CLINICAL OUTCOMES FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT) WITH OMIDUBICEL OR OTHER DONOR SOURCES IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES: COMPARISON OF CLINICAL TRIAL RESULTS TO CENTER FOR INTERNATIONAL BLOOD AND MARROW TRANSPLANT RESEARCH (CIBMTR) DATABASE CONTROLS

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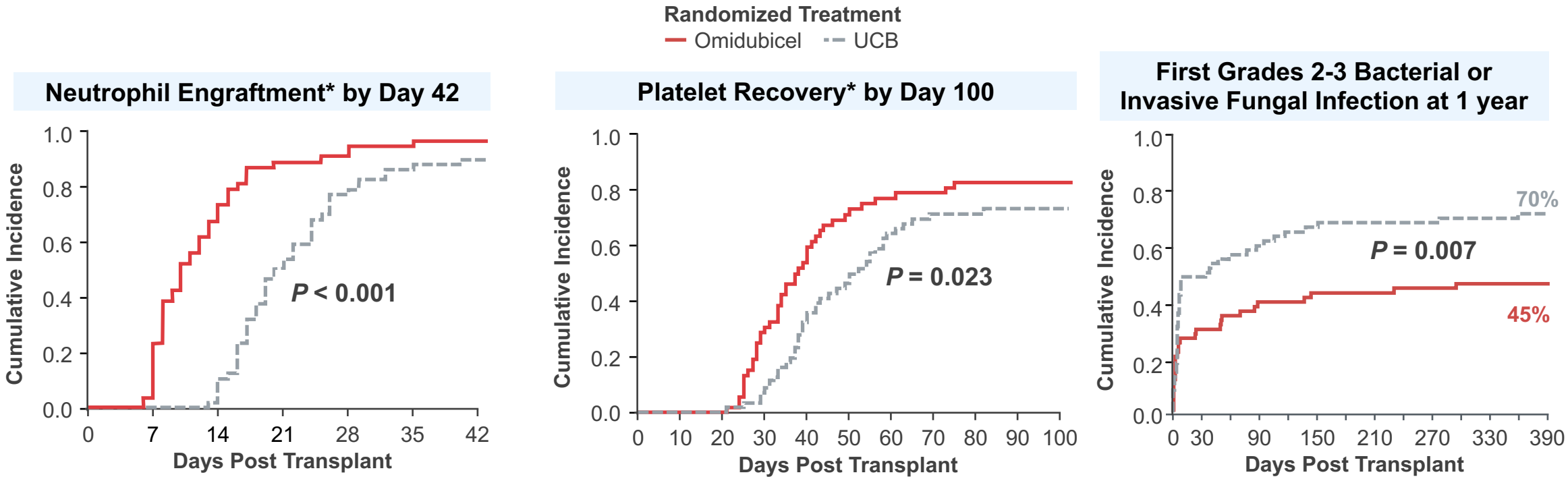
BACKGROUND

- In a global randomized Phase 3 trial, omidubicel, an investigational advanced cell therapy donor source for allogeneic HCT in patients with hematologic malignancies, has demonstrated significantly accelerated time to engraftment, reduced risk of infections and shortened hospital stays vs transplantation with UCB



Median time to neutrophil engraftment*	*P*-value
Omidubicel: 10 (95% CI: 8-13) days	<0.001
UCB: 20 (95% CI: 18-24) days	

Median time to platelet engraftment*	*P* value
Omidubicel: 37 (95% CI: 33-42) days	0.023
UCB: 50 (95% CI: 42-58) days	

*The time to engraftment of neutrophils ≥500 cells/μL and platelets ≥20 000/μL was defined according to CIBMTR standards, requiring donor chimerism for neutrophil engraftment.
CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; HCT, hematopoietic cell transplantation; UCB, umbilical cord blood.
Horwitz ME, et al. *Blood*. 2021;138:1429-1440.

OBJECTIVE

- Comparative efficacy of omidubicel vs. other donor sources (MUD, MMUD, Haplo) used in clinical practice is unknown
  - CIBMTR registry data can provide valuable evidence in the absence of head-to-head clinical trial data
- The objective of this study was to compare outcomes of patients in the phase 3 omidubicel trial to outcomes in selected patients reported to CIBMTR
- Outcomes studied included:
  - Neutrophil and platelet engraftment
  - Overall survival (OS)
  - Disease free survival (DFS)
  - Non-relapse mortality (NRM)
  - Disease relapse
  - Acute GvHD grades II-IV, acute GvHD grades III-IV
  - Chronic GvHD

CIBMTR, Center for International Blood and Marrow Transplant Research; GvHD, graft-versus-host disease; Haplo, haploidentical donor; MMUD, mismatched unrelated donor; MUD, matched unrelated donor.

METHODS: PATIENT INCLUSION AND EXCLUSION CRITERIA

- **CIBMTR cohort selection criteria were harmonized with the omidubicel trial**
  - Key inclusion/exclusion criteria from the trial were applied to the CIBMTR cohort
    - First allo-HCT in the US between January 1, 2017, and December 31, 2019
    - Age at transplant 12-65 years
    - AML/ALL/other leukemia (in CR), CML, MDS, or lymphoma
      - Exclude AML t(8:21), inv(16), or t(16:16)
    - Karnofsky/Lansky performance score ≥ 70
    - Myeloablative conditioning regimen
- **Donor sources included from omidubicel clinical trial**
  - Per protocol ‘as-treated’ population from omidubicel and UCB arms
- **Donor sources included from CIBMTR database**
  - 8/8 matched unrelated donor (MUD)
  - 7/8 matched unrelated donor (MMUD)
  - Haploidentical donor (Haplo) with post transplant cyclophosphamide based GvHD prophylaxis

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; CML, chronic myeloid leukemia; CR, complete remission; GvHD, graft-versus-host disease; Haplo, haploidentical donor; HCT, hematopoietic cell transplantation; MDS, myelodysplastic syndrome; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

METHODS: STATISTICAL ANALYSES

- The following baseline characteristics were included in all adjusted analyses:
  - Age
  - Sex
  - Weight
  - Race
  - Primary diagnosis
  - Karnofsky/Lansky performance score
  - Hematopoietic cell transplant-comorbidity index (HCT-CI)
  - Disease risk index (DRI)*
  - Year of transplant
  - Conditioning regimen
- Kaplan-Meier analyses and Cox proportional hazard models were used for OS and DFS
- Cumulative incidence functions (CIF) and Fine-Gray analyses were used for neutrophil and platelet engraftment, non-relapse mortality, disease relapse, and GvHD outcomes

*For omidubicel trial groups, DRI is based on the refined DRI described by Armand et al. (2014).[1] For patients with rare disease types not classified by Armand et al., disease risk was assigned by the site investigator. For CIBMTR groups, we recalculated DRI to harmonize disease category definitions between the trial and CIBMTR data as much as possible.
CIBMTR, Center for International Blood and Marrow Transplant Research; DFS, disease-free survival; GvHD, graft-versus-host disease; OS, overall survival.
1. Armand et al. *Blood* 2014;123:3664-3671.

RESULTS : BASELINE CHARACTERISTICS

	Omidubicel (N=52)	MUD (N=450)	MMUD (N=65)	Haplo (N=328)	UCB (N=56)	*P* value
Age at transplant (years), mean ± SD	38.9 ± 16.0	45.8 ± 13.8	42.9 ± 15.2	40.0 ± 15.3	35.6 ± 15.1	**< 0.001**
Male, n (%)	27 (51.9)	268 (59.6)	32 (49.2)	186 (56.7)	35 (62.5)	
Caucasian, n (%)	31 (59.6)	367 (81.6)	33 (50.8)	195 (59.4)	29 (51.8)	**< 0.001**
Disease n (%)						**< 0.01**
AML	22 (42.3)	158 (35.1)	25 (38.5)	116 (35.4)	27 (48.2)	
ALL	18 (34.6)	118 (26.2)	24 (36.9)	99 (30.2)	19 (33.9)	
MDS	5 (9.6)	118 (26.2)	8 (12.3)	58 (17.7)	3 (5.4)	
CML	4 (7.7)	16 (3.6)	4 (6.2)	18 (5.5)	2 (3.6)	
Lymphoma	2 (3.9)	37 (8.2)	3 (4.6)	34 (10.4)	3 (5.4)	
Other	1 (1.9)	3 (0.7)	1 (1.5)	3 (0.9)	2 (3.6)	

- Compared with CIBMTR patients, patients from omidubicel trial were significantly
  - Younger when they received transplant
  - More likely to have AML than other malignancies
- Race distribution differs significantly across donor sources
  - More Caucasian patients in the MUD arm

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; CML, chronic myeloid leukemia; Haplo, haploidentical donor; MDS, myelodysplastic syndrome; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; SD, standard deviation; UCB, umbilical cord blood.

RESULTS : BASELINE CHARACTERISTICS (CONT'D)

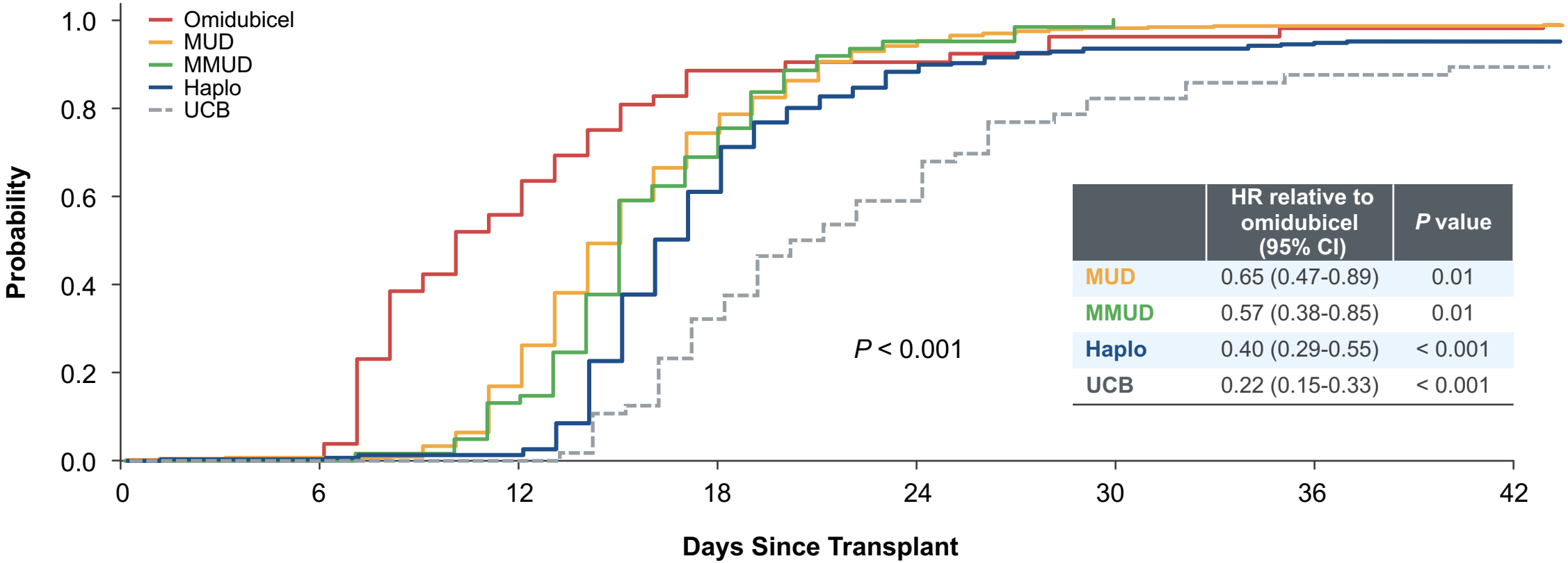
	Omidubicel (N=52)	MUD (N=450)	MMUD (N=65)	Haplo (N=328)	UCB (N=56)	*P* value
Karnofsky/Lansky PS <90, n (%)	12 (23.1)	170 (37.8)	24 (36.9)	131 (39.9)	14 (25.0)	
HCT-CI ≥3, n (%)	27 (51.9)	201 (44.7)	29 (44.6)	137 (41.8)	28 (50.0)	
Body weight (kg), mean ± SD	78.0 ± 21.2	85.7 ± 22.3	79.9 ± 25.1	85.9 ± 23.5	77.5 ± 19.6	**< 0.01**
TBI used in conditioning regimen, n (%)	27 (51.9)	131 (29.1)	27 (41.5)	183 (55.8)	28 (50.0)	**< 0.001**
Year of transplant						**< 0.001**
2017	5 (9.6)	206 (45.8)	35 (53.8)	113 (34.4)	4 (7.1)	
2018	14 (26.9)	157 (34.9)	22 (33.8)	109 (33.2)	19 (33.9)	
2019/2020	33 (63.5)	87 (19.3)	8 (12.3)	106 (32.3)	33 (58.9)	

- PS and HCT-CI are relatively similar across arms
- There are differences across donor sources in body weight, use of TBI in conditioning regimen, and year of transplant

Haplo, haploidentical donor; HCT-CI, hematopoietic cell transplant-comorbidity index; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; PS, performance score; SD, standard deviation; TBI, total body irradiation; UCB, umbilical cord blood.

RESULTS: NEUTROPHIL ENGRAFTMENT

- Omidubicel was associated with faster rates of neutrophil engraftment compared with other donor sources after adjusting for baseline variables

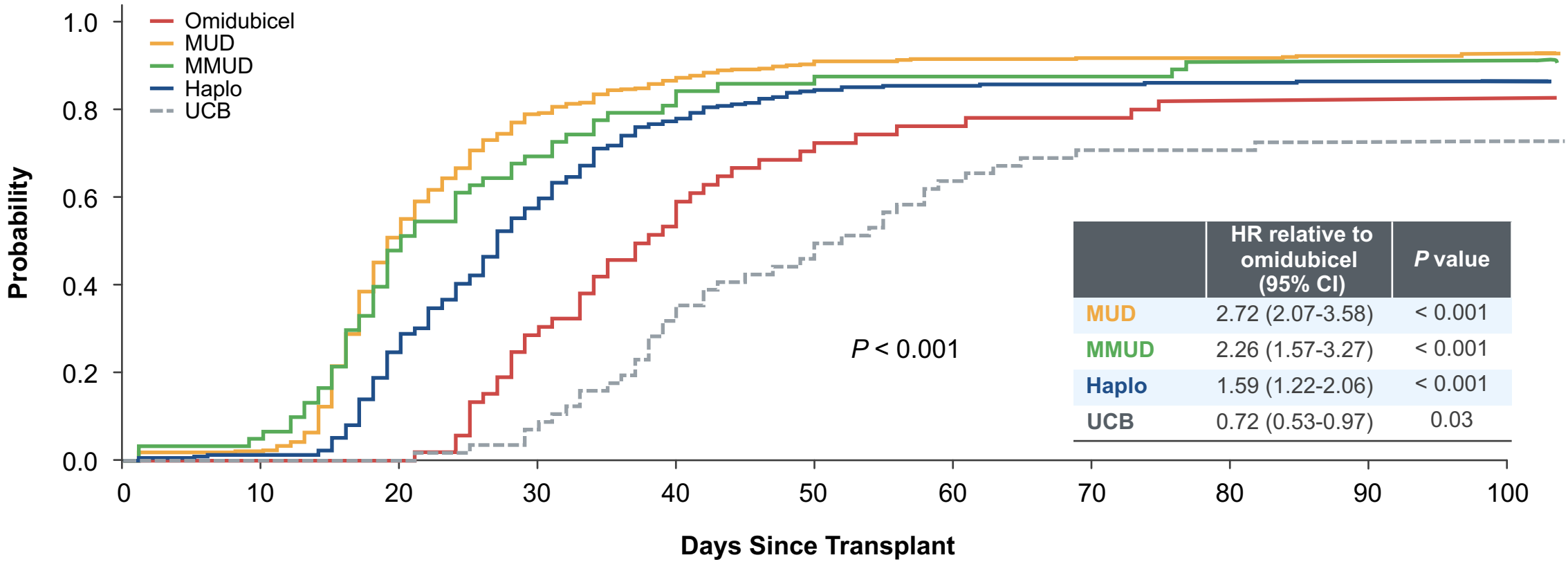


	HR relative to omidubicel (95% CI)	*P* value
MUD	0.65 (0.47-0.89)	0.01
MMUD	0.57 (0.38-0.85)	0.01
Haplo	0.40 (0.29-0.55)	< 0.001
UCB	0.22 (0.15-0.33)	< 0.001

The cumulative incidence function plots for neutrophil engraftment are unadjusted for baseline variables. CI, confidence interval; Haplo, haploidentical donor; HR, hazard ratio; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

RESULTS: PLATELET ENGRAFTMENT

- Omidubicel was associated with a slower rate of platelet engraftment compared with other donor sources except UCB after adjusting for baseline variables



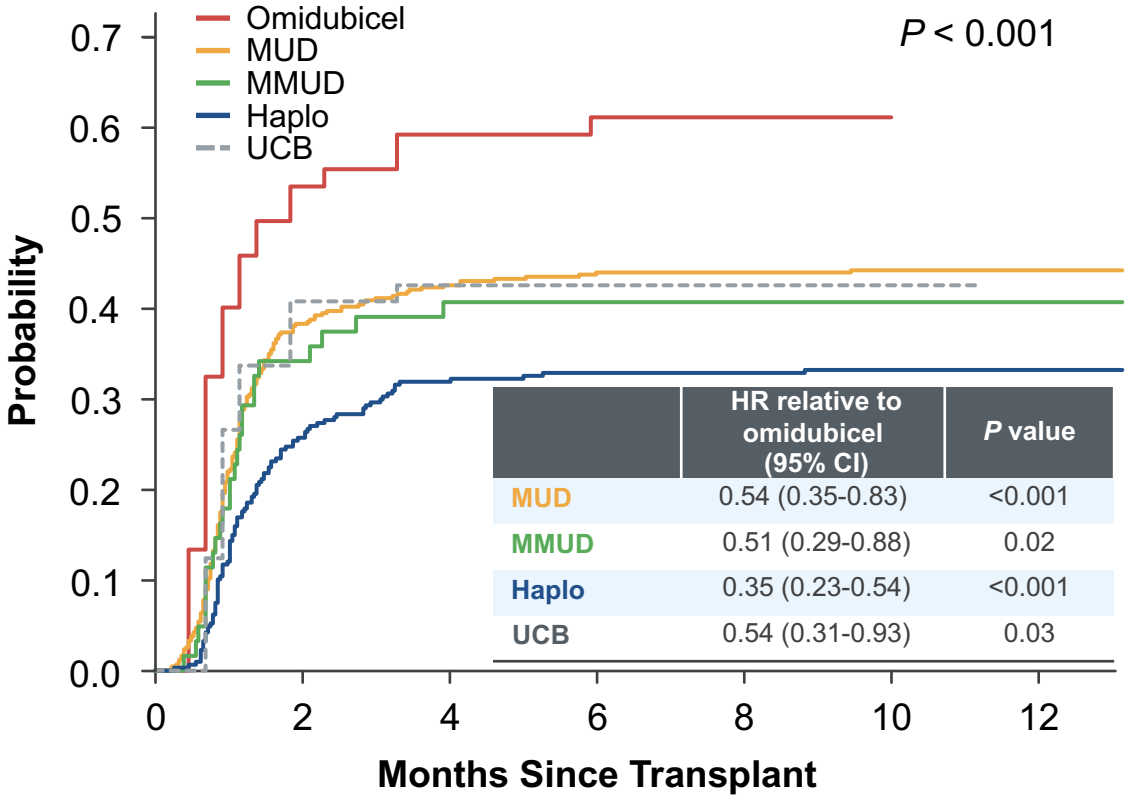
	HR relative to omidubicel (95% CI)	*P* value
MUD	2.72 (2.07-3.58)	< 0.001
MMUD	2.26 (1.57-3.27)	< 0.001
Haplo	1.59 (1.22-2.06)	< 0.001
UCB	0.72 (0.53-0.97)	0.03

The cumulative incidence function plots for platelet engraftment are unadjusted for baseline variables. CI, confidence interval; Haplo, haploidentical donor; HR, hazard ratio; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

RESULTS: ACUTE GVHD

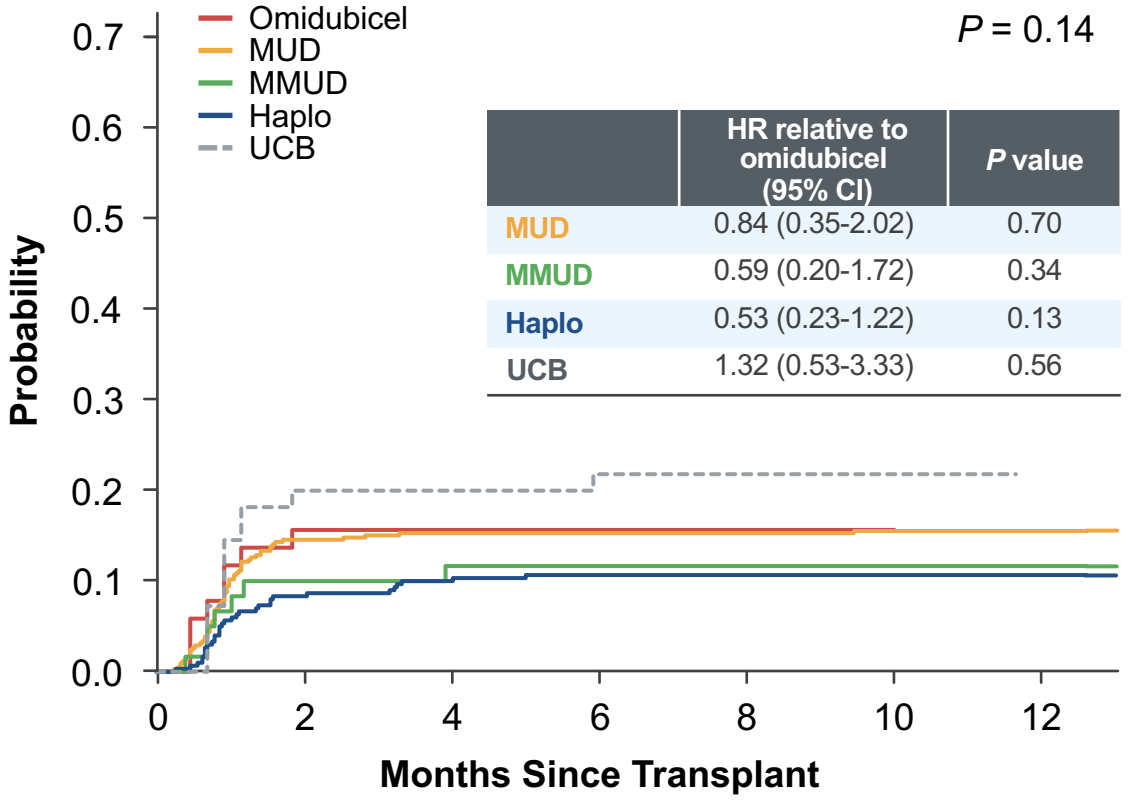
- Compared with other donor sources, omidubicel had significantly higher rates of acute GvHD Grade II-IV, however no significant differences were observed for severe acute GvHD (grade III-IV)

Grade II-IV



	HR relative to omidubicel (95% CI)	*P* value
MUD	0.54 (0.35-0.83)	<0.001
MMUD	0.51 (0.29-0.88)	0.02
Haplo	0.35 (0.23-0.54)	<0.001
UCB	0.54 (0.31-0.93)	0.03

Grade III-IV



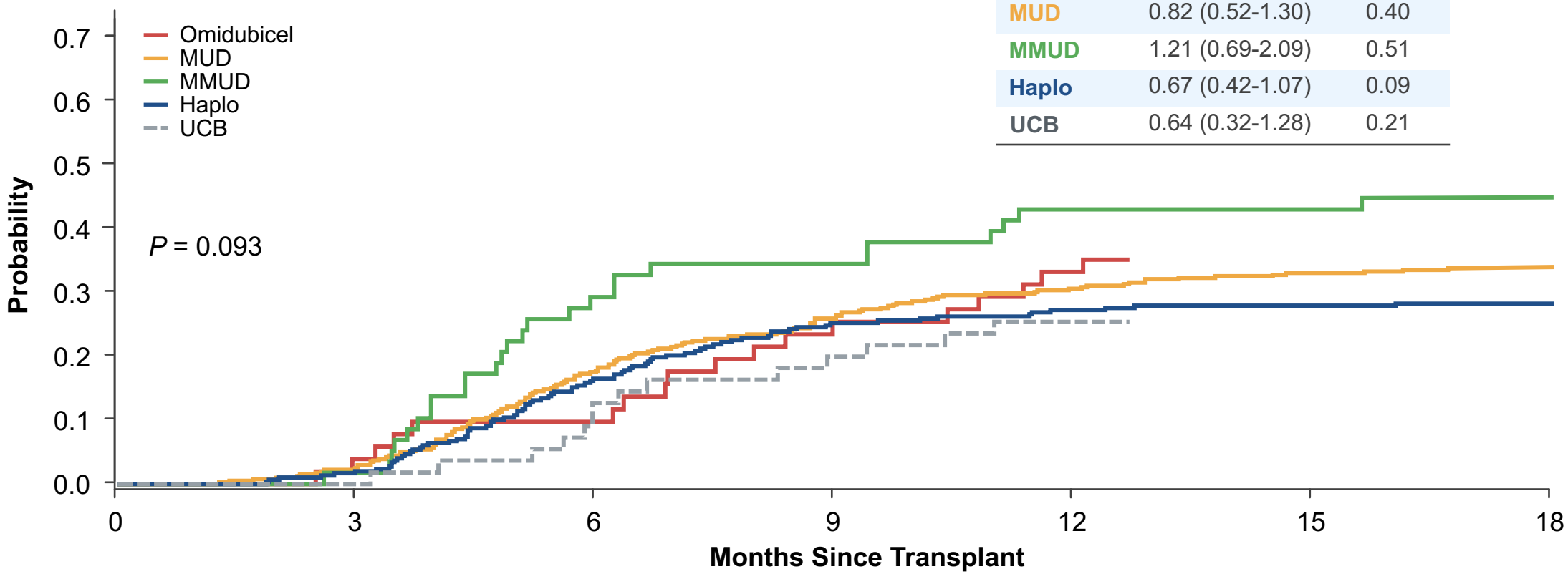
	HR relative to omidubicel (95% CI)	*P* value
MUD	0.84 (0.35-2.02)	0.70
MMUD	0.59 (0.20-1.72)	0.34
Haplo	0.53 (0.23-1.22)	0.13
UCB	1.32 (0.53-3.33)	0.56

The cumulative incidence function plots for acute GvHD are unadjusted for baseline variables. GvHD, graft-versus-host disease; Haplo, haploidentical donor; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

RESULTS: CHRONIC GVHD

- No statistically significant difference for chronic GvHD between omidubicel and other donor sources after adjusting for baseline variables

	HR relative to omidubicel (95% CI)	*P* value
MUD	0.82 (0.52-1.30)	0.40
MMUD	1.21 (0.69-2.09)	0.51
Haplo	0.67 (0.42-1.07)	0.09
UCB	0.64 (0.32-1.28)	0.21

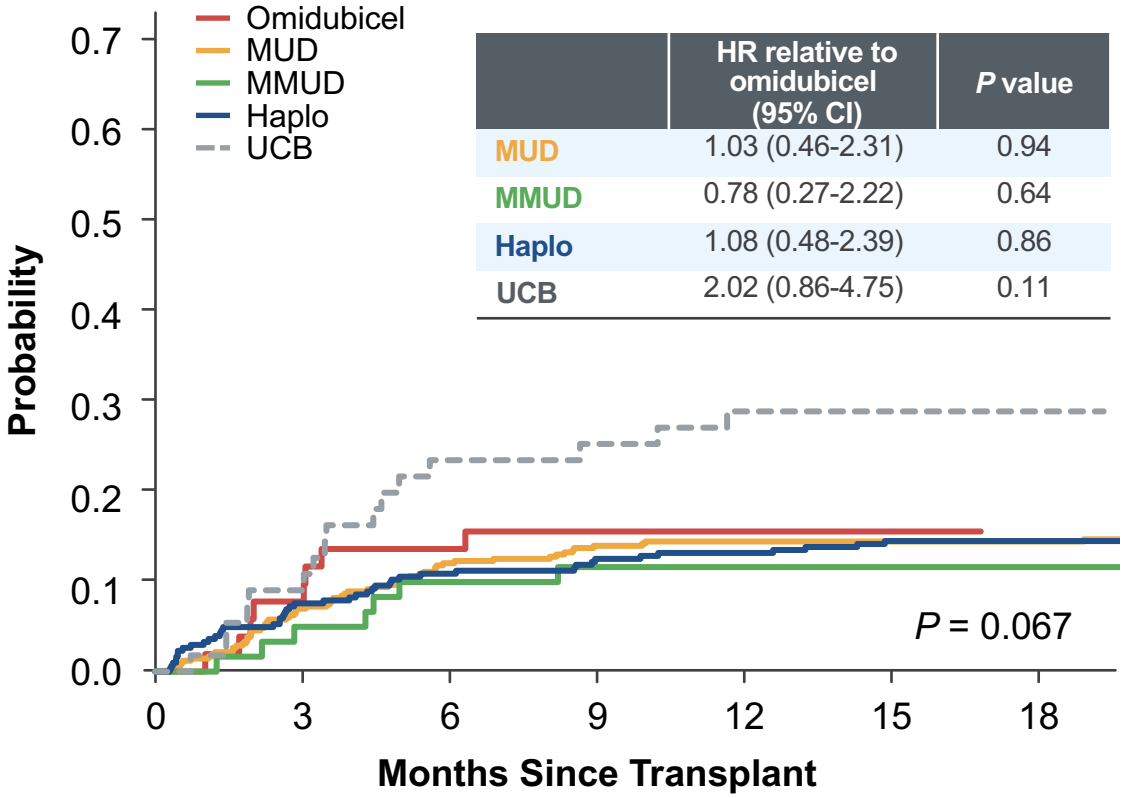


The cumulative incidence function plots for chronic GvHD are unadjusted for baseline variables. CI, confidence interval; GvHD, graft-versus-host disease; Haplo, haploidentical donor; HR, hazard ratio; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

RESULTS: NON-RELAPSE MORTALITY AND DISEASE RELAPSE

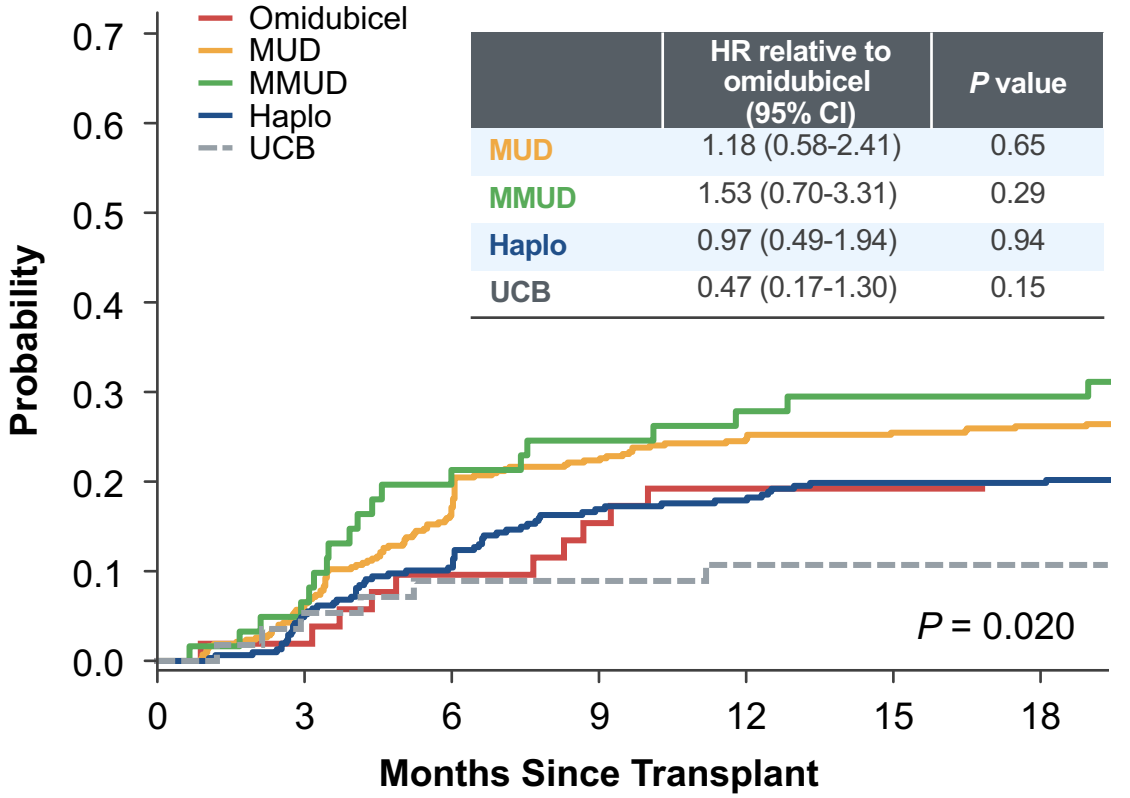
- The differences in relapse and non-relapse mortality between omidubicel and other donor sources were not statistically significant after adjusting for baseline variables

Non-relapse mortality



	HR relative to omidubicel (95% CI)	*P* value
MUD	1.03 (0.46-2.31)	0.94
MMUD	0.78 (0.27-2.22)	0.64
Haplo	1.08 (0.48-2.39)	0.86
UCB	2.02 (0.86-4.75)	0.11

Disease relapse

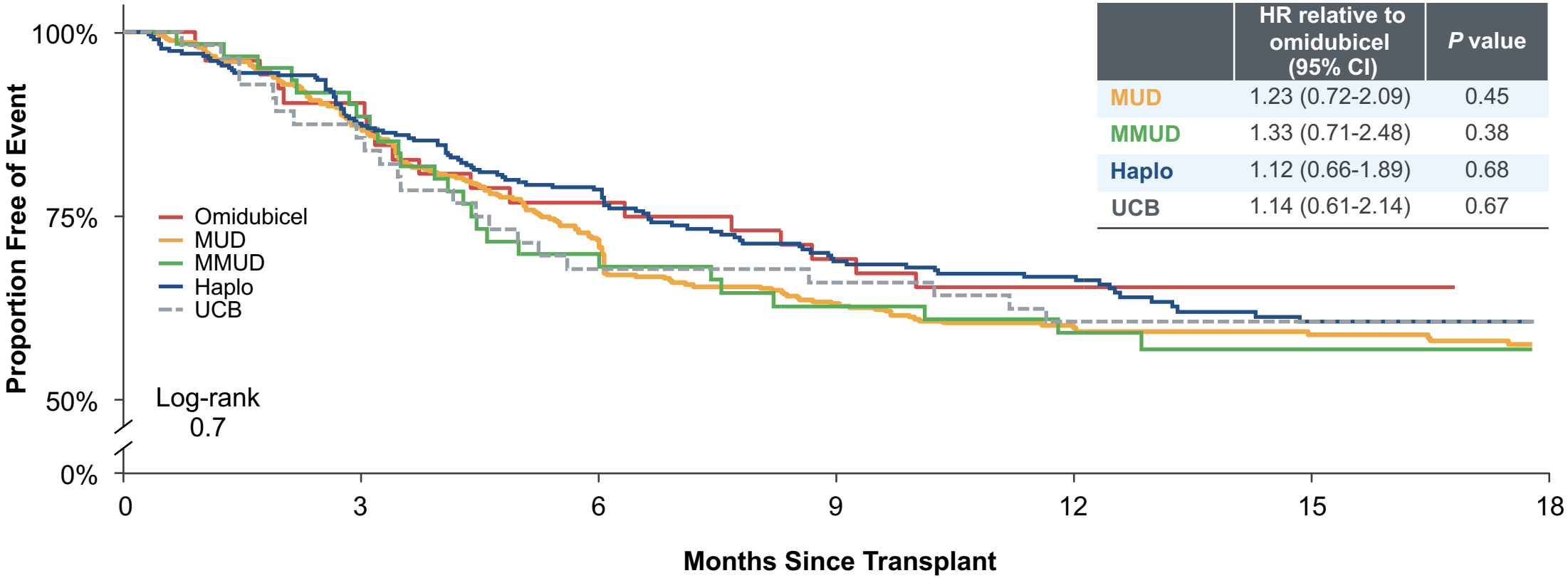


	HR relative to omidubicel (95% CI)	*P* value
MUD	1.18 (0.58-2.41)	0.65
MMUD	1.53 (0.70-3.31)	0.29
Haplo	0.97 (0.49-1.94)	0.94
UCB	0.47 (0.17-1.30)	0.15

The cumulative incidence function plots for non-relapse mortality and disease relapse are unadjusted for baseline variables. Haplo, haploidentical donor; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

RESULTS: DISEASE-FREE SURVIVAL (DFS)

- No statistically significant difference between omidubicel and other donor sources for DFS after adjusting for baseline variables



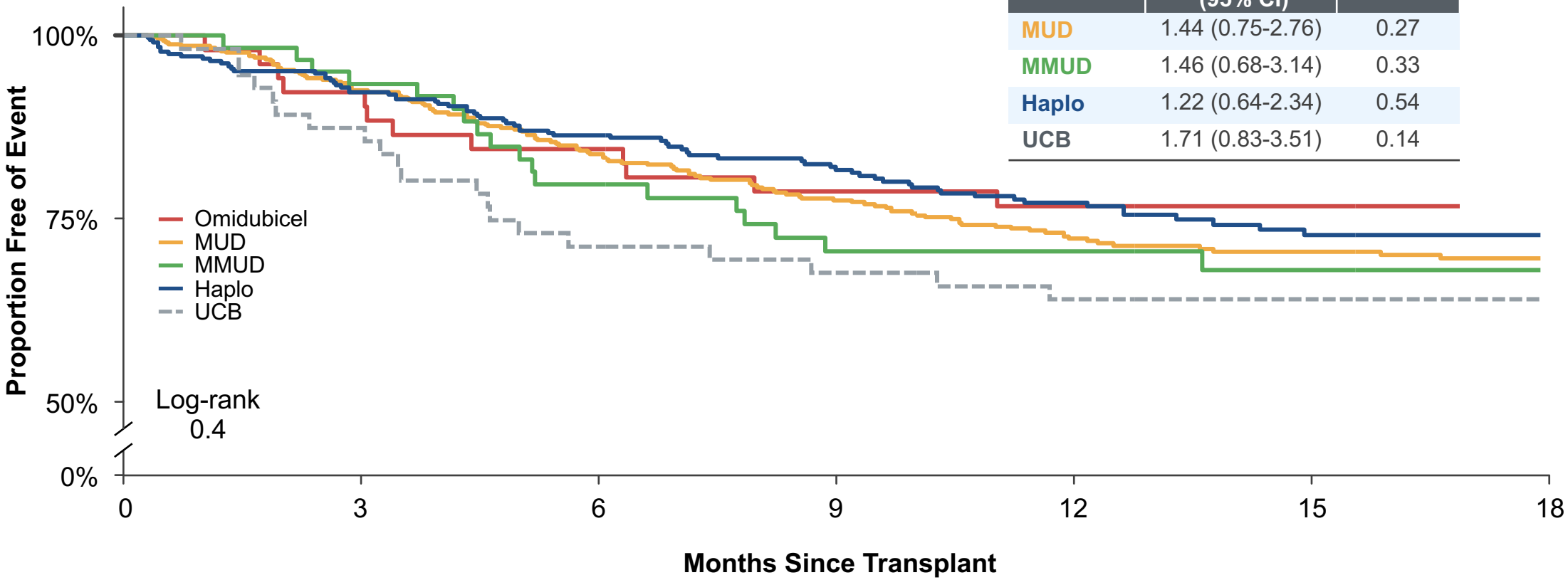
	HR relative to omidubicel (95% CI)	*P* value
MUD	1.23 (0.72-2.09)	0.45
MMUD	1.33 (0.71-2.48)	0.38
Haplo	1.12 (0.66-1.89)	0.68
UCB	1.14 (0.61-2.14)	0.67

The cumulative incidence function plots for DFS are unadjusted for baseline variables. CI, confidence interval; DFS, disease-free survival; Haplo, haploidentical donor; HR, hazard ratio; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

RESULTS: OVERALL SURVIVAL

- No statistically significant differences for overall survival between omidubicel and other donor sources after adjusting for baseline variables

	HR relative to omidubicel (95% CI)	*P* value
MUD	1.44 (0.75-2.76)	0.27
MMUD	1.46 (0.68-3.14)	0.33
Haplo	1.22 (0.64-2.34)	0.54
UCB	1.71 (0.83-3.51)	0.14



The cumulative incidence function plots for overall survival are unadjusted for baseline variables. CI, confidence interval; Haplo, haploidentical donor; HR, hazard ratio; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.

LIMITATIONS OF CURRENT RESEARCH

- Comparisons between clinical trial and registry data are limited by:
  - Heterogeneity in baseline characteristics
  - Inconsistent definitions of outcomes
  - Differences in standard of care between patients in registry vs clinical trial setting
    - Intensity and schedule of assessments and reporting (eg, ability to capture infections comprehensively, etc)
- Statistical adjustment was adopted to mitigate these biases to the extent possible (eg, multivariable regression adjustments for available baseline variables)

CONCLUSIONS

Compared with results from existing donor sources (MUD, MMUD, Haplo) reported to CIBMTR, omidubicel was associated with

- More rapid rate of neutrophil engraftment
- Slower rate of platelet engraftment
- Comparable rates of grade III-IV acute GvHD and chronic GvHD
- Comparable overall survival

These results suggest that omidubicel may be an effective and important new donor source option, broadening the availability of allogeneic HCT for patients

CIBMTR, Center for International Blood and Marrow Transplant Research; GvHD, graft versus host disease; Haplo, haploidentical donor; HCT, hematopoietic cell transplant; MMUD, mismatched unrelated donor; MUD, matched unrelated donor.

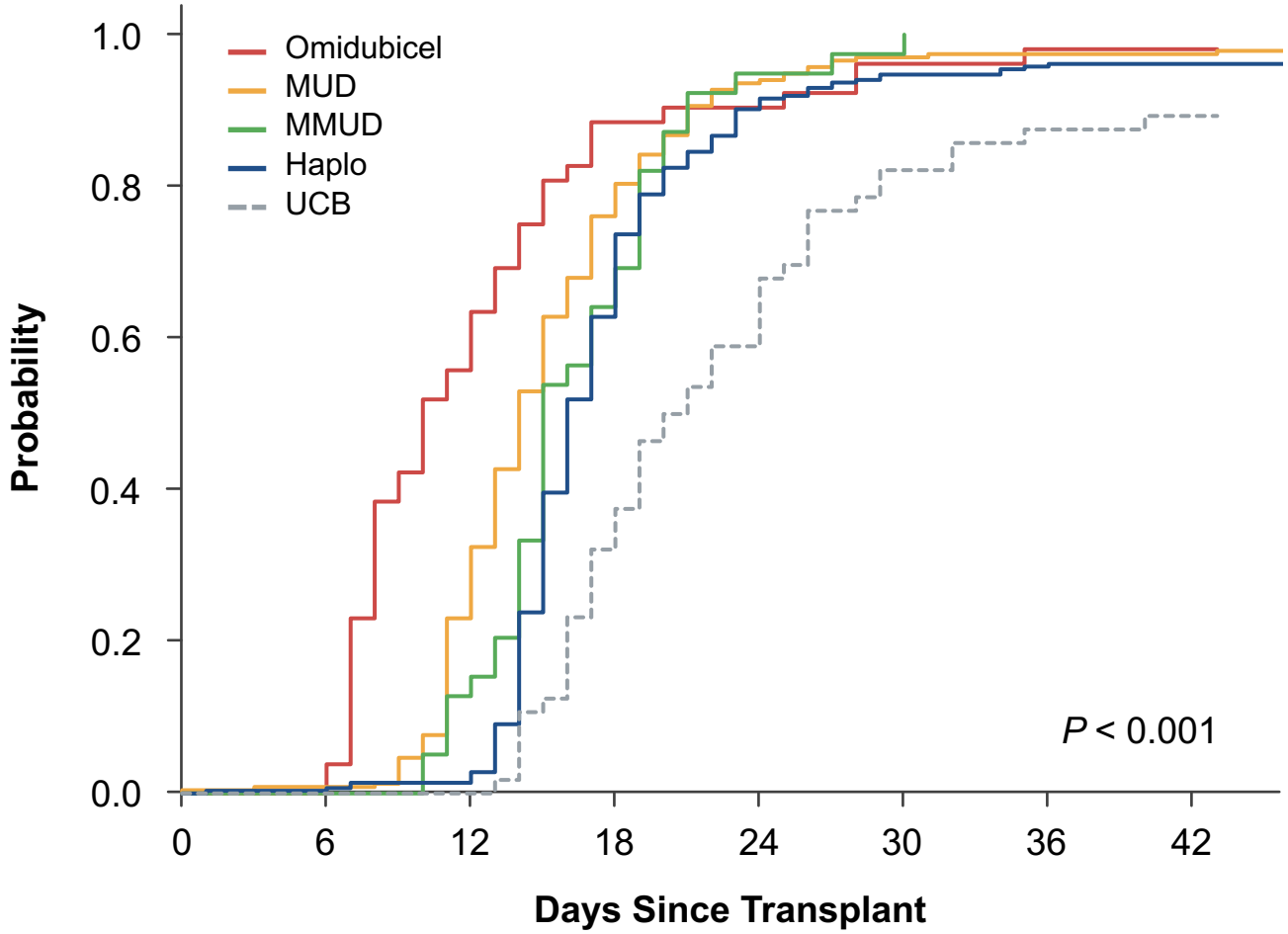
ACKNOWLEDGEMENTS

- We thank:
  - The investigators and patients who participated in the clinical trial
  - The centers who contributed data to the CIBMTR database
  - The patients who provided consent for their data to be used by the CIBMTR in research
  - Everyone at CIBMTR who contributed to this research

BACKUP

RESULTS: SUBGROUP ANALYSIS OF NEUTROPHIL ENGRAFTMENT AMONG THOSE RECEIVING GROWTH FACTORS (N=708)

- There were similar results for neutrophil engraftment in subgroup analyses restricting to patients who received G-CSF/GM-CSF (n=108 in omidubicel trial, n=600 across CIBMTR groups)
- Compared with omidubicel, other donor sources had significantly slower rates of neutrophil engraftment after adjusting for baseline variables



CIBMTR, Center for International Blood and Marrow Transplant Research; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; Haplo, haploidentical donor; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; UCB, umbilical cord blood.