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Continuing Medical Education (CME) Questions

Germ line predisposition in BM hypocellularity

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Molteni E, Bono E, Gallì A, Elena C, Ferrari J, Fiorelli N, Pozzi S, Ferretti VV, Sarchi M, Rizzo E, Camilotto V, Boveri E, Cazzola M, Malcovati L. Prevalence and clinical expression of germ line predisposition to myeloid neoplasms in adults with marrow hypocellularity. *Blood.* 2023;142(7):643-657.

1. **Your patient is a 64-year-old man with unexplained cytopenias with an age-adjusted hypocellular bone marrow. On the basis of the large cohort study using germ line and somatic targeted sequencing by Molteni and colleagues, which one of the following statements about prevalence and spectrum of germ line predisposition to myeloid neoplasms and other genetic variants in adults with cytopenias and age-adjusted hypocellular bone marrow is correct?**
   - ☐ 8 of 402 patients (~2%) had germ line variants causing a predisposition syndrome/disorder
   - ☐ Shwachman-Diamond syndrome (SDS) was the most frequent predisposition disorder
   - ☐ Most patients with germ line predisposition had homozygous mutations in genes causing autosomal recessive syndromes
   - ☐ 111 germ line variants of unknown significance (VUS) were identified in 38 genes linked to myeloid neoplasm predisposition in 21.9% of patients

2. **According to the large cohort study using germ line and somatic targeted sequencing by Molteni and colleagues, which one of the following statements about clinical correlates of predisposition syndromes/disorders and diagnostic implications of germ line mutations in adults with suspected myeloid neoplasm is correct?**
   - ☐ One third of patients with causative germ line genotype were diagnosed with myeloid neoplasm
   - ☐ Patients with predisposition syndrome/disorder were older than the other patients and had lower risk for advanced myeloid malignancy
   - ☐ Increased risk for progression to acute myeloid leukemia
   - ☐ Family history of cancer was significantly associated with a predisposition syndrome/disorder

3. **On the basis of the large cohort study using germ line and somatic targeted sequencing by Molteni and colleagues, which one of the following statements about clinical implications of prevalence and phenotypic expressivity of germ line variants predisposing to myeloid neoplasms among adults with cytopenia and hypoplastic bone marrow is correct?**
   - ☐ Patients with myeloid neoplasm and predisposition variants have more severe disease and bone marrow failure and increased risk for leukemic progression
   - ☐ The study proves that older adults with age-adjusted hypocellularity should undergo germ line genetic testing
   - ☐ Patients not diagnosed with myeloid neoplasm but with underlying genetic predisposition did not have higher risk for progression to myeloid cancer
   - ☐ Combining all potentially informative clinical variables is the best way to predict underlying genetic predisposition to myeloid cancer

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