Clinical Group

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Editorial

Hematopoietic stem cell transplantation (HSCT) is an important life-saving procedure which is applied in cases of genetic defects or malignant tumors. Hematopoietic stem cells (HSCs), reside in certain “niches” within the bone marrow allowing them to reproduce themselves and remain in undifferentiated state [1,2], whereas there are evidence that HSC population is not homogenous and can be divided into subtypes [2]. Dependent on the donor of HSC, HSCT can be autologous (if the donor and the recipient is the same person), allogeneic (HSC come from a different person) or syngeneic (HSC donor is identical twin).

The first step in HSCT requires stem cell mobilization using G-CSF or, in the autologous HSCT, various chemotherapeutics in combination with G-CSF [3]. Disruption of CXCL12 binding to CXCR4 has been shown to mobilize HSCs; this is the case in mechanisms of mobilization by G-CSF, FLT-3L, SCF, plerixafor, LECT2 and chemotherapy-driven mechanism [4–6]. Important data have been presented for plerixafor in autologous and allogeneic HSCT [7,8], in HSCT for pediatric patients [9,10], showing superior activity from established treatments such as G-CSF [11,12]. The introduction of plerixafor in clinical practice for HSC mobilization has increased the efficiency of the procedure allowing more patients, which were poorly mobilized to produce stem cells by conventional agents, to take advantage of this therapeutic strategy [13,14]. This is due mainly to the fact that more stem cells can be collected in a single session decreasing, thus, the necessary apheresis sessions [15]. whereas, for NHL and multiple myeloma patients receiving autologous HSCT, plerixafor in combination with GCS–F led to an increase in the efficiency of stem cell regrowth [13,14]. Novel CXCR4 antagonists seem to be more promising than plerixafor such as POL5551 [16,17], increasing the yield of HSCs. Alternative targets such as integrin/ligand receptor interactions (VLA-4, VCAM-1) are also explored, whereas cell signaling pathways such as Rac1 have been shown to mobilize HSCs in mice. A potential target for HSCs mobilization is the activity of various proteases and their ability to degrade chemokines and other adhesive targets. Such proteases are the members of the MMP family, CD26, neutrophil elastase and carboxypeptidase M and N [18]. Other potential targets in HSCs mobilization include the sphingosin 1-phosphate (S1P), SNS neurotransmitters and the compliment cascade.

The second step in HSCT must secure that the donor will escape immune rejection by the recipient and that the transplanted cells will have access to niche spaces in the recipient bone marrow [19–21]. Current strategies involve conditioning regimens with radiation or/and chemotherapy which lead to lymphoablation and elimination of resident HSCs. Those procedures, however, are non-specific and can cause serious complications [22,23]. A novel procedure that eliminates HSCs without radiation of chemotherapy has recently been published by Chhabra et al. [24] and Yokoi et al. [25] using anti–c–Kit monoclonal antibodies. The use of such biological agents makes the procedure safer eliminating the dangerous acute and long-term side effects including non-malignant organ dysfunction (reproductive inability, endocrinopathy, cardiopathy), secondary tumors, infections and changes in life quality [26]. An alternative strategy to secure niche spaces in the recipient bone marrow has recently been introduced by Taya et al. [27]; in their paper they presented convincing results that dietary valine starvation leads to dramatic reduction of HSCs within 1 week in the bone marrow.

Overall, those recent advances, the use of more effective mobilization regimens and the use of biological agents or valine starvation to secure niche spaces for HSCs, will transform HSCT since the procedure will become more efficient and safer. The use of HSCT in the treatment of other conditions, the combination of HSCT with gene therapy and the development of protocols for ex vivo HSCs expansion are intense fields of research and soon clinical applications will be available.
Plerixafor in combination with granulocyte-colony-stimulating factor after the experience. Anticancer Drugs. 25:841-847.


