A PROSPECTIVE STUDY OF 338 PATIENTS WITH POLYCYTHEMIA VERA: THE IMPACT OF JAK2 (V617F) ALLELE BURDEN AND LEUKOCYTOSIS ON FIBROTIC OR LEUKEMIC DISEASE TRANSFORMATION AND VASCULAR COMPLICATIONS


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SUMMARY

A modification of the clinical features characterized by evolution in secondary myelofibrosis, or more rarely in acute leukemia, may occur in the course of polycythemia vera and essential thrombocythemia. Previous studies have shown that leukocyte counts greater than $15 \times 10^9 / L$ and a long duration of the disease are risk factors for evolution into secondary myelofibrosis, while leukocyte values greater than $15 \times 10^9 / L$ and age affect the evolution in acute leukemia. Patients with polycythemia vera present in approximately 95% of cases the V617F mutation of JAK2 gene. This mutation may be present in varying amounts in peripheral blood cells, meaning that a cell can have both alleles of the gene JAK2 normal or one mutated and one normal (condition defined “heterozygosity”), or both mutated (homozygous). The term “allelic burden” gives the percentage of mutant allele compared to normal in a sample of peripheral blood leukocytes. Previous retrospective studies, conducted mostly in Italy, had shown that the allele burden (= load of mutated allele) was associated with clinical features of hematologic disease, including increased severity of clinical symptoms and increased risk of evolution in myelofibrosis.

The purpose of the study published in Leukemia by colleagues of group of prof. M. Cazzola, Pavia, was to define the prognostic significance of the mutated allele burden in predicting complications of the disease. The relevance of the study is that it is a prospective assessment, and not retrospective, and that the number of patients analyzed were significant (= 338). The results of this study have largely confirmed the phenotypic associations of disease with the mutational load, particularly as regards the risk of evolution into myelofibrosis, which was significantly higher in patients who had an allele burden exceeds 50%. In addition to the prognostic implications, these observations may have a relapse also therapeutic, as it will determine whether new drugs JAK2 inhibitors currently under study, may reduce the risk of evolution into myelofibrosis through control, and if possible reduce, the allele burden of the mutated gene.

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