JAK2 46/1 HAPLOTYPE – CORRELATIONS WITH JAK2 V617F STATUS, HAEMATOLOGICAL FEATURES AND THROMBOTIC EVENTS IN 172 PATIENTS WITH MYELOPROLIFERATIVE NEOPLASMS

Trifa AP[1], Cucuianu A[2], Popp RA[1], Urian L[2], Dima D[2], Petrov L[2], Militaru M[1], Pop I.V.[1]
[1]Department of Medical Genetics, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca
[2] "Ion Chiricuță" Oncology Institute, Hematology Dept., Cluj-Napoca

The JAK2 46/1 haplotype has been recently described as a major risk factor for the development of JAK2 V617F-positive myeloproliferative neoplasms (MPN). We investigated the rs10974944 SNP, in which the G allele tags the JAK2 46/1 haplotype, in 172 MPN patients (69 with polycythemia vera, 89 with essential thrombocythemia and 14 with primary myelofibrosis), and in 150 healthy controls, by a PCR-RFLP assay. All the patients have been assessed for the JAK2 V617F mutational status by a semiquantitative tetra-primer PCR assay.

Overall, 120 patients (69.8%) were JAK2 V617F-positive. One hundred and thirty patients (75.6%) had the CG or GG genotypes, compared to 68 controls (45.3%) (OR = 3.7; 95% CI = 2.3 – 6; p-value < 0.0001). One hundred out of 120 patients (83.4%), positive for JAK2 V617F mutation, carried the CG/GG genotypes, compared to 68 controls (OR = 6; 95% CI = 3.4 – 10.7; p<0.0001). The CG/GG genotypes were also enriched in JAK2 V617F-positive compared to JAK2 V617F-negative patients (OR = 3.6; 95% CI = 1.8 – 7.6; p-value = 0.0008), but not in JAK2 V617F-negative patients compared to controls (OR = 1.6; 95% CI = 0.9 – 3.1; p-value = 0.14). JAK2 V617F status significantly influenced the haematocrit, the haemoglobin, the red and the white blood cells counts (p < 0.0001), and the platelets count (p-value = 0.02), while the CG/GG genotypes correlated significantly only with the red and the white blood cells counts (p-value = 0.01), independently of JAK2 V617F status. Fifty-six patients (32.6%) had thrombotic complications; JAK2 V617F contributed significantly to the risk of thrombotic events (p-value = 0.03), but not the CG/GG genotypes (p-value = 0.18).

Our study confirms the strong relationship between the JAK2 46/1 haplotype and the JAK2 V617F mutation. Our study suggests that the JAK2 46/1 haplotype might also have some consequences not only on the acquisition of somatic mutations, but also on some biological features displayed by the MPN patients.