Patients undergoing peripheral blood stem cell mobilization for autologous transplantation may fail to achieve the generally accepted minimum threshold for transplantation ($\geq 2 \times 10^6$ CD34/kg) despite using optimal doses of granulocyte-colony stimulating factor (G-CSF) or chemotherapy plus G-CSF. Failure rates vary from center to center but are felt to be highest in certain diseases such as non-Hodgkin’s lymphoma (NHL), Hodgkin’s disease (HD), and in heavily pretreated patients with multiple myeloma (MM). Although there is both vigorous debate and varying understanding of the optimal methods for mobilization (G-CSF alone versus chemotherapy plus G-CSF) there is general agreement that these diseases and various risk factors are associated with high rates of stem cell collection failure. The known risk factors include age, high-risk diseases such as lymphoma, progressive disease, bone marrow involvement, previous radiation therapy, premobilization platelet counts, exposure to repetitive cycles of chemotherapy with specific chemotherapies such as fludarabine and biologic therapies such as lenalidomide ($>3$-6 cycles). There are likely other risk factors that are either poorly understood (SDF-1 and CXCR4 single nucleotide polymorphisms, sympathetic nervous system function, and innervation of the bone marrow) or not yet identified (diabetes, germ line polymorphisms in genes that control stem cell quiescence and mass) [1,2]. Because the SDF-1/CXCR4 axis is critical for stem cell trafficking and homing any agent that modulates this axis or interrupts this ligand-receptor interaction would be expected to promote stem cell trafficking from the bone marrow to the peripheral blood yielding enhanced stem cell collections.

The largest retrospective analysis of patients undergoing stem cell mobilization for NHL, HD, and MM demonstrated that magnitude of mobilization failure is greatest in NHL ($\sim 25\%$) and lowest in MM ($\sim 8\%$) [3]. These data have now been confirmed and validated by many groups. Pusic et al. [3] also found that although chemotherapy plus G-CSF mobilized higher median Cd34/kg than G-CSF alone the failure rates of achieving a minimum threshold of $\geq 2 \times 10^6$ CD34/kg after a maximum of 5 20-liter apheresis procedures were identical in each disease group (NHL, HD, and MM) whether the patients were mobilized with G-CSF plus chemotherapy or G-CSF alone. Furthermore, a subset analysis of over 280 patients who required remobilization demonstrated that a second mobilization attempt was successful only $\sim 25\%$ of the time regardless of the use of G-CSF, granulocyte macrophage-colony stimulating factor plus G-CSF or chemotherapy plus G-CSF as an alternative remobilization strategy while remobilization with G-CSF plus plerixafor resulted in successful remobilization in approximately $60\%$ of patients.

The report of Attolica et al. [4] reported similar results in a small cohort of patients ($n = 37$) with NHL and MM who failed initial mobilization (or were considered high risk for mobilization failure) with either G-CSF or G-CSF plus chemotherapy. The authors found, similar to other groups, that the addition of plerixafor to chemotherapy plus G-CSF was well tolerated and dramatically reduced mobilization failure rates, similar to those reported by Pusic et al, from $75\%$ to $27\%$. Although their study could not compare the failure rates of second mobilization with G-CSF plus chemotherapy plus plerixafor to G-CSF plus perixafor other reports suggest that the 2 approaches are similar and point to the key role of adding plerixafor to either backbone in NHL and MM patients who fail initial mobilization [5,6]. Therefore, this study represents one of many that have demonstrated that the addition of plerixafor will increase the CD34/µL by 2- to 4-fold (in 4-12 hours) and will reduce the failure of second mobilization by 2- to 3-fold. In fact, the largest retrospective study of remobilization in MM, HD, and NHL patients who failed initial mobilization performed by the European Consortium of Stem Cell Mobilisation ($n = 580$) revealed almost
identical results with 75% of all patients receiving plerixafor with either G-CSF or chemotherapy plus G-CSF successfully achieving the threshold of ≥2 × 10^6 CD34+/kg. This report recapitulated the results of Attolica et al. [4] demonstrating that the yields of CD34+/kg after remobilization with plerixafor are the best in MM patients (88% success), the worst in NHL patients (63% success) and, most importantly, that G-CSF plus plerixafor was at least as effective at remobilization as G-CSF plus chemotherapy plus plerixafor [6].

The report of Attolica et al. [4] confirm and validate the results of many other groups suggesting that the addition of a small molecule competitive inhibitor of CXCR4, plerixafor, provides new hope for those unfortunate patients with limited marrow reserves and who fail initial mobilization and provides a pathway to autologous stem cell transplantation as potentially curative therapy for patients with hematologic malignancies. Although this and other reports are consistent and compelling, prospective randomized trials will be needed to definitively confirm the role of plerixafor to enhance the mobilization of peripheral blood stem cells in patients who are undergoing mobilization or remobilization with a backbone of chemotherapy plus G-CSF.

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REFERENCES


My AML Cytogenetics Classification Scheme Is Better Than Yours

Mikkael A. Sekeres

Growing up in Rhode Island, my brother and I spent hours riving and fighting over which baseball team was better: the Yankees or the Red Sox. I rooted for the Yankees, just like my father and his father, while my brother, the second born, favored the Sox. This was the late 1970s, and we compared player to player (Jackson vs Rice, Guidry vs Tiant), position to position, tirelessly trying to convince the other, based on the past performance of our teams, which was superior, and each of us leaving the quarrel convinced the other was a complete idiot.

Fast forward a few decades, transform the 2 brothers into hematologic malignancy doctors and the schoolyard into a windowless pathology conference room, and the same passionate dispute shifts to which acute myeloid leukemia (AML) cytogenetic risk scheme is the most predictive of survival. The most widely used are those from the Medical Research Council of the United Kingdom (now the National Council Research Institute), each of the 3 U.S. Cooperative Groups, and the European Organization for Research and Treatment of Cancer/Gruppo Italiano Malattie Ematologiche Dell’Adulto [1-5]. They overwhelmingly share similar characteristics (everyone agrees core binding factors are good, complex cytogenetics are bad, and most