

HEALTH-RELATED QUALITY OF LIFE (HRQL) FOLLOWING TRANSPLANTATION WITH OmidubICEL VERSUS Umbilical Cord Blood (UCB) IN PATIENTS WITH Hematologic Malignancies: Results from a Phase III Randomized, Multicenter Study

Chenyu Lin,¹ Gautam Sajeev,² Anthony D Sung,¹ Patrick Stiff,³ Claudio Brunstein,⁴ Corey Cutler,⁵ Guillermo Sanz,⁶ Caroline A Lindemans,⁷ Andrew R Rezvani,⁸ Rabi Hanna,⁹ Liang Pi Koh,¹⁰ Richard T Maziarz,¹¹ William Y K Hwang,¹² Yan Song,² Qing Liu,² Rocio Manghani,¹³ Smitha Sivaraman,¹³ James Signorovitch,² Mitchell Horwitz¹

¹Adult Stem Cell Transplant Program, Division of Cellular Therapy, Department of Medicine, Duke University Medical Center, Durham, NC, USA; ²Analysis Group Inc., Boston, MA, USA; ³Loyola University Medical Center, Chicago, IL, USA; ⁴Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, MN, USA; ⁵Dana-Farber Cancer Institute, Boston, MA, USA; ⁶Servicio de Hematología, Hospital Universitari i Politècnic La Fe, Valencia, Spain; ⁷Division of Pediatrics, University Medical Center Utrecht, Utrecht, Netherlands; ⁸Department of Medicine, Division of Blood and Marrow Transplantation, Stanford University School of Medicine, Stanford, CA, USA; ⁹Department of Pediatric Hematology, Oncology, and Bone Marrow Transplantation, Cleveland Clinic Children's Hospital, Cleveland, OH, USA; ¹⁰Department of Hematology-Oncology, National University Cancer Institute, Singapore; ¹¹Knight Cancer Institute, Oregon Health and Science University, Portland, OR, USA; ¹²Department of Hematology, Singapore General Hospital, Singapore; ¹³Gamida Cell Ltd., Boston, MA, USA

BACKGROUND

- Patients with hematologic malignancies undergoing allogeneic hematopoietic cell transplant (HCT) experience notable deficits in health-related quality of life (HRQL)¹⁻³
- Omidubicel is an investigational advanced cell therapy, derived from an appropriately HLA-matched single umbilical cord blood (UCB) unit
- Omidubicel manufacturing in the presence of nicotinamide (NAM) allows for inhibition of differentiation and enhances the functionality and number of hematopoietic stem and progenitor cells⁴
- HCT with omidubicel has demonstrated significantly faster and robust neutrophil and platelet engraftment; shorter hospitalization; and lower rates of bacterial, viral, and invasive fungal infections as compared with UCB in a phase III randomized trial (NCT02730299)⁵
- An understanding of the impact of omidubicel from the patient perspective is important to stakeholders and decision-makers, including providers, payers, caregivers, and the patients themselves

OBJECTIVE

- To compare patient-reported HRQL outcomes between treatment groups receiving HCT with omidubicel versus UCB in a phase III randomized trial

METHODS

Data source and sample selection

- A phase III randomized controlled trial of omidubicel (NCT02730299; data cutoff: April 2021) included patients with high-risk hematologic malignancies, aged 12–65 years
- The present analysis included patients who received protocol-defined treatment and provided HRQL evaluations at baseline and at least one follow-up visit

Study measures

- HRQL measures were assessed prospectively at screening (treated as baseline) and days 42, 100, 180, and 365 post-transplant. Higher HRQL scores indicate better quality of life. Specifically, HRQL measures include:
 - Functional Assessment of Cancer Therapy-General (FACT-G) domains
 - Physical well-being (7 items, domain score ranges from 0 to 28)
 - Social/family well-being (7 items, domain score ranges from 0 to 28)
 - Emotional well-being (6 items, domain score ranges from 0 to 24)
 - Functional well-being (7 items, domain score ranges from 0 to 28)
 - FACT-G total score (sum of the 4 FACT-G domain scores)
 - Bone marrow transplantation (BMT) subscale score (10 items, each item score ranges from 0 to 4)
 - FACT-BMT total score (comprised of all FACT-G domains plus BMT-specific subscale items)
 - EuroQol 5-dimension scale 3-level instrument (EQ-5D-3L) index score
 - A range from less than 0 (where 0 is a health state equivalent to death and negative values indicate states worse than death) to 1 (perfect health)

Statistical methods

- Patient baseline characteristics were described and compared between the omidubicel and UCB groups
- Changes in HRQL measures over time were compared between treatment groups
 - Mixed effect models with repeated measures (MMRM) were used to analyze changes from baseline during the first year post-transplant
 - Models were adjusted for time (categorical by visit), treatment group, interaction between treatment and time, baseline HRQL score, region, age group, sex, race, HCT-specific comorbidity index, and primary diagnosis
 - Correlations across repeated HRQL measures from the same individual were accounted for via an unstructured covariance matrix
 - Areas under the mean HRQL trajectory curve (AUCs), which represent the average HRQL experience over time, were compared between treatment groups⁶

RESULTS

Study sample

- 125 patients were randomized and 108 patients were transplanted
- 33 transplanted patients were excluded from the HRQL population due to missing HRQL at baseline (n=14) or during follow-up (n=19)
 - Rates of missing HRQL data were comparable between treatment groups, although slightly higher in general for UCB
- HRQL population (N=75)
 - 75 patients had >50% non-missing items for FACT-G domains and BMT subscales at both the baseline and at least one follow-up visit
 - 37 patients were transplanted with omidubicel and 38 patients were transplanted with UCB

Baseline characteristics

- Demographics and HRQL scores were comparable between the 2 treatment groups (Table 1)

TABLE 1. BASELINE CHARACTERISTICS

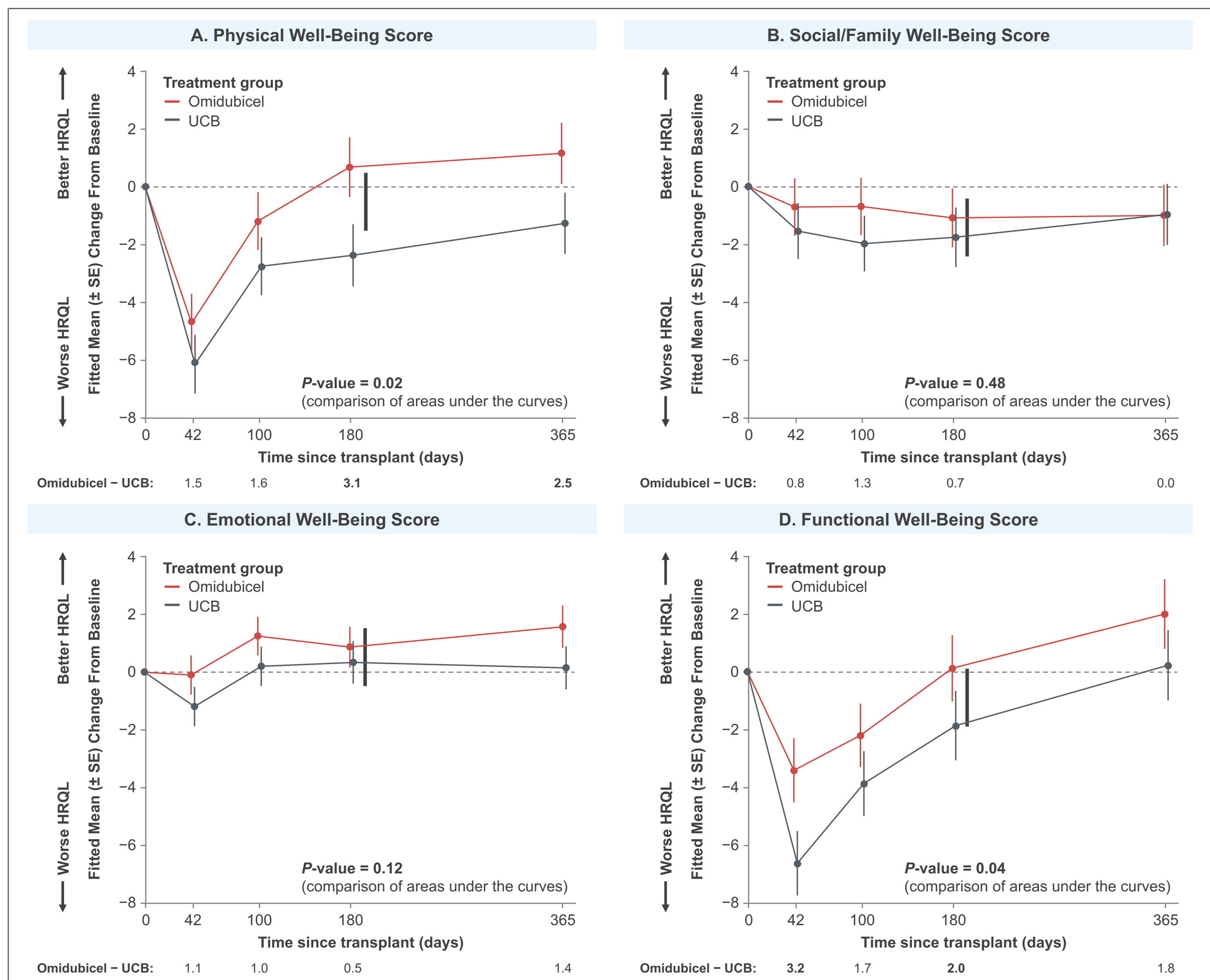
	Omidubicel (n=37)	UCB (n=38)
Demographics		
Age (years), mean ± SD	37.3 ± 15.5	35.1 ± 14.8
12–17, n (%)	5 (13.5)	5 (13.2)
18–39, n (%)	15 (40.5)	16 (42.1)
40–65, n (%)	17 (45.9)	17 (44.7)
Male, n (%)	20 (54.1)	24 (63.2)
Weight (kg), mean ± SD	82.4 ± 20.5	79.7 ± 21.3
White, n (%)	24 (64.9)	20 (52.6)
US participants, n (%)	27 (73.0)	28 (73.7)
Clinical measures		
Primary diagnosis, n (%)		
Acute myelogenous leukemia	17 (45.9)	17 (44.7)
Acute lymphoblastic leukemia	12 (32.4)	14 (36.8)
Chronic myelogenous leukemia	3 (8.1)	2 (5.3)
Myelodysplastic syndrome	3 (8.1)	2 (5.3)
Lymphoma	1 (2.7)	2 (5.3)
Other	1 (2.7)	1 (2.6)
Disease risk index, n (%)		
Low risk	11 (29.7)	6 (15.8)
Intermediate risk	12 (32.4)	17 (44.7)
High risk	14 (37.8)	15 (39.5)
HCT-specific comorbidity index, n (%)		
0	8 (21.6)	6 (15.8)
1–2	11 (29.7)	12 (31.6)
3+	18 (48.6)	20 (52.6)
HRQL measures, mean ± SD		
FACT-G total score	80.2 ± 14.3	83.9 ± 11.9
Physical well-being score	22.3 ± 5.1	23.6 ± 4.5
Social/family well-being score	22.2 ± 5.2	24.1 ± 3.6
Emotional well-being score	18.1 ± 4.4	18.4 ± 3.6
Functional well-being score	17.6 ± 6.2	17.9 ± 5.7
BMT subscale score	28.2 ± 5.7	27.9 ± 6.6
FACT-BMT total score	108.4 ± 19.1	111.8 ± 17.3
EQ-5D-3L index score	0.86 ± 0.16	0.87 ± 0.13

BMT: bone marrow transplant; EQ-5D-3L: EuroQol 5-dimension scale 3-level instrument; FACT-BMT: Functional Assessment of Cancer Therapy-Bone Marrow Transplant; FACT-G: Functional Assessment of Cancer Therapy-General; HCT: hematopoietic cell transplantation; SD: standard deviation; UCB: umbilical cord blood; US: United States.

Comparison of HRQL changes between groups during the first year post-transplant

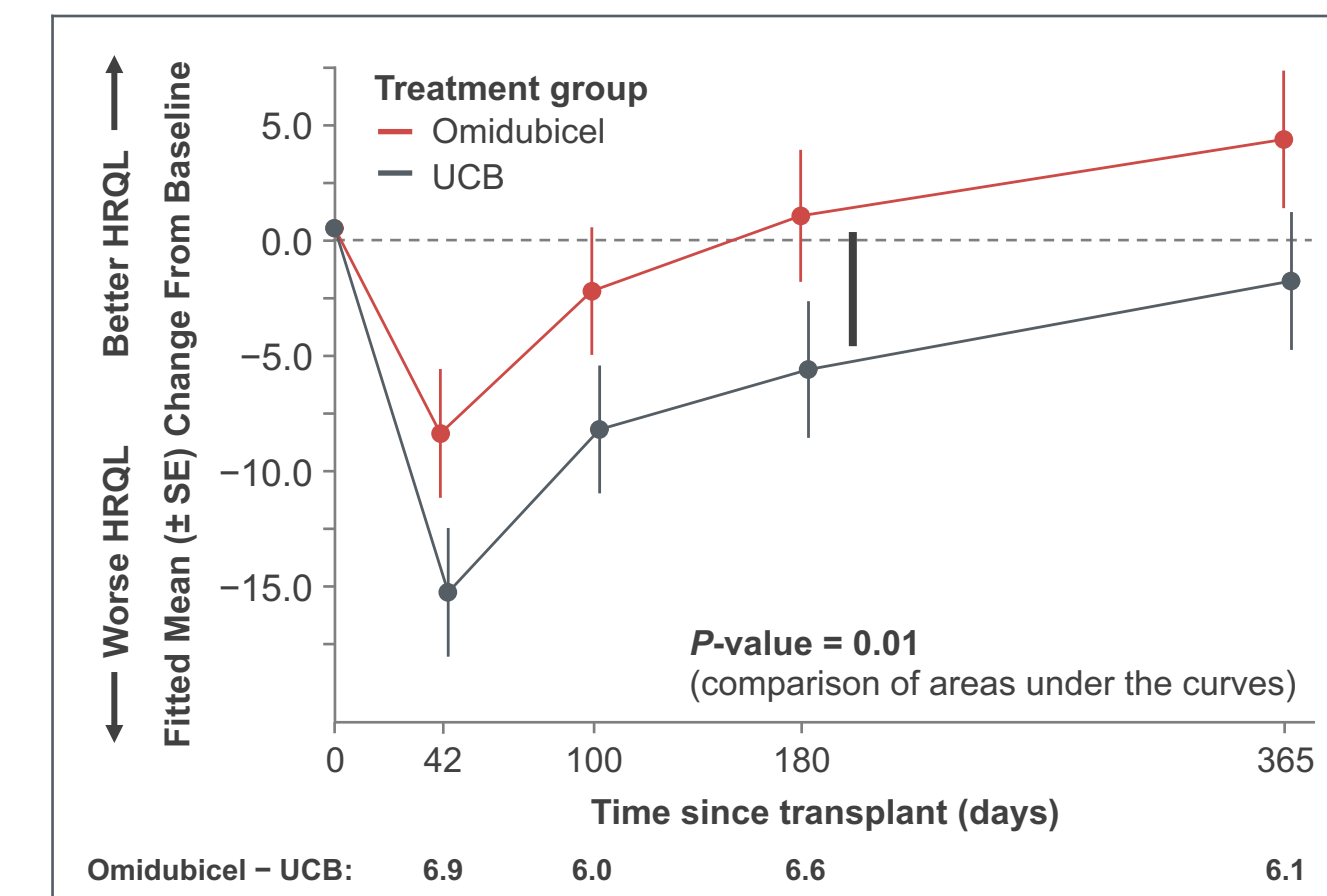
- An initial decline in mean scores for all HRQL measures was observed at day 42 post-transplantation in both treatment groups. The mean declines were consistently numerically smaller in the omidubicel group compared to the UCB group
- FACT-G domain scores
 - Average change in physical well-being domain score (Figure 1A) was significantly better with omidubicel (P=0.02). The minimal clinically important difference (MCID) of 2 units⁷ was exceeded at days 180 and 365
 - Numerically superior changes in average social/family well being and emotional well being domain scores were observed in the omidubicel group, but were not significant (Figures 1B, 1C)
 - Average change in functional well-being domain score (Figure 1D) was significantly better with omidubicel (P=0.04) and exceeded the MCID of 2 units⁷ at day 42
- Changes in FACT-G, FACT-BMT and BMT subscale scores also indicated better average HRQL over time in the omidubicel group relative to the UCB group (Figures 2–4)
 - FACT-G: Mean differences exceeded the MCID of 5 units⁷ at all time points (P=0.01)
 - BMT subscale: Mean differences exceeded the MCID of 2 units⁸ at days 42, 100, and 180 (P=0.04)
 - FACT-BMT: Mean differences exceeded the MCID of 7 units^{7,8} across all time points (P=0.01)
- Average EQ-5D-3L index (Figure 5) was numerically superior with omidubicel (P=0.06) and exceeded the MCID of 0.07 units⁹ at days 100 and 180
- In a regression analysis correlating HRQL with clinical outcomes, neutrophil engraftment by day 42 was associated with better HRQL scores in certain domains; grade 3 viral infections, grade 2/3 bacterial infections, grade 3 fungal infections, and longer hospitalizations in the first 100 days post-transplant were associated with worse HRQL scores (data not shown)

FIGURE 1. CHANGES FROM BASELINE IN FACT-G DOMAINS



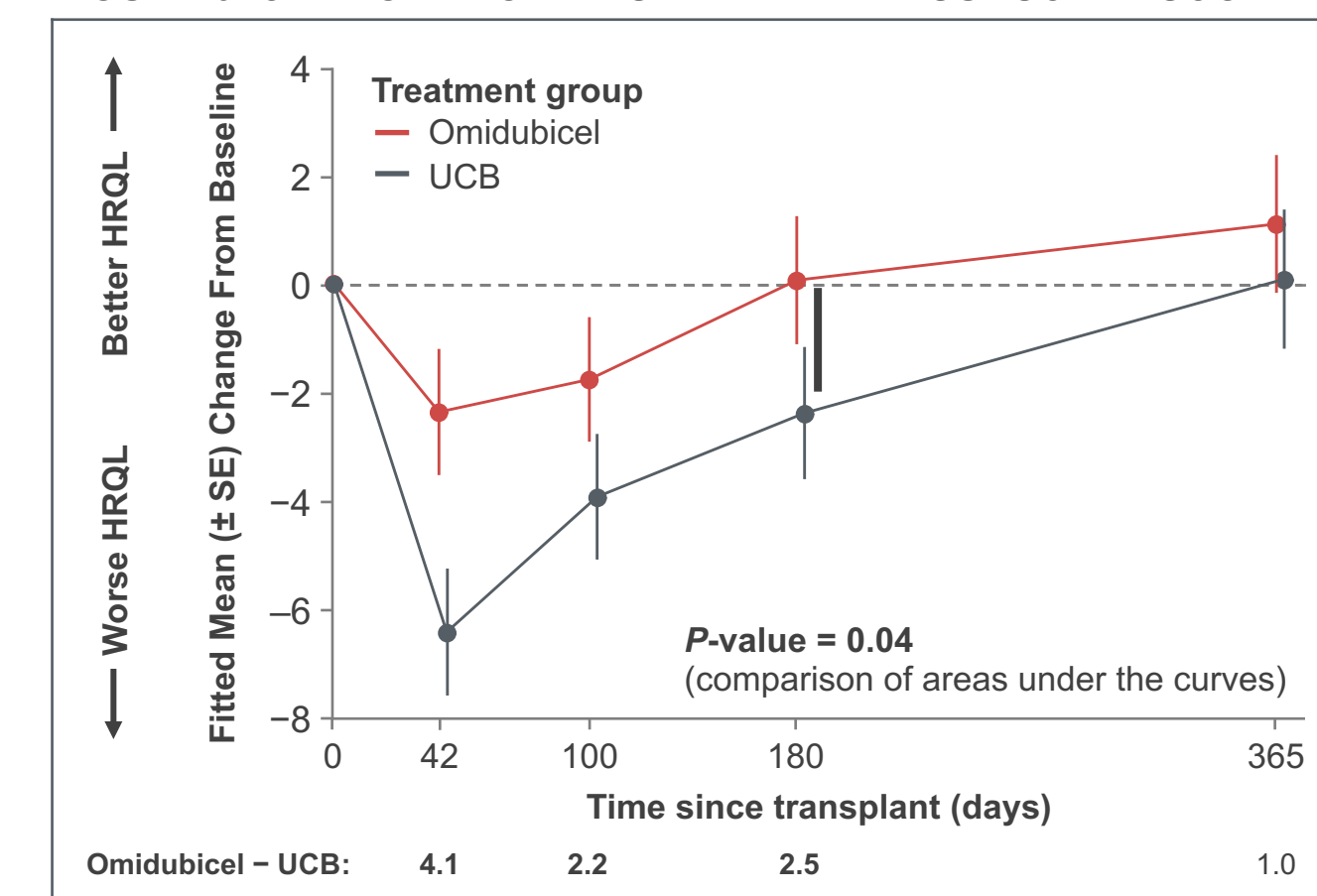
Note: The dark vertical lines denote the MCIDs for physical well-being, social/family well-being, emotional well-being, and functional well-being scores, which are 2 points.⁷ The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID. FACT-G: Functional Assessment of Cancer Therapy-General; HRQL: health-related quality of life; MCID: minimal clinically important difference; SE: standard error; UCB: umbilical cord blood.

FIGURE 2. CHANGE FROM BASELINE IN FACT-G TOTAL SCORE



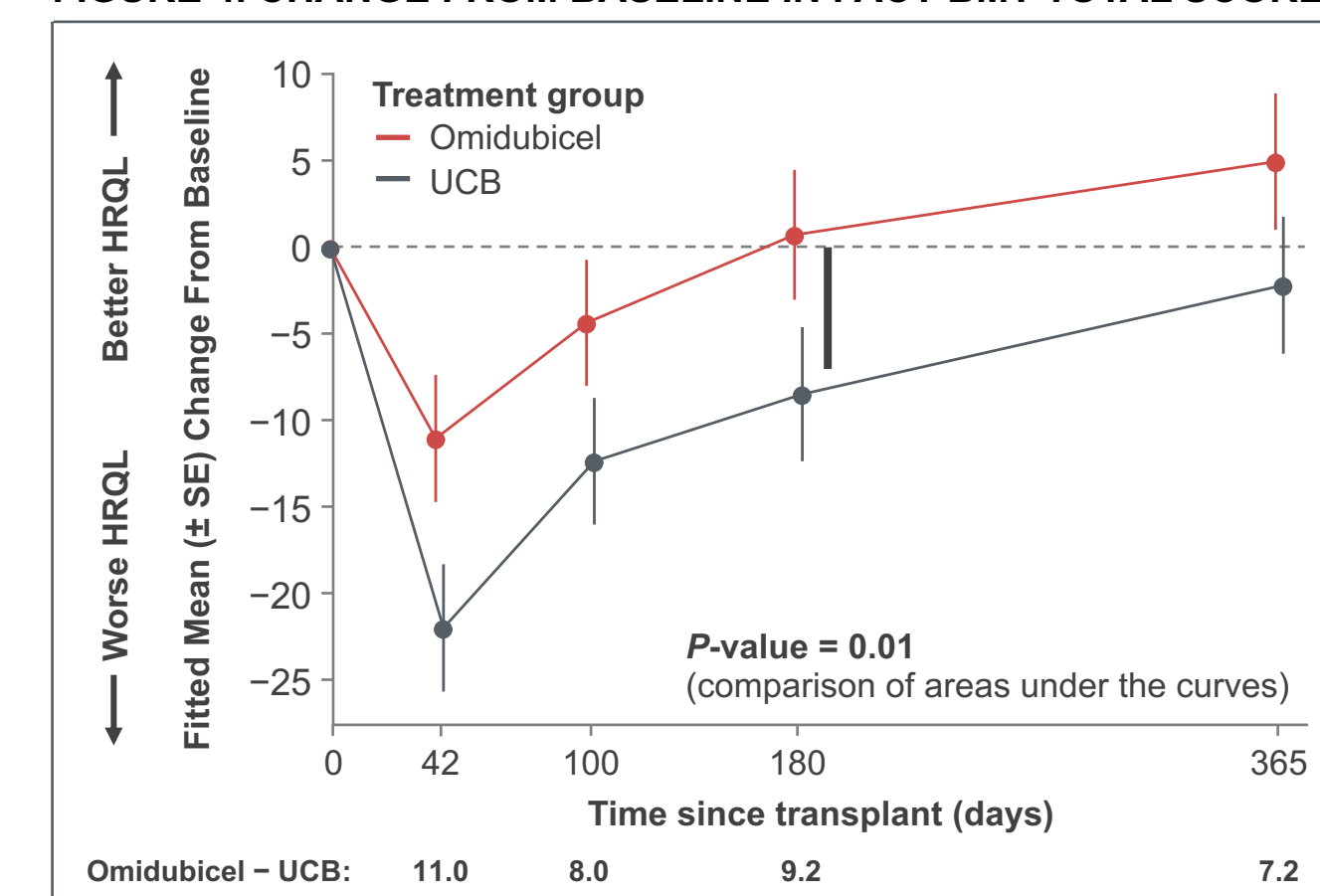
Note: The dark vertical line denotes the MCID for FACT-G total score, which is 5 points.⁷ The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID. FACT-G: Functional Assessment of Cancer Therapy-General; HRQL: health-related quality of life; MCID: minimal clinically important difference; SE: standard error; UCB: umbilical cord blood.

FIGURE 3. CHANGE FROM BASELINE IN BMT SUBSCALE SCORE



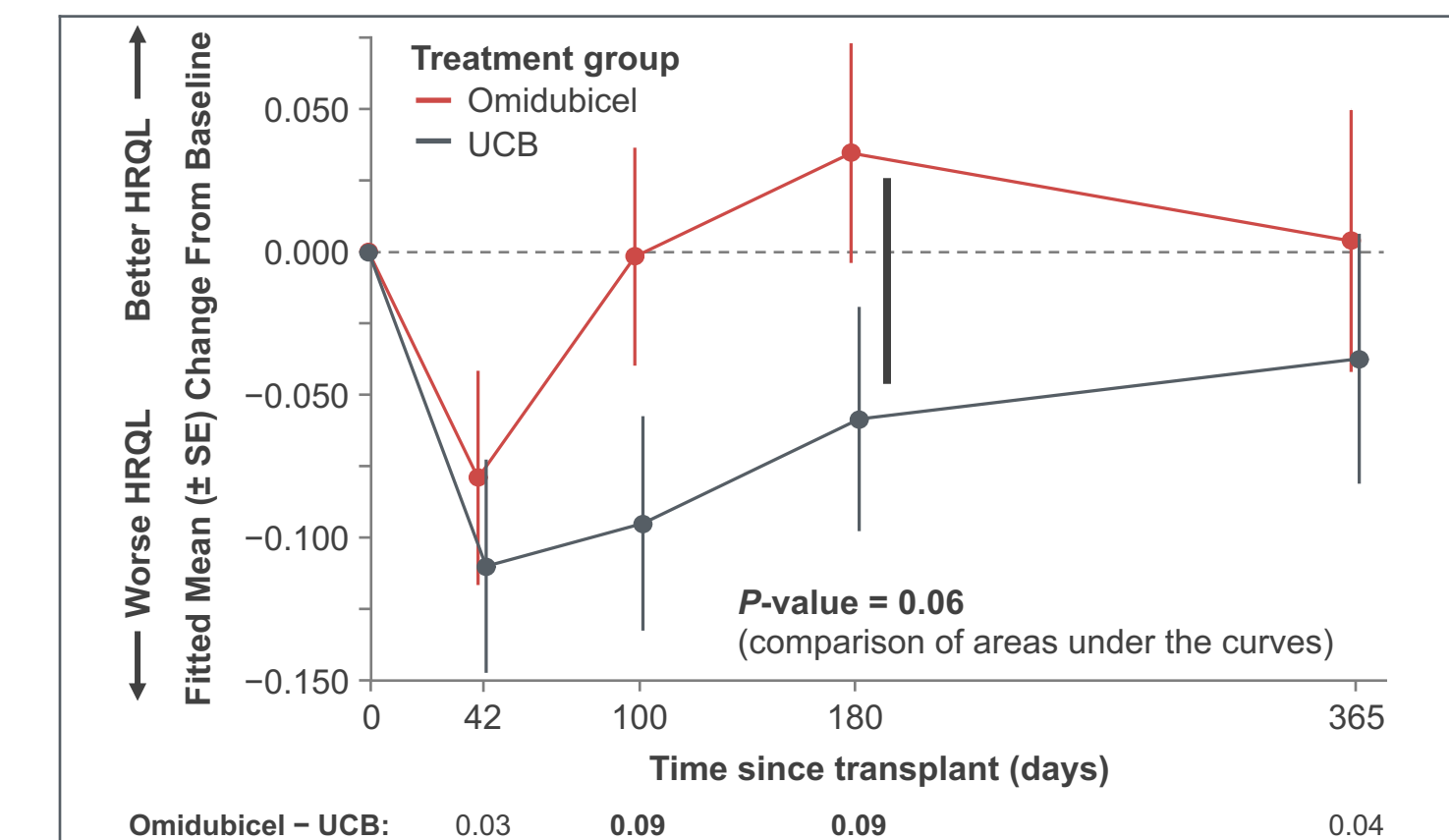
Note: The dark vertical line denotes the MCID for BMT subscale score, which is 2 points.⁸ The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID. BMT: bone marrow transplantation; FACT-G: Functional Assessment of Cancer Therapy-General; HRQL: health-related quality of life; MCID: minimal clinically important difference; SE: standard error; UCB: umbilical cord blood.

FIGURE 4. CHANGE FROM BASELINE IN FACT-BMT TOTAL SCORE



Note: The dark vertical line denotes the MCID for FACT-BMT total score, which is 7 points.^{7,8} The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID. FACT-BMT: Functional Assessment of Cancer Therapy-Bone Marrow Transplant; HRQL: health-related quality of life; MCID: minimal clinically important difference; SE: standard error; UCB: umbilical cord blood.

FIGURE 5. CHANGE FROM BASELINE IN EQ-5D-3L INDEX SCORE



Note: The dark vertical line denotes the MCID for EQ-5D-3L index total score, which is 0.07 points.⁹ The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID. EQ-5D-3L: EuroQol 5-dimension scale 3-level instrument; HRQL: health-related quality of life; MCID: minimal clinically important difference; SE: standard error; UCB: umbilical cord blood.

DISCUSSION

- As patients with better HRQL are generally more likely to provide data, HRQL benefits estimated for omidubicel may be conservative. More patients in the UCB group had missing follow-up data, which was likely attributable to inferior outcomes including worse HRQL
- Missing data may limit interpretability of results and underestimate HRQL burden
- The AUC approach is well-suited to settings in which HRQL can both worsen and improve on average over time, such that no single time point is representative of the full patient experience
- Long-term HRQL changes >1-year post-transplant were not studied here, but are important to patients and caregivers
- This was an exploratory study and statistical analyses were performed post hoc; no multiplicity corrections were performed

CONCLUSIONS

- In a phase III randomized trial, omidubicel demonstrated significantly faster neutrophil and platelet engraftment, shorter hospitalizations, and lower infection rates compared to UCB⁵
- This current study demonstrated that, in addition to clinical endpoint benefits, omidubicel was associated with meaningful improvements or greater preservation of several important and well-established patient-reported HRQL measures
- HRQL improvements from omidubicel were observed as early as 42 days post-transplant and persisted throughout the first year, indicating potential long-term benefits
- Achieving neutrophil engraftment by day 42 was associated with better HRQL outcomes
- The regression analysis correlating HRQL with clinical outcomes suggested a relationship between the known clinical benefits of omidubicel and the improvements seen in HRQL

DISCLOSURES

MEH is a consultant for AbbVie, CareDx, Kadmon, and Magenta; and receives research support from Gamida Cell. PS is a consultant for CRISPR; receives research support from Amgen, Alara Biotherapeutics, Eisai, Gamida Cell, Incyte Corp, MacroGenics, and Takeda. CB receives research support from Astex, Gamida Cell, and Magenta; and is a consultant for AlloVir. CC is a consultant for Incyte Corporation, Jazz Pharmaceuticals, Kadmon, Medscape, Mesoblast, and Regenon. GS is an advisor for AbbVie, Helsinn, Hoffmann-La Roche, and Takeda. ARR receives research support from Pharmacia, RTM is an advisor or consultant for AlloVir, Ariva, CRISPR Therapeutics, Incyte Corporation, and Novartis; reports honoraria from Incyte Corporation and Vor Pharma; receives research support from BMS and Oncores; participates in a data safety monitoring board for Athersys, Novartis, and Vor Pharma; and has a patent with Athersys. RM is an employee of Gamida Cell Inc., Kite Inc., and Tricida Corporation. SS is an employee of Gamida Cell Inc. and Incyte Corporation. GS, YS, QL, and JS are employees of Analysis Group Inc., which received consulting fees from Gamida Cell Inc. for this research.

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