

# C1. CALR AND JAK2 V617F MUTATIONS DELINEATE SUBGROUPS OF PATIENTS WITH ESSENTIAL THROMBOCYTHAEMIA AND PRIMARY MYELOFIBROSIS DISPLAYING DISTINCT BIOLOGICAL FEATURES. A MULTICENTRIC STUDY ON 199 PATIENTS

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## Introduction

Essential thrombocythemia (ET) and primary myelofibrosis (PMF) represent non-BCR-ABL classical myeloproliferative neoplasms characterized in around half of cases by the somatic mutation JAK2 V617F. Around 5-10% of the JAK2-negative patients harbour somatic mutations within the c-MPL gene. Recently, the CALR gene (Calreticulin) has been shown to be mutated in 60-70% of the JAK2-negative patients.

## Material and methods

This a multicentric study, including 199 patients (153 with ET and 46 with PMF), diagnosed and followed in haematology clinics and departments from

Cluj-Napoca, București, Tîrgu-Mureș, Baia-Mare and Sibiu. JAK2 V617F was analyzed by a tetra-primer PCR assay, the c-MPL W515L/K/A and S505N mutations were analyzed by a multiplex alle-specific PCR assay. In order to analyze the type 1 (a 52-bp deletion) and type 2 (a 5-bp insertion) mutations of the CALR gene, making roughly 90% of all the CALR mutations described, we developed and validated by DNA sequencing an own simplex PCR assay.

## Results

JAK2 V617F was the most frequent mutation, seen in 83 patients with ET (54.2%) and 20 patients with PMF (43.5%). The CALR mutations were seen in 43 patients with ET (28.1%) and 13 patients with PMF (28.3%). The c-MPL mutations were rare events, seen in 3 patients with ET (2%) and 2 patients with PMF (4.3%). Twenty-four patients with ET (15.7%) and 11 patients with PMF (23.9%) were triple-negative.

CALR-positive patients displayed: a more important thrombocytosis and a less important leucocytosis than their JAK2-positive or triple-negative counterparts, regardless of disease (ET or PMF). They also had less frequently thrombosis or splenomegaly, than those JAK2-positive or triple-negative ones.

## Conclusions

CALR-mutated ET and PMF represent entities with a distinct phenotype, compared to those JAK2-positive or triple-negative. This phenotype is „milder”, probably conferring a better survival.

**Key-words:** essential thrombocythemia, primary myelofibrosis, JAK2 V617F, CALR, c-MPL