	*P*=0.28	*P*=1.00
MSD/MUD	55	58	56	46	33
UCB	27	25	25	24	29

A robust recovery of NK cells is also evident



	Pre	1.5	3	6	12
	P=0.03	*P*=1.00	*P*<0.01	*P*<0.01	*P*<0.01
MSD/MUD	58	60	59	47	33
UCB	26	26	26	24	19

MSD, matched sibling donor; MUD, matched unrelated donor; NK, natural killer; UCB, umbilical cord blood.

Kanda J, et al. *Biol Blood Marrow Transplant* 2012;18:1664-1676.

OMIDUBICEL USING NICOTINAMIDE TECHNOLOGY DELIVERS A SPECTRUM OF CD34+ PROGENITOR CELLS AND IMMUNE CELLS

- Omidubicel is an advanced cell therapy for allogeneic HSCT that uses nicotinamide based proprietary technology to preserve multipotency of progenitor cells and increase cell quantity for transplantation

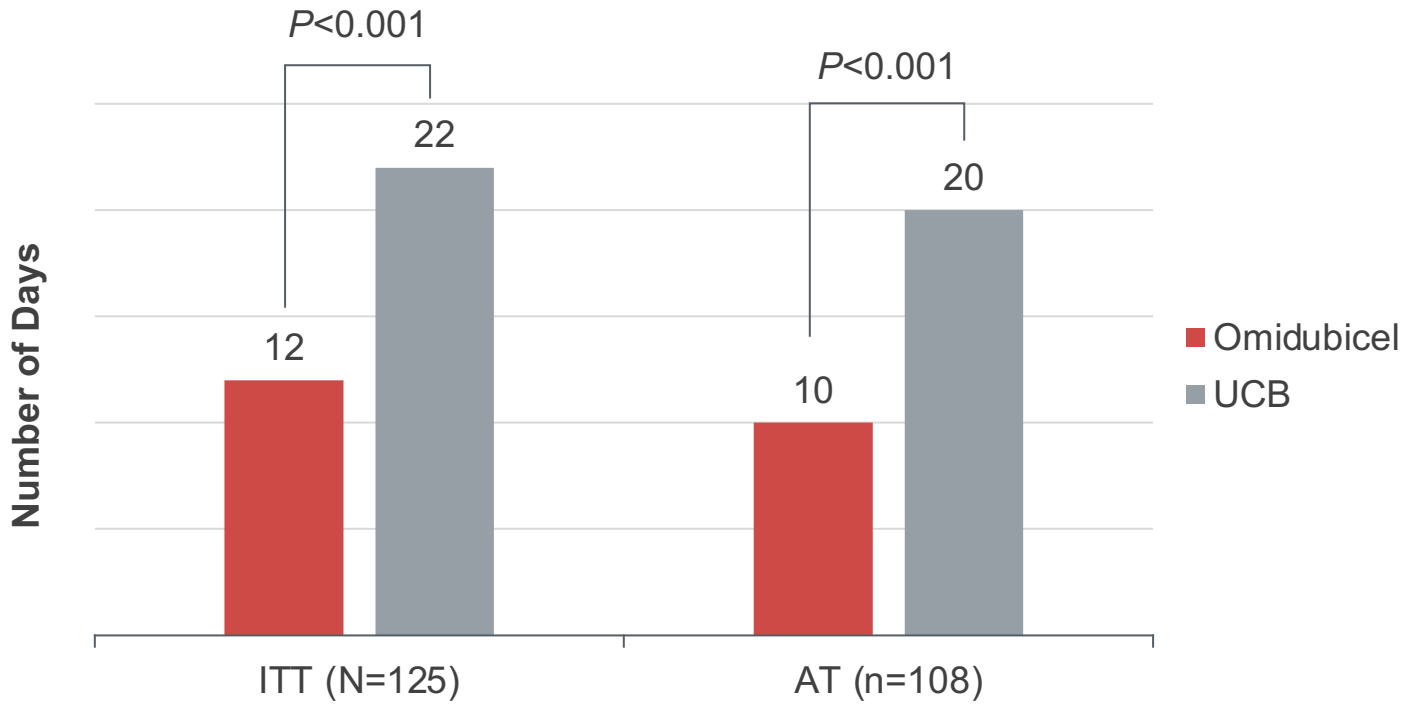
Graft characteristics of omidubicel compared with unmanipulated cord blood

	Omidubicel (n=52)	Unmanipulated UCB (n=56)
Total CD34+ cells/kg, median (range)	9.0×10^6 (2.1–47.6)	0.2×10^6 (0.0–0.08)
Total CD3+ cells/kg, median (range)	3.0×10^6 (1.1–12.4)	5.3×10^6 (1.8–14.8)*

*n=25.
HSCT, hematopoietic stem cell transplantation; UCB, umbilical cord blood.
1. Lodie T, et al. *Blood* 2019;134(supp1):3718. 2. Horwitz ME, et al. *Blood* 2021;138:1429-1440.

TRANSPLANT WITH OMIDUBICEL: SIGNIFICANTLY FASTER TIME TO ENGRAFTMENT

Median Time to Neutrophil Engraftment (1° endpoint)

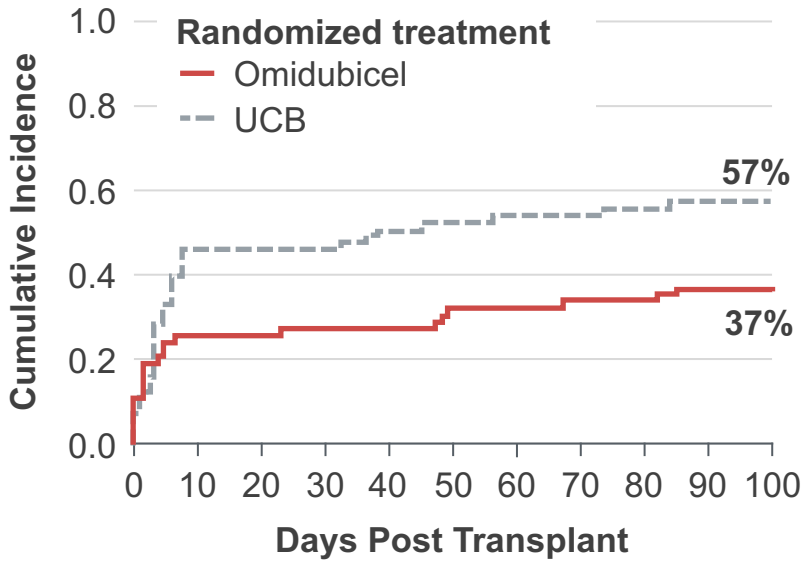


AT, as-treated; ITT, intent-to-treat; UCB, umbilical cord blood.

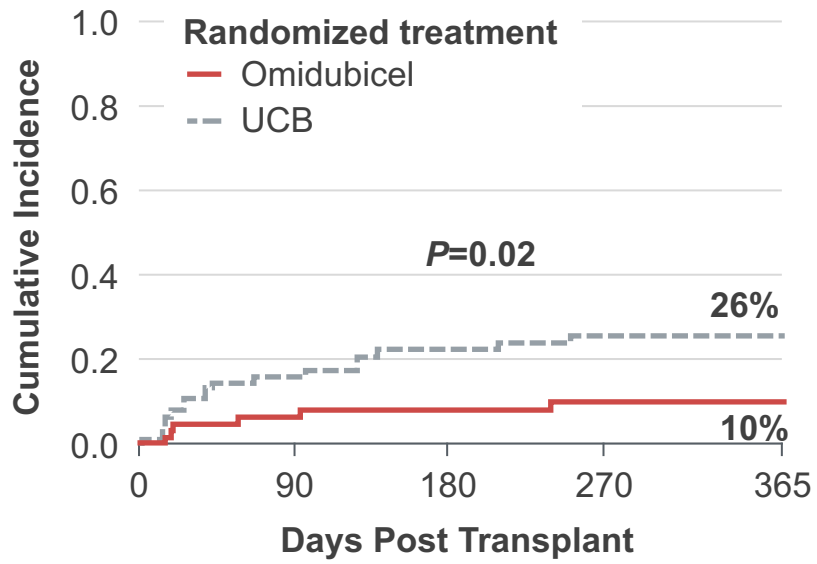
Horwitz ME, et al. *Blood* 2021;138:1429-1440.

TRANSPLANT WITH OMIDUBICEL: REDUCED RISK OF BACTERIAL, FUNGAL, AND VIRAL INFECTIONS

First Grades 2/3 Bacterial or Invasive Fungal Infection*



First Grade 3 Viral Infection*



Rates of acute and chronic GvHD were similar in both groups

*Intent-to-treat population (N=125).
GvHD, graft-versus-host disease; UCB, umbilical cord blood.
Horwitz ME, et al. *Blood* 2021;138:1429-1440.

IMMUNE RECONSTITUTION SUBSTUDY FOLLOWING OMIDUBICEL TRANSPLANTATION

Research questions:

1. Is rapid neutrophil engraftment followed by rapid recovery of other cell lineages?
2. What is driving the reduced risk of infections?

Methods:

- Optional substudy
  - 14 clinical centers participating
- 37 patients
  - 17 omidubicel and 20 UCB
- TCR diversity analysis samples were collected at Screening and Days 100, 180, and 365
- Samples were collected at intervals between Day 7 through Day 365 for the immunophenotyping analysis
- Immunophenotyping and TCR diversity analyses were performed at central laboratories

TCR, T cell receptor; UCB, umbilical cord blood.

BASELINE PATIENT AND GRAFT CHARACTERISTICS

	Omidubicel (n=17)	UCB (n=20)
Median age (range), years	30 (13–62)	43 (19–55)
Male, n (%)	10 (59)	12 (60)
Primary diagnosis, n (%)		
Acute leukemia (ALL, AML)	14 (82)	18 (90)
Other (CML, MDS, lymphoma)	3 (18)	2 (10)
Disease risk, n (%)		
Medium – high/very high	12 (70)	15 (75)
Myeloablative conditioning, n (%)		
TBI-based	8 (47)	14 (70)
CMV status, n (%)		
Positive	10 (59)	13 (65)
CD3+ cell dose/kg, × 10^6	1.8 (1.2–7.6)	6.0 (1.7–10.2)*

*n=9.

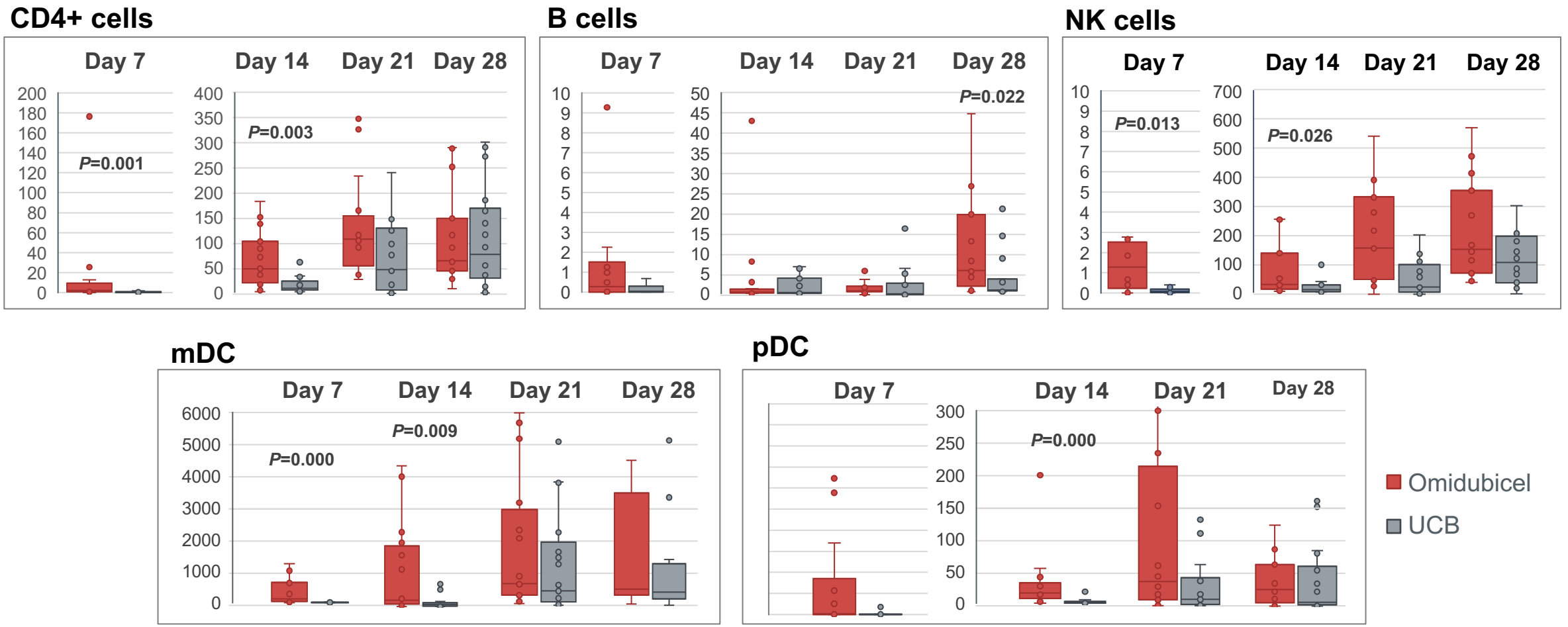
ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; CMV, cytomegalovirus; MDS, myelodysplastic syndrome; TBI, total body irradiation; UCB, umbilical cord blood.

PATIENT OUTCOMES

	Omidubicel (n=17)	UCB (n=20)	*P*-value
Median time to neutrophil engraftment (range), days	10 (6–28)	18.5 (14–40)	<0.001
Patients with >95% chimerism, n (%) Day 21/28 Day 100	 17 (100) 16 (100)*	 20 (100) 18 (100)†	 – –
Grade 2/3 infections over 365 days, n (%) Bacterial infections Viral infections	 7 (41) 1 (6)	 14 (70) 9 (45)	 0.037 0.010
Patients with steroid use in first month, n (%)	3 (18)	5 (25)	–
Median (range) number of days of steroid use in first month	13 (11–20)	13 (3–16)	–

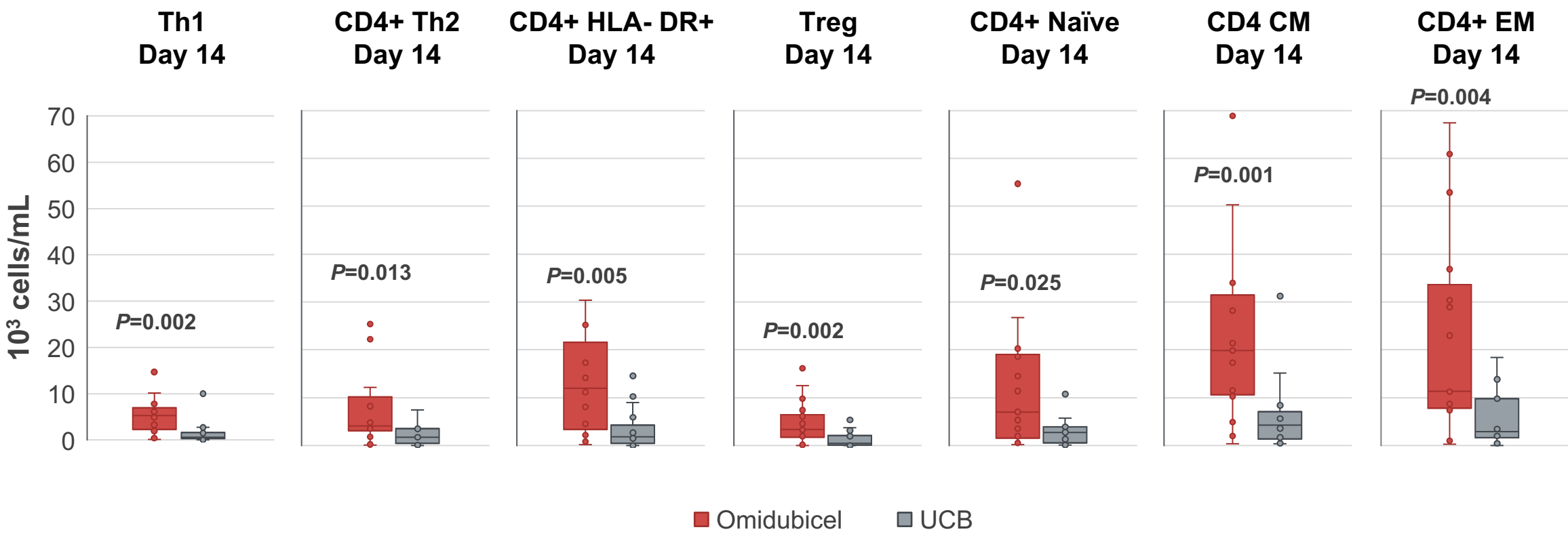
*n=16. †n=18.
UCB, umbilical cord blood.

ROBUST EARLY RECOVERY OBSERVED FOR T CELL, B CELL, NK CELL, AND DENDRITIC CELL SUBSETS (DAY 0 TO DAY 28)



mDC, myeloid dendritic cell; NK, natural killer; pDC, plasmacytoid dendritic cell; UCB, umbilical cord blood.

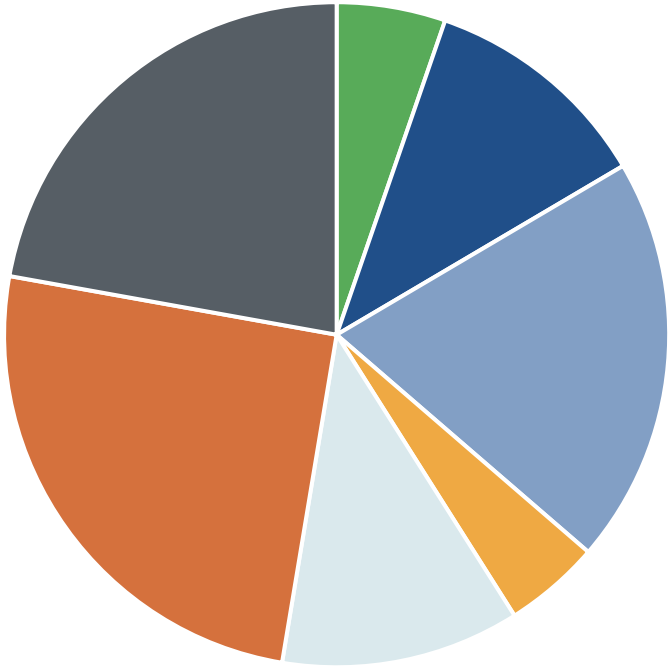
DESPITE A LOWER T CELL INPUT, CD4+ SUBSETS AT 2 WEEKS ARE HIGHER IN PATIENTS WHO RECEIVED OMIDUBICEL

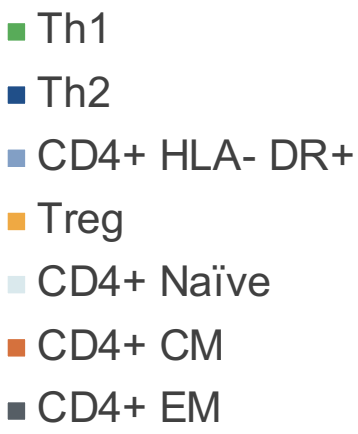


CM, central memory cells; EM, effector memory cells; HLA, human leukocyte antigen; Th, T helper cells; Treg, T regulatory cells; UCB, umbilical cord blood.

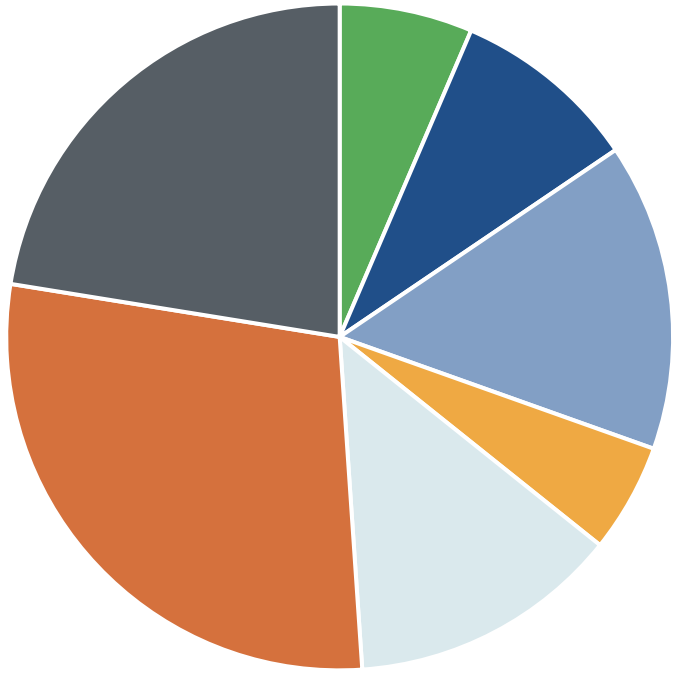
THE PROPORTIONAL RECOVERY OF DIFFERENT CD4+ SUBSETS IS COMPARABLE

CD4+ Subgroups Day 14 – OMIDUBICEL



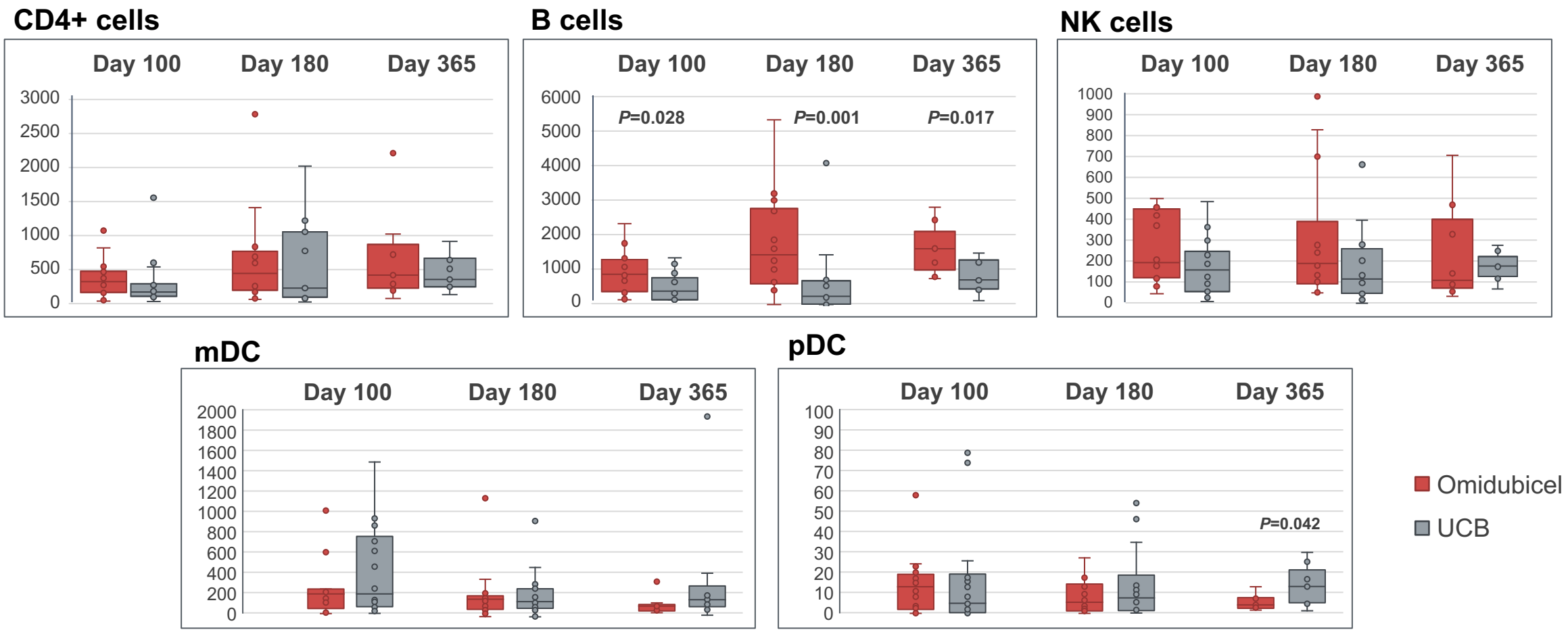


CD4+ Subgroups Day 14 – UCB



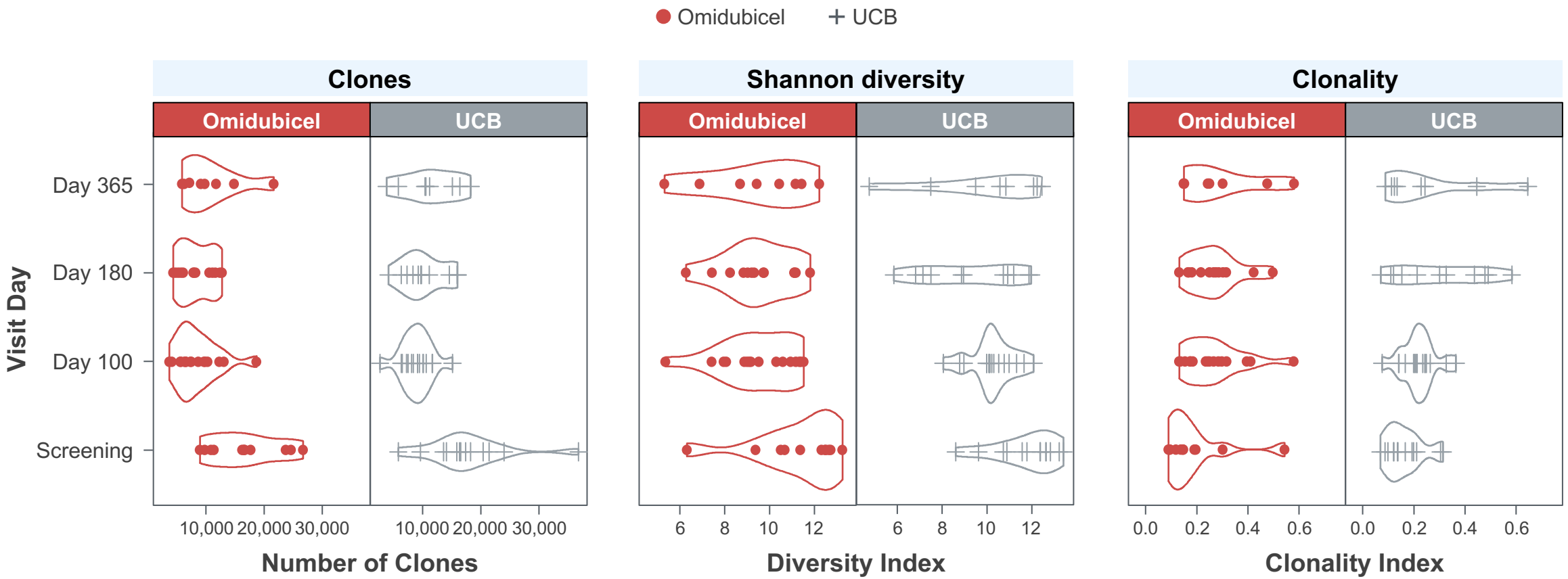
CM, central memory cells; EM, effector memory cells; HLA, human leukocyte antigen; Th, T helper cells; Treg, T regulatory cells; UCB, umbilical cord blood.

DURABILITY OF RECOVERY OBSERVED FOR UP TO 1 YEAR POST-TRANSPLANT (DAY 100 TO DAY 365)



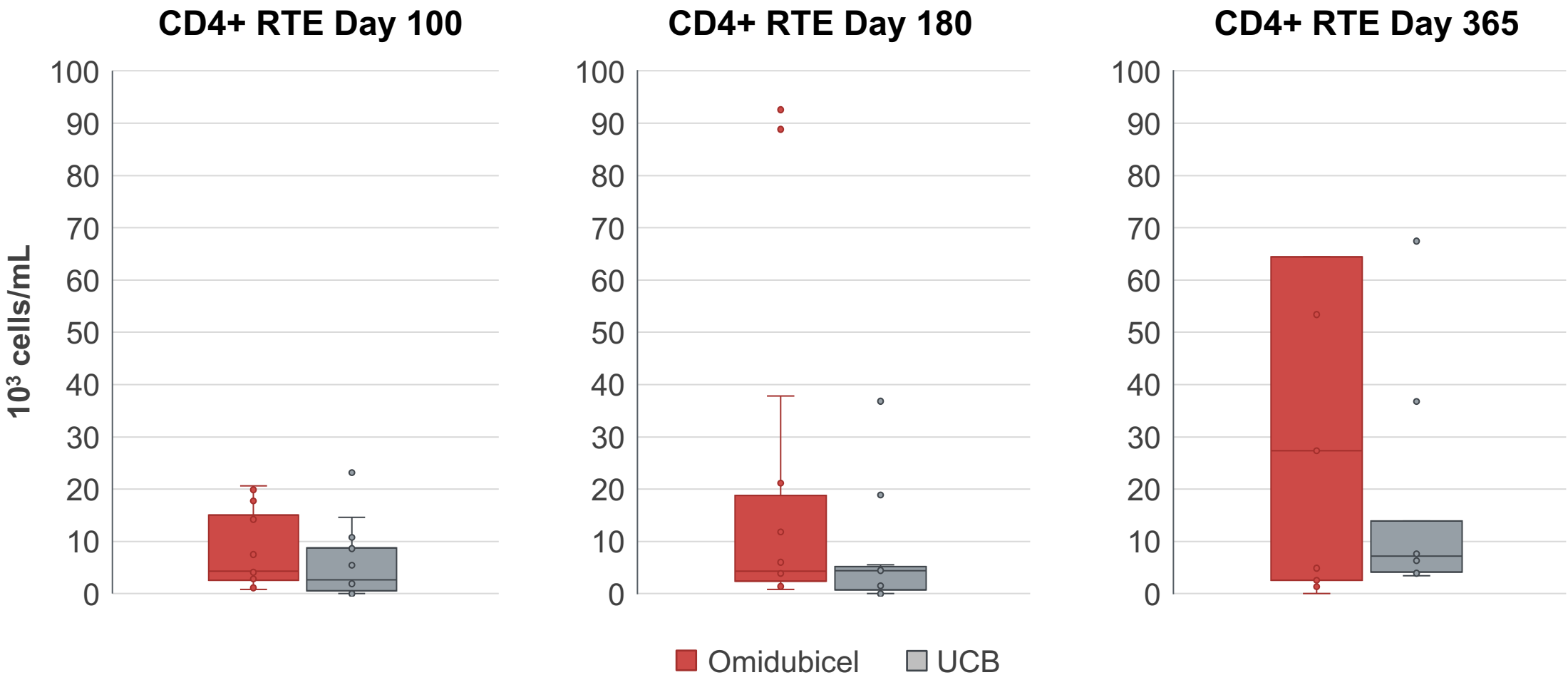
mDC, myeloid dendritic cell; NK, natural killer; pDC, plasmacytoid dendritic cell; UCB, umbilical cord blood.

OMIDUBICEL SUPPORTS A COMPARABLE TCR REPERTOIRE DIVERSITY AND THYMIC T CELL OUTPUT POST-TRANSPLANTATION



All *P* values in the comparison are insignificant (*P*>0.05, range: 0.17-0.93).
TCR, T cell receptor; UCB, umbilical cord blood.

CD4+ RECENT THYMIC EMIGRANTS (RTE) DEMONSTRATE RECOVERY BY ONE YEAR



CD4+ subset / CD4+, CD31, CD45RA subset.
RTE, recent thymic emigrant; UCB, umbilical cord blood.

CONCLUSIONS

HSCT with omidubicel results in rapid hematopoietic recovery, reduced rates of infections, and no increase in GvHD rates compared with standard UCB

In the omidubicel group, enhanced recovery of circulatory mDC, pDC, NK cell, and CD4+ T cells within the first 28 days and sustained B-cell recovery from Day 28 onwards were observed

- The faster immune recovery with omidubicel:
  - occurred despite a lower number of T cells (CD3+) infused
  - was sustained throughout the first year post transplant

These additional analyses of CD4+ subsets, TCR repertoire diversity, and RTE support the long-term durability and functionality of the omidubicel graft

These results provide potential mechanistic support for the lower rates of severe infection observed in patients treated with omidubicel

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