CALR MUTATIONS IN SICILIAN ESSENTIAL THROMBOCYTHEMIA AND MYELOFIBROSIS PATIENTS.

Di Piazza F[1], Accurso V[2], Caracciolo C[2], Mulè L[1], Bono M[1], Perez A[1], Castiglia M[1], Calò V[1], Massihnia D[1], Barraco N[1], Cangemi G[1], Maragliano R[1], Listì A[1], Galluccio N[1], Bazan V[1], Siragusa S[2], Russo A[1].

[1]Department of Surgical, Oncological and Oral Sciences, Section of Medical Oncology, University of Palermo, 90127 Palermo, Italy
[2] Section of Hematology, A.O.U.P. "Paolo Giaccone", Palermo

Background. Essential thrombocythemia (ET) and primary myelofibrosis (MF) are myeloproliferative neoplasms characterized by the overproduction of mature cells such as platelets (ET) or early bone marrow fibrosis due to scarring induced by highly proliferating myeloid progenitors and pathological stimulation of local fibroblasts (MF). Somatic mutations in CALR gene have recently identified in the majority of JAK2-V617F and MPL negative ET and MF patients. In this study we evaluated the frequency and type of CALR mutations and their clinical and hematological features.

Methods. A total of 54 patients, 29 ET and 25 MF patient, was included in this study. All patients were JAK2 V617F and MPL negative. We registered clinical and hematological characteristics of patients i.e. age, hemoglobin level, white blood cell count, platelet count, International Prognostic Scoring System (IPSS**),** risk of thrombosis. Samples were collected from peripheral blood and DNA was extracted by using the QIAamp DNA mini kit (QIAGEN); CALR mutations were analyzed by direct sequencing method.

Results. CALR mutations were present in 20.4 % of patients (4 ET; 7 MF). Four types of CALR mutations were detected; type 1 (p.L367fs*46) was isolated in 6 MF patient, type 2 (p.K385fs*47) was isolated in 3 ET patient; we also found 2 deletion mutations (p.E371fs*49 and D373fs*47), which are less common deletions, in the remaining patients. Patients carrying CALR mutations were younger (mediane age: 50 *vs* 65; p=0.2) than CALR negative patients. Furthermore, they did not show thrombosis and IPSS high risk.

Conclusions. Our observations are in agreement with the findings of literature. We can assert an improved outcome of CALR mutated patients and we can also speculate a possible protective role of CARL mutations given the absence of thrombosis events and of IPSS high risk. However, the cohort of patients with myeloproliferative disease need to be implemented to draw final conclusion.