CT-039

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

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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 cells[4]
- 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 groups[6]

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

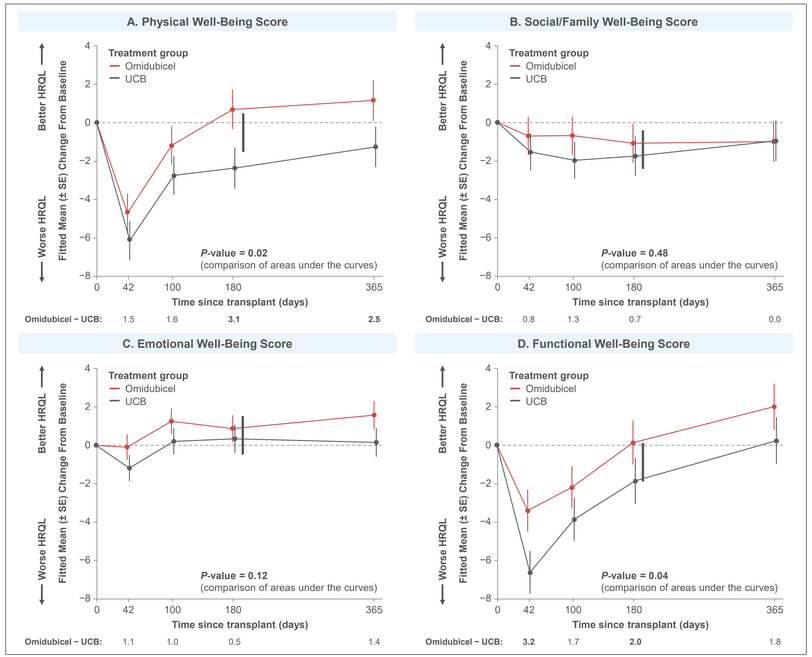
	Omidubicel (n=37)	UCB (n=38)
Demographics		
Age (years), mean ± SD	37.3 ± 15.5	35.1 ± 14.8
12–17, n (%)	5 (13.5)	5 (13.2)
18–39, n (%)	15 (40.5)	16 (42.1)
40–65, n (%)	17 (45.9)	17 (44.7)
Male, n (%)	20 (54.1)	24 (63.2)
Weight (kg), mean ± SD	82.4 ± 20.5	79.7 ± 21.3
White, n (%)	24 (64.9)	20 (52.6)
US 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

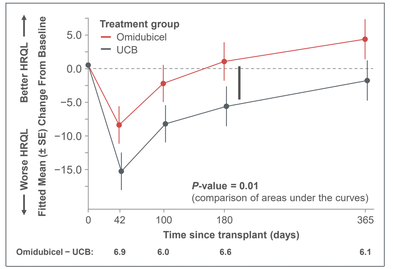
- An initial decline in mean scores for all HRQL measures was observed at day 42 post-transplantation in both treatment groups. The mean declines were consistently numerically smaller in the omidubicel group compared to the UCB group
- FACT-G domain scores
  - Average change in physical well-being domain score (**Figure 1A**) was significantly better with omidubicel (P=0.02). The minimal clinically important difference (MCID) of 2 units[7] 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 units[7] 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 units[7] at all time points (P=0.01)
  - BMT subscale: Mean differences exceeded the MCID of 2 units[8] 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 units[9] 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



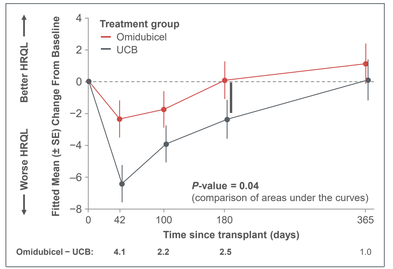
Note: The dark vertical lines denote the MCIDs for physical well-being, social/family well-being, emotional well-being, and functional well-being scores, which are 2 points.[7] The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID.
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



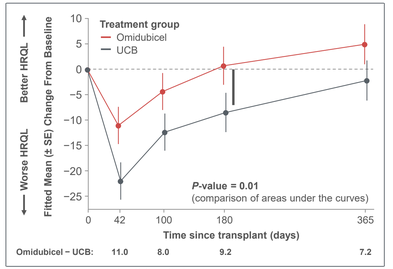
Note: The dark vertical line denotes the MCID for FACT-G total score, which is 5 points.[7] The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID.
FACT-G: Functional Assessment of Cancer Therapy–General; HRQL: health-related quality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

FIGURE 3. CHANGE FROM BASELINE IN BMT SUBSCALE SCORE



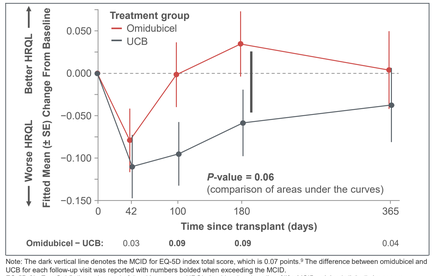
Note: The dark vertical line denotes the MCID for BMT subscale score, which is 2 points.[8] The difference between omidubicel and UCB for each follow-up visit was reported with numbers bolded when exceeding the MCID.
BMT: bone marrow transplantation; FACT-G: Functional Assessment of Cancer Therapy–General; 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 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 UCB[5]
- 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, Atara Biotherapeutics, Eisai, Gamida Cell, Incyte Corp, Macrogenics, and Takeda. CB receives research support from Astex, Gamida Cell, and Magenta; and is a consultant for AbbVir. CC is a consultant for Incyte Corporation, Jazz Pharmaceuticals, Kadmon, Medsenic, Mesoblast, and Regeneron. GS is an advisor for AbbVie, Helsinn, Hoffmann-LaRoche, and Takeda. ARR receives research support from Pharmacyclics. RTM is an advisor or consultant for AbbVir, Artiva, CRISPR Therapeutics, Incyte Corporation, and Novartis; reports honoraria from Incyte Corporation and Vor Pharma; receives research support from BMS and Omeros; participates in a data safety monitoring board for Athenyx, Novartis, and Vor Pharma; and has a patent with Athenyx. RM is an employee of Gamida Cell Inc., Kite Inc., and Tricida Corporation. SS is an employee of Gamida Cell Inc. and Incyte Corporation. EG-C is a former employee of Gamida Cell Inc. 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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