



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242 Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com <http://www.wjgnet.com>

Name of Journal: *World Journal of Transplantation*

ESPS Manuscript NO: 20447

Manuscript Type: Minireviews

REPLY To REVIEWER's comments/ suggestions:

REVIEWER 1 :

COMMENT 1- Clinically, the incidence and severity of CMV infection (including CMV diseases and seropositivity) is closely associated with the transplantation patterns. In haplo-identical hematopoietic stem cell transplantation, the incidence of CMV infection is usually high and that is commonly low in the setting of HLA matched related HSCT. It might be appropriate if the authors had detailed the differences and the underlying mechanisms.

REPLY- We have added points suggested by reviewer in introduction and pathogenesis sections with proper references.

COMMENT 2 - Treatment of CMV infection with the commonly used drugs usually result in therapy associated nephrotoxicity and hematopoietic suppression, which is the problematic issue in the control of CMV disease. The authors may add some detailed discussion about this issue.

REPLY- We have described the treatment related nephrotoxicity and myelosuppressive issues as suggested by reviewer with appropriate references.

COMMENT 3- Further, cellular therapy with CMV- specific CTL and other therapeutic options should be discussed.

REPLY- Reviewer suggestion has been included in treatment section with references.

REVIEWER 2:

COMMENT - The manuscript by Bhat V et al. is well structured and written. A clear definition as well as correct description of possible complication and management of the CMV effects in transplant patients, have been done by the authors. Nevertheless, I feel that considering the relevance of the topic, the authors

should update the references since they include very old references, I just have found one reference from 2012. In the sense, many articles have been published in the last 3 years regarding the topic, due to the relevance and the increase in the amount of transplanted patients.

REPLY- As suggested by reviewer we have included additional text and recent references in manuscript as follows:

- Ariza-Heredia EJ, Neshor L, Chemaly RF. Cytomegalovirus diseases after hematopoietic stem cell transplantation. *Cancer Letters* 342 (2014) 1-8 PMID:24041869 DOI:10.1016/j.canlet.2013.09.004
- Luo XH, Chang YJ and Huang XJ. Improving Cytomegalovirus-Specific T Cell Reconstitution after Haploidentical Stem Cell Transplantation. *Journal of Immunology Research* Volume 2014, Article ID 631951. <http://dx.doi.org/10.1155/2014/631951>
- Lu DP, Dong L, Wu T, Huang XJ, Zhang MJ, Han W, Chen H, Liu DH, Gao ZY, Chen YH, Xu LP, Zhang YC, Ren HY, Li D, Liu KY. Conditioning including antithymocyte globulin followed by unmanipulated HLA mismatched/ haploidentical blood and marrow transplantation can achieve comparable outcomes with HLA-identical sibling transplantation, *Blood*, vol. 107, no. 8, pp. 3065-3073, 2006.
- Marty FM, Boeckh M . Maribavir and human cytomegalovirus-what happened in the clinical trials and why might the drug have failed? *Curr Opin Virol.* 2011 Dec;1(6):555-62 PMID:22440913 DOI:10.1016/j.coviro.2011.10.011
- Feuchtinger T, Opherk K, Bethge WA, Topp MS, Schuster FR, et al. Adoptive transfer of pp65-specific T cells for the treatment of chemorefractory cytomegalovirus disease or reactivation after haploidentical and matched unrelated stem cell transplantation *Blood.* 2010 Nov 18;116(20):4360-7. . PMID:20625005 DOI: <http://dx.doi.org/10.1182/blood-2010-01-262089>
- George B, Pati N, Gilroy N. et al. Pre-transplant cytomegalovirus (CMV) serostatus remains the most important determinant of CMV reactivation after allogeneic hematopoietic stem cell transplantation in the era of surveillance and preemptive therapy," *Transplant Infectious Disease*, vol. 12, no. 4, pp. 322-329, 2010. PMID: 20487414 DOI: 10.1111/j.1399-3062.2010.00504.x