genes; in 1 case for 2 genes) clearly support a common clonal cell origin. One MPL gene mutation was found in CEC but not in HSC, while no CARL gene mutation was found.

Conclusions: HSC and EC in PMF share one or more mutations of genes, which are known to be correlated with the onset and pathogenesis of PMF. These first *in vivo* findings support the theory that PMF may harbor from a common HSC/EC precursor. Further data are needed to validate these findings.

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CYTOGENETIC ABNORMALITIES IN PRIMARY MYELOFIBROSIS: CLINICAL ASSOCIATION AND OUTCOME IN AN ITALIAN MULTICENTER SERIES

A. Iurlo, D. Cattaneo, F. Palandri, E.M. Elli, B. Martino, C. Bucelli, M. Sciumè, D. Vincelli, G. Auteri, F. Brioschi, G.A. Croci, I. Cortinovis, A. Bossi, V. Rosti, L. Baldini, U. Gianelli

Hematology Division, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan; Institute of Hematology "L. and A. Seràgnoli", S. Orsola - Malpighi Hospital; Hematology Division, San Gerardo Hospital, ASST Monza; Division of Hematology, Azienda Ospedaliera "Bianchi Melacrino Morelli"; Division of Pathology, Department of Pathophysiology and Transplantation, University of Milan, and Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico; Laboratory G. A. Maccacaro, Department of Clinical Sciences and Community Health, University of Milan; Center for the Study of Myelofibrosis, Laboratory of Biochemistry, Biotechnology, and Advanced Diagnosis, IRCCS Policlinico San Matteo Foundation

Cytogenetic abnormalities have been reported in 30-70% of primary myelofibrosis (PMF) patients (pts) and specific alterations have been associated with worse outcome. We analyzed cytogenetic data at diagnosis in 395 out of 480 PMF pts to evaluate any possible association between karyotype and clinical phenotype and its impact on prognosis. All the cases were diagnosed at five Italian Hematological Centers between November 1983 and December 2016. G-banding technique were used and at least 20 metaphases analyzed. Bone marrow (BM) biopsies were reviewed to adhere to WHO 2016 criteria. An abnormal karyotype (AK) was found in 69 (17.5%) pts: 56 (81.2%) were sole abnormality, 10 (14.5%) double abnormalities, and three (4.3%) complex karyotype (of which one was monosomal karyotype).

Table 1. Presenting clinical and laboratory features of the 395 PMF patients according to karyotype.

	Total N=395	Abnormal N = 69	Normal N = 326	*P value*
Male gender, n (%)	204 (51.6)	49 (73.1)	155 (47.6)	**<0.001**
Age ≥ 65 years, n (%)	201 (50.9)	42 (60.9)	159 (48.8)	**0.007**
Pre-fibrotic PMF, n (%)	280 (70.9)	38 (55.1)	242 (74.2)	**0.002**
Overt fibrotic PMF, n (%)	115 (29.1)	31 (44.9)	84 (25.8)	
Hb < 10 g/dl, n (%)	53 (13.4)	20 (29.0)	33 (10.1)	**<0.001**
WBC ≥ 25 x 10^9/L, n (%)	13 (3.3)	1 (1.45)	12 (3.68)	0.345
PLT < 100 x 10^9/L, n (%)	12 (3.0)	7 (10.1)	5 (1.5)	**0.001**
Blasts ≥ 1%, n (%)	28 (9.5)	13 (18.8)	15 (4.6)	**<0.001**
Splenomegaly, n (%)	178 (45.1)	41 (59.4)	137 (42.0)	**0.008**
Constitutional symptoms, n (%)	45 (11.4)	11 (16.2)	34 (10.4)	0.175
Driver mutation type:				
CALR type 1, n (%)	50 (12.7)	8 (11.6)	42 (12.9)	
CALR type 2 or other / *JAK2*V617F / *MPL*, n (%)	312 (79.0)	55 (79.7)	257 (78.8)	0.955
Triple-negative, n (%)	33 (8.4)	6 (8.7)	27 (8.3)	
IPSS risk category:				
Low, n (%)	141 (35.7)	15 (21.7)	126 (38.7)	
Intermediate-1, n (%)	186 (47.1)	31 (44.9)	155 (47.6)	**<0.001**
Intermediate-2 / High, n (%)	68 (17.2)	23 (33.3)	45 (13.8)	

Abbreviations: PMF: primary myelofibrosis; Hb: hemoglobin; WBC: white blood cells; PLT: platelets; IPSS: international prognostic scoring system.

Table 1 reports clinical and laboratory features of PMF pts according to AK and normal karyotype (NK) status. AK clustered differently according to BM fibrosis grade as it was found in 31 (27.0%) cases with overt fibrotic and 38 (13.6%) with pre-fibrotic PMF (p=0.001). Male sex, older (>65 years) age, anemia (Hb <10 g/dl), thrombocytopenia (PLTs <100x10^9/L), circulating blasts >1%, splenomegaly and higher LDH were significantly associated with AK. A significant association was also found between higher IPSS and AK (p<0.001). Concerning driver mutations, chromosomal abnormalities were described in eight (16.0%) out of 50 type 1 CALR-mutated, in 55 (17.6%) out of 312 non-type 1 CALR / JAK2 or MPL-mutated, and in six (18.2%) out of 33 triple-negative pts. After a follow-up of >6 years, 101 deaths (25.6%) were recorded. Survival was different between AK and NK patients with an estimated median OS of 8.9 and 25.7 years, respectively (p=0.015). Blast phase (BP) transformation occurred in 20 (5.1%) pts and 82 (20.8%) suffered from thrombosis. Any relationship between karyotype and BP, nor between karyotype and thrombotic events was observed. In conclusion, around 20% of pts showed an AK, with the latter clustering more frequently in pts with an advanced BM fibrosis grade and clinical-laboratory features indicative of a more aggressive disease. As in secondary myelofibrosis (MYSEC project), any significant difference in AK distribution according to driver mutations was found. This present study showed that an AK confers a more severe clinical phenotype and significantly influenced OS, thus representing an additional tool to be considered in the evaluation of PMF prognosis.

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DO DIRECT ORAL ANTICOAGULANTS PROVIDE A LIMITED PROTECTION AGAINST RECURRENCES IN MPN PATIENTS WITH VENOUS THROMBOEMBOLISM?

V. De Stefano[1], S. Betti[1], T. Za[1], A. Ciminello[1], F. Bartolomei[1], F. Di Landro[1], P. Chiusolo[1], E. Rossi[1], T. Barbui[2]

[1]Istituto di Ematologia, Università Cattolica, Fondazione Policlinico A. Gemelli IRCCS; [2]Fondazione FROM, Ospedale Papa Giovanni XXIII

In patients with Ph-negative myeloproliferative neoplasms (MPN) and venous thromboembolism (VTE) long-term treatment with vitamin K-antagonists (VKA) is suggested. However, there is concern about the hemorrhagic risk, being the MPN pts. more prone to bleeding. In no-cancer and non-MPN pts. with VTE direct oral anticoagulants (DOACs) are suggested over VKA, because of a non-inferior efficacy and a lower hemorrhagic risk. Efficacy and safety of DOACs in the MPN pts. are unknown. We analysed the medical records of 13 pts. (M/F 8/5, median age at diagnosis 66 yrs, range 37-82) with MPN (polycythemia vera=7, essential thrombocythemia=4, myelofibrosis=2) receiving DOACs after VTE. Thrombosis involved leg veins (n=6), splanchnic veins (n=3), cerebral veins (n=2), and pulmonary arteries (n=2). Eleven pts. took rivaroxaban, and 2 apixaban; circulating levels were checked once in all pts. and were found at therapeutic levels. Five pts. had been shifted from VKA, and 8 received DOACs as first therapy. The median time on DOACs was 18 months (range 1-39), for overall 19.8 pt-yrs, and 14.5 months (range 1-39) in the first-users. Eleven pts. took hydroxyurea. Three recurrent thromboses were recorded in first-users of DOACs: 1 pulmonary embolism 1 month after leg deep vein thrombosis (DVT) (progression), 1 cerebral vein thrombosis (CVT) 21 months after leg DVT, and 1 TIA 18 months after splanchnic vein thrombosis (SVT). A fourth patient with previous CVT was shifted to DOACs after 18 years on VKA because of intracranial hemorrhage and developed a SVT 27 months later. No major bleeding was recorded on DOACs; a clinically relevant non-major bleeding (epistaxis) was recorded in the only patient receiving also aspirin. The incidence of thrombosis on DOACs resulted 20 per 100 pt-yrs (95%CI 5.4-51.2), with a cumulative probability at 2 years of 36.7% (95%CI 1.5-71.8). This compares unfavourably with the 10.7% cumulative probability of thrombosis at 2 years recorded on VKA in pts. with MPN and VTE (Leukemia 2016;30:2032). Obvious limitations of this study are the small number of pts., the short duration of exposure to DOACs, and the retrospective design, and no firm conclusion can be reached. However our data induce some caution in prescribing DOACs after VTE in MPN pts., particularly after CVT and SVT. Those findings urgently call for a multicenter study aimed to assess efficacy and safety of DOACs in this setting on a statistically powered patient sample size.