# WHAT DOES THE FUTURE HOLD IN MPNs?


## Professor Jean-Jacques Kiladjian

Clinical Investigation Centre,
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**Biography**

Jean-Jacques Kiladjian is Professor of Clinical Pharmacology, consultant Haematologist, and head of the Clinical Investigation Centre of the Hôpital Saint-Louis, and Paris Diderot University, Paris, France.

Professor Kiladjian's research has centred on myeloproliferative neoplasms and myelodysplastic syndromes. In these disorders, he has been very active in evaluating novel therapeutics and implementing clinical trials. He is published in many peer-reviewed journals including *The New England Journal of Medicine, Journal of Clinical Oncology, Blood, Leukemia, Seminars in Thrombosis and Haemostasis, Haematologica and British Journal of Haematology,* and has authored several book chapters. He is an active member of many societies including the French Société Française d'Hématologie (SFH), the European Haematology Association (EHA), the American Society of Haematology (ASH). Pofessor Kiladjian was elected President of the French Intergroup of Myeloproliferative disorders (FIM group) and held this position since 2008.


## ABSTRACT

**The discovery of mutations such as *JAK2, MPL, CALR* to name a few have contributed greatly to our understanding in the pathogenesis of Philadelphia negative myeloproliferative neoplasms (MPNs). The question that we now ask ourselves is if such mutations can be incorporated and used in reproducible diagnostic and prognostic models. Histology still plays an important role for diagnosis in MPNs, however, we have already seen change over the years with the bone marrow biopsy no longer being indispensable to diagnose polycythaemia vera (PV) with the discovery of the *JAK2* mutation. Currently essential thrombocythaemia (ET) and primary myelofibrosis (PMF) still require a histological diagnosis according to WHO guidelines. Regarding the molecular landscape of MPNs, knowledge has dramatically evolved in the past 10 years. What was once thought to be as a single mutation leading to classic MPNs, we now know consists of a much more complex story, very different from our past experience in chronic myeloid leukemia. The pathogenesis of classical MPNs is ever evolving and as we move forward, we look to further clarify these intricate connections.**





**References:**

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**Conflict of interest:**

- NOVARTIS
- SHIRE
- AOP ORPHAN
- INCYTE

# WHAT DOES THE FUTURE HOLD IN MPNs?

**Professor**
**Alessandro M. Vannucchi**

Department of Experimental and Clinical Medicine, University of Florence, Italy

**Biography**

Alessandro M. Vannucchi is an Associate Professor of Haematology, past Director of the Specialty School in Haematology 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. 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 Disorders Research Consortium (MPD-RC), funded by the National Institutes of Health, USA. He is the past Vice-President of the Italian Society of Experimental Haematology and is now on the Board of Directors of the Italian Society of Haematology.
Professor 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

**Both the WHO (World Health Organisation) and ELN (EuropeanLeukemia.Net) guidelines have undergone revisions recently. The ELN response criteria that have been developed specifically for assessing the effects of new drugs/treatment in the settings of clinical trials for the daily management of MPNs, which is a useful tool, with the latest revision in 2013, published by Barosi G, *et al.* One of the topics of interest was if molecular response criteria were going to be included in the overall ELN response criteria for essential thrombocythaemia and polycythaemia vera. The current stance is that it is unclear whether remission of a particular malignant clone will always translate to complete remission, as suggested by persistence of *TET2*-mutated clones in patients who lose the *JAK2* V617F mutated clone under interferon treatment. The proposed revisions of the WHO guidelines, however, have included molecular markers in the diagnostic criteria over the years including the addition of the latest discovery of the *CALR* mutation. The proposed revision of WHO criteria was prompted by the addition of the *JAK2* mutation as major diagnostic criteria. Histopathology still remains as a key factor in diagnosis, particularly when looking at ET, but the question beckons to what extent do we see these guidelines changing in the future and what could we expect?**



**References:**

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- Tefferi, *et al. Leukemia.* 2014;28:1407-13.

**Conflict of interest:**

- NOVARTIS
- SHIRE

# WHAT DOES THE FUTURE HOLD IN MPNs?

**Professor Tiziano Barbui**

Division of Haematology, Riunti Di Bergamo Hospital, Italy

**Biography**

Tiziano Barbui was graduated at the University of Padua (Italy). He was Consultant in Haematology at San Bortolo Hospital in Vicenza and founded the Department of Haematology at the Ospedali Riuniti di Bergamo where he was the Director from 1981 to 2008. Professor Barbui is currently the Scientific Director of the Research Foundation at Ospedale Papa Giovanni XXIII, Bergamo (Italy). He has served as Chairman on the Subcommittee on Lupus Anticoagulant of the International Society of Thrombosis and Haemostasis, and as President of the Italian Society of Haematology. Currently, he leads the EuropeanLeukemia.Net WP-9 on Myeloproliferative Disorders and the Italian GIMEMA group on Philadelphia negative myeloid neoplasms. He is one of the founders of the US-NIH Myeloproliferative disorders Consortium. Professor Barbui published so far more than 600 scientific articles in International peer reviewed journals (total citations 18194, h-index 68) and is among the top 50 Italian scientists according to the Virtual Italian Academy. During decades he significantly contributed to many fields of general Haematology. Professor Barbui has been the principal investigator in several academic clinical trials. In 2013, he received the Jean Bernard award by EHA for his contribution to optimisation of diagnosis, prognosis and therapy of myeloproliferative neoplasms and for establishing international networks for clinical research in Haematology.

## ABSTRACT

**One of the key aspects when looking at myeloproliferative neoplasms (MPNs), are risk factors for disease complications. A more accurate prognosis of a disease and its progression is a key factor to ensure that a patient is managed in the most appropriate manner as early as possible. One example is essential thrombocythaemia (ET) and the development of the International Prognostic Score of thrombosis in World Health Organization – Essential Thrombocythaemia (IPSET). Thrombosis still remains a major complication with this disease and the associated risk factors can be perceived as 'patient related' and 'disease related'. Age, previous thrombosis and cardiovascular risk factors can be grouped into the 'patient related' category whereas platelet counts, genetic mutations and bone marrow reticulin fibrosis (to name a few) can be considered as 'disease related'. The question remains, with ongoing research and discussions about new genetic and biological markers along with potential revisions of diagnostic criteria, will we see a change in prognostic criteria for this disease in the future?**



**References:**

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**Conflict of interest:**

- NOVARTIS
- SHIRE

# WHAT DOES THE FUTURE HOLD IN MPNs?

**Professor Carlos Besses**

Department of Clinical Haematology, Hospital del Mar, Barcelona, Spain

**Biography**

Dr Carlos Besses is the head of the Clinical Haematology Department in the Hospital del Mar, Barcelona, Spain. He is also the leader of the Group of Translational Clinical Research in Haematology of the Cancer Research Program and is responsible for the Essential Thrombocythemia Spanish Registry. Currently, he is the President of the Spanish Group for Philadelphia-negative Myeloproliferative Neoplasms. His major interests in the clinical area focus on the natural history, prognosis and treatment of essential thrombocythemia and polycythemia vera. Professor Besses' research interests lie in the diagnostic and prognostic role of genes and other biomarkers in myeloproliferative neoplasms as well as in the clinical implications of *JAK2* V617F modulation by therapy. His most recent research activity focuses in the analysis of clonal evolution by next-generation sequencing in PV patients, and the diagnostic accuracy and reproducibility of WHO-histologic criteria for myeloproliferative neoplasms.

## ABSTRACT

**A multidisciplinary approach for the management of patients with Philadelphia-chromosome negative myeloproliferative neoplasms (MPNs) is of utmost importance to offer the patient the best diagnosis and optimal therapeutic options. A practical example is the management of pregnancy in essential thrombocythaemia (ET). Although a close collaboration between the gynecologist and the hematologist is required throughout pregnancy, a protocolled agenda of visits and tests to be performed is usually not well defined. The role of cardiovascular risk factors as prognostic factors of thrombotic risk is another issue surrounded with uncertainty. In addition, there is no consensus about the adverse prognostic weight of each individual factor in predicting the risk of vascular occlusions. Refinement in the assessment of the individual risk is an emerging need. Cardiologists and epidemiologists may contribute with their expertise in this particular matter. Transformation to myelofibrosis during the clinical course of patients with PV and ET is one of the major life-threatening complications. Currently, conventional therapeutic options are not able to prevent the appearance of this problem. Consequently, collaboration with molecular pharmacologists in the search for drugs able to interfere with abnormal formation of fibers is essential in the near future. These examples are some of the unmet needs and challenges that remain to be addressed by a true collaborative effort of teamwork in the management of patients with MPNs.**



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**Conflict of interest:**

- NOVARTIS
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