




Emostasi e Tumori

# OUTCOMES OF PATIENTS WITH JAK2V617F VAF ≤2% EVALUATED FOR SUSPECTED MYELOPROLIFERATIVE NEOPLASMS

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Detection of the JAK2V617F mutation is central to the diagnosis of myeloproliferative neoplasms (MPNs). In clinical practice, a variant allele frequency (VAF) >2% is considered unequivocally positive and is also used to define clonal hematopoiesis of indeterminate potential (CHIP). Current WHO/ICC recommendations advocate the use of highly sensitive methods to detect JAK2V617F when the VAF is below 1%. However, interpretation of low-level JAK2V617F positivity remains challenging, as the mutation can be detected in individuals without hematologic disease and no validated diagnostic cut-off for MPNs has been established.To investigate the clinical and molecular characteristics of patients referred for suspected MPN with a JAK2V617F VAF <2%. Fifty-five patients evaluated for erythrocytosis (n=31) or thrombocytosis (n=24) and harboring a JAK2V617F VAF <2% were included. Median age was 64 years (range: 15–86). JAK2V617F analysis was performed on granulocyte DNA at diagnostic suspicion using quantitative PCR (ipsogenR JAK2MutaQuantR, limit of detection 0.0014%). At referral, median JAK2V617F VAF was 0.354% (range: 0.02–1.975), significantly higher in patients with thrombocytosis than in those with erythrocytosis (0.451% vs 0.25%, p=0.047). Median erythropoietin level was 5.4 mU/mL (range: 1–16.8), with 51% of erythrocytosis cases showing subnormal levels. None of the patients met diagnostic criteria for MPN at the time of the initial JAK2 assessment. Among patients with erythrocytosis, 4 (12.9%) were subsequently diagnosed with polycythemia vera and 1 with prefibrotic myelofibrosis. Median hematocrit was 50.2%, ten patients required phlebotomy, and two received cytoreductive therapy. Among patients with thrombocytosis, 7 (22.5%) were diagnosed with essential thrombocythemia; CALR mutations were identified in three cases, all fulfilling ET criteria. Median platelet count was 564 × 109/L, and three patients received cytoreductive treatment. The median time from first quantitative JAK2 assessment to MPN diagnosis was 21.1 months. Patients who later developed MPN had a higher median VAF at baseline compared with those who did not (0.532% vs 0.24%, p=0.02). Sequential samples available in 27 patients confirmed persistence of JAK2V617F with stable VAF <2% over a median follow-up of 31.7 months. The median time from first quantitative JAK2 assessment to MPN diagnosis was 21.1 months. Patients who later developed MPN had a higher median VAF at baseline compared with those who did not (0.532% vs 0.24%, p=0.02). Sequential samples available in 27 patients confirmed persistence of JAK2V617F with stable VAF <2% over a median follow-up of 31.7 months. The median time from first quantitative JAK2 assessment to MPN diagnosis was 21.1 months. Patients who later developed MPN had a higher median VAF at baseline compared with those who did not (0.532% vs 0.24%, p=0.02). Sequential samples available in 27 patients confirmed persistence of JAK2V617F with stable VAF <2% over a median follow-up of 31.7 months.Overall, 17 patients (30.9%) experienced thrombotic events, occurring a median of 4.3 months after molecular testing. Thrombotic rates were similar in patients with and without subsequent MPN diagnosis (25% vs 32.5%, p=0.57). However, patients with thrombosis had a significantly higher median JAK2V617F VAF than those without events (0.44% vs 0.23%, p=0.038).