Correcting 2 more myths regarding transplants for AML in second remission

A recent Blood Perspective report by Forman and Rowe challenged the myth that in persons with acute myeloid leukemia (AML) in first remission, one can take a wait-and-see approach: if relapse occurs persons in second remission can undergo transplantation. The authors correctly suggest that few people with recurrent AML achieve second remission and are fit to proceed to a transplant. This leads them to conclude that transplants in persons with AML in first remission should be more often considered, especially persons with minimal residual disease (MRD) who may have an increased likelihood of relapse. What precisely MRD is and how it is defined are not specified, which is potentially problematic. Although we agree that second remissions are infrequent in persons who relapse, these data do not necessarily result in recommending transplants in first remission because it perpetuates 2 other myths: (1) that only persons who achieve a second remission benefit from a transplant and (2) that we can accurately predict at the subject level which persons with AML in first remission are likely to relapse.

Results of transplants in persons achieving second remission are clearly better than results of transplants in those who fail to achieve second remission but receive a transplant anyway. But this is a self-fulfilling prophecy based predominately on data from observational databases of transplant recipients rather than the entire relapse cohort including persons who could have received a transplant but did not. Moreover, some persons, albeit few, who relapse may achieve long-term survival or even cure with reinduction chemotherapy, especially those whose first remission was >18 months. Results of MRD testing in the only prospective study in persons with AML were informative regarding a transplant decision in <20% of the starting cohort.

Although most persons who relapse never achieve a second remission, many could receive a transplant without further therapy or with additional therapy aimed at disease control rather than remission reinduction. Importantly, there are no convincing data from prospective studies that giving antileukemia drugs to persons with AML who relapse and then proceed to a transplant improves outcomes. Data from a recent large clinical trial support this conclusion.

Much of the variance in the outcome of persons with AML in first remission remains unexplained. It follows that the best predictor of relapse is relapse. The only potential disadvantage of using relapse to trigger a transplant decision is if the outcome of transplants in relapsing persons is compromised by waiting for relapse in precisely the same subjects. This is not proved.

We appreciate Forman and Rowe’s thoughtful discussion of the myth of transplants in second remission but suggest current data are inconclusive as to whether to recommend transplants in persons with standard- or high-risk AML in first remission, even those with MRD. More importantly, we want to disarm 2 other myths: (1) that only those achieving second remission benefit from a transplant and (2) that we can, at the subject level, accurately predict which persons with AML in first remission will relapse. More data are needed on these complex issues.

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References

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Association of a single-nucleotide polymorphism in the SH2B3 gene with JAK2V617F-positive myeloproliferative neoplasms

In a recent paper, Perez-Garcia et al described an inherited mutation in the SH2B3 gene associated with the development of acute lymphoblastic leukemia. SH2B3 encodes the lymphocyte adaptor protein (LNK) that negatively modulates the signaling of several cytokine receptors, including the thrombopoietin receptor (myeloproliferative leukemia virus oncogene [MPL]) and the erythropoietin
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