FISH and mutational screening of the Abl, Syk and Jak tyrosine kinase family genes in *BCR-ABL1* negative and *JAK2*V617F negative chronic myeloproliferative neoplasms (CMPNs)

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Keywords: Myeloproliferative neoplasms, tyrosine kinases

Abstract

Chronic myeloproliferative neoplasms (CMPNs) are clonal disorders of the hematopoietic stem cells, characterized by abnormal proliferation and survival of one or more cells of the myeloid lineage. *BCR-ABL1* negative CMPNs are a heterogeneous group of diseases for which the molecular pathogenesis is not well understood. Over the last years some genetic alterations have been described, most of them activating some tyrosine kinase genes playing a role similar to *ABL1* in CML. Tyrosine kinases (TK) have an important role in cell growth and oncogenesis. Deregulation of TK genes (mainly due to translocations, amplifications or point mutations) can result in constitutive activation of the signalling pathways in which they are involved, causing the abnormal proliferation and survival that characterize these pathologies. In this study, we have analysed all genes from the families Jak (*JAK1*, *JAK2*, *JAK3* and *TYK2*), Abl (*ABL1* and *ABL2*) and Syk (*SYK* and *ZAP70*) of TKs. All of them code for cytoplasmic tyrosine kinase proteins and some of them have been found mutated in CMPNs and in other tumor types. We have used FISH to detect cryptic rearrangements and dHPLC to detect sequence mutations on samples from 44 *BCR-ABL1* negative and V617F*JAK2* negative CMPN patients. Both analyses have shown that these genes are no frequently mutated in these diseases, implying that lesions in other genes must be involved in the pathogenesis of these diseases.

Abstract #1496. Haematologica/The Hematology Journal 2009;94 (Suppl. 2): pp. 581. XIVth Congress of the European Haematology Association. Berlin Alemania. 4-7 Junio, 2009