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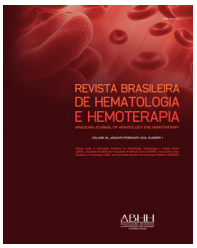

Scientific Comment

Hematopoietic stem cell mobilization for autologous transplantation in multiple myeloma patients previously exposed to cyclophosphamide, thalidomide, and dexamethasone: is granulocyte-colony stimulating factor alone enough?☆

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The paradigm for multiple myeloma (MM) therapy has evolved markedly in the past decade with the introduction of numerous new drugs and improved patient outcomes.[1]

Autologous hematopoietic stem cell transplantation (aHSCT) is widely used as part of first line therapy in the treatment of transplant-eligible patients with MM.[2] In these patients, hematopoietic stem cell (HSC) mobilization for aHSCT has commonly been performed using cyclophosphamide plus granulocyte-colony stimulating factor (G-CSF) or G-CSF alone.[3,4] However, the induction regimens should not increase the mobilization failure risk. This concern has been especially pertinent to patients previously exposed to cyclophosphamide or lenalidomide during induction, as these drugs appear to hamper HSC mobilization. In the article that accompanies this comment, Crusoe et al. demonstrate the feasibility of using G-CSF alone to mobilize progenitor cells in MM patients induced with a cyclophosphamide, thalidomide and dexamethasone regimen.[5] The number of $CD34^+$ cells mobilized was assessed after using G-CSF with or without cyclophosphamide.

The retrospective study of Crusoe et al. included eighty-eight MM patients who underwent aHSCT at two Brazilian centers.[5] Collection of $>2.0 \times 10^6$ $CD34^+$ cells/kg was considered sufficient. The group that received cyclophosphamide collected a higher median number of progenitor cells [3.8 (range: 3.1–4.4) vs. 3.2 (range: 2.3–3.8) – p-value = 0.008]. However, the cyclophosphamide used in mobilization did not show advantages in terms of mobilization, or improved response or survival.

Indeed, we have to consider that cyclophosphamide used for mobilization may have some disadvantages, such as raising the cost of the procedure due to hospitalization, higher toxicity as patients treated with cyclophosphamide require more time for engraftment of platelets and neutrophils, and potentially a higher incidence of post-transplant infections. Eliminating cyclophosphamide from the mobilization regimen has improved patient convenience and has decreased the duration of mobilization treatment by approximately nine days.[6]

We might also argue that the higher number of progenitor cells collected with cyclophosphamide plus G-CSF would enable the storage of more HSC for a second salvage transplant. However, the utilization of stored autologous HSC to support a second aHSCT in MM patients in the era of novel agent therapies has been addressed. Data from Seattle showed that of 726 patients who had residual HSC in storage after their first aHSCT, only 135 patients underwent a second aHSCT.[7] The percentage of patients receiving a second aHSCT has declined over time. The resources required to collect and store

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☆ See paper by Crusoe et al. in Rev Bras Hematol Hemoter. 2016;38(4):302–309.
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unused HSC added up to 336 extra patient days of apheresis and 41,587 extra patient months of cryopreservation, translating into a higher average cost per patient. The authors concluded that a reconsideration of conventional HSC collection and storage practices would save significant cost for the majority of MM patients who never undergo a second aHSCT.[6] We do not know whether the results from Seattle might be translated to the reality of Brazilian patients treated within the Brazilian National Health System (SUS) that, in some centers, precludes the use of novel and more effective agents that would lead to better responses before and after aHSCT.

In conclusion, the study by Crusoe et al. showed that sufficient progenitor cells can be mobilized to perform at least one aHSCT with the use of G-CSF alone in patients induced using the cyclophosphamide, thalidomide and dexamethasone protocol. This strengthens the current study as it makes a valuable judgment regarding the limitations of performing aHSCT in Brazil and the need to cut costs. The questions addressed here will have a practical impact on the clinical practice.

Conflicts of interest

The author declares no conflicts of interest.

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