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Clinical, laboratory, molecular and pathological (CLMP) Euro-Asian classification and treatment options of prefibrotic JAK2, CALR AND MPL mutated myeloproliferative neoplasms

The broad spectrum of JAK2 V617F mutated trilinear phenotypes varies from essential thrombocythemia (ET), prodromal polycythemia vera (PV), masked PV, erythrocythemic PV, classical PV, and PV complicated by splenomegaly and myelofibrosis (MF). ET heterozygous for the JAK2 V617F mutation is associated with normal life expectancy. JAK2 mutation load increases from less than 50% in early stage PV to 100% in overt and advanced PV and MF. Pretreatment bone marrow morphology and cellularity distinguish JAK2 V617F mutated trilinear MPN from calreticulin (CALR) and MPL mutated MPN. The morphology of clustered large pleomorphic megakaryocytes with hyperlobulated nuclei are similar in JAK2 V67F ET and PV patients. CALR mutated thrombocythemia shows characteristic bone marrow features of primary dual megakaryocytic granulocytic myeloproliferation (PMGM) without features of PV. MPL515 mutated thrombocythemia is featured by monolinear proliferation of large to giant megakaryocytes with hyperlobulated staghorn like nuclei. JAK2, CALR and MPL allele burden slowly increases together with the degree of splenomegaly, myelofibrosis and constitutional symptoms during life long follow-up. The presence of epigenetic mutations at increasing age predicts unfavorable outcome in JAK2, CALR and MPL mutated MPN. Low dose aspirin in ET and phlebotomy on top of aspirin in PV is mandatory to prevent platelet-mediated microvascular circulation disturbances. Pegaylated interferon is the first line myeloreductive treatment option in prodromal and early stage JAK2 mutated PV and in CALR and MPL mutated thrombocythemia to postpone the use of hydrozyurea as long as possible.

Biography

Jan Jacques Michiels is a Multidisciplinary Internist in Blood Coagulation & Vascular Medicine Center, Erasmus Tower, NL. He is the Professor of *Nature Medicine* & Health, Clinical and Molecular Genetics, Blood & Coagulation Research, University Hospitals Antwerp, Brussels and Martin-Bratislava International Consultant of Blood Coagulation & Vascular Medicine. He is also an Academic Consultant of Pharmaceutical and Industrial Medicine. He is Editor of *Journal of Hematology & Thromboembolic Diseases and World Journal of Hematology*, and Editor in Chief of *World Journal of Clinical Cases*.

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