ALLOGENEIC STEM CELL TRANSPLANTATION WITH OMIDUBICEL: LONG-TERM FOLLOW-UP FROM A SINGLE CENTER

#1827

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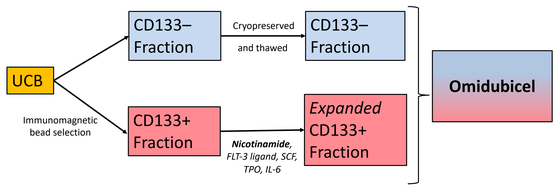
INTRODUCTION

- Umbilical cord blood (UCB) is an important source of stem cells in hematopoietic cell transplantation (HCT), especially for non-White patients underrepresented in marrow registries, but it is afflicted by delayed hematopoietic recovery and immune reconstitution
- **Omidubicel** is a hematopoietic stem cell graft derived from umbilical cord blood, composed of an *ex vivo* nicotinamide-expanded CD133+ stem cell fraction and a non-expanded CD133– T-cell-containing fraction[1,2]



FLT3, fms-like tyrosine kinase 3; IL-6, interleukin 6; SCF, stem cell factor; TPO, thrombopoietin

- Omidubicel was the first *ex vivo* expanded stem cell graft to be transplanted as a single, standalone graft following myeloablative conditioning[3]
- Prospective trials have established omidubicel's short-term safety and improvements in early hematopoietic recovery, but long-term outcomes of hematopoiesis and graft durability have not been well described[3,4]

METHODS

- Single institution retrospective study
- **Inclusion criteria:** All patients with hematologic malignancies who had undergone HCT and engrafted with omidubicel between Nov 2010 and Jan 2020
- **Exclusion criteria:** Primary graft failure or full engraftment with an unmanipulated cord unit
- R 4.1.0 was used to perform Kaplan-Meier and competing risk analyses via Gray's method

RESULTS

- 26 patients received omidubicel: 3 engrafted with an unmanipulated graft while 1 had primary graft failure, leaving 22 evaluable patients
- Median follow-up of 2.3 years (range, 0.1–10 years)
- 11 patients have died due to disease relapse (64%), acute graft-versus-host disease (GvHD) (27%), and infection (9%)
- One patient had secondary graft failure requiring a rescue haploidentical transplant on day 202
- No incidences of secondary hematologic malignancies were reported, although clonal hematopoiesis was not specifically evaluated in the post-transplant period

TABLE 1: Baseline Characteristics

	Omidubicel, *N* = 22
Male sex (%)	8 (36)
Median age (range)	48 years (18–62)
Median weight (range)	88.9 kg (49.6–130.5)
Non-White race (%)	8 (36)
Disease type (%)	
AML	8 (36)
MDS	7 (32)
ALL	4 (18)
CML, HL, TCL	1 (5), 1 (5), 1 (5)
Disease risk (%)	
High risk	5 (23)
Intermediate risk	13 (59)
Low risk	3 (14)
Unevaluable	1 (5)
Conditioning regimen (%)	
TBI / Flu	8 (36)
TBI / Flu / Cy	6 (27)
TBI / Flu / Thio	8 (36)
Graft(s) received (%)	
Standalone omidubicel graft	15 (68)
Double cord*	7 (32)
Engraftment of double cords* (%), *N* = 7	
Full engraftment of omidubicel	4 of 7 (57)
Chimeric CD3, omidubicel in CD15 and whole blood	2 of 7 (29)
Chimerism in all fractions	1 of 7 (14)

Table 1. **In the phase I trial, patients received a double cord transplant with omidubicel and an unmanipulated cord unit.[2] ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; TCL, T-cell leukemia; HL, Hodgkin lymphoma; MDS, myelodysplastic syndrome; Cy, cyclophosphamide; Flu, fludarabine; TBI, total body irradiation; Thio, thiotepa.*

FIGURE 1: Survival Analysis

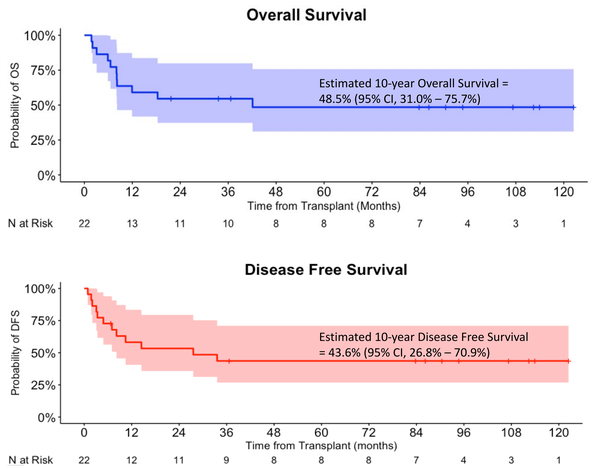


Fig 1. *Kaplan-Meier survival analysis. There is a plateau of the survival curves after 4 years, suggesting good graft durability and prolonged survival for a subset of patients. The shaded areas depict the 95% confidence interval (CI); DFS, disease-free survival; OS, overall survival.*

FIGURE 2: Long-term Hematopoiesis

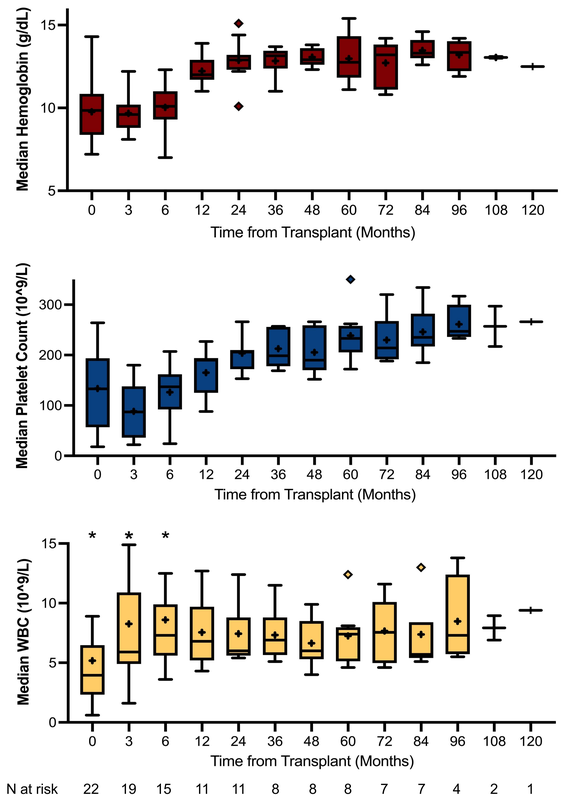


Fig 2. *Tukey boxplots demonstrate durable trilineage hematopoiesis at up to 10 years of follow-up. + indicates mean value. * indicates additional outliers not shown.*

FIGURE 3: Immune Reconstitution

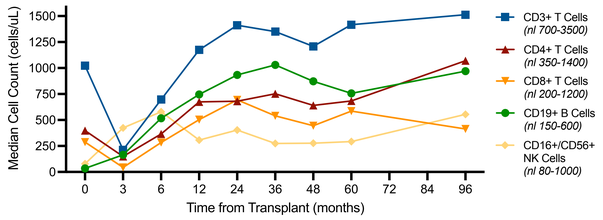


Fig 3. *Serial quantitative assessments showed recovery of lymphocyte subsets. Median levels of lymphocyte subsets reached normal ranges starting at ~6 months post-transplant and maintained stability at up to 8 years of follow-up. NK, natural killer.*

FIGURE 4: Chronic GvHD and Relapse

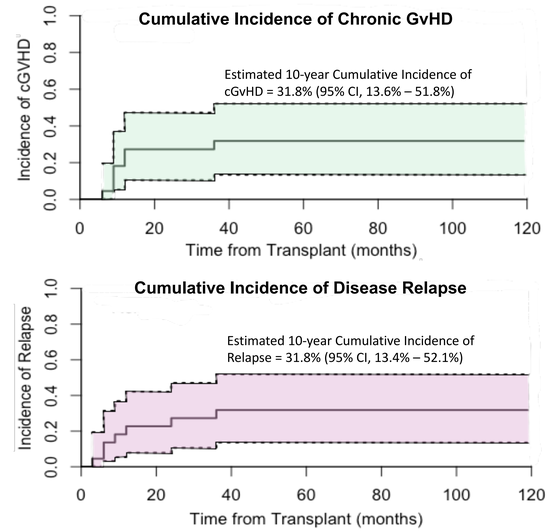


Fig 4. *Competing risk analysis of cumulative incidence of chronic GvHD (cGvHD) and disease relapse. Shaded regions indicate 95% CI. Max grades of cGvHD were 2 (mild), 4 (moderate), and 1 (severe). Only 2 of the 7 patients with cGvHD still required systemic immunosuppression at last follow-up.*

CONCLUSIONS

- Omidubicel is a safe and reliable stem cell source that can provide long-term sustainable hematopoiesis and immune competence at follow-up periods of 10 years
- Despite historical concerns that *ex vivo* expansion may compromise the integrity of long-term repopulating HSCs, there was only one case of secondary graft failure in this cohort and no secondary malignancies were observed
- All but one case of cGvHD was mild or moderate disease and no deaths were attributed to cGvHD

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ACKNOWLEDGEMENTS

This research was supported by Gamida Cell Ltd and the Duke Cancer Institute. Author CL is supported by the Duke Hematology & Transfusion Med T32 training grant (NIH/NHLBI HL007057-46).