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WILL THE LATEST GENETIC DISCOVERIES HAVE AN IMPACT ON CLINICAL MANAGEMENT IN ET AND MF?

BIOGRAPHY

Alessandro Vannucchi is an Associate Professor of Hematology, past Director of the Specialty School in Hematology and a member of the Board of Doctorate School in Experimental and Clinical Oncology at the University of Florence.

His main interests relate to the myeloproliferative neoplasms and molecular genetics of myeloid neoplasia. He is the Principal Investigator of several Research Projects supported in the last 5 years by the Associazione Italiana per la Ricerca sul Cancro, Ministero per la Università e la Ricerca Scientifica e Tecnologica, and the Istituto Toscano Tumori. Principal Investigator and Italian coordinator of the AIRC 5perMille project-funded AGIMM group, http://www.progettoagimm.it.

Board of the Working Party of Myeloproliferative Disorders of GIMEMA, Italy; the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT); the European LeukemiaNet Work Package 9. He is an Investigator of the Myeloproliferative Disorder Research Consortium (MPD-RC), funded by the National Health Institute, USA.

Past Vice-President of the Italian Society of Experimental Hematology, he is now on the Board of Directors of the Italian Society of Hematology. Prof. Vannucchi has more than 250 peer-reviewed publications and has provided lectures at several national and international meetings, including SIE, SIES, EHA, ASH and several others.

ABSTRACT

The recent discovery of mutations in the calreticulin (*CALR*) gene had an important impact in the field of *JAK2* V617F and *MPL* unmutated essential thrombocythemia (ET) and primary myelofibrosis (PMF). Currently, only 10-15% of ET and PMF patients lack a recurrent mutation and are defined as "triple negative". In addition to their diagnostic value, that supported the inclusion of the *CALR* mutation as a major diagnostic criterium in the recommended revision of the WHO classification, mutations in the *CALR* gene have resulted in a better understanding of the phenotypic characteristics of patients along with greater accuracy in prognostic stratification. In particular, several studies have pointed to mutated *CALR* ET patients as being at lower risk of vascular events compared to mutated *JAK2* V617F and *MPL*, although a group of triple negative patients appear to have the lowest rate of thrombosis. On the other hand, patients with PMF harboring *CALR* mutations have better overall survival than mutated *JAK2* and *MPL*, and particularly triple negative patients who demonstrate lower survival rates. Mutated *CALR* patients had overall better disease state than the others, with a lower risk of developing anaemia, thrombocytopenia or leukocytosis. There may also be differences between the two major types of *CALR* mutations, with type 1 (i.e. deletion of 52 bp) being associated with longer survival than type 2 (i.e. insertion of 5 bp) in PMF in at least some studies. Overall, the three phenotype driver mutations in *JAK2*, *MPL* and *CALR* are providing valuable information for ET and PMF patients in terms of disease presentation and progression as well as overall prognosis. However whether this information can be translated into different therapeutic approaches remains to be further explored.

CONFLICT OF INTEREST:

• NOVARTIS • SHIRE

Presentation references:

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