How can the mutational profile in myeloproliferative neoplasms (MPN) help to inform diagnosis and prognosis?

Aaron Gerds, MD
Associate Professor of Medicine
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Cleveland, Ohio

Driver mutations can play important roles in MPN, and characterization of the mutational profile of each patient is essential to better understand the disease. For example, some reports suggest that patients with primary myelofibrosis who lack one of the three classic driver mutations – referred to as 'triple-negative' patients – have an adverse prognosis compared to patients who have one or more of these mutations.[1-4] As an additional example, patients with essential thrombocythemia (ET) due to CALR mutations have a different thrombosis risk than those who have JAK2 V617F mutations.[5] Moreover, an alternate diagnosis may be considered if patients with Philadelphia chromosome-negative MPN lack one of the three classic driver mutations that are associated with this disease.

Still, it is important to remember that multiple mutations generally occur within these malignant cells. For example, approximately one-fourth of patients with ET have a second or third mutation, and about 35% of patients with polycythemia (PV) and ET have a second, third, or fourth mutation.[6,7] Thus, the mutational profile of each patient must be considered in whole prior to developing a definitive treatment plan.

For more information on MPN driver genes and the importance of molecular genetic testing, please view the full newsletter by clicking here.

This activity is supported by educational grants from Bristol-Myers Squibb and Incyte Corporation.

References:

1. Tefferi A, Barbui T. Polycythemia vera and essential thrombocythemia: 2017 update on diagnosis, risk-stratification, and management. *Am J Hematol*. 2017;92:94-108.
2. Rumi E, Cazzola M. Diagnosis, risk stratification, and response evaluation in classical myeloproliferative neoplasms. *Blood*. 2017;129:680-692.
3. Zaidi U, Sufaida G, Rashid M, et al. A distinct molecular mutational profile and its clinical impact in essential thrombocythemia and primary myelofibrosis patients. *BMC Cancer*. 2020;20:205.
4. Pettit KM, Kandarpa M, Robinson D, et al. Genomic landscape and clinical features of triple-negative myelofibrosis. *Clin Lymphoma Myeloma Leuk*. 2018;18(Suppl):Abstr MPN-285.

5. Guglielmelli P, Carobbio A, Rumi E, et al. Validation of the IPSET score for thrombosis in patients with prefibrotic myelofibrosis. *Blood Cancer J*. 2020;10:21.
6. Asp J, Andréasson B, Hansson U, et al. Mutation status of essential thrombocythemia and primary myelofibrosis defines clinical outcome. *Haematologica*. 2016;101:e129-e132.
7. Grinfeld J, Nangalia J, Baxter J, et al. Classification and personalized prognosis in myeloproliferative neoplasms. *N Engl J Med*. 2018;379:1416-1430.