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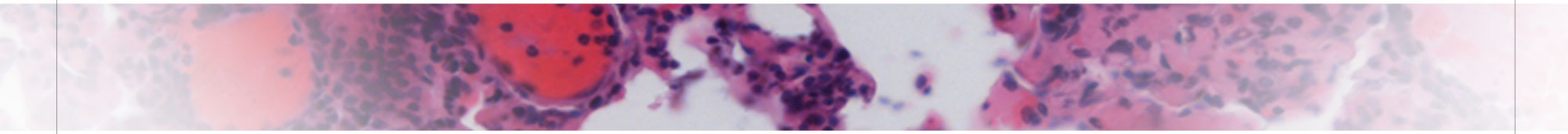

Hematopoietic Stem Cell Transplantation (HSCT) With Omidubicel Is Associated With Robust Immune Reconstitution and Lower Rates of Severe Infection Compared to Standard Umbilical Cord Blood Transplantation

Paul Szabolcs, MD[1], Stuart Levy, MPH[2], Dima Yackoubov, MSc[2], Aviad Pato, PhD[2], Einat Galamidi-Cohen, MD, MSc[2], and Mitchell E. Horwitz, MD[3]

[1]Division of Blood and Marrow Transplantation and Cellular Therapy, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA; [2]Gamida Cell, Jerusalem, Israel; [3]Division of Hematologic Malignancies and Cellular Therapy, Duke University Medical Center, Durham, NC

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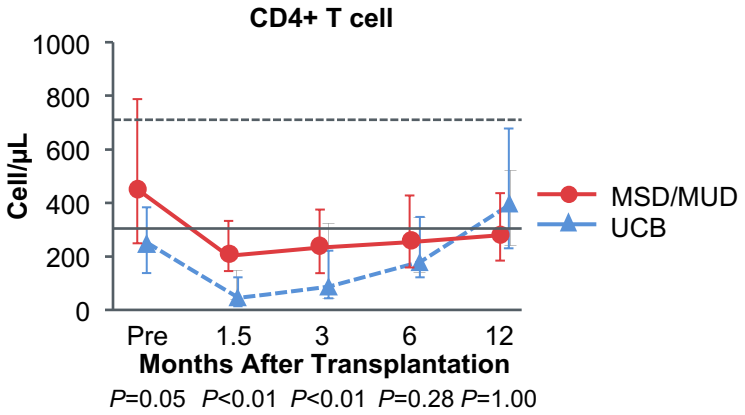
Limitations of Cord Blood Transplantation

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

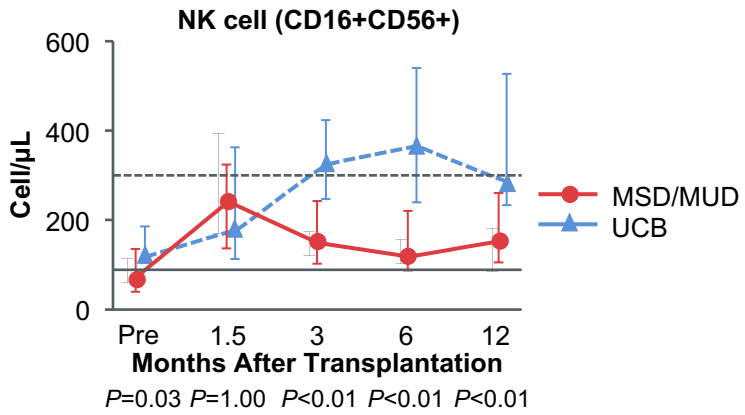
Potential solution: *ex vivo* manipulation of cord blood stem cells (omidubicel)

Historical data show that 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

However, a robust recovery of NK cells is 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 Full Complement of CD34+ Progenitors Cells and Immune Cells

- Using nicotinamide-based proprietary technology to expand UCB CD34+ cells preserves the multipotency of progenitor cells for long-term repopulation, while increasing cell quantity for transplantation
- Omidubicel is an advanced cell therapy for allogeneic HSCT that preserves stem cell function to optimize homing, engraftment, and differentiation

Graft characteristics of omidubicel compared with unmanipulated cord blood

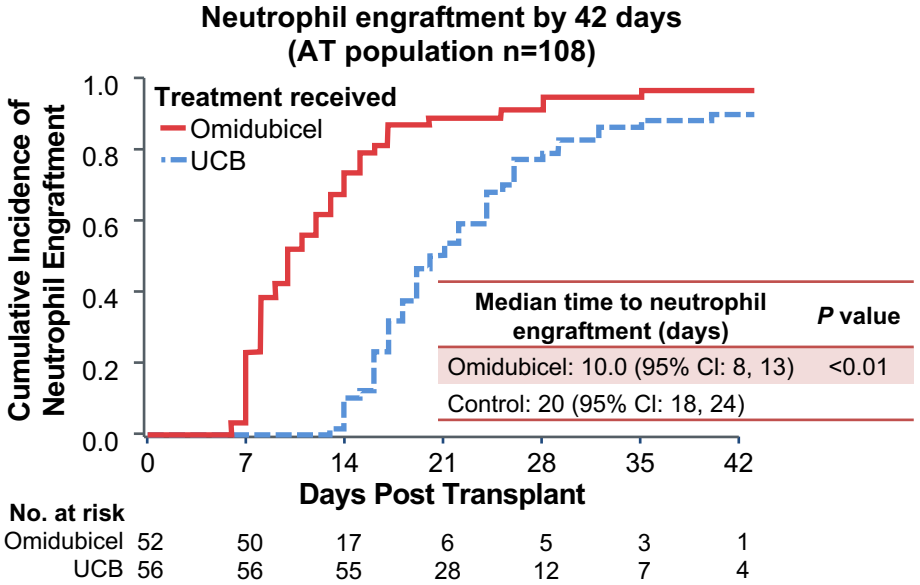
	Omidubicel (n=52)	Unmanipulated UCB (n=56)
Total CD34+ cells/kg, median (range)	9.0×10^6 (2.1–47.6)	0.2×10^6 (0.0–0.08)
Total CD3+ cells/kg, median (range)	3.0×10^6 (1.1–12.4)	4.6×10^6 (0.0–14.8)*

*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

Completed global phase III trial (n=125); 108 patients with hematologic malignancies treated with omidubicel vs standard UCB transplantation following myeloablative conditioning and with no serotherapy

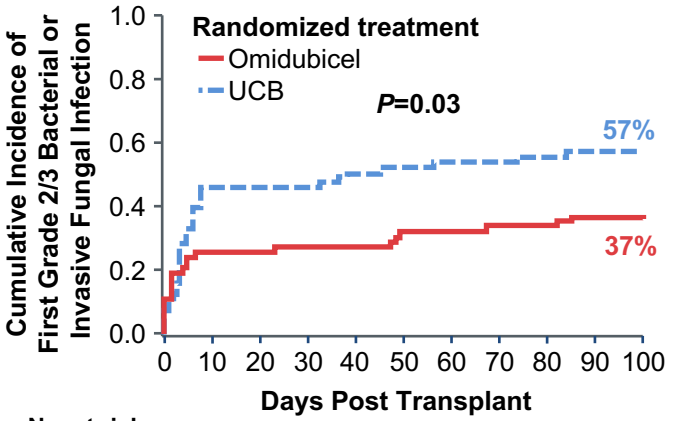
Faster neutrophil engraftment by 42 days (AT population, n=108)



AT, as-treated; CI, confidence interval; UCB, umbilical cord blood.
Horwitz ME, et al. *Blood* 2021;138:1429-1440.

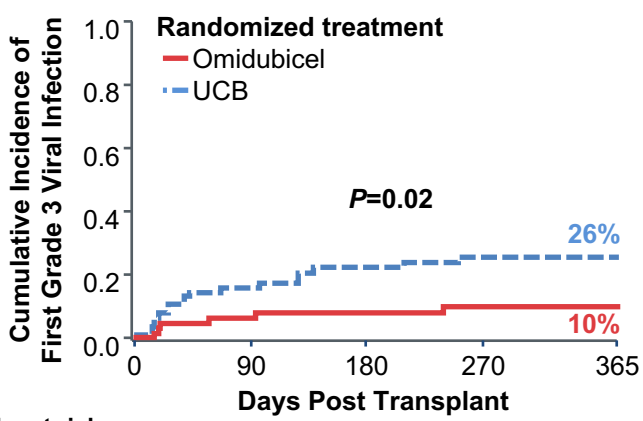
Transplant With Omidubicel: Reduced Risk of Bacterial, Fungal, and Viral Infections

Incidence of first grade 2/3 bacterial or invasive fungal infections (ITT; N=125)



No. at risk											
Omidubicel	62	46	46	45	43	42	39	38	37	35	33
UCB	63	34	34	34	30	29	27	27	26	25	25

Incidence of first grade 3 viral infection (ITT; N=125)



No. at risk					
Omidubicel	62	55	46	36	28
UCB	63	48	36	27	19

Rates of acute and chronic GvHD were similar in both groups

GvHD, graft-versus-host disease; ITT, intent-to-treat; 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 participating clinical centers
- 37 patients
  - 17 omidubicel and 20 UCB
- Samples collected at intervals from Day 7 through Day 365
- Immunophenotyping analysis at central laboratory
- T-cell (CD4+, CD8+), NK cells, B-cell, monocyte, and DC subsets
- Summary statistics by treatment and *P*-values based on Wilcoxon rank-sum test (without multiplicity adjustment)

DC, dendritic cell; NK, natural killer; UCB, umbilical cord blood.

Substudy: 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)*

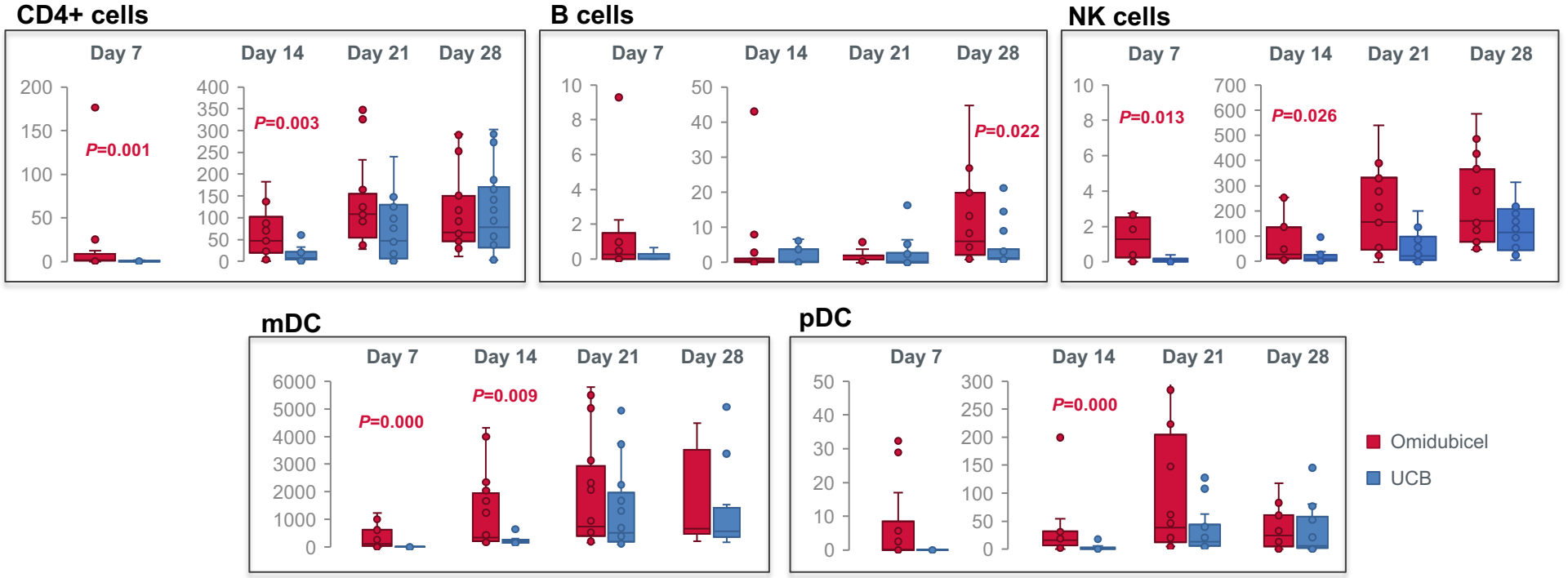
*n=9.
ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; CMV, cytomegalovirus; MDS, myelodysplastic syndrome; TBI, total body irradiation; UCB, umbilical cord blood.

Substudy: 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
Grade 2/3 infections over 365 days, n (%)			
Bacterial Infections	7 (41)	14 (70)	=0.037
Viral Infections	1 (6)	9 (45)	=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)	–

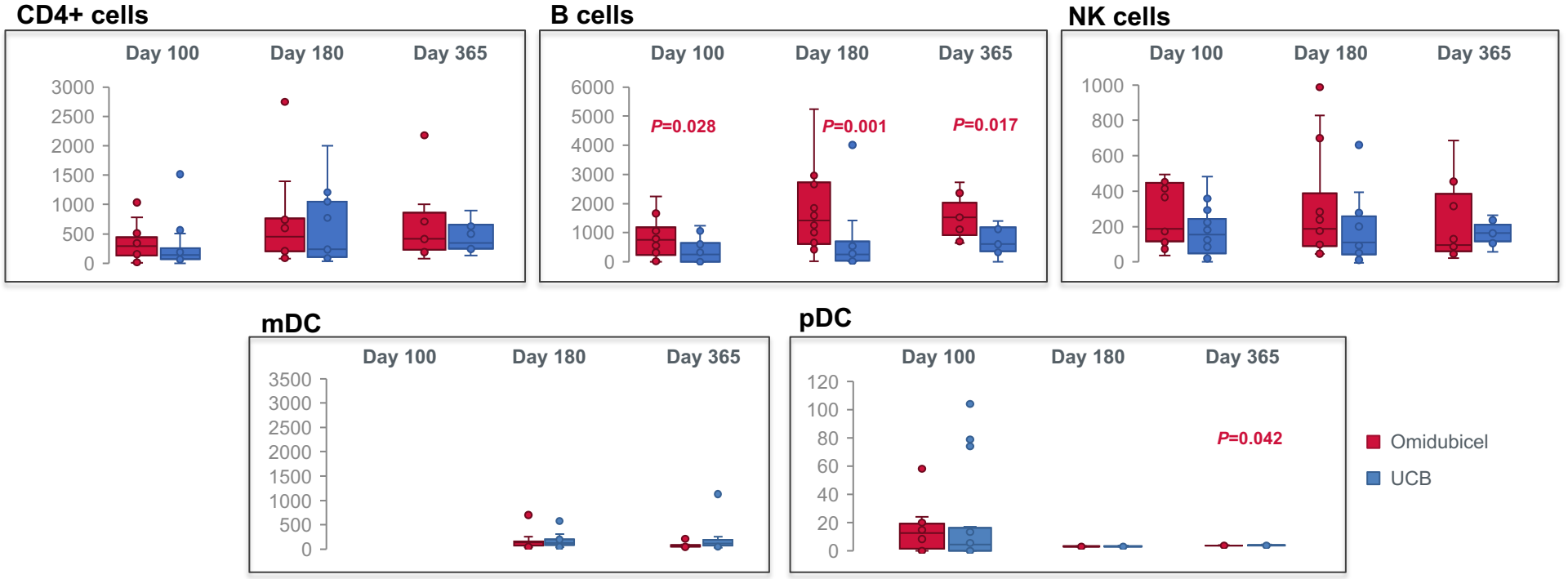
UCB, umbilical cord blood.

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.

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.

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 immediate post-transplant period (up to Day 28), immune cell recovery was significantly faster with omidubicel compared with standard UCB transplantation despite receiving a lower number of T cells at transplant
- Enhanced recovery of circulatory mDC, pDC, NK, and CD4+ T cells within the first 28 days, and sustained B-cell recovery from Day 28 through the first year were observed
- Additional analysis on thymic reconstitution is ongoing
- These results demonstrate rapid and functional reconstitution of T and B cell subsets following transplant with omidubicel, which provides mechanistic support for the lower rates of severe infection observed in the omidubicel-treated patients

GvHD, graft versus host disease; HSCT, hematopoietic stem cell transplantation; mDC, myeloid dendritic cell; NK, natural killer; pDC, plasmacytoid dendritic cell; UCB, umbilical cord blood.