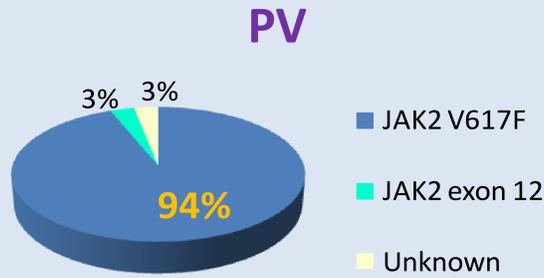
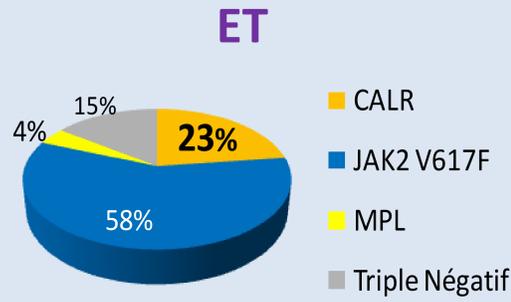


1. Introduction

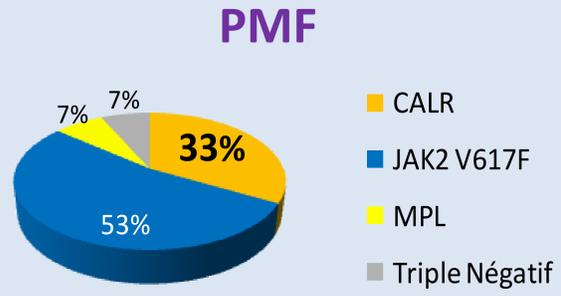
Within the 2008 World Health Organization classification (WHO), **Polycythemia Vera (PV)**, **Essential Thrombocythemia (ET)** and **Primary Myelofibrosis (PMF)** belong to the "Philadelphia Chromosome–Negative" Myeloproliferative Neoplasms (MPNs) entity.



The majority of **PV** carries a **JAK2-V617F** mutation (JAK2V617F).



The recently described **calreticulin (CALR)** mutations are preferentially associated with **JAK2-V617F-negative** and **Myeloproliferative Leukemia Virus Oncogene (MPL)** mutations negative **ET** or **PMF**. (Cross N.C., 2011).



However, retrospective studies recently revealed that:

CALR mutations could be detected in **JAK2-negative PV**. (Broseus J. et al, 2014)

JAK2-V617F can coexisting with **CALR** mutations in rare **ET/PMF** cases (McGaffin G. et al, 2014; Lim K.H. et al, 2015)

Here, we describe **TWO** of such atypical cases:

JAK2-V617F/exon12-negative presumptive **PV** with a **CALR** mutation

ET carrying both **CALR** and **JAK2-V617F** mutations

2. Clinical

CALR mutation in JAK2-negative PV

Patient 1	
Age, y	62
Sexe, M/F	M
Hemoglobin (g/dL)	17.8
Hematocrit (%)	58
Platelets (g/L)	466
EPO (mUI/mL)	8.7
Red cell mass (%)	N/A
Bown marrow biopsy	No fibrosis
RCM	Negative
JAK2-V617F mutation	Negative
JAK2 exon 12 mutation	Negative
MPL mutation	Negative
BCR-ABL1	Negative
CALR mutation	Positive

WHO Criteria-Polycythemia Vera
2 Major Criteria +1 Minor Criteria
or First Major Criteria + 2 Minor Criteria

Major Criteria if Hb > 18.5 g/dL

Major Criteria if Hct increased

Minor Criteria if Subnormal

Evocative of a PV

JAK2V617F coexisting with CALR mutation in ET

Patient 2	
Age, y	44
Sexe, M/F	M
Hemoglobin (g/dL)	14.1
Hematocrit (%)	40.3
Platelets (g/L)	800
Bown marrow biopsy	- Dystrophic megakaryocytes - No reticulin and/or collagen fibrosis
JAK2-V617F mutation	Positive
MPL mutation	Negative
BCR-ABL1	Negative
CALR mutation	Positive

WHO Criteria- Essential Thrombocythemia
4 Criteria

No PV

Platelets count >450x10⁹/L

Megakaryocyte proliferation/No PMF

Demonstration of JAK2-V617F

No CML

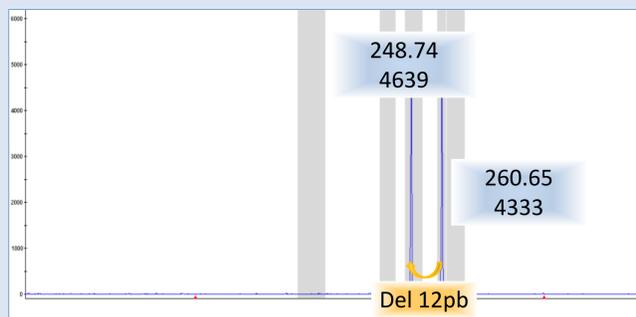
ET Diagnosis

3. Results

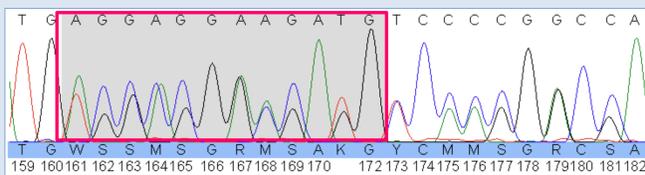
CALR mutation in JAK2-negative PV

Exon 9 of CALR: c.1214-1225del;p.Glu405-Val409del

Fragment Analysis



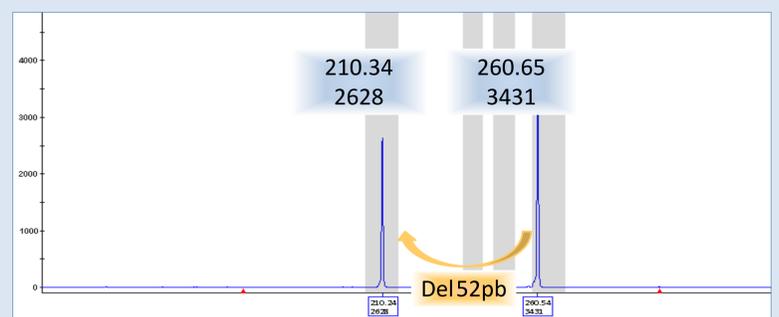
Sanger Sequencing



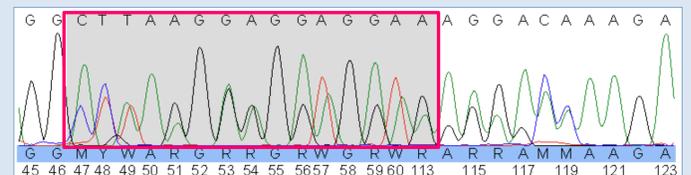
JAK2-V617F coexisting with CALR mutation in ET

Exon 9 of CALR: c.1099-1150del;p.Leu367-Glu383del

Fragment Analysis



Sanger Sequencing



4. Conclusion

In conclusion, we report **CALR** mutations in two atypical cases, one presumptive **JAK2-negative PV** and one **JAK2V617F-positive/CALR-positive ET**.