RETROVIROLOGY

MEETING ABSTRACT Open Access

Can allo-SCT with RIC cure ATLL? Long-term survivors with excellent PS and with heterogenous HTLV-1 proviral load level

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From 15th International Conference on Human Retroviruses: HTLV and Related Viruses
Leuven and Gembloux, Belgium. 5-8 June 2011

Background

Adult T-cell leukemia/lymphoma(ATLL) has so far had a very poor prognosis by chemotherapy. From the long-term observations of our previous clinical trials (NST-1/NST-2; allogeneic hematopoietic stem cell transplantation with reduced-intensity conditioning regimen (RIC) for ATLL patients), we suspect that RIC strategy might have a possible curative power for ATLL patients (pts).

Objective

We evaluated the safety and feasibility of allogeneic hematopoietic stem cell transplantation with RIC from matched sibling donors (MSD) for ATLL pts using a conditioning regimen consisting of fludarabine and busulfan. Low-dose antithymocyte globulin was added in the 1st study (NST-1), while it was omitted for the 2nd study (NST-2). We present the results of long-term follow-up of the two trials as well as the longitudinal patterns of changes in HTLV-1 proviral load in survivors.

Patients and methods

Between Apr, 2001 and Feb, 2006, 30 pts ranged from 50 to 67 years of age were enrolled in NST-1(16 pts) and NST-2 (14 pts). After undergoing the conditioning regimen, they received G-CSF-mobilized peripheral blood (PB) stem cells from HLA-matched sibling donors (MSD). Half of the donors were HTLV-1 carriers. The primary end points in both studies were achievement of complete donor chimerism before day 90, and absence of early transplant-related mortality (TRM) before day100. The HTLV-1 proviral load was estimated using PB samples serially after RIC. HTLV-1 proviral DNA was measured by the quantitative PCR amplification of HTLV-1 pX DNA. The detection limit of the HTLV-1 proviral load was 0.5 The overall survival (OS) curve was estimated by the Kaplan–Meier method.

Results

The results have been already published elsewhere (Okamura, Blood, 2005, Tanosaki, BBMT, 2008, Choi, BMT, 2011) . Ten of the29 evaluable patients have survived for a median of 115 months (range, 85-130 months) after RIC. All of them maintain their good health (Karnofsky PS score ?90%).The majority of survivors have developed the graft-versus host disease (GVHD) (10/10 pts for acute GVHD and 9/10 pts for chronic GVHD). Overall and progression free survival rates at 5 years for the studies were 36% (95% IC, 21 to 51%) and 31% (95% IC, 17 to 45%), respectively. Serial changes in the HTLV-1 proviral load after RIC in the pts are heterogeneous but can be roughly classified into 3 patterns. In the first pattern, seen in 3 pts, the proviral load became undetectable after RIC and continued to remain so. In the second pattern, seen in 3 pts who had received RIC from HTLV-1 negative donors, the proviral load had become undetectable but returned to detectable levels thereafter. Lastly, in the third pattern, seen in 4 pts who had received the grafts from HTLV-1-carrier donors, the proviral load had remained at the carrier level. All the 10 survivors continue to show complete donor chimera during the observation period regardless of the HTLV-1 proviral load level.

Conclusion

The long-trem follow–up in our study indicates not only that RIC from MSD is a feasible treatment modality for ATL, but also that one third of the pts may be cured

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with this procedure because all survivors are good for health. As for post-RIC changes in HTLV-1 proviral load in long-term survivors it seems heterogenous, which may be categoryzed into 3 patterns.

Acknowledgements
(Other coauthors ; T Fukushima, M Harada, T Etoh, Y Saburi, H Kikuchi, M Hidaka, M Matsuoka, M Kannagi, T Yamanaka. Supported by a grant for anticancer project from Ministry of Health, Welfare, and Labor of Japan.)

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Published: 6 June 2011

doi:10.1186/1742-4690-8-S1-A33
Cite this article as: Uike *et al.*: Can allo-SCT with RIC cure ATLL? Long-term survivors with excellent PS and with heterogenous HTLV-1 proviral load level. *Retrovirology* 2011 **8**(Suppl 1):A33.