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Continuing Medical Education (CME) Questions

Mutant *CALR* in MPN

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How J, Hobbs GS, Mullally A. Mutant calreticulin in myeloproliferative neoplasms. *Blood*. 2019;134(25):2242-2248.

1. Your patient is a 61-year-old man with essential thrombocythemia (ET) and mutant *CALR*. According to the review by How and colleagues, which one of the following statements about mechanistic and biochemical data regarding mutant *CALR*'s role as a driver mutation in myeloproliferative neoplasms (MPNs) is correct?

- ☐ Whole-exome sequencing has shown recurrent mutations in *CALR* in approximately one-quarter of patients with ET and primary myelofibrosis (PMF) without a *JAK2* or *MPL* mutation
- ☐ *CALR* mutations consist of insertions and/or deletions in exon 9, generating a novel, mutant-specific, positively charged amino acid sequence in the carboxyl (C) terminus
- ☐ The 2 most common *CALR* mutations are a 10 base-pair deletion and a 15 base-pair insertion
- ☐ The only biologic requirement for mutant *CALR*-induced oncogenesis is the mutant-specific C terminus of mutant *CALR* and its positive electrostatic charge

2. According to the review by How and colleagues, which one of the following statements about clinical data regarding mutant *CALR*'s role as a driver mutation in MPNs is correct?

- ☐ Compared with patients with *JAK2*-mutant ET, patients with *CALR*-mutant ET tend to be older with increased leukocytosis
- ☐ Compared with patients with *MPL*-mutant ET, patients with *CALR*-mutant ET are more likely to be female and have less platelet count elevation
- ☐ Compared with *JAK2*-mutant ET, patients with *CALR*-mutant ET tend to be younger and have less erythrocytosis and leukocytosis and higher platelet counts
- ☐ The improved prognosis of *CALR* in PMF may be restricted to only type 2-like *CALR* mutations

3. According to the review by How and colleagues, which one of the following statements about current treatment of MPNs with mutant *CALR* and therapeutic targeting of *CALR* is correct?

- ☐ At this time, no rationally designed treatments target *CALR* mutations, but *CALR* mutations affect clinical risk stratification, and thus initial treatment decisions
- ☐ Cytoreductive therapies for MPNs (eg, hydroxyurea, interferon-α, and ruxolitinib) are more effective in patients with *CALR* mutations
- ☐ The mutant-specific C terminus of mutant *CALR* is not likely to be a good site for immunological targeting
- ☐ Clinical studies of a synthetic peptide to competitively inhibit mutant *CALR*-MPL binding have shown efficacy and safety in patients with MPN and *CALR* mutations

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