received consolidation and 86% had response improvement within 1 cycle. At 12 months, the complete response rate was 58% and at 24 months, organ response rates were 70%.

The major barrier to widespread implementation of stem cell transplantation is the high treatment-related mortality. In the current article, Sanchorawala et al. report therapy-related mortality of 8.5%. The group from Oregon had therapy-related mortality of 9.6% [7], and the group at Memorial reported 10% treatment-related mortality [8]. These therapy-related mortality rates are increasingly difficult to justify as new active agents for the treatment of immunoglobulin light chain amyloidosis become available. It will be important to properly select patients at high risk of therapy-related death for exclusion to achieve the optimal outcomes when combining new antiplasma cell agents with myeloablative therapy and stem cell rescue.

ACKNOWLEDGMENTS

Financial disclosure: The authors have nothing to disclose.

Conflict of interest statement: There are no conflicts of interest to report.

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How Do Pretransplantation Peripheral Blood Counts Inform Us about Post-Transplantation Outcomes in Acute Myeloid Leukemia?

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Article history:
Received 1 May 2015
Accepted 15 May 2015

It is an old platitude that peripheral blood counts are important in acute myeloid leukemia (AML). Most immediately, they are directly related to the risk of potentially life-threatening medical events such as bleeding or infections and, to prevent these events, costly supportive care needs that are associated with unwanted side effects and reduced quality of life. For patients who have undergone initial chemotherapy and have achieved significant cytoreduction, as indicated by the presence of $< 5\%$ blasts by morphology in the bone marrow and resolution of extramedullary leukemia, peripheral blood counts also provide relevant prognostic information. Specifically, among such responders, patients who show complete recovery of their neutrophil and platelet counts have repeatedly demonstrated better overall survival, higher expectation of long-term survival ("cure"), and lower risk of disease recurrence than those who fail to fully recover either neutrophils or platelets [1-3]. These differences support and validate the current recommendations by international working groups to separate patients who have

Financial disclosure: See Acknowledgments on page 1341.

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http://dx.doi.org/10.1016/j.bbmt.2015.05.014

achieved a complete remission (CR) from those who either obtained a CR with incomplete platelet recovery (CRp) or a CR with incomplete blood count recovery (CRi) [4,5].

However, blood counts are not independent of other risk factors. The likelihood of achieving a CRp rather than a CR is associated with adverse disease characteristics, including cytogenetic risk and a history of antecedent hematological disorder or prior exposure to radiation or chemotherapy [2]. Moreover, higher proportions of patients with CRi or CRp have morphologic remissions with persistence of minimal residual disease (MRD) [3]. Still, even after adjustment for pretreatment risk factors and MRD status, blood counts at the time of response convey prognostic information for reasons that are currently not understood [3]. Given the prognostic role of peripheral blood counts following chemotherapy after initial diagnosis, it is natural to wonder what peripheral blood counts at the time of allogeneic hematopoietic cell transplantation (HCT) tell us about post-transplantation outcomes in patients with AML.

This question underlies the study by Vu et al. reported in this issue of *Biology of Blood and Marrow* Transplantation [6]. The investigators analyzed a cohort of 270 patients with AML in morphologic remission who underwent a first matched related or matched unrelated allogeneic HCT after myeloablative or reduced-intensity conditioning at their institution between 2006 and 2013. In line with other studies analyzing AML patients in remission [1-3,7], the vast majority of subjects in their cohort met criteria for CR (n = 206 [76%]); smaller numbers of patients were in CRp (n = 45 [17%]) or morphologic leukemia-free state (MLFS, n = 19 [7%]), and there were no CRi patients. International working groups have attempted to distinguish MLFS (no requirement for peripheral blood count recovery) from CRi (residual neutropenia and/or thrombocytopenia) for patients with < 5% marrow blasts and lack of extramedullary leukemia [4,5]. Nonetheless, in clinical practice, the separation is oftentimes blurry, and some of the patients with MLFS in this study may have met the criteria for CRi.

The findings by Vu et al. are reassuring for patients presenting with CRp at the time of allogeneic HCT. Although the 3-year event-free survival appeared slightly lower (36% versus 45%), their overall and event-free survival were not statistically significantly different from those for patients in CR after adjustment for various risk factors (including age, donor-patient gender mismatch, disease etiology, and cytogenetic risk) using propensity-score matching. This observation is consistent with data obtained in a cohort of 99 patients undergoing allogeneic HCT for AML in first CR at the Fred Hutchinson Cancer Research Center: in these patients, we found that the lack of full blood count recovery was associated with only a trend toward worse outcomes in univariate analyses (eg, unadjusted hazard of overall mortality, failure for disease-free survival relapse, and nonrelapse mortality of 2.2 [$P = .08$], 2.0 [$P = .10$], 1.7 [$P = .36$], and 2.8 [$P = .12$]), respectively [8]. One can merely speculate why there is no significant difference in outcome between CR and CRp patients in this treatment situation. As an exciting possibility, it is conceivable that allogeneic HCT could overcome the negative effect associated with incomplete blood count recovery, as the authors posit. However, alternative explanations, such as sample size limitations and imbalances in patient- and treatment-characteristics for which appropriate adjustments could not be made, will need to be considered for the lack of independent association between CR/CRp status and outcome. The latter possibilities are suggested by a relatively large study by Alatrash et al. [7]. In their cohort of 334 patients with AML (n = 324) and high-risk myelodysplastic syndrome (n = 10), the unadjusted hazards for overall mortality, failure of progression-free survival, and nonrelapse mortality were 2.0 ($P < .001$), 1.7 ($P = .001$), and 1.7 ($P = .03$), respectively, for the 78 CRp patients—hazard estimates that are remarkably similar to those found in the Fred Hutchinson Cancer Research Center cohort [8]. Although results from formal multivariate analyses were not reported, Alatrash et al. noted that the CR/CRp status was the only significant predictor of survival in univariate analyses [7].

On the other hand, the data presented by Vu et al. for the 19 MLFS patients are much more troubling: although after adjustment their overall survival and event-free survival at 3 years was not statistically significantly different from patients in CR, their nonrelapse mortality was much higher than that for CR or CRp patients (58% versus 22% versus 16%). Given the very small sample size, drawing firm conclusions is obviously difficult, and it is plausible that this high nonrelapse mortality rate is a chance finding; some of the causes of death listed indeed suggest that this might be the case. However, it is interesting to note that MLFS patients more likely had persistent cytogenetic and/or molecular abnormalities in the pretransplantation bone marrow sample than the CR and CRp patients did. Although not collected systematically in this cohort, this suggests that MLFS patients more likely had MRD at the time of transplantation. In our own AML remission patients, we have repeatedly observed that, at least after myeloablative conditioning, nonrelapse mortality is higher for those presenting with MRD [8,9]. Thus, despite the limitation of small sample size, the study by Vu et al. suggests the possibility that the tolerance for allogeneic HCT is significantly lower if the patient presents with lack of peripheral blood count recovery at the time of transplantation. If substantiated by future studies, it will be important to understand the basis for this association, ie, to dissect whether this association is the direct results of low blood counts are a consequence of another factor that tracks along with low blood counts, to devise the best possible strategy to render transplantation safer for these patients.

ACKNOWLEDGMENTS

Financial disclosure: The author has nothing to disclose.

Conflict of interest statement: There are no conflicts of interest to report.

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