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Commentary
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The Haploidentical Family Donor: A New Weapon against Hodgkin's Lymphoma

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Commentary

The fraction of patients with Hodgkin's Lymphoma (HL) who are not responsive to first-line or salvage therapy have a poor outcome and deserve investigation for the search of newer and effective drugs. Fortunately, those drugs are there and showed efficacy in late stages as well as in earlier phases of treatment [1-5]. Some are new, like Brentuximab Vedotin and Nivolumab, whereas others are not properly a novelty, like Bendamustin or Gemcitabine. Furthermore, we are at the beginning of a new era in oncology, where we have the possibility to effectively re-direct the patient's immune system against cancer cells, thus widening the multitude of options for cancer treatment [6,7].

Allogeneic hematopoietic stem cell has shown to be effective in HL and this procedure is now reserved to patients relapsed after autologous stem cell transplantation and who are fit to receive such an intensive and complex treatment [8]. Few years ago, Sureda A et al. [9], on behalf of the European Group for Blood and Marrow Transplantation, demonstrated that allogeneic HSCT has to be performed using a reduced-intensity conditioning regimen, which improves the outcome by reducing the toxicity associated with the "traditional", myeloablative allogeneic HSCT. This enhanced the rationale, proposed from 1979, of allogeneic HSCT as an effective form of immunotherapy [10] other than as a procedure relying solely on high-dose chemotherapy to eradicate cancer.

Recently, a platform of allogeneic HSCT from a HLA-mismatch donor, that foresees an unmanipulated stem cell graft from such a donor together with high-dose post-transplant cyclophosphamide as part of GvHD prophylaxis (haplo-HSCT with PT-Cy), has been introduced11 and, like in many other blood diseases, also employed for those HL patients who deserved allogeneic HSCT but lacked a compatible donor. The "haplo-HSCT with PT-Cy" platform has been pioneered by the colleagues from Baltimore [11] and in few years has replaced cord blood as source of hematopoietic stem cells in adult patients [12] and challenges the results with allogeneic HSCT from unrelated donors [13,14]. Interestingly, such haplo-transplant showed to be particularly effective in HL, as reported by two independent groups [15,16] and thereafter confirmed by others [17-20]. The reason for that is not completely understood: a role might be played by high-dose cyclophosphamide, or by the dramatic reduction of toxic mortality associated with this platform, or we could even call for a putative "haplo-vs-lymphoma" effect, taking into account the immunological implication in the pathogenesis and pathophysiology of HL. Nonetheless, as it is the case for diseases with relatively little numbers of patients, at this moment no uniform indication for the choice of donor type exists for allogeneic HSCT in patients with this unlucky form of HL, and haplo-HSCT with PT-Cy still has not a well-established place in HL treatment, despite having shown those very promising results. A randomized scomparison between stem cell donors setting is poorly feasible in this setting of relatively low numbers of patients and of heterogeneity of transplant algorithms for donor choice among transplant centers; moreover, a true randomization should involve only those patients with HLA-matched donor [21], thus restraining furthermore the already low numbers. Alternatively, potential data from genetic randomization studies, observational registry ones, or any retrospective comparisons will provide the best evidence in this field. In the era of precision medicine in oncology, where targeted therapies are tested on subgroups of cancers or distinct cancers sharing the same mutation (i.e. the basket trials or the umbrella trials), recommendations may be provided although the traditional, phase III randomized controlled trial is not there.

At the moment, unless new data will appear, the prognosis of relapsed or refractory HL patients seems to be affected by disease features among which the most important is the sensitivity to the therapy administered before transplant, but not by the type of stem cell donor [19,20], thus depending this latter on each center's policy. This means that haplo-HSCT with PT-Cy is part of this choice; and this choice will integrate into the framework of multiple, effective weapons that now we have against HL.

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