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EBMT 2019 | Umbilical cord blood transplantation in adolescents and young adults with acute myeloid leukemia

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Data regarding the use of hematopoietic stem cell transplantation (HSCT) is limited and controversial in adolescents and young adults (AYAs), which is also true of studies using umbilical cord blood (UCB) as an alternative donor source.

On Tuesday 26 March 2019, during the 45th European Society for Blood and Marrow Transplantation (EBMT), Hiromi Hayashi, Eurocord, Hôpital Saint Louis, APHP and IUH, Paris, FR, presented the outcomes of AYAs with acute leukemia who received an umbilical cord blood transplantation (UCBT) following a myeloablative conditioning regimen. The study was conducted on behalf of Eurocord, the Cellular Therapy and Immunobiology Working Party (CTIWP) and Paediatric Diseases Working Party (PDWP) and was presented during the meeting in Frankfurt, Germany.[1]

Background

AYAs represent a heterogeneous population of patients for whom the treatment protocols are not well defined; some are treated with pediatric regimens whereas others may receive more intensive chemotherapy traditionally given to adults. Additionally, the age range represented by AYAs is not mutually agreed upon, with some definitions ranging from 15 to 39.

This study aimed to investigate the use of UCBT in patients aged 15–25 with acute leukemia following a myeloablative conditioning regimen. By restricting the age range, the authors aimed to make the population more homogenous.

Study design and patient characteristics

- Eligibility:
  - Patients (age 15–25 at UCBT) with acute leukemia who received an unrelated UCBT (single or double UCB source), in EBMT centers between 2004 and 2016, as their first allogeneic-HSCT, with a myeloablative conditioning regimen
  - Patients were ineligible if they had received manipulated or expanded cord blood or UCB co-infused with other stem cell sources
- Patient characteristics:
  - N = 504
  - Median age at UCBT: 19 years (16–22)
  - Median time from diagnosis to UCBT: 11 months (5–29)
  - Acute myeloid leukemia (AML) *vs* acute lymphoblastic leukemia (ALL): 41% *vs* 59%
  - Disease status (complete remission 1 [CR1] *vs* CR2 *vs* advanced): 42% *vs* 38% *vs* 20%
- UCBT and treatment regimen:

- HLA mismatches (matched or 1 mismatch *vs* ≥2 mismatches): 38% *vs* 62%
- Stem cell source (single *vs* double): 58% *vs* 42%
- Anti-thymoglobulin (ATG) was used in 54%
- In 40% of cases, the donor was female and the recipient was male
- Most frequently used myeloablative conditioning regimen: cyclophosphamide + total body irradiation + fludarabine: 45%
- Most frequently used GvHD prophylaxis: cyclosporine A + mycophenolate mofetil: 44%
- Cumulative incidence function (CIF) for neutrophil engraftment at day-60: 87.7%

Table 1: Summary of patient outcomes

Outcome measure	**Result (95% CI)**
3-year leukemia free survival (LFS) (n = 504):	40.9 ± 2.3%
- CR1 (n = 207)	48.5 ± 3.7%
- CR2 (n = 183)	48.1 ± 3.9%
- Advanced (n = 96)	19.8 ± 4.3%
CIF Graft-*versus*-host disease (GvHD):	
- Grade II–IV acute GvHD (aGvHD), day 100	27.8% (23.8–31.9)
- Chronic GvHD (cGvHD), 3-years	25.3% (21.4–29.3)
Relapse	27.9% (23.9–32.1)
- CR1	27.6% (21.4–31.4)
- CR2	24.3% (8.1–31.1)
- Advanced	36.8% (26.7–46.9)

3-year overall survival (OS)	45 ± 2%
By disease status (P < 0.001):	
- CR1	54 ± 4%
- CR2	48 ± 4%
- Advanced	20 ± 4%
3- year refined GvHD relapse free survival (rGRFS)	31.5 ± 2%
3-year CIF transplant related mortality (TRM)	31.1% (24–33)
Main causes of death:	
- Relapse	41%
- TRM	57%

Table 2: Factors associated with outcome in multivariate analysis

Outcome measure	**Factor associated**	***P* value (95% CI)**	**HR (95% CI)**
3-year LFS	Improved LFS:		
	More recent UCBT (2010–2016 *vs* 2004–2009)	0.02	0.73 (0.56–0.95)
	Poor LFS:		
	Use of ATG	0.02	1.42 (1.05–1.92)
	Advanced disease status (*vs* CR1)	>0.001	2.50 (1.81–3.45)

aGvHD	Reduced risk aGvHD:		
	Use of ATG	0.01	0.54 (0.34–0.86)
	More recent UCBT	0.03	0.67 (0.46–0.97)
	Higher risk aGvHD:		
	Double UCBT	0.02	1.65 (1.07–2.53)
Relapse	Higher relapse rate:		
	Advanced disease status (vs CR1)	0.01	1.89 (1.15–3.11)
3-year OS	Increased OS:		
	More recent UCBT	0.002	0.76 (0.62–0.90)
	Better disease status	< 0.001	0.36 (0.24–0.53)
3-year rGRFS	Higher rGRFS:		
	More recent UCBT	0.47	0.85 (0.73–0.99)
	Better disease status	0.008	0.60 (0.41–0.88)
	Negative cyto-megalovirus serology	0.037	0.77 (0.60–0.99)

Changes in outcomes in AYAs with UCBT

Between 2004–2009 and 2010–2016, the 3-year OS for AYAs has improved from 36.8% ± 3.2 to 53.8% ± 3.5, bringing this in line with the OS seen in children.

Conclusion

- In AYA patients without an alternative donor source, UCBT is a viable option. However, in this setting, UCBT should be used with caution
- This study has contributed to further understanding of HSCT in this age group, for which there was limited prior data available

- Key risk factors for outcome: advanced disease status at UCBT, the use of ATG and UCBT performed between 2004-2009

References

1. Hayashi H. *et al.* Outcomes after umbilical cord blood transplantation in adolescents and young adults with acute leukemia: on behalf of Eurocord, CTIWP and PDWP of EBMT. Abstract OS3-8. 2019 March 26. 45th Annual Meeting of the European Society of Blood and Marrow Transplantation (EBMT), Frankfurt, DE
