
# Paziente con “masked PV”

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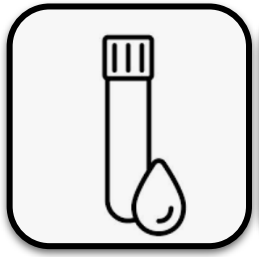
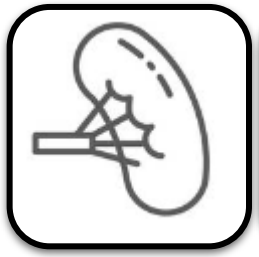
**No Disclosures**

# CLINICAL CASE – Apr 2007

MEN 63 years-old – Thalassemic trait, arterial hypertension, non smoker

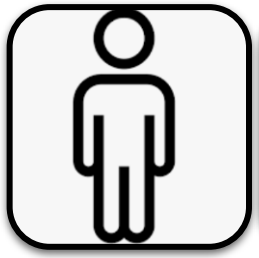


WBCs 8.5 x$10^9$/L (normal differential count, no myeloid precursors or blasts), Hb 14.9 g/dl, RBCs 5.9 x $10^{12}$/L, Hct 46% MCV 61 fl, PLT 540 x$10^9$/L, LDH within normal limit



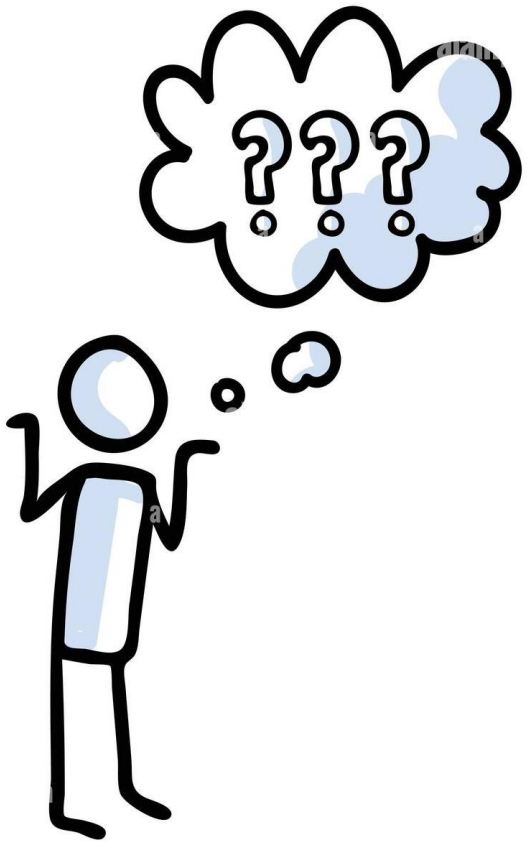
Splenomegaly palpable at 5 cm from LCM

No epatomegaly



No relevant symptoms

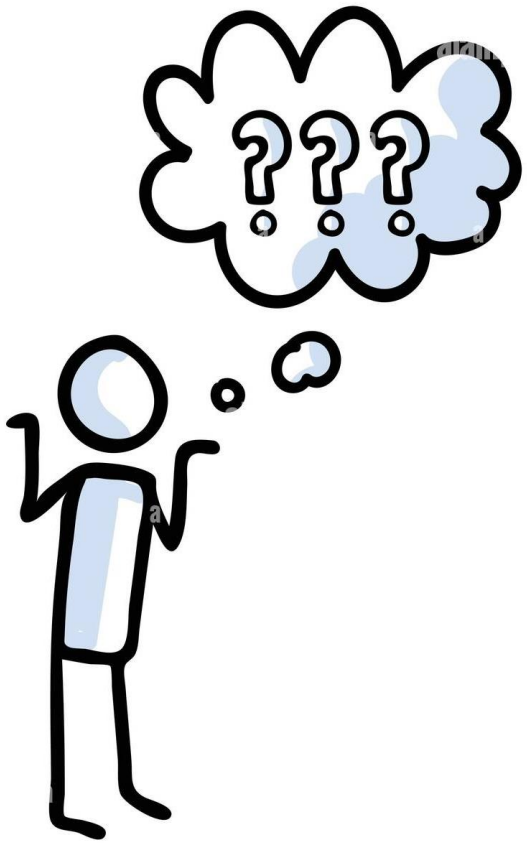
# CLINICAL CASE



**Does this patient have polycythemia vera?**

1. **Yes**
2. **No**
3. **Don’t know**

# CLINICAL CASE



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# Heterogeneous clinical presentation of PV

**PV can present as isolated erythrocytosis, leukocytosis, thrombocytosis,or splenomegaly, with fibrosis, or any combination of these.**

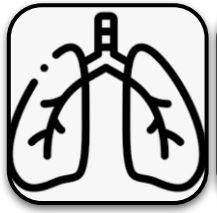
| | PVSG, % | Sweden |
|---|---|---|
| Erythrocytosis alone | 0 | 17 |
| **Erythrocytosis and** | | |
| Leukocytosis | 13 | 29 |
| Thrombocytosis | 30 | 16 |
| Leukocytosis and thrombocytosis | 57 | 38 |
| Splenomegaly (palpable) | 70 | 58 |
| **Splenomegaly and** | | |
| Leukocytosis | ND | 66 |
| Thrombocytosis | ND | 54 |

ND, not determined; PVSG, Polycythemia Vera Study Group.

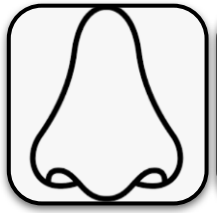
Spivak JL. *Blood* (2019) 134 (4): 341–352.

# CLINICAL CASE – Apr/may 2007

## Diagnostic work-up

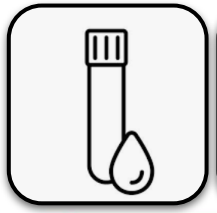


Normal respiratory function tests and thorax XR



Nocturnal snoring with exceptional hyponea

Splenomegaly (19 cm)



Normal metabolic pannel and coagulation, low EPO (0,3 mIU/mL)

JAK2 V617F 35%

# Masked PV - Definition

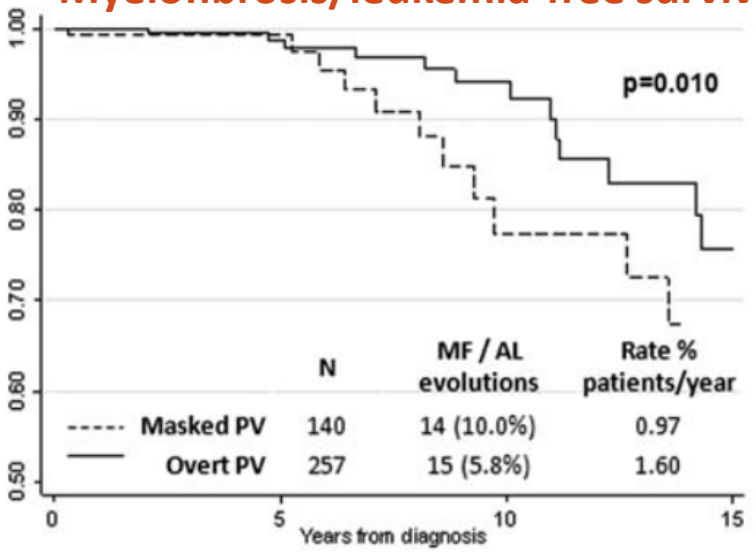
The term "masked PV" has been used for those patients not meeting the cut-offs of haemoglobin and haematocrit established in the WHO and the BCSH criteria, but showing histological data characteristic of PV.

In the 2016 WHO of MPN was proposed as a new JAK2V617F-positive entity with a phenotypic presentation mimicking ET (apparently isolated thrombocytosis) but associated to endogenous erythroid colony formation (EEC) as found in PV or histological findings of PV (initially described as *latent* or *inapparent* PV).

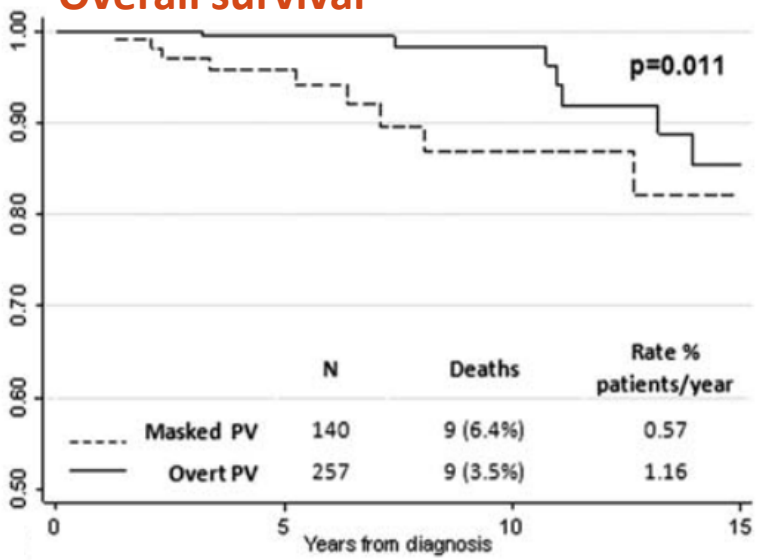
Barbui T. et al. Blood Cancer J. 2018;8(2):15.

# Masked PV - *Outcome*

**Myelofibrosis/leukemia-free survival**




**Overall survival**



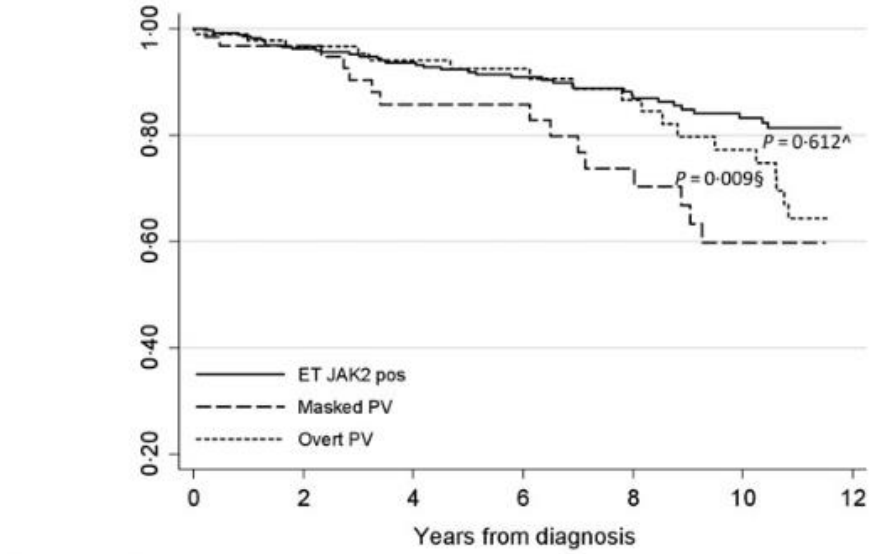

- A worsening of OS was documented in mPV patients in comparison with overt PV.
- The annual rate of death in mPV was almost twice that of overt PV, mainly due to an excess of hematological transformation (overt MF and AL).

**Individuals suffering from this condition have a worse outcome, possibly owing to missed or delayed diagnoses and, as a consequence, a lower intensity of treatment.**

Barbui T. et al. Am J Hematol 2014 Jan;89(1):52-4

# Masked PV - *Outcome*

- mPV was characterized by a higher platelet count, lower leucocyte count and included a prevalence of males compared to overtPV.
- mPV patients have an increased rate of thrombosis compared to overt PV and this difference may be accounted for by the less intensive treatment prescribed in this previously unrecognized category ofpatients.
- These results emphasize the need to treat these patients to maintain their haematocrit level<45%




Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ET JAK2 pos | 348 | (12) | 285 | (7) | 222 | (6) | 182 | (6) | 142 | (6) | 96 | (2) | 79 |
| Masked PV | 62 | (2) | 50 | (5) | 33 | (0) | 29 | (4) | 22 | (4) | 14 | (0) | 12 |
| Overt PV | 96 | (3) | 78 | (2) | 65 | (1) | 51 | (3) | 41 | (4) | 30 | (5) | 22 |

§ Masked PV vs overt PV; ^ *JAK2* mutated ET vs overt PV

Lussana, F et al. Br. J. Haematol. 2014167, 541–546.

**BUT**

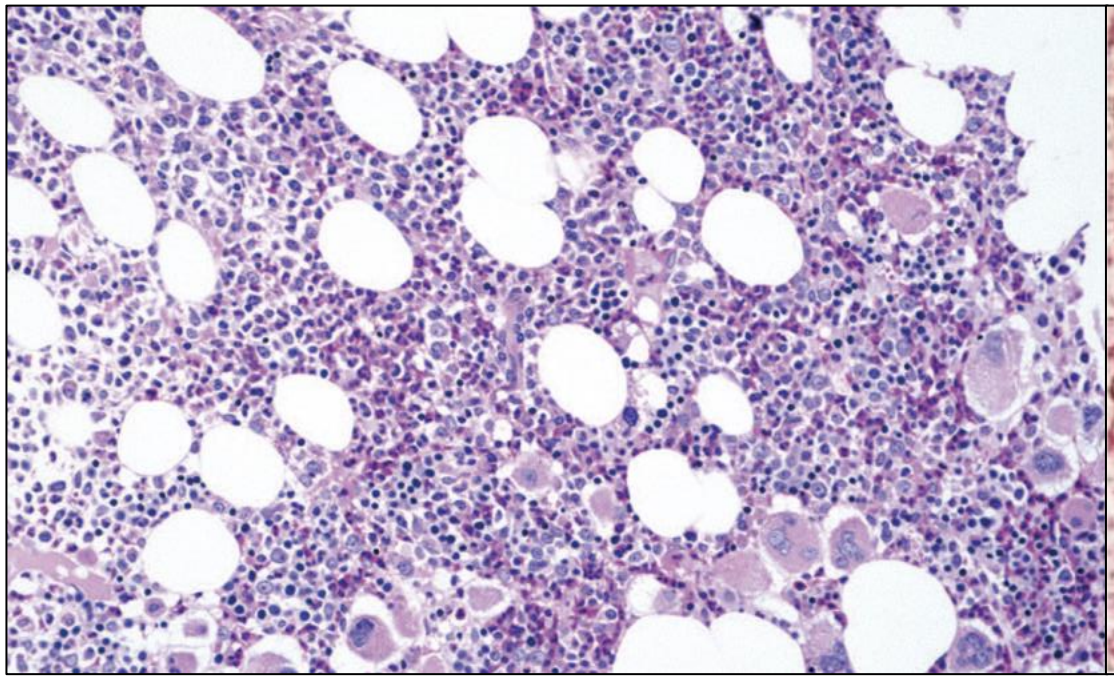
- No differences in the frequency of thrombosis have been observed between masked and overt PV.
- Overall survival and probability of transformation were similar in patients with masked and overt-PV using either WHO or BCSH diagnostic criteria

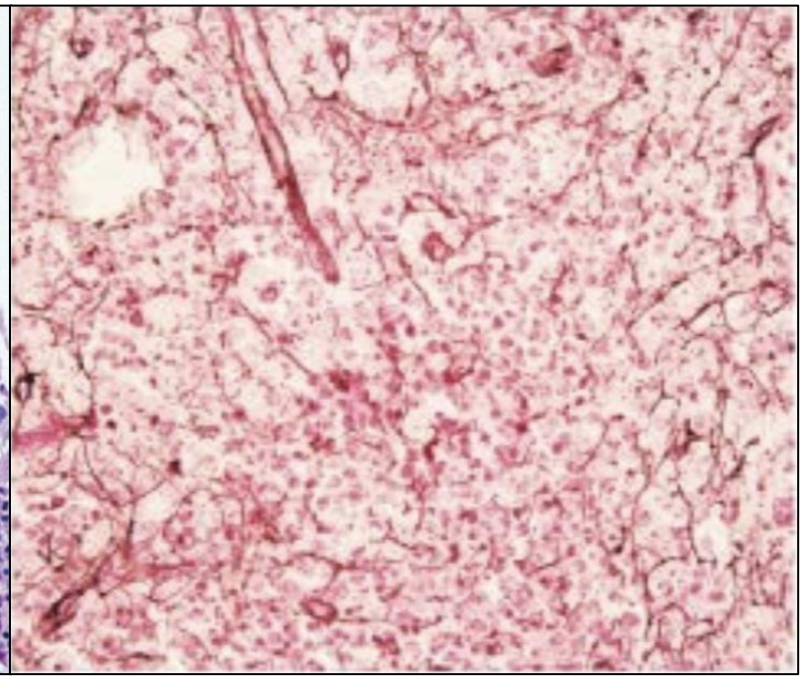
Alvarez-Larràn A. et al Eur J Haematol. 2016 Jan;96(1):83-9.

# CLINICAL CASE – Jul 2007

## Diagnostic work-up

**BMB → PV**



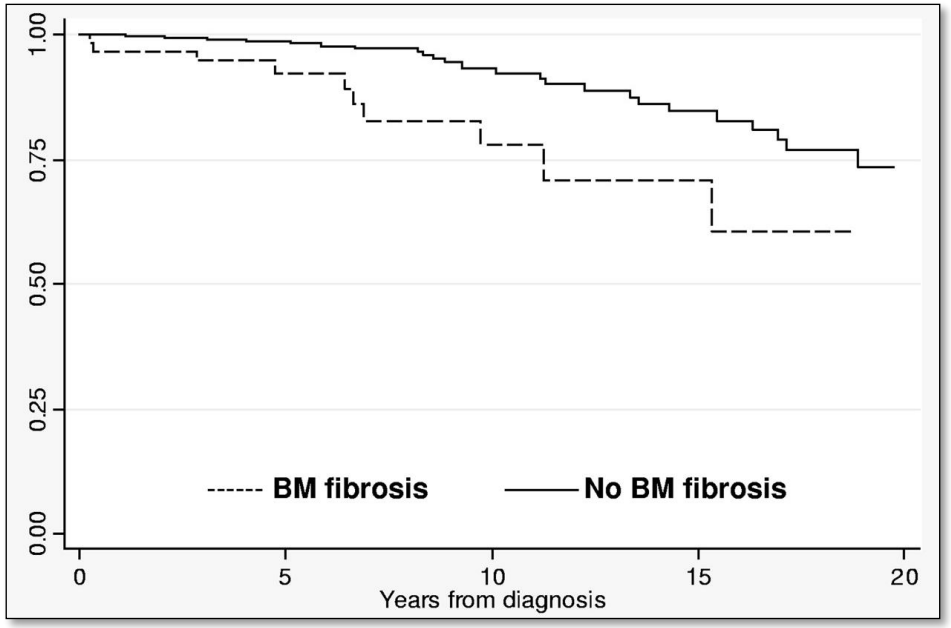


Hypercellular marrow with increased numbers of erythroid, megakaryocytic, and granulocytic precursor cells; increase in the number of reticulin fibers (G1)

# The role of bone marrow hystology

Bone marrow biopsy may detect an **initial myelofibrosis** (up to 20%) that indicates a more rapid progression to overt myelofibrosis (post-PV MF).

Patients with increased RCM also had BM morphology typical of PV both in overt PV and in cases with early PV disease.

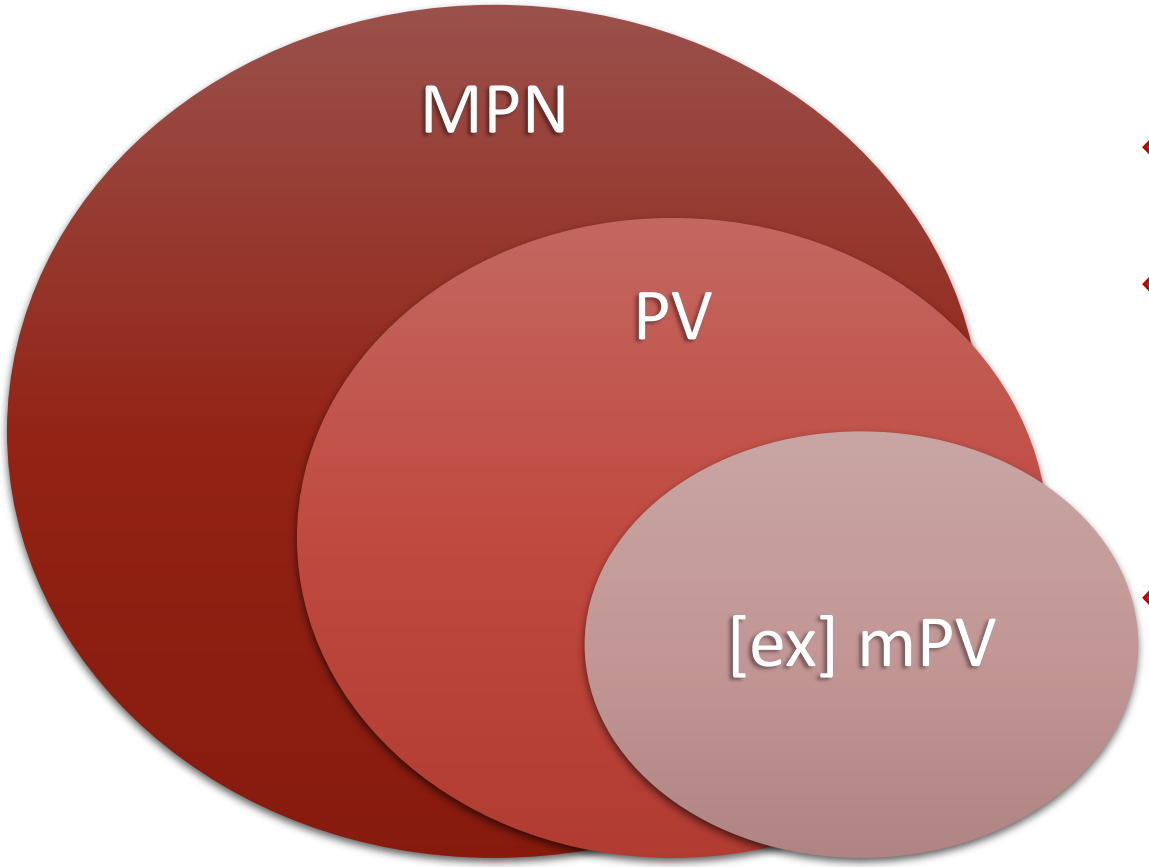



*At presentation, 74 (14%) of the 526 WHO-defined PV patients displayed an increase in BM fiber content.*

*The degree of fibrosis was G1 in all but 3 cases*

Barbui T et al. Blood. 2012;119(10):2239-2241; Barraco D et al. Blood Cancer J. 2017 Mar 10;7(3):e538

# The role of bone marrow hystology




JAK2 mutation

Hb >18.5 g/dL or HCT >55.5% (M)
Hb >16.5 g/dL or HCT > 49.5% (F)

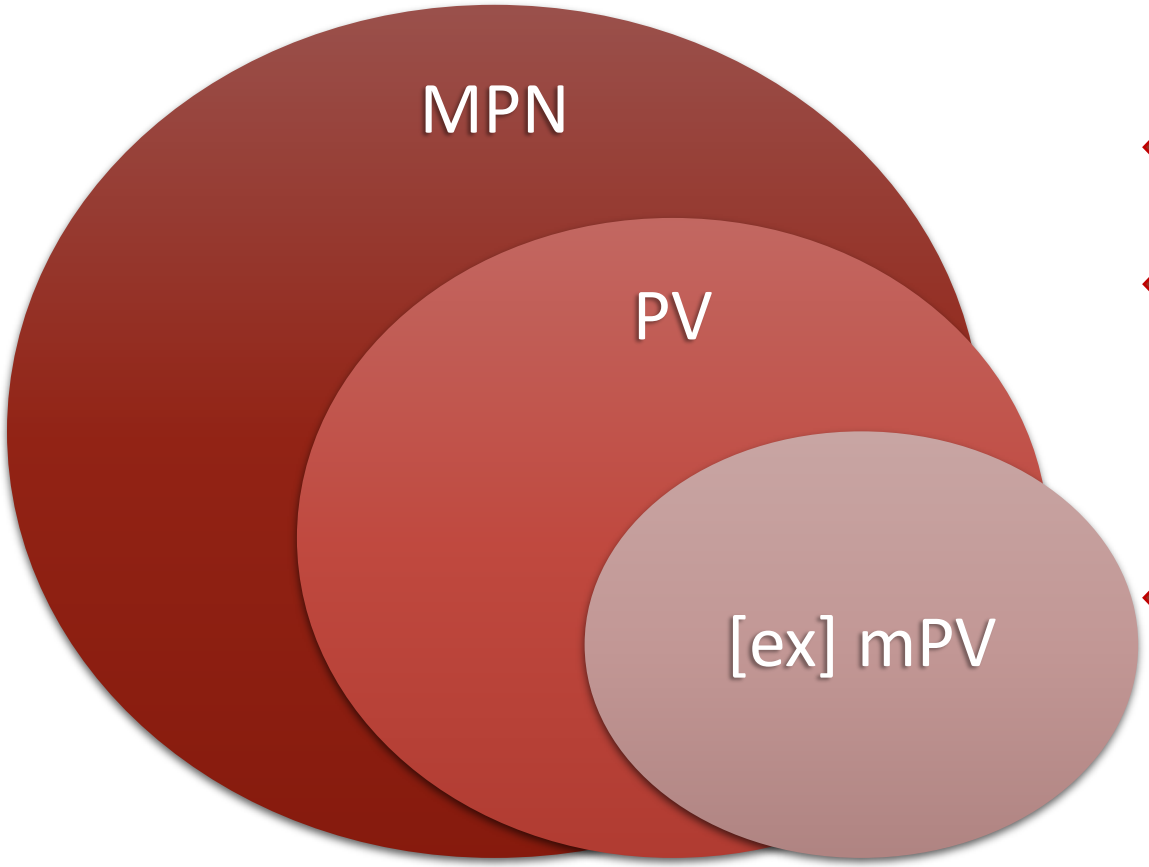
**BIOPSY is not mandatory**

**(EPO reduced)**

Hb >16.5 g/dL or HCT >49 % (M)
Hb >16 g/dL or HCT >48% (F)

**BIOPSY is mandatory**

# The role of bone marrow hystology




JAK2 mutation

Hb >18.5 g/dL or HCT >55.5% (M)
Hb >16.5 g/dL or HCT > 49.5% (F)

**BIOPSY is suggested**

**(EPO reduced)**

Hb >16.5 g/dL or HCT >49 % (M)
Hb >16 g/dL or HCT >48% (F)

**BIOPSY is mandatory**

# CLINICAL CASE – Jul 2007

## Management – PV HR (age > 60)


**ASA**

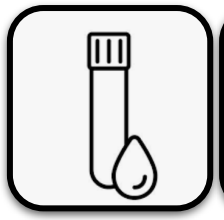
**Suggested phlebotomies if Hct > 45%**

**Cardiovascular risk factor control**

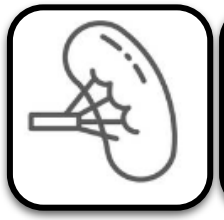
**HU start**

# CLINICAL CASE – Jan 2015

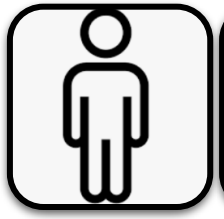
## PV HU resistant



WBCs 9.3 x$10^9$/L (normal differential count, no myeloid precursors or blasts), Hb 11.3 g/dl, MCV 59 fl, PLT 370 x$10^9$/L, no phlebotomy need



Splenomegaly palpable at 16 cm from LCM



Mild fatigue, rare night sweats, moderate itching

PV fibrosis G1 confirmed

# Inadequately controlled PV

*when switching to a second-line therapy?*

## HU switch must be recommended
**(at any HU dose)**

- **Non hema intolerance**
  G3–4 or prolonged G2 toxicity
- **Hema intolerance**
  Hb<10 g/dL, PLT<100 ×$10^9$/L, or PMN<1 ×$10^9$/L) at the lowest dose to achieve a response
- **NMSC**
- **Vascular events**
  (clinically relevant bleeding, venous or arterial thrombosis)

## HU switch must be considered
**(after ≥1.5 g/d for 4 mos)**

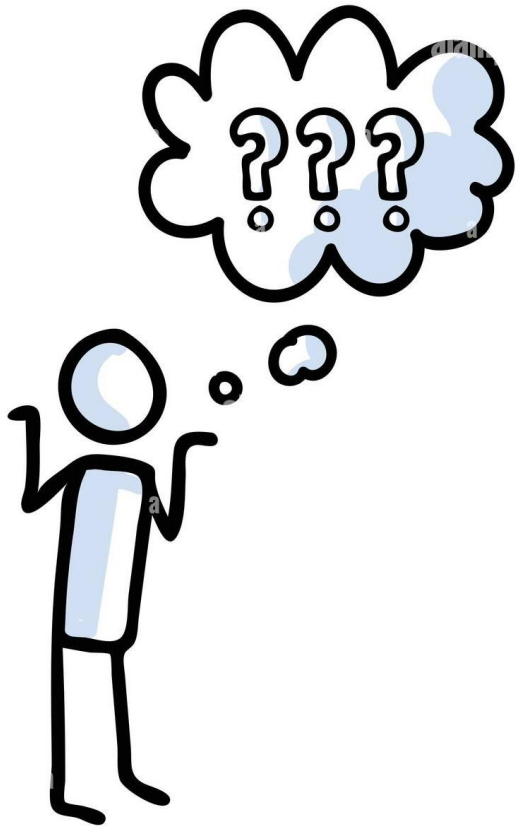
- TSS ≥20 and/or Itching ≥5 for >6 mos
- PLT>1000 x $10^9$/L for >3 mos
- Symptomatic/progressive splenomegaly
- Progressive/persistent leukocytosis
- ≥ 6 PHL to keep HCT<45%

Symptomatic/progressive splenomegaly: increased spleen size by more than 5 cm from the left costal margin in one year

Leukocytosis
-progressive (at least 100% increase if baseline count is <10 x$10^9$/L or >50% increase if baseline count is > 10 x$10^9$/L)
-persistent (WBC> 15 x$10^9$/L for >3 mos)

Marchetti M et al, Lancet Haematol . 2022 Apr;9(4):e301-e311.

# CLINICAL CASE



## Which second-line therapy would you choose?

1. Ruxolitininb
2. Interferons
3. No need to change therapy
4. Busulfan

# CLINICAL CASE

High risk PV patient

Progressive symptomatic *s*plenomegaly

Moderate itching

No dermatological toxicity during HU

## RUX

Highly effective in spleen and itching control

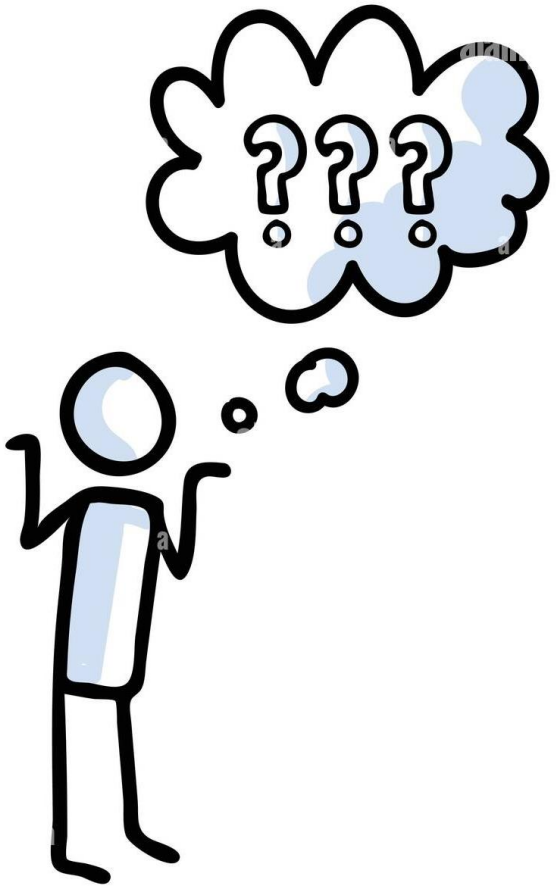
Rapid response

Well tolerated

PO formulation (patient preference)

Peg INF not available

# CLINICAL CASE

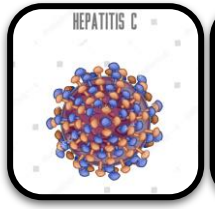


## Which salvage therapy would you choose?

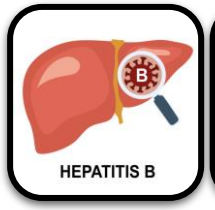
1. Peg-rIFN-a
2. No need to change therapy
3. **Ruxolitininb**
4. Busulfan

# CLINICAL CASE

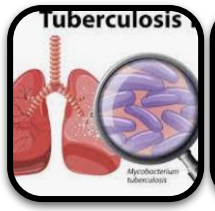
## Screening for RUX start



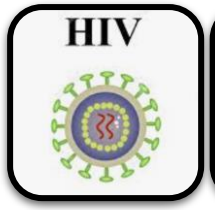

**HCV IgG neg**




**HBV serology neg**



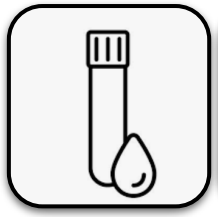

**Quantiferon neg**




**HIV neg**

# CLINICAL CASE – Jan 2015

## PV HU resistant



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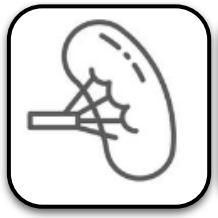

Splenomegaly palpable at 16 cm from LCM

Mild fatigue, rare night sweats

PV fibrosis G1 confirmed

**RUX switch**

# Conclusions

- PV has heterogeneous clinical presentations.
  - *Distinguishing between PV, ET and MF in important because they arbour different thrombotic risk (highest risk for PV), treatments options and prognosis.*

- Hemoglobin and hematocrit aren't alway adequate surrogate markers of erythrocytosis
  - *They cannot be used due to the effects of iron deficiency or plasma volume expansion.*
  - *RBC count has been recognized as a more accurate indicator of erythrocytosis*.

- BM morphology is mandatory for diagnosis if Hb <18.5 g/dL or HCT <55.5% (M)/ Hb >16.5 g/dL or HCT > 49.5% (F).

- Individuals suffering from formerly known mPV have a worse outcome if not treated as PV
  - *Possible correlation with missed or delayed diagnoses and lower intensity of treatment.*

BOLOGNA
17 FEBBRAIO 2023
NH De La Gare

# POLICITEMIA VERA NEL 2023:

## qualcosa è cambiato

# GRAZIE!