BOLOGNA
17 FEBBRAIO 2023
NH De La Gare

POLICITEMIA VERA NEL 2023:

qualcosa è cambiato

Paziente in terapia con idrossiurea mal tollerata e con scarso controllo di piastrinosi, i sintomi, la splenomegalia, switch a RUX o IFN?

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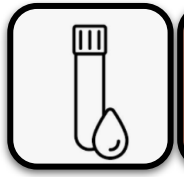
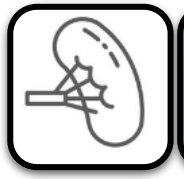
No Disclosures

CLINICAL CASE – Nov 2013

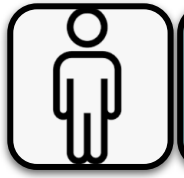
Female, 35 yo–no CV risk factors



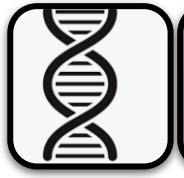
WBCs 11.1 x10^9/L (normal differential count), Hb 16.2 g/dl, Hct 51.7% MCV 77 fl, PLT 440 x10^9/L, LDH 244 U/L, EPO 3.5 mIU/mL, ferritin 5 ng/ml



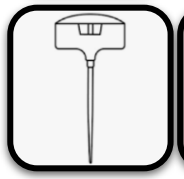
No splenomegaly or hepatomegaly



Moderate itching after water contact

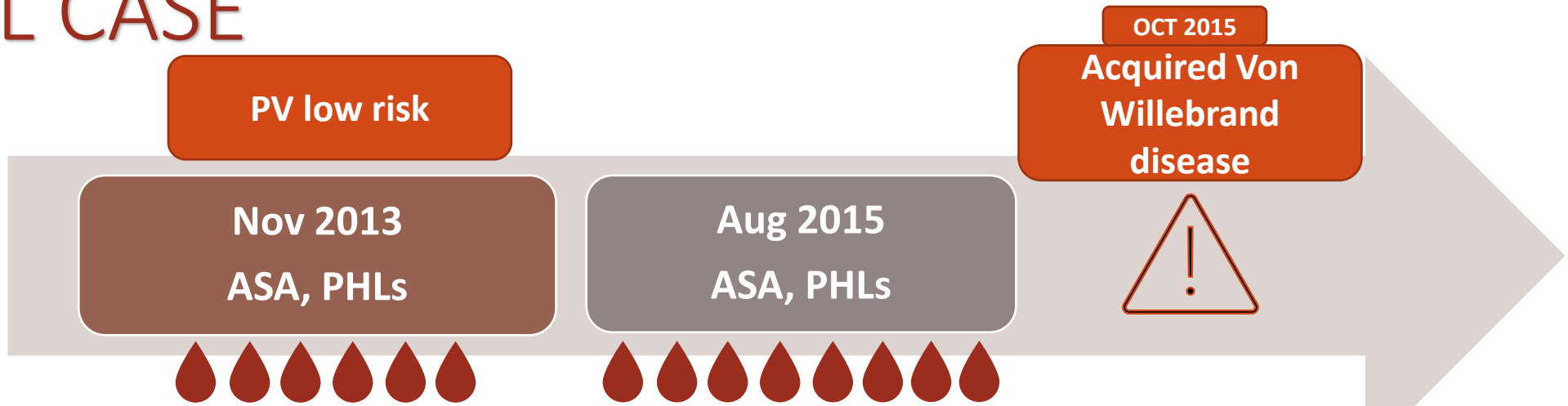


JAK2 V617F (VAF 58%)



Trilinear expansion, CD34+ preceursors < 5 %, fibrosis G0

CLINICAL CASE



	Nov 2013 PV diagnosis	Aug 2015
WBC	11.1 k/µL	11.4k/µL
Hgb	16 g/dL	13.9 g/dL
PLTs	412 k/µL	554 k/µL
Hct	54%	44%
No of PHL/yr	**6**	**9**
MPN-related symptoms	Itching +++	Itching +

CLINICAL CASE

Low risk young PV patient

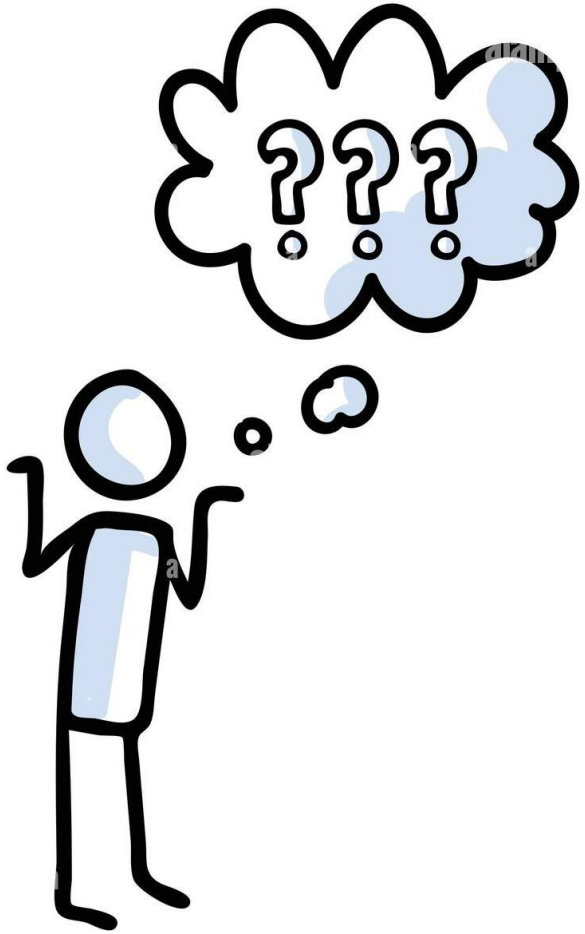
No Splenomegaly

Mild, sporadic itching

Childbearing age

Frequent PHL need

Paraneoplastic vW disease



What to do next?

1. HU
2. IFN
3. Ruxolitinib
4. Continue with phlebotomies only

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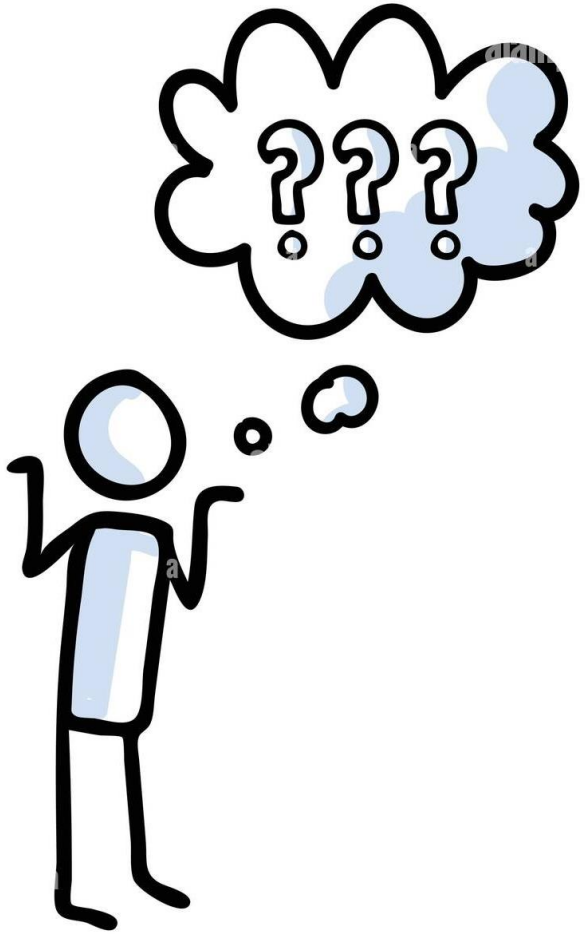

What to do next?

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2. **IFN**
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Prevention of vascular complications in PV

High-risk PV

Cytoreduction is mandatory if

- Age > 60 yrs
- Previous thrombosis

Low-risk PV

Cytoreduction is recommended if

- Poor PHL intolerance
- Symptomatic/progressive splenomegaly (increase by >5 cm in the past year)
- Persistent leukocytosis (WBC >20 × 10^9/L for 3 months)

Cytoreduction should be considered if

- Progressive leukocytosis (increase >100% if WBC<10x10^9/l; >50% if WBC>10x10^9/l)
- Persistent leukocytosis (>15x10^9/l for 3 months)
- PLT>1500x10^9/l for >3 mos
- ≥ 6 PHL to keep HCT<45%

Cytoreduction can be considered if

- TSS ≥20 and/or Itching ≥5 for >6 mos despite PHL, asa and antihistamines
- Relevant uncontrolled CVRF

McMullin MF, Br J Haematol. 2019 Jan;184(2):176-191. Spivak JL, Blood. 2019 Jul 25;134(4):341-352; Barbui T, Leukemia. 2018 May;32(5):1057-1069; Vannucchi AM, Haematologica. 2017 Jan;102(1):18-29. Marchetti M. et al. Lancet Haematol 2022 Apr;9(4):e301-e311.

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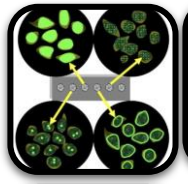
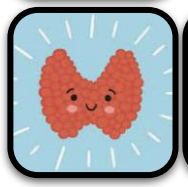
CLINICAL CASE

Screening for IFN start



ANA reflex neg



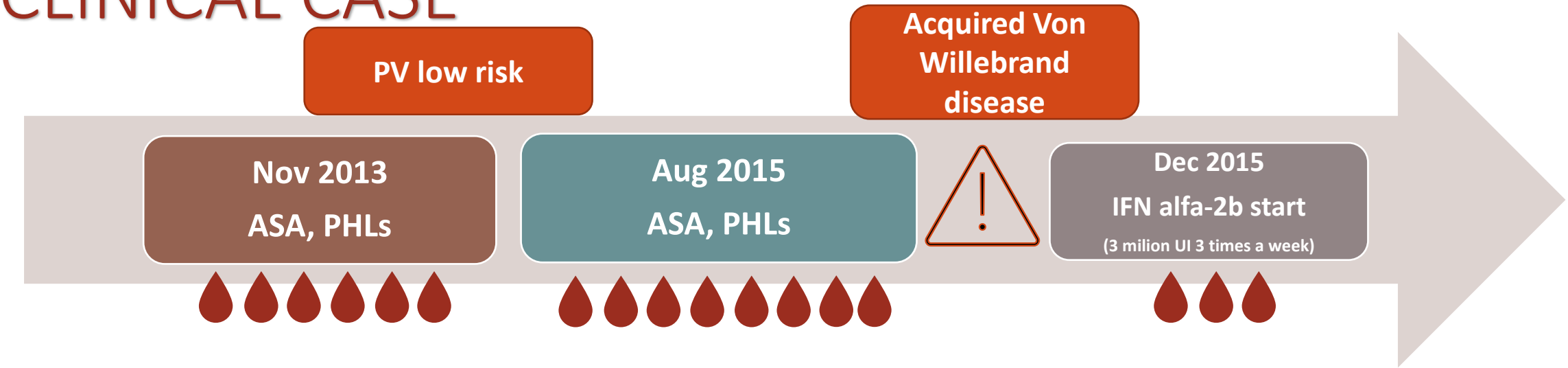
Anti tyreo-globulin and anti tyreo-peroxidase antibodies neg

Rheumatoid factor and anti phospholipid antibodies within normal limits

No history of diabetes nor other autoimmune disease

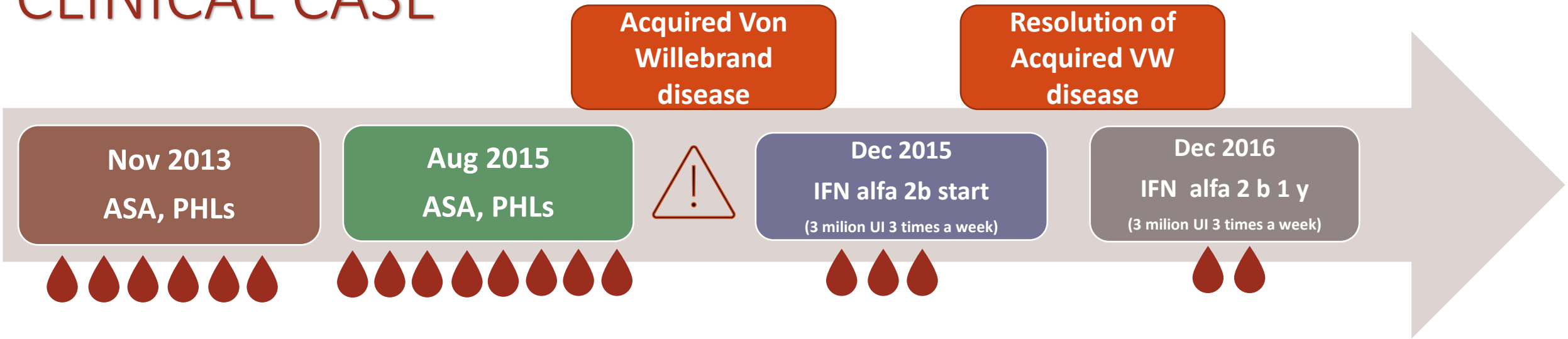
No history of psychiatric disorders

CLINICAL CASE



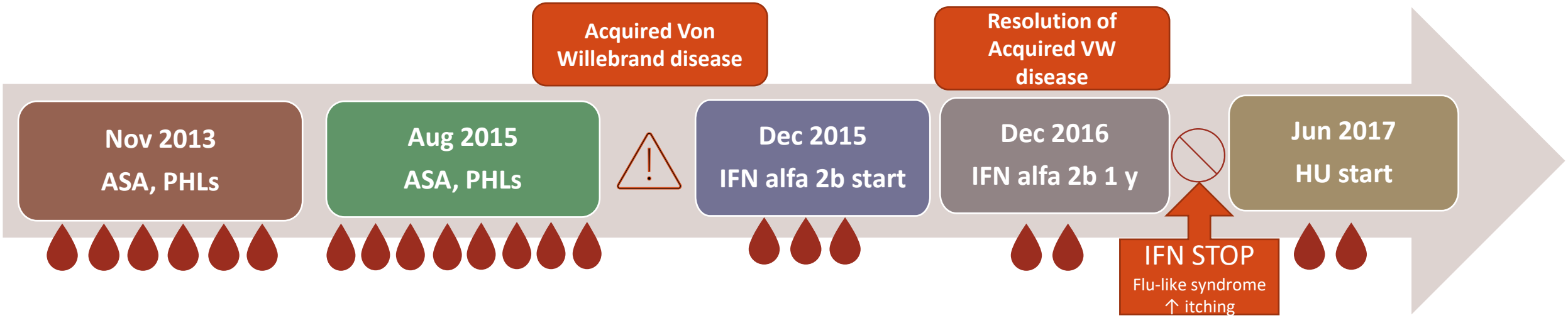
	Nov 2013 PV diagnosis	Aug 2015	Dec 2015 IFN start
WBC	11.1 k/μL	11.4k/μL	16 k/μL
Hgb	16 g/dL	13.9 g/dL	13.0 g/dL
PLTs	412 k/μL	554 k/μL	556 k/μL
Hct	54%	44%	46%
No of PHL/yr	6	9	3 (4 months)
MPN-related symptoms	Itching +++	Itching +	Itching ++

CLINICAL CASE



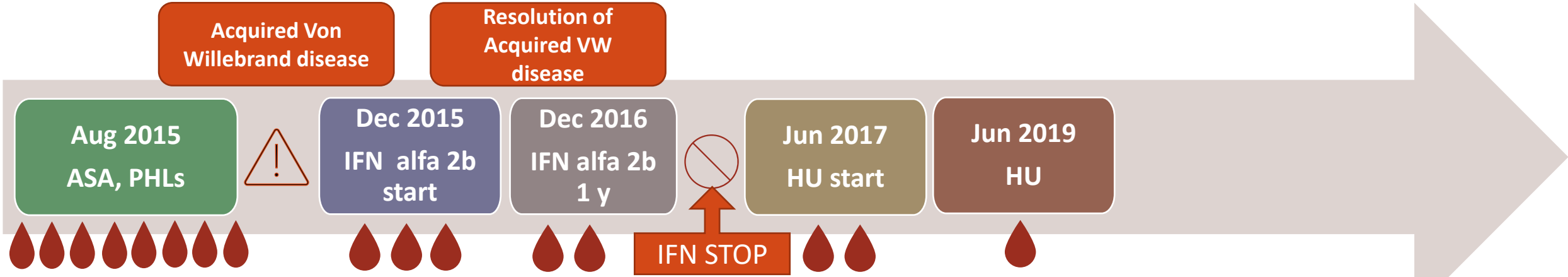
	Nov 2013 PV diagnosis	Aug 2015	Dec 2015 IFN start	Dec 2016 IFN 1 y
WBC	11.1 k/µL	11.4k/µL	16 k/µL	10.9 k/µL
Hgb	16 g/dL	13.9 g/dL	13.0 g/dL	12.0 g/dL
PLTs	412 k/µL	554 k/µL	556 k/µL	416 k/µL
Hct	54%	44%	46%	40.8%
No of PHL/yr	6		12	2
MPN-related symptoms	Itching +++	Itching +	Itching ++	-

CLINICAL CASE



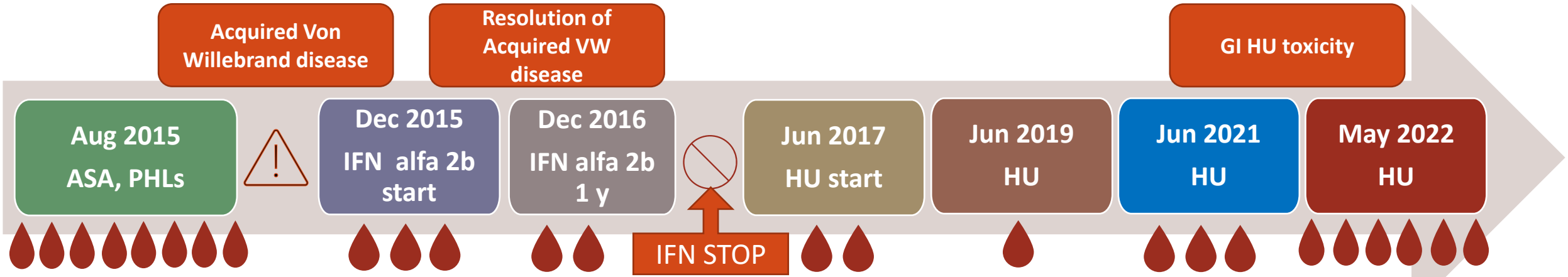
	Nov 2013 PV diagnosis	Aug 2015	Dec 2015 IFN start	Dec 2016 IFN start	Jun 2017
WBC	11.1 k/µL	11.4k/µL	16 k/µL	10.9 k/µL	10.7 k/µL
Hgb	16 g/dL	13.9 g/dL	13.0 g/dL	12.0 g/dL	12.7 g/dL
PLTs	412 k/µL	554 k/µL	556 k/µL	416 k/µL	441 k/µL
Hct	54%	44%	46%	40.8%	42 %
No of PHL/yr	6	12		2	2
MPN-related symptoms	Itching +++	Itching +	Itching ++	-	Itching ++++

CLINICAL CASE



	Dec 2015 IFN start	Dec 2016 IFN start	Jun 2017 HU start	Jun 2019 HU 2 y
WBC	16 k/µL	10.9 k/µL	10.7 k/µL	10.0 k/µL
Hgb	13.0 g/dL	12.0 g/dL	12.7 g/dL	12.9 g/dL
PLTs	556 k/µL	416 k/µL	441 k/µL	250 k/µL
Hct	46%	40.8%	42 %	43 %
No of PHL/yr	-	2	2	1
MPN-related symptoms	Itching ++	-	Itching +++	-

CLINICAL CASE



	Dec 2015 IFN start	Dec 2016 IFN start	Jun 2017 HU start	Jun 2019 HU 2 y	Jun 2021 HU 4 y	May 2022 HU 5 y
WBC	16 k/µL	10.9 k/µL	10.7 k/µL	10.0 k/µL	14.9 k/µL	12.4 k/µL
Hgb	13.0 g/dL	12.0 g/dL	12.7 g/dL	12.9 g/dL	14.2 g/dL	13.4 g/dL
PLTs	556 k/µL	416 k/µL	441 k/µL	250 k/µL	660 k/µL	358 k/µL
Hct	46%	40.8%	42 %	43 %	49.7 %	46.6%
No of PHL/yr	-	2	2	1	3	6
MPN-related symptoms	Itching ++	-	Itching +++	-	Fatigue + Itching ++	TSS 40 (itching, fatigue, sweats, weight loss)

Definition of resistance/intolerance to Hydroxyurea

Need for phlebotomy to keep hematocrit < 45% after 3 months of at least 2 g/d oh HU OR

Uncontrolled myeloproliferation (ie, platelet count > 400 x 10^9 AND WBC count > 10 x 10^9) after 3 months of at least 2 g/d of HU OR

Failure to reduce massive splenomegaly by > 50% as measured by palpation OR failure to completely relieve symptoms related to splenomegaly after 3 months of at least 2 g/d of HU OR

Absolute neutrophil count < 1.0 x 10^9/L OR platelet count < 100 x 10^9 OR hemoglobin < 10 g/dl at the lowest dose of HU required to achieve a complete or partial clinico-hematologic response OR

Presence of leg ulcers or other unacceptable HU-related toxicities, such as mucocutaneous manifestations, GI symptoms, pneumonitis or fever at any dose of HU.

Barbui T, Barosi G, Birgegard G, et al. Philadelphia-negative classical myeloproliferative neoplasms: Critical concepts and management recommendations from European LeukemiaNet. J Clin Oncol 2011;29:761-770.

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 x10^9/L or >50% increase if baseline count is > 10 x10^9/L)
-persistent (WBC> 15 x10^9/L for >3 mos)

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

CLINICAL CASE

Low risk young PV patient

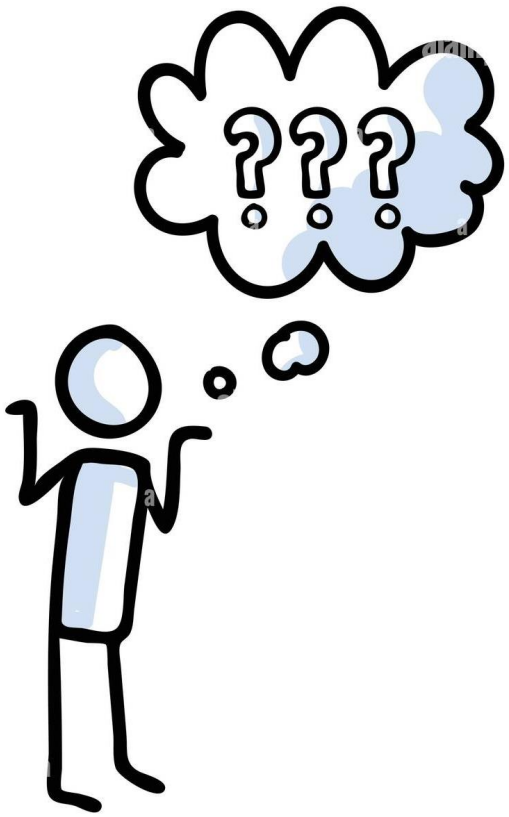
Mild splenomegaly

Severe Symptoms (constitutional symptoms, Itching 10/10)

No motherhood desire

Frequent PHL need

Intollerant to IFN, resistant & intollerant to HU (GI toxicity)



How to go on?

1. Just keep it up with HU
2. PHLs only
3. Start Peg-rIFN-a (new formulation)
4. Start RUX

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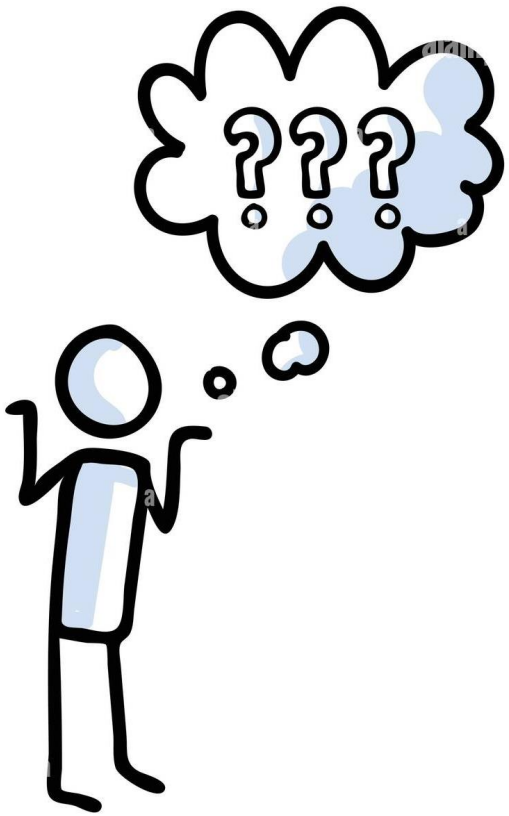
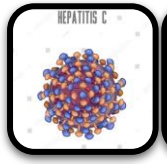


How to go on?

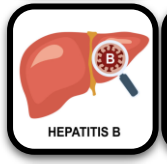
1. Just keep it up with HU
2. PHLs only
3. Start Peg-rIFN-a (new formulation)
4. **Start RUX**

CLINICAL CASE – May 2022

Screening for RUX start



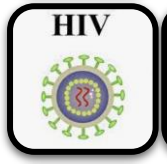
HCV IgG neg



Anti Hbc neg

HBV DNA neg

Quantiferon neg

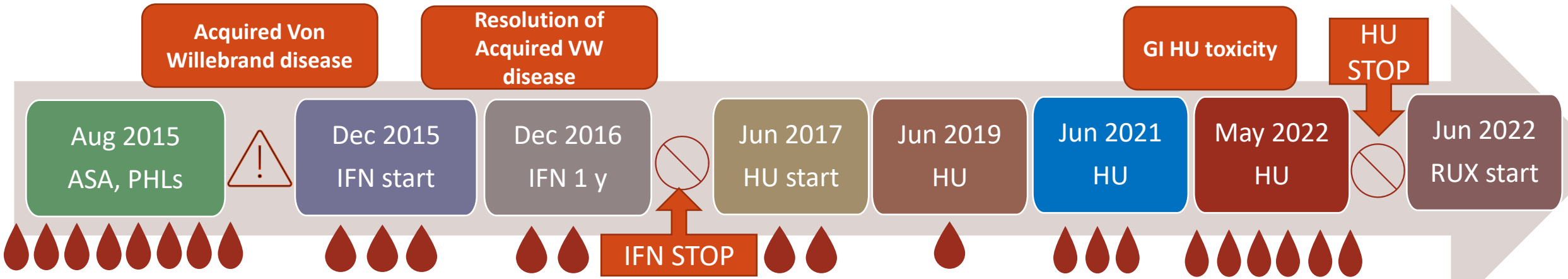


HIV neg

Splenomegaly 17 cm

PV, fibosis G1

CLINICAL CASE



	Dec 2015 IFN start	Dec 2016 IFN start	Jun 2017 HU start	Jun 2019 HU 2 y	Jun 2021 HU 4 y	May 2022 HU 5 y	Jun 2022 Rux start
WBC	16 k/µL	10.9 k/µL	10.7 k/µL	10.0 k/µL	14.9 k/µL	12.4 k/µL	21.48 k/µL
Hgb	13.0 g/dL	12.0 g/dL	12.7 g/dL	12.9 g/dL	14.2 g/dL	13.4 g/dL	12.7 g/dL
PLTs	556 k/µL	416 k/µL	441 k/µL	250 k/µL	660 k/µL	358 k/µL	590 k/µL
Hct	46%	40.8%	42 %	43 %	49.7 %	46.6%	44.1 %
No of PHL/yr	-	2	2	1	3	6	
MPN-related symptoms	Itching ++	-	Itching +++	-	Fatigue + Itching ++	TSS 40 (itching, fatigue, sweats, weight loss)	

CLINICAL CASE

Oct 2022 (RUX 3 months)

WBCs 12.05 x10^9/L, Hb 12.1 g/dl, Hct 42.2% MCV 75 fl, PLT 530 x10^9/L

Spleen 130 mm

TSS 6/100 (itching 2)

No PHL

IFN VS RUX: PROS and CONS

RUX

PO administration	2 daily doses (low compliance!!)
No food interference	↑ infectuos risk (viral and mycobacterial infections)
Well tollerated, few non haematological SE	Weight gain common
Highly active on severe Itching and splenomegaly	Cutaneous toxicity
Rapid onset of response	Risk of hematological tox with cytopenias

IFN

Administration every 2 weeks	Slow onset of response (often needs initial embrication with other therapy)
No infectious risk or cutaneous tox	Flu-like syndrome
Possible disease modifying action	↑ autoimmune diseases and severe depression*
Possibility of long «therapeutic holidays»	Risk of hematological tox with cytopenias
	* ↓ with new formulation

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GRAZIE!