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Continuing Medical Education (CME) Questions

Clone metrics in clonal cytopenia

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Gallì A, Todisco G, Catamo E, Sala C, Elena C, Pozzi S, Bono E, Ferretti VV, Rizzo E, Molteni E, Zibellini S, Sarchi M, Boveri E, Ferrari J, Fiorelli N, Camaschella C, Gasparini P, Toniolo D, Cazzola M, Malcovati L. Relationship between clone metrics and clinical outcome in clonal cytopenia. *Blood*. 2021;138(11):965-976.

1. Your patient is a 62-year-old man with idiopathic cytopenia of undetermined significance (ICUS). According to the prospective cohort study by Gallì and colleagues, which of the following statements about features of the mutant clone(s) associated with clinical phenotype and progression in patients with ICUS, in community-dwelling individuals, and in patients with an overt myeloid neoplasm (MN) is correct?

- ☐ Ten percent of patients with ICUS carried a somatic genetic lesion indicating that the diagnosis had progressed to clonal cytopenia of undetermined significance (CCUS)
- ☐ Prevalence of clonal hematopoiesis (CH) did not differ significantly between nonanemic and anemic community-dwelling individuals
- ☐ At the time of progression to MN, 13 of 20 patients with CCUS had clonal expansion without acquisition of additional mutations (median variant allele frequency [VAF] increase = 0.1 [range, 0.03-0.39])
- ☐ In community-dwelling individuals, *DNMT3A* mutations independently predicted anemia

2. According to the prospective cohort study by Gallì and colleagues, which of the following statements about the use of molecular profiling and clone metrics in patients with CCUS is correct?

- ☐ Recurrent mutation patterns exhibited different VAF values associated with marrow dysplasia (0.17-0.48; $P < .001$), indicating variable clinical expressivity of mutant clones
- ☐ Unsupervised clustering analysis based on mutation profiles identified 3 major clusters that did not differ in overall survival
- ☐ In patients with CCUS, clusters based on mutation profiles did not differ significantly in their risk for progression to MN
- ☐ Clone metrics did not identify distinct subsets with different risks for progression to MN

3. According to the prospective cohort study by Gallì and colleagues, which of the following statements about clinical implications of features of the mutant clone(s) associated with clinical phenotype and progression in patients with CCUS, community-dwelling individuals, and patients with MN is correct?

- ☐ The findings show marked consistency in the clinical expressivity of myeloid driver genes
- ☐ The findings support the use of morphologic dysplasia for clinical staging of mutant hematopoietic clones
- ☐ The findings rule out CCUS being a transition state between clonal hematopoiesis of indeterminate potential and MN
- ☐ Clone metrics enable estimation of disease progression risk and appear to be critical to inform clinical decision making in patients with clonal cytopenia

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