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EDITORIAL

To G or not to G: is this still a question in allogeneic transplantation?

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In this issue of *Bone Marrow Transplantation*, Battiwalla *et al.*[1] review the role of G-CSF in allogeneic hematopoietic stem cell transplantation providing an overview of the mechanism of action, the use of G-CSF in healthy HSC donors, chronic neutropenia patients, post-chemotherapy and post-hematopoietic stem cell transplantation. They carefully highlight controversies surrounding the use of G-CSF and appropriately recommend continuous pharmacovigilance. What is the take home message for transplant physicians caring for the donor considering progenitor cell mobilization and for the allograft recipient?

For healthy donors, based on years of monitoring and despite theoretical concerns raised by *in vitro* studies,[2] short-course exposure to G-CSF is safe. The few cases of acute myeloid leukemia reported in healthy donors,[3] are rather consistent with the age-adjusted incidence of leukemia in adults;[4] and in one case, offers some insights into the mechanisms of leukemogenesis.[5] Fortunately, G-CSF, at least in the unrelated donor setting remains listed under the IND protocols, which implies that every donor provides informed consent for the research, including agreement for perpetual annual follow-up.

For the myeloid leukemia allograft recipient in first remission or in chronic phase, post-transplant G-CSF to hasten neutrophil recovery is neither beneficial nor harmful. Shortening time to neutrophil engraftment with G-CSF does not translate into reduced infections, shorter transplant hospitalization or better early survival.[6] In the long run, the short course of G-CSF post-transplant, should not be a reason for concern with regards to chronic GVHD or secondary acute myeloid leukemia. Indeed, despite its *in vitro* immunomodulatory effects, G-CSF, in the clinic, does not affect acute or chronic GVHD, or the risk for opportunistic infections. It is unlikely that short exposure to G-CSF will have a leukemogenic effect similar to what is observed in a subgroup of severe congenital neutropenia patients with monosomy 7,[7] who, after many years of exposure to G-CSF, acquire somatic mutations in the G-CSF receptor and are more prone to develop acute myeloid leukemia. Nevertheless, two reports suggest that children and adolescents in general,[8] and the allograft recipient with acute leukemia in $>$CR1[9] receiving G-CSF post-transplant, should be cautioned about the potential harmful effects on GVHD and survival.

So, to answer the question 'to G or not to G: is this still a question in allogeneic transplantation?' one can conclude that G-CSF is a safe and effective stem cell mobilizing agent for donors; and perhaps with the faster neutrophil engraftment post-peripheral blood stem cell transplantation and the increasing use of effective prophylactic antibiotics post-transplant, there are no indications, with the exception of cord blood transplantation, to routinely administer G-CSF post-allogeneic transplantation.

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