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Review

Autologous hematopoietic progenitor cell mobilization and collection in adult patients presenting with multiple myeloma and lymphoma: A position-statement from the Turkish Society of Apheresis (TSA)

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ABSTRACT

Autologous hematopoietic cell transplantation (AHCT) is a routinely used procedure in the treatment of adult patients presenting with multiple myeloma (MM), Hodgkin lymphoma (HL) and various subtypes of non-Hodgkin lymphoma (NHL) in upfront and relapsed/refractory settings. Successful hematopoietic progenitor cell mobilization (HPCM) and collection are the rate limiting first steps for application of AHCT. In 2015, almost 1700 AHCT procedures have been performed for MM, HL and NHL in Turkey. Although there are recently published consensus guidelines addressing critical issues regarding autologous HPCM, there is a tremendous heterogeneity in terms of mobilization strategies of transplant centers across the world. In order to pave the way to a more standardized HPCM approach in Turkey, Turkish Society of Apheresis (TSA) assembled a working group consisting of experts in the field. Here we report the position statement of TSA regarding autologous HPCM mobilization strategies in adult patients presenting with MM and lymphoma.

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1. Introduction

Autologous hematopoietic cell transplantation (AHCT) is a routinely used procedure in the treatment of adult patients presenting with multiple myeloma (MM), Hodgkin lymphoma (HL) and various subtypes of non-Hodgkin lymphoma (NHL) in upfront and relapsed/refractory settings [1,2]. On the other hand the application of second AHCT is recommended in MM patients with high-risk cytogenetic features as part of a tandem approach [3] or relapsed disease following a reasonable duration (>18 months) of initial remission following upfront AHCT [4]. There is a global shift from bone marrow to peripheral blood (PB) as the preferred source of $CD34^+$ hematopoietic progenitor cells because faster engraftment kinetics and better quality of life compared to bone marrow harvesting.

Successful hematopoietic progenitor cell mobilization (HPCM) and collection are the rate limiting first steps for application of AHCT. Although there are recently published consensus guidelines addressing critical issues regarding autologous HPCM [5–8], there is a tremendous heterogeneity in terms of mobilization strategies of transplant centers across the world. Mobilization policies of centers depend not only on institutional perception of up-to-date data regarding HPCM or preference of a specific guideline-driven strategy but also on resource availability and local regulations of each country, where the center is located. In order to pave the way to a more standardized HPCM approach in Turkey, Turkish Society of Apheresis (TSA) assembled a working group consisting of experts in the field. Here we report the position statement of TSA regarding autologous HPCM mobilization strategies in adult patients presenting with MM and lymphoma.

2. Methods

TSA established a working group consisting of experts in the field of adult clinical hematopoietic cell transplantation (HCT). The position statement included frequently asked questions, relevant issues regarding HPCM and organized in a user-friendly way for transplant physicians. A core panel of experts prepared a draft including most current data and local regulations in Turkey regarding HPCM, which was thoroughly evaluated by all members of the working group to finalize the manuscript.

3. Position statement

3.1. The choice and schedule of the myeloid growth factors

Original filgrastim (Neupogen®) with its various biosimilars and lenograstim (Granocyte®) are currently available in Turkish market. Although we have robust data indicating similarity in terms of efficacy and safety of pegylated G-CSF compared to non-pegylated G-CSF [9], pegylated G-CSF is not licensed yet in the country. Equivalence of biosimilar filgrastim as originator G-CSF or lenograstim in terms of safety and efficacy has been reported in steady-state [10–15], chemomobilization [16–21] and G-CSF + plerixafor HPCM [22] settings in patients who underwent autologous HCT and healthy donors of allogeneic HCT recipients. All available G-CSFs (original/biosimilar filgrastim and lenograstim) can be used in approved doses and schedules for steady-state (10 μg/kg/day subcutaneously) and chemomobilization (5 μg/kg/day subcutaneously) as recommended by guidelines [8].

Although widely used, one study conducted in breast cancer patients found no advantage of split dose injection of filgrastim over once daily schedule [23]. Because of cost savings compared to lenograstim, original or biosimilar filgrastim seems to be the most feasible agent for steady-state HPCM in Turkey.

3.1.1. Position statement on the choice and schedule of the myeloid growth factors

Original filgrastim, biosimilar forms of filgrastim and lenograstim in recommended doses and schedules are reasonable G-CSF options for steady-state mobilization and chemomobilization in patients undergoing HPCM. Original or biosimilar filgrastim may be preferred over lenograstim because of cost-effectivity.

3.2. Progenitor cell dose and duration of leukapheresis

There is general agreement that infusion of at least 2×10^6/kg $CD34^+$ cells are needed for successful engraftment, although restoration of normal hematopoiesis is possible below this threshold [7]. Because the infusion of higher dose of progenitor cells result in faster engraftment and decreased transfusion support, optimal dose of $CD34^+$ cells needed to support one AHCT were accepted as $>4 \times 10^6$/kg [24] or $>5 \times 10^6$/kg [7,25–27]. There are also centers using disease-specific targets for $CD34^+$ cells ($>4 \times 10^6$/kg for MM and $>5 \times 10^6$/kg for lymphoma patients required for supporting one AHCT) [28]. In fact, two phase-III trials, which resulted the approval of plerixafor in combination with G-CSF for HPCM in patients with MM and NHL defined achievement of $>6 \times 10^6$/kg and $>5 \times 10^6$/kg $CD34^+$ cells as the primary end point for target stem cell yield in patients presenting MM and NHL, respectively [29,30]. Although an evidence-based threshold for optimal stem cell dose cannot be defined at this moment, targeting optimal progenitor cell dose for one AHCT as $4-5 \times 10^6$/kg seems to be reasonable. Even in the era of novel agents, AHCT is an indispensible treatment option for MM patients in upfront and relapsed/refractory settings. Indeed, many MM patients may need two AHCT procedures during the course of their disease either as a tandem approach (patients with high-risk cytogenetic features at diagnosis) or in relapsed disease with a long remission duration following first AHCT [3,4]. Therefore, achievement of minimal stem cell yield required for supporting two AHCT procedures should be aimed in patients presenting with MM.

Currently, there is no consensus on the maximal duration of leukapheresis. Defining the optimal trade-off between prolonged HPCM procedure and higher progenitor cell yield is an important issue for all transplant centers. It is often difficult to decide whether to stop or continue leukapheresis to reach the optimal cell dose in a patient after achievement of minimal stem cell dose. Italian Group for Stem Cell Transplantation (GITMO) defined proven poor mobilization as inability to harvest at least 2×10^6/kg $CD34^+$ cell dose in ≤3 apheresis sessions [31]. With judicious use of plerixafor in almost one third of the patients, City of Hope group was able to collect at least 2×10^6/kg $CD34^+$ cells in 2.8 days (mean) [28]. In the plerixafor era, keeping the duration of progenitor cell collection at a maximum of 4 days seems to be rational [8,29,30,32].

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