MULTICENTER LONG-TERM FOLLOW-UP OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION WITH OMIDUBICEL: A POOLED ANALYSIS OF FIVE PROSPECTIVE CLINICAL TRIALS

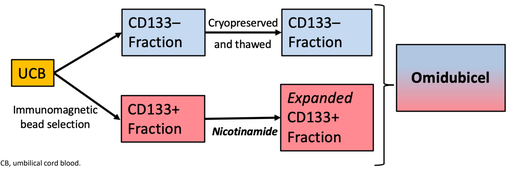
CT-314

Chenyu Lin, MD[1], Aurelie Schwarzbach, MSc[2], Pau Montesinos, MD, PhD[3], Patrick Stiff, MD[4], Suhag Parikh, MD[1], Claudio Brunstein, MD, PhD[5], Corey Cutler, MD[6], Caroline A. Lindemans, MD, PhD[7], Rabi Hanna, MD[8], Liang Piu Koh, MBBS[9], Madan H. Jagasia, MBBS[10], David Valcarcel, MD, PhD[11], Richard T. Maziarz, MD[12], Amy K. Keating, MD[13], William Y.K. Hwang, MBBS[14], Andrew R. Rezvani, MD[15], Nicole A. Karras, MD[16], Juliana F. Fernandes, MD[17], Vanderson Rocha, MD, PhD[17], Isabell S. Badell, MD, PhD[18], Ron Ram, MD[19], Gary J. Shiller, MD[20], Leonid Volodin, MBBS[21], Mark Walters, MD[22], Nelson Hamerschlak, MD, PhD[23], Daniela Cilloni, MD, PhD[24], Olga Frankfurt, MD[25], Joel A. Brochstein, MD[26], Joseph P. McGuirk, DO[27], Joanne Kurtzberg, MD[1], Guillermo Sanz, MD[3], Ronit Simantov, MD[2], Mitchell E. Horwitz, MD[1]

[1]Duke University, USA; [2]Gamida Cell Ltd, Israel; [3]Hospital Universitari I Politecnic La Fe, Spain, [4]Loyola University, USA, [5]University of Minnesota, USA, [6]Dana Farber Cancer Institute, USA, [7]University Medical Center Utrecht, Netherlands, [8]Cleveland Clinic, USA, [9]National University Cancer Institute, Singapore, [10]Vanderbilt University, USA, [11]University Hospital Vall d'Hebron, Spain, [12]Oregon Health and Science University, USA, [13]Children's Hospital Colorado, USA, [14]Singapore General Hospital, Singapore, [15]Stanford University, USA, [16]City of Hope, USA, [17]Universidade de Sao Paulo, Brazil, [18]Hospital de la Santa Creu, Spain, [19]Tel Aviv Sourasky Medical Center, Israel, [20]University of California Los Angeles, USA, [21]University of Virginia, USA, [22]University of California San Francisco, USA, [23]Hospital Israelita Albert Einstein, Brazil, [24]University of Turin, Italy, [25]Northwestern University, USA, [26]Cohen Children's Medical Center, USA, [27]University of Kansas, USA

INTRODUCTION

- Umbilical cord blood (UCB) is an important source of stem cells in hematopoietic cell transplantation (HCT), but it is often limited by low cell dose[1]
- **Omidubicel** is an *ex vivo* expanded stem cell graft derived from UCB, which has demonstrated faster engraftment, fewer infections, and shorter durations of hospitalization in a recent multicenter phase III trial[2]
- While omidubicel has demonstrated early benefits, its long-term outcomes are still unknown



UCB, umbilical cord blood.

METHODS

- Multi-institutional pooled analysis of long-term outcomes of omidubicel transplantation from 5 prospective clinical trials[2-5]
- **Inclusion criteria:** All patients with hematologic malignancies or sickle cell hemoglobinopathy who had undergone HCT with omidubicel between 2010 and 2020 as part of 5 clinical trials
- **Exclusion criteria:** Full engraftment with an unmanipulated UCB (if received a double cord with omidubicel + an unmanipulated UCB)

RESULTS

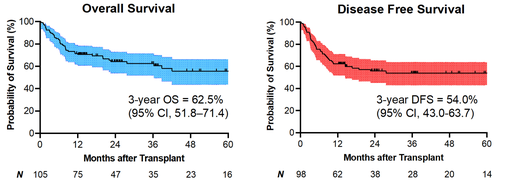
- 116 patients across 26 academic transplant centers worldwide underwent omidubicel transplantation, either as a standalone unit (n=92) or together with an unmanipulated UCB (n=24)
- 11 patients were excluded after engrafting fully with an unmanipulated UCB, leaving **105 patients** in the study:
  - 97 (93%) patients engrafted fully with omidubicel
  - 2 (2%) had mixed chimerism between omidubicel and UCB
  - 5 (5%) had primary graft failure
  - 1 patient was unevaluable for engraftment
- All patients received myeloablative conditioning regimens and standard graft versus host disease (GVHD) prophylaxis with a calcineurin inhibitor and mycophenolate mofetil
- Median follow-up of 22 months (range, 0.3–122.5) overall and 35.7 months (range, 11.7–122.5) among survivors

TABLE 1: Baseline Characteristics by Clinical Trial

	NCT01221857 (N=9)	NCT01816230 (N=36)	NCT02730299 (N=52)	NCT01590628 (N=7)	NCT02504619 (N=1)	Total (N=105)
Phase	I	I / II	III	I	I / II	
Disease type, N (%)						
AML	4 (44%)	17 (47%)	22 (42%)	0	0	43 (41%)
ALL	1 (11%)	9 (25%)	18 (35%)	0	0	28 (27%)
MDS	2 (22%)	6 (17%)	5 (10%)	0	0	13 (12%)
Sickle cell disease	0	0	0	7 (100%)	1 (100%)	8 (8%)
Other	2 (22%)	4 (11%)	7 (13%)	0	0	13 (12%)
Disease Risk Index, N (%)						
Low/Moderate	6 (67%)	22 (61%)	34 (65%)	0	0	62 (59%)
High/Very high	2 (22%)	12 (33%)	18 (35%)	0	0	32 (30%)
Unknown/Unevaluable	1 (11%)	2 (6%)	0	7 (100%)	1 (100%)	11 (10%)
Transplantation strategy, N (%)						
Double cord	9 (100%)	0	0	4 (57%)	0	13 (12%)
Single cord	0	36 (100%)	52 (100%)	3 (43%)	1 (100%)	92 (88%)
Engraftment outcome, N (%)						
Omidubicel	7 (78%)	33 (92%)	50 (96%)	6 (86%)	1 (100%)	97 (92%)
Mixed chimerism	1 (11%)	0	0	1 (14%)	0	2 (2%)
Primary graft failure	1 (11%)	2 (6%)	2 (4%)	0	0	5 (5%)
Unevaluable	0	1 (3%)	0	0	0	1 (1%)
Male Sex, N (%)	4 (44%)	20 (56%)	27 (52%)	3 (43%)	1 (100%)	55 (52%)
Non-White or Hispanic, N (%)	3 (33%)	7 (19%)	23 (44%)	7 (100%)	1 (100%)	41 (39%)
Median age at transplant, N (range)	45 (21–61)	44 (13–62)	40 (13–62)	14 (8–16)	2	42 (2–62)
Karnofsky PS ≥ 80%, N (%)	9 (100%)	35 (97%)	51 (98%)	6 (86%)	1 (100%)	102 (97%)

ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; PS, performance status.

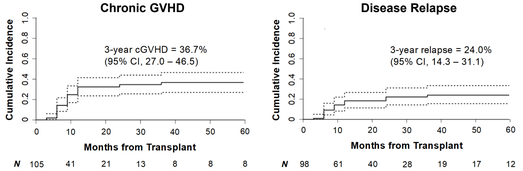
FIGURE 1: Survival Analysis



The most common causes of death were disease relapse (n=16), infection (n=11), and acute GVHD (n=6).

CI, confidence interval; DFS, disease free survival; OS, overall survival.

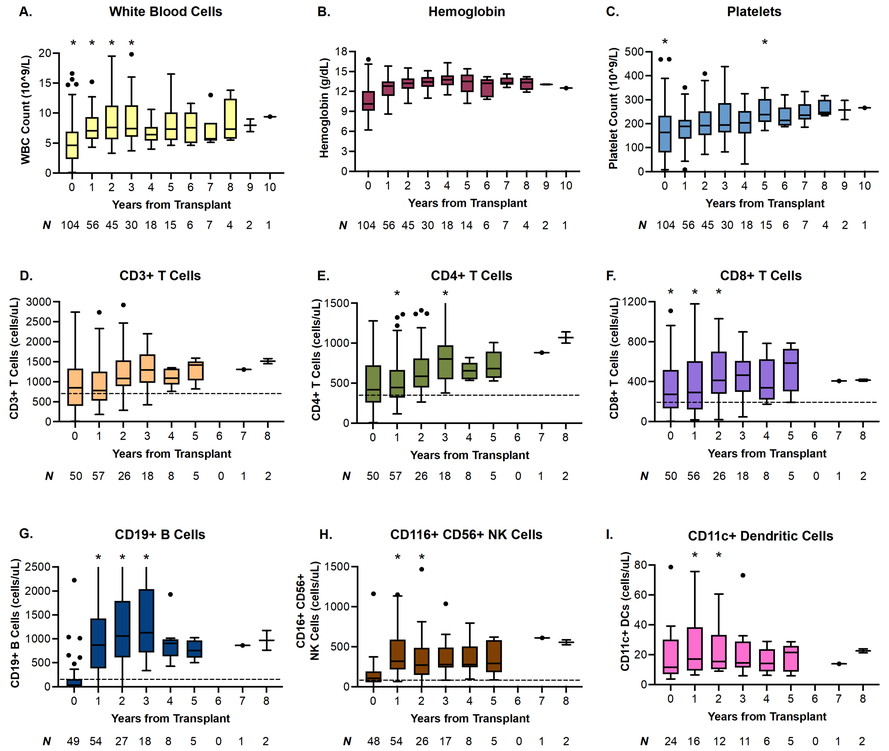
FIGURE 2: Chronic GVHD and Cancer Relapse



Most chronic GVHD cases were mild (54%), with 33% and 13% having moderate and severe disease, respectively. No deaths were primarily attributed to chronic GVHD.

cGVHD, chronic graft versus host disease; CI, confidence interval; GVHD, graft versus host disease.

FIGURE 3: Long-term Hematopoiesis and Immune Competence



NK, natural killer; WBC, white blood cell.

Figure 3. Tukey box plots showing trends in hematopoiesis (**3A-3C**) and immune competence (**3D-3I**) over extended follow-up. Omidubicel provided durable trilineage hematopoiesis at up to 10 years of follow-up. Similarly, serial quantitative assessments of lymphoid subsets demonstrated that median counts of CD3+, CD4+, and CD8+ T cells, as well as CD19+ B cells, CD16+CD56+ NK cells, and CD11c+ dendritic cells remained within the normal range at up to 8 years. The dotted lines indicate the lower limit of normal for the respective lymphoid subset. Asterisk * indicate that outliers exist beyond the range of the figure.

Notably, while 5 patients (5%) experienced secondary graft failure within the first year, no late graft failures occurred beyond what had already been reported in the primary analyses. Three of these patients received a second rescue allogeneic transplant, while 1 patient with sickle cell disease received only an autologous stem cell infusion. Two of the 5 patients remained alive at last follow-up.

TABLE 2: Secondary Hematologic Malignancies

Transplant	Patient	AE	Time	Clinical Outcome
Single cord [omidubicel]	Adult M, AML	dd-MDS	40 months post-tx	Haplo transplant at 46 months, in CR
Single cord [UCB]*	Ped F, B-ALL	dd-AML	35 months post-tx	Passed away from dd-AML
Single cord [omidubicel]	Adult F, T-ALL	PTLD, DLBCL	17 months post-tx	Passed away from PTLD
Single cord [omidubicel]	Adult M, T-ALL	PTLD, DLBCL	20 months post-tx	Treated with rituximab/RT, in CR

AE, adverse event; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CR, complete response; dd, donor-derived; DLBCL, diffuse large B cell lymphoma; F, female; M, male; MDS, myelodysplastic syndrome; PTLD, post-transplant lymphoproliferative disorder; RT, radiation therapy; tx, treatment; UCB, umbilical cord blood.

Table 2. One patient (1%) with AML who received omidubicel developed a donor-derived MDS at 40 months post-transplant, requiring a rescue haploidentical transplant. Interestingly, a patient with ALL who received only an unmanipulated UCB also developed donor-derived AML at 35 months. Donor cell origins were confirmed by sex mismatch in both cases. *This second patient was enrolled in the control arm of the phase III study (NCT02730299) and was therefore not included in this study cohort, but is reported here for comparison.

CONCLUSIONS

- In addition to the known early benefits, omidubicel demonstrated long-term graft durability, with preserved trilineage hematopoiesis and immune competence at up to 10 years of follow-up
- No late cases of secondary graft failure were observed, beyond the 5 patients reported in the primary analysis
- One case (1%) of a donor-derived MDS was observed in a patient who received omidubicel. This incidence is consistent with previous reports of donor-derived myeloid neoplasms after cord blood transplants (0.6–2%).[6-7] A case of donor-derived AML was also observed in the phase III control arm

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