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Continuing Medical Education (CME) Questions

Genetics and outcome in older AML transplant

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Murdock HM, Kim HT, Denlinger N, Vachhani P, Hambley B, Manning BS, Gier S, Cho C, Tsai HK, McCurdy S, Ho VT, Koreth J, Soiffer RJ, Ritz J, Carroll MP, Vasu S, Perales M-A, Wang ES, Gondek LP, Devine S, Alyea EP III, Lindsley RC, Gibson CJ. Impact of diagnostic genetics on remission MRD and transplantation outcomes in older patients with AML. *Blood.* 2022;139(24):3546-3556.

1. You are considering treatment options for your 70-year-old patient with acute myeloid leukemia (AML). According to the analysis by Murdock and colleagues, which of the following statements about baseline clinical and genetic determinants of posttransplant leukemia-free survival (LFS) in older patients with AML is correct?

- ☐ *DDX41* and *DNMT3A* mutations present at diagnosis have unfavorable associations with LFS
- ☐ *TP53* and *JAK2* mutations present at diagnosis have favorable associations with LFS
- ☐ Baseline molecular risk, karyotype, hematopoietic cell transplantation comorbidity index (HCT-CI) score, complete response with incomplete blood recovery (CRi), and clinically defined secondary AML all have independent associations with LFS in a multivariable frailty model
- ☐ At baseline, fewer than 10% of patients had somatic mutations indicating evolution from antecedent myelodysplastic syndromes (MDSs), which are associated with poor outcome

2. According to the analysis by Murdock and colleagues, which of the following statements about molecular genetics of CR and measurable residual disease (MRD) associations with baseline characteristics and posttransplant outcomes in older patients with AML is correct?

- ☐ In a multivariable model accounting for baseline risk, MRD positivity was significantly associated with LFS
- ☐ Patients with sole persisting *DNMT3A* or *TET2* mutations (DT) had posttransplant LFS similar to that of patients who cleared all mutations at remission, whereas patients with other persisting mutations (including in *ASXL1)* had inferior LFS
- ☐ MRD positivity was random and not associated with any pretreatment characteristics of the leukemias
- ☐ Posttreatment-emergent mutations always reflect outgrowth of chemoresistant leukemic subclones

3. According to the analysis by Murdock and colleagues, which of the following statements about clinical implications of factors that drive outcomes of allogeneic HCT for AML in older patients is correct?

- ☐ Because older patients with AML are at increased risk of transplant-related toxicity, alternatives to high-intensity conditioning regimens will be necessary to mitigate MRD-associated relapse risk
- ☐ Molecular associations with MRD positivity and transplant outcomes in older patients with AML are driven primarily by mutations present in remission
- ☐ High baseline molecular risk was driven solely by *JAK2* mutations
- ☐ In older patients with AML, persistent AML mutations should be eradicated with intensive myeloablative conditioning regimens

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