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ESPS Peer-review Report
Name of Journal: World Journal of Transplantation
ESPS Manuscript NO: 5319
Title: Optimal choice of stem cell source for allogeneic hematopoietic stem cell transplantation in patients with hematological malignancies
Reviewer code: 00742009
Science editor: Cui, Xue-Mei
Date sent for review: 2013-08-29 16:39
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This is an interesting review on the choice of different sources of hematopoietic stem cells for the sake of transplantation for patients with hematologic malignancies. 1. The author is justified, based on the review of the published literature, that bone marrow (BM), peripheral blood stem cells (PBSC), and cord blood (CB) are the usual options, and that transplantation with either BM or PBSC results in comparable outcomes in terms of overall survival. 2. Most of the discussions go around the choice of stem cells from the patients' perspective, there are, however, important considerations looking from the donors' perspective. Potential complications, time to off work, and donors' discomfort post-harvest are different with respect to BM harvest and PBSC collection. This deserves a separate column for discussion. 3. Leukemia patients who require stem cell transplantation are by nature having high risk disease. When the author mentions about "high risk" leukemia patients in the manuscript, he is actually referring to a subset of patients. He might want to elaborate how this "high risk" group is defined. 4. Given the complex interplay between stem cell source, disease characteristics, and graft-versus-host disease (GVHD), how does the choice of stem source affect the approach to GVHD prophylaxis? 5. To what extent is recipient's cytomegalovirus status determining in the choice of stem cells source? 6. When choosing the appropriate stem cell source from unrelated donors, the transplant physician has to take into consideration of other important factors such as cost and ABO mismatch. For instance, if a cord blood is found locally and a walking donor is found in an overseas country, the price tags for the procurement of the 2 sources of stem cells are substantially different. In the case of major ABO mismatch, obtaining PBSC from the donor can be more convenient as the small amount of red cells in the final product can obviate the need for red cell

depletion whereas bone marrow obtained from the same donor needs to be processed, which takes time and there will be some loss in stem cells. Randomized studies are not needed. 7. Table 1 is not very informative. I would suggest the author to re-organize it so as to focus on unrelated donor transplantation for leukemia patients. "Availability" to be replaced by "typical time frame" from initiation of search to transplantation. To specify the actual volume in "Volume" so that the risk of volume overload can be appreciated. To specify the "speed of engraftment" in terms of neutrophils and platelet in figures. With this information, "stem cell proliferation rate" becomes unimportant. "Amount of stem cell" to be replaced by "optimal or minimum cell doses for transplant". "Freshness of stem cell" is not an important feature but potential "exposure to dimethyl sufloxide" is. "Collection process", "Duration of collection process", and "Age of stem cell" are irrelevant in clinical practice. The author may also want to include a certain subset of patients (high risk), red cell content, CMV status for comparison among the different sources of stem cells. The resultant Table will be useful for the transplant physician to put it side by side with the patient and see which source of stem cell has the most advantages.

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[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

- The paragraph entitled “Selection among different stem cell sources” could be improved by a tentative flow-chart presenting a point-to-point approach to HSCT in hematologic malignancies, e.g: 1) matched sibling donor (MSD)available > when BM, PBSC, UCB; 2) if MSD not available > if not urgency > matched unrelated donor (MUD); 3) if MUD not available … - A brief paragraph could be worth, discussing how the major differences in blood cell composition among the three sources of stem could impact the outcome of HSCT, in terms of engraftment, GvHD and, possibly graft versus tumor. - The following paragraphs (page 5 – 13) report relevant data from RCT and meta-analyses that would assist hematologists in choosing the appropriate source of stem cells in different conditions. However, the structure is a bit repetitive and can slow the reading. To improve readability, most of data from RCT could be reported in a table and the text of the manuscript could be reserved to a more articulated discussion of results. - The practice of HSCT is continuously evolving. In the last paragraph (conclusions), it could be advisable to briefly discuss how novel procedures may impact on the choice of SC source. In particular, manipulation of cells (stem cell enrichment, depletion of lymphocytes subsets or allo-reactive cells), mesenchymal stem cells, novel treatments of GvHD have recently been used to improve haploidentical SCT. Minor comment: - page 5, 6th row from the bottom: please check data with ref 8 and make more clear what group percentages are referring to.

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		[ ] No records	

COMMENTS TO AUTHORS
Good overall review of choosing a donor stem cell source for HSCT. The review of the available studies of BM vs. PBSC vs. cord blood is quite good and will be useful to readers. Since the review is relatively brief, I would like to see a little more detail about double cord transplants and haploidentical transplants, as these are becoming more attractive options. Specific comments: Please make sure that, when discussing double cord transplants, it is stated that the two cords be at least 4/6 HLA matched to the patient as well as to each other. Last paragraph, first sentence on p. 9, discussing the meta analysis of ref. #29: I think the statement that "disease free survival was significantly lower in the PBSC group" is incorrect. To my reading of the referenced paper, DFS was better in the PBSC group. Please provide a little more detail on the pros and cons of haploidentical transplants (e.g., worse GVHD and engraftment failure if T cell replete; increased relapse rate and delayed immune reconstitution if T cell depleted). This is an area of growing interest due to the greater availability of haplo donors, if some of these problems can be overcome. There are several good recent reviews which can be cited in the interest of brevity. In the author's center 8 antigen HLA matching may be performed, but in many centers 10 antigen matching is used. I would ask the author to consider changing (or adding) that 10/10 or 9/10 HLA matches are optimal.