THE JAK2 MUTATIONAL STATUS AND CYTOREDUCTIVE THERAPY - THE ROLE IN MPN PROGRESSION TO AML

Elena Coles, Nicoleta Berbec, Andrei Coliță, Oana Ciocan, Mihaela Lebedenco, Cecilia Draghici, Carmen Saguna, Anca Ciobanu, Irina Triantafyllidis, Mihaela Tevet, Cornel Dragan, Raluca Manolache, Geanina Ofițeru, Gabriela Barca, Ștefan Marin, Ana Maria Ivănescu, Anca Roxana Lupu
Haematology Department, Colțea Clinical Hospital

MPN represent a complex group of hematological malignancies both genetically and phenotypically. They are characterized by a single or multilineage overproduction of terminally differentiated blood elements and pronounced predisposition to thrombosis, bleeding and leukemic transformation.

Although most of the patients have a stable disease that can prolong for many years, in the past years we have noticed a more accelerated progression of PV or ET to secondary myelofibrosis, variable degrees of pancytopenia, and accumulation of blasts in the bone marrow and peripheral blood, and even conversion to acute leukemia.

The majority of myeloid cells in MPN are derived from a stem cell clone dominating the whole hematopoiesis. A series of acquired molecular mutations play an important role in the initiation of the clonal hematopoiesis and they were associated with a more agressive outcome. The first lesion studied was the JAK2 V617F, thus the high V617F burden had been associated with secondary myelofibrosis, and the homozygous genotype with the refractory disease and tranformation to AML. In the last years the JAK2 mutation has proven to be a reliable molecular marker for PV and potentially useful in monitoring treatment effect.

Though many somatic defects involved in MPN pathogenesis were discovered, the mutations in the JAK2 domain remain the most proeminent, and show a high specificity for MPN.

A major challenge arises to what degree pharmacologic management of MPN can induce the transformation to AML. Long term treatment with DNA damage-inducing agents can facilitate mutagenesis and thus the clonal progression.