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The PVSG/WHO versus the clinical, laboratory, molecular and pathological (2018 CLMP) defined myeloproliferative neoplasms caused by $JAK2^{V617F}$ $JAK2^{EXON12}$, CALR, MPL and TPO driver mutations are distinct blood & coagulation disorders: Prognostic and therapeutic implications towards 2020 and beyond

The $JAK2^{V617F}$ mutated trilinear myeloproliferative neoplasms (MPN) include a broad spectrum of clinical laboratory and bone marrow features in essential thrombocythemia (ET), prodromal polycythemia vera (PV) and erythrocythemic PV, classical PV and advanced stages of masked PV and PV complicated by splenomegaly and secondary myelofibrosis (MF). Heterozygous $JAK2^{V617F}$ mutated ET is associated with low JAK2 allele and MPN disease burden and normal life expectance. In combined heterozygous and homozygous or homozygous $JAK2^{V617F}$ mutated trilinear MPN, the JAK2 mutation load increases from less than 50% in prodromal and early stage PV to above 50% up to 100%in classical PV, advanced PV and PV with MF. Bone marrow histology features show various degrees of diagnostic erythrocytic, megakaryocytic and granulocytic (EMG) myeloproliferation in $JAK2^{V617F}$ mutated trilinear MPN clearly differ from monolinear megakaryocytic (M) in MPL or dual megakaryocytic granulocytic (MG) myeloproliferation in calreticulin (CALR) mutated thrombocythemia without features of PV. The morphology of clustered large pleomorphic megakaryocytes with hyperlobulated nuclei are similar in JAK2V67F thrombocythemia, prodromal PV and classical PV patients. Monolinear megakaryocytic (M) myeloproliferation of large to giant megakaryocytes with hyperlobulated staghorn like nuclei is the hallmark of MPL515 mutated normocellular thrombocythemia. CALR mutated thrombocythemia usually presents with high platelet count around $1000x10^9$/l and normocellular megakaryocytic (M) proliferation of immature megakaryocytes with cloud-like hyperchromatic nuclei or prefibrotic dual megakaryocytic granulocytic (MG) myeloproliferation followed by various degrees of bone marrow fibrosis. Natural history and life expectancy of MPN patients are related to the response to treatment and the degree of anemia, splenomegaly, myelofibrosis and constitutional symptoms. The acquisition of epigenetic mutations at increasing age on top of MPN disease burden independently predict unfavorable outcome in $JAK2^{V617F}$, MPL^{515} and CALR mutated MPNs, which mutually exclude each other. Current treatment options in MPN include low dose aspirin in JAK2 and MPL mutated ET, phlebotomy on top of aspirin in PV, pegylated interferon in intermediate stages of PV and CALR and MPL mutated ET followed by hydroxyurea and or ruxolitinib in the hypercellular stages of PV and MF.

Speaker Biography

Jan Jacques Michiels is a Lifestyle Physician and Medical Doctor, MD, educated in Internal Medicine, Hematology, Bloodcoagulation and Vascular Medicine and graduated as PhD at the Erasmus University Medical Center, Rotterdam. He frequently served as Guest Editor and was the Founder and Editor in Chief of Seminars in Vascular Medicine. He is the Founder of the Thrombocythemia Vera Study Group, the European Working Group on Myeloproliferative Disorders and Myeloproliferative Neoplasms as scientific working groups of the European Hematology Association. He is the founder of the Goodheart Institute & Foundation in Nature Medicine & Health, Rotterdam, The Netherlands.

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