Poor peripheral blood stem cell collection in patients with multiple myeloma: a new predictive model based on clinical parameters from a GIMEMA retrospective study

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A still not well defined proportion of patients with multiple myeloma (MM) and eligible for autologous stem cell transplantation (AuSCT) fails to mobilize CD34+ peripheral blood stem cells (PBSC) at all or to collect an adequate number for a safe procedure or sufficient for multiple transplants. The percentage of these 'poor mobilizers', however, differs across studies, depending on definitions, parameters utilized to evaluate collections, age, disease type, phase and characteristics, treatments applied, objectives to reach, and practices for mobilization and apheresis. Due to such heterogeneity, data are difficult to analyse and to compare.

We aimed to develop a method based on easily available clinical parameters for predicting unsuccessful (< 2 x 10^6/kg) or sub-optimal (< 5 x 10^6/kg) collections of CD34+ PBSC in newly diagnosed MM patients eligible for AuSCT, treated with novel agents and receiving an homogeneous mobilizing therapy with cyclophosphamide and granulocyte-colony stimulating factor (G-CSF). To this purpose, 1.348 patients enrolled in five consecutive Italian clinical trials were retrospectively analysed. Age, baseline low peripheral blood cell counts, use of lenalidomide, and haematological toxicity developed during induction were taken into account as possible factors associated with poor mobilization.

Overall, 280 patients (20.8%) showed either sub-optimal (167 patients, 12.4%) or unsuccessful (113 patients, 8.4%) collections. All analysed parameters negatively influenced the procedure, but only age and haematological toxicity during induction maintained their significance at multivariate analysis. Based on ordinal logistic regression model, we constructed a risk heat-map where the four parameters were pooled and weighted according to their relevance as single or combined variables. This model was predictive for different probabilities of failure, suboptimal or optimal outcomes. According to the cumulative probability of unsuccessful collections (failures + suboptimal), four different areas were identified, respectively, at low (range 14% to 18%), intermediate-1 (21% to 30%), intermediate-2 (39% to 46%), and high (50% to 63%) risk (Figure 1).

An insufficient availability of PBSC may be a relevant clinical problem in patients otherwise eligible for AuSCT, a procedure that represents the best therapeutic approach in MM. We quantified this phenomenon, showing that a significant proportion of previously untreated MM patients completely fails CD34+ PBSC collection or does not reach an adequate number after a standard mobilizing procedure. To conclude, about 20% of newly diagnosed MM fail to collect an adequate number of PBSC.

Our simple 'risk card', based on the largest group of patients treated frontline with novel agents and receiving the most popular mobilizing approach currently employed in Europe so far reported in this setting, is applicable in individual patients with MM and may contribute to the early identification of 'poor mobilizer' phenotypes. Although certainly ameliorable, this model increases our awareness in this field, representing a novel possible framework to select patients in whom to plan alternative mobilizing strategies. Therefore, its validation in prospective series is required, possibly even in the setting of potentially more effective chemotherapy-free-mobilizing regimens, which have been recently reported as superior to the cyclophosphamide and G-CSF combination.

Stem Cell Res Ther. 2015 Apr 17;6(1):64.