From Thrombophilia to Thrombosis: Budd–Chiari Syndrome and Splanchnic Vein Thrombotic Events in the Liver

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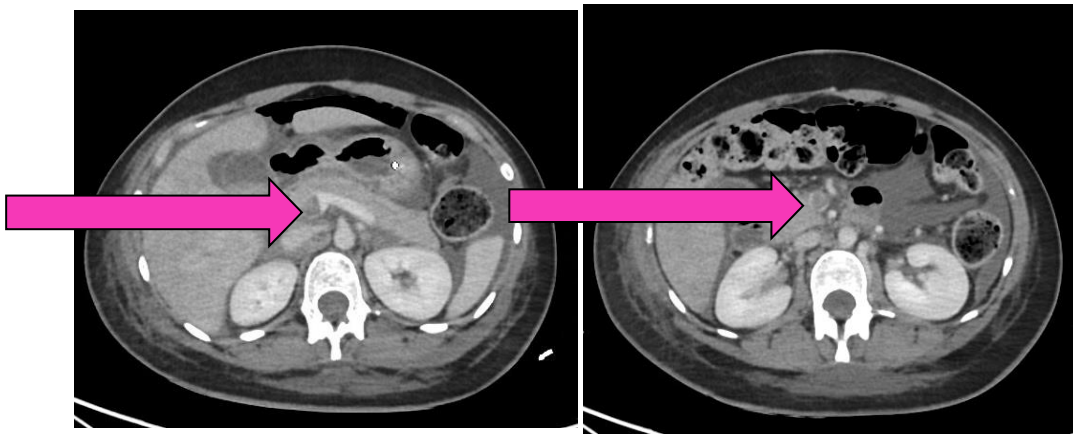
- 15-year-old female,

Abdominal pain
Colitis
ileo colic
Surgical resection

Porto-mesenteric vein thrombosis



PT 50%, Bili T 29 µmol/L, ASAT/ALAT: 566/685, PAL/GGT: 103/87 U/L.

08 Jan 2026

13 January 2026

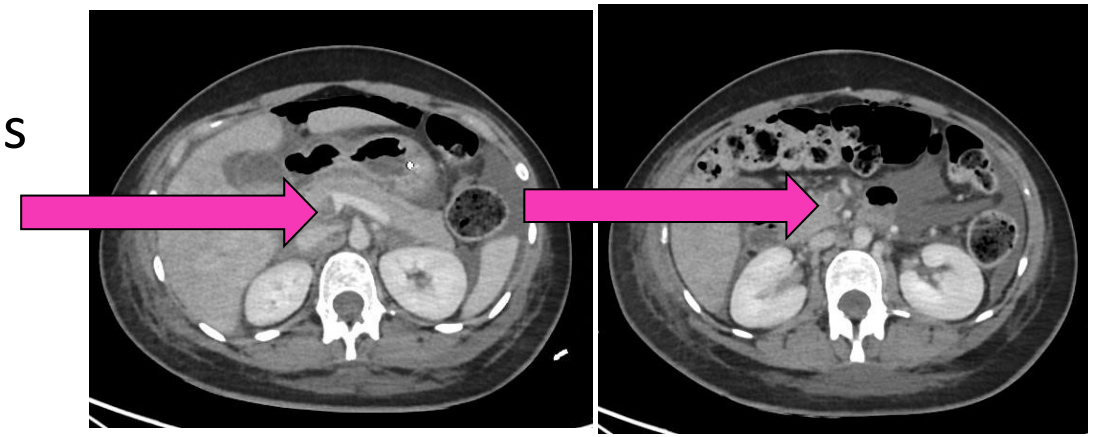
18 January 2023

- What were my hypothesis?
- What cause (s) did I suspect?

- 15-year-old female, abdominal pain after atb for UT infection

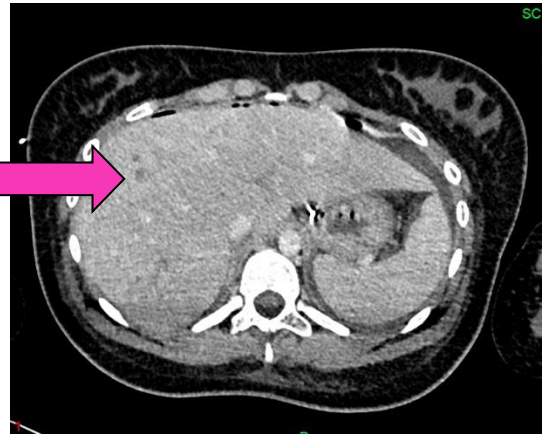
Abdominal pain
Colitis
ileo colic Surgical resection:
complete necrosis

Porto-mesenteric vein thrombosis



Budd Chiari syndrome

PT 50%, Bili T 29 µmol/L, ASAT/ALAT: 566/685, PAL/GGT: 103/87 U/L. Ascites
LS 60, SS 70



08 Jan 2026

13 Jan2026

18 Jan 2023

- What was our diagnosis hypothesis? Confirmed radiological review of CT scans

BCS and porto mesenteric vein thrombosis

- What cause (s) did I suspect? What questions did I ask?
  - PNH, MPN: hgb, platelets, LDH, spleen size
  - APLS, ….immune disorders, activated partial thromboplastin time?
  - Behcet disease: aphtosis, GI disease, inflammation..
  - V leiden, f 2 mutation, PC PS deficiency: personnal or family history?
  - Local or provoking cause: **covid**, CMV,, OC oral contraception, **Surgery**….
  - Complete thrombophilia screening negative but…

- BCS occuring after surgery in a patient with portomesenteric vein thrombosis, thrombophilia = idiopathic or secondary hypereosinophilic syndrome

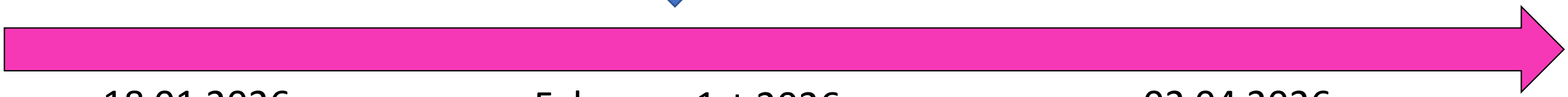
Eosinophils fluctuating from 1500 to 3000

LMWH

Parasitic screening Mutation
FIP1L1-PGFRA : negative
Tryptase nle
IgE elevated

Corticosteroids and anti IL 5

Recanalisation of hepatic veins and Portomesenteric veins
Eosinophils= 200/mm3
Mepolizumab and
Apixaban 5mgx2
LS 7, SS 20



18 01 2026

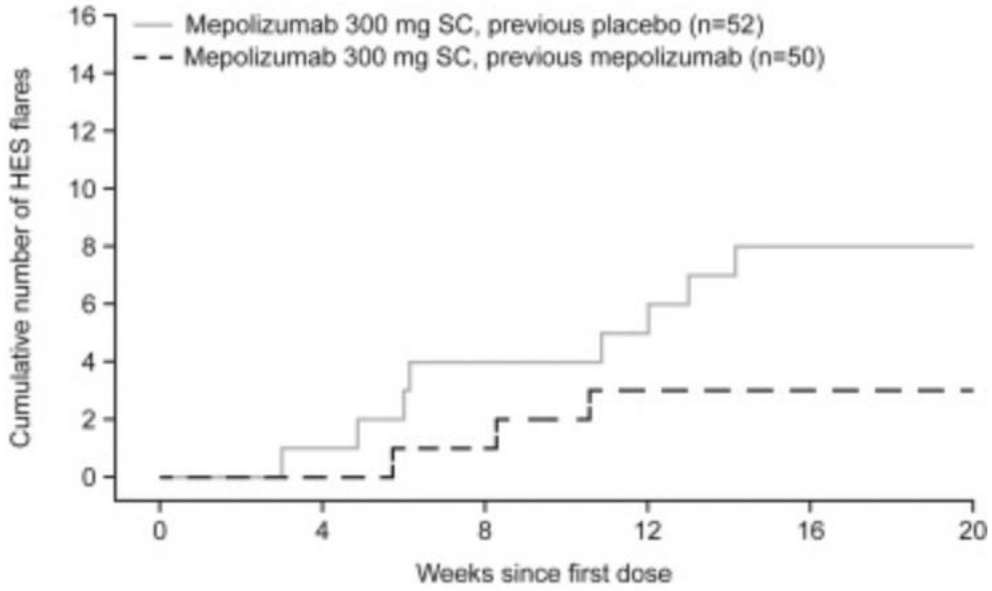
February 1st 2026

02 04 2026

Key messages

Multiple, progressive and proximal thromboses

Young age and hypereosinophilia



Message 1:

Context: Young age, PVT … **and** liver failure complicated by PHT+ eosinophils = should raise suspicion of BCS and secondary hypereosinophilic syndrome

Message 2: risk of recurrent thrombosis, avoid treat the triggers (hypereosinophilia, surgery)

Message 3: Favourable outcome with medical treatment alone using effective treatment fo the cause and anticoagulants, and PHT gradually resolved

Message 4: Requires rapid and effective collaboration between the referring centre, a haematologist, internal medicine and an expert hepatologist (pediatrics and adults).

Message 5: patient's empowerment critically needed

Outline

- Thrombophilia in VLD : BCS and PVT
- Caracteristic of thrombosis according to the cause
- Prognosis variability according to the cause
- Impact of treating the cause
- Impact of cause on anticoagulation regimen

What is thrombophilia ?

- *Thrombophilia* defines conditions that are associated with an increased risk of VTE and are characterized by a hypercoagulable state or alterations in the fibrinolytic system leading to hypofibrinolysis

Kyrle PA, Eichinger S. Deep vein thrombosis. Lancet. 2005; Smallberg Arterioscler Thromb Vasc Biol. 2011

Splanchnic vein thrombosis and thrombophilia

Common clinical features of thrombophilia	BCS %	NC- PVT %
Risk factor	76	58
Multiple causes	19	15-36
Thrombosis at a young age	35-40 Western 20-40 Eastern	+
Recurrent thrombosis in the absence of ATC	High	7-20
Positive family history of VTE	NA	23
Obstetric complications %	Pre eclampsia 5 IPC 17	Pre eclampsia 4
Thrombosis at unusual sites: cerebral, retinal	PNH, MPN, APLS Behcet	PNH, MPN, APLS Behcet

Risk factors for vascular liver diseases

Local « provoked » causes

- Liver stiffness=exclude cirrhosis
  Injected cross-sectional imaging
  Total colonoscopy
- Infectious
  Inflammatory
  Post-surgical
  Abdominal trauma
  Neoplastic

Thrombophilia

Acquired factors

Myeloproliferative neoplasia

Antiphospholipid syndrome

Behcet's disease

Paroxysmal nocturnal hemoglobinuria

Hereditary factors

Coagulation gene mutations

General causes

- Obesity and metabolic syndrome
- Pregnancy and post-partum
- Estrogen-progestin oral contraception
- Systemic diseases
  CMV infection, Covid
- 1er degree personal or family history of deep vein thrombosis

1. *Seijo S et al, Dig Liver Dis*
2. *Plessier A et al, Hepatol Baltim Md, January 2010*
3. *EASL Clinical Practice Guidelines: Vascular diseases of the liver. J Hepatol, January 2016 and 2025*
4. *Condat B et al. Hepatol Baltim Md, September 2000, debroucker J Hepatology 2022 , Elkrief Lancet gastro 2024*

VLD risk factors : Multifactorial

In adults without cirrhosis, VLD are frequently associated with ≥1 risk factor(s), which may be occult at presentation and should systematically be investigated with a **comprehensive workup**.

%	BCS	PVT
At least one cause	76	50
Multiple causes	19	10

Etiological workup should include the screening for **permanent and reversible risk factors.** Permanent risk factors can be further classified into major and not major risk factors (including thrombophilia and myeloproliferative neoplasm), depending on the risk of thrombosis recurrence.

EN-Vie BCS/TVP Cohort. Darwish Murad Ann Intern Med 2009, Plessier hepatology 2010, EASL CPG 2025, BAVENO VIII 2026

Cause varies according to geographic origins

%	Europe N=157	Algeria N=115	China N=92
MPN/Jak2 +	49/29	34	4
APLS	37	22	
V Leiden	19	11	0
PNH	15	4	1,6
Coeliac / Behcet's disease	1/4	**12**/ **>3**	
Oral contraceptive	33	34	4
Pregnancy	6	4	

Selectively screen for MPN, PNH and APLS in China. Factor II and V mutation screening inappropriate. Hyperhomocysteinemia,Poverty, bacterial infection, pregnancy

Afredj 2015 Apr 28;7(6):903-9. doi: 10.4254/wjh.v7.i6.903 Cheng J Gastroenterol Hepatol 2013

Risk factors for portal vein thrombosis

Local causes (*21%*) ‘induced’

- Injected cross-sectional imaging
  Total colonoscopy
- Infectious
  Inflammatory
  Post-surgical
  Abdominal trauma
  Neoplastic

Thrombophilia (*60%*)[2]

- [4,5] work-up
- **Acquired factors**
  Myeloproliferative neoplasm
  Antiphospholipid syndrome
  Behcet’s disease
  Paroxysmal nocturnal haemoglobinuria
  Hereditary factors
  F2 gene mutation

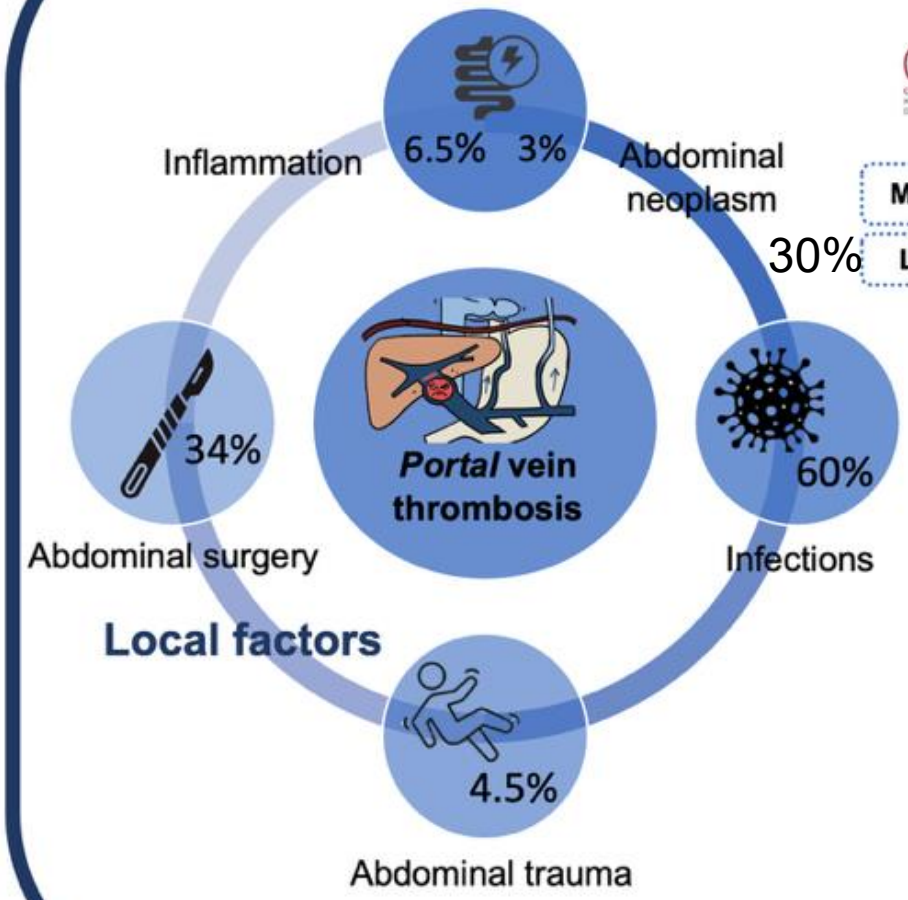
General causes

- Obesity and metabolic syndrome
- Pregnancy and postpartum
- Oestrogen- oral contraceptives
- Systemic diseases
  CMV infection, Covid
- Personal or family history

1. *Seijo S et al, Dig Liver Dis: Official Journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver, October 2012*
2. *Plessier A et al, Hepatology, January 2010*
3. *Vascular diseases of the liver: AFEF recommendations 2018. Hépato-Gastro Oncol Dig, Sept 2018*
4. *EASL Clinical Practice Guidelines: Vascular diseases of the liver. J Hepatol, January 2016*

Local Causes in NC-PVT: Major Risk Factor Identified in One-Third of Cases

Retrospective study including recent non-cirrhotic portal vein thrombosis associated with local factors



Baseline
154 patients

Follow-up

140 patients

Major-risk prothrombotic factors : 50/154 (32,5%)	**Major-risk prothrombotic factors** : 47/140 (33,6%)
Low-risk prothrombotic factors : 33/154 (21,4%)	**Low-risk prothrombotic factors** : 16/140 (11,4%)

17 new thrombotic events occurred after a median follow-up of 52 months (IQR 14-62) (min–max 3.0-69.0)

Multivariate analysis		p	HR	CI 95%
Gender	*Female vs. male*	0.197	1.985	0.701-5.618
Prothrombotic factors	*High-risk PTF vs. Low-risk or No PTF*	0.015	3.817	1.303-11.180
Continuous exposure to anticoagulation either until date of last news or date of discontinuation or date of the first new thrombotic event (max. 84 months)		0.016	0.976	0.956-0.995
Recanalization	*Complete or partial vs. absent*	0.005	0.222	0.078-0.635

Pancreatitis Very rare in the study

Ollivier Hourmand J Hepatol 2024

Splanchnic vein thrombosis (SVT) associated with SARS-CoV-2 infection

VALDIG Network

27 patients with recent SVT and SARS-CoV-2 infection

Comparison to 494 patients with recent SVT before the SARS-CoV-2 pandemic

At inclusion:

Fever (52% vs. 15%, p <0.001) and respiratory symptoms (44% *vs.* 0%, p <0.001) were more frequent, and median lymphocyte count was lower (1.1 10^3/mm *vs.* 1.6 10^3/mm^3, p = 0.043) in patients with infection compared to those without SARS-CoV-2 infection.

A prothrombotic condition was identified in 44% and 52% in patients with and without SARS-CoV-2 infection, respectively (p = 0.5).

During a median follow-up of 250 days:

All SARS-CoV-2 patients received anticoagulation therapy.

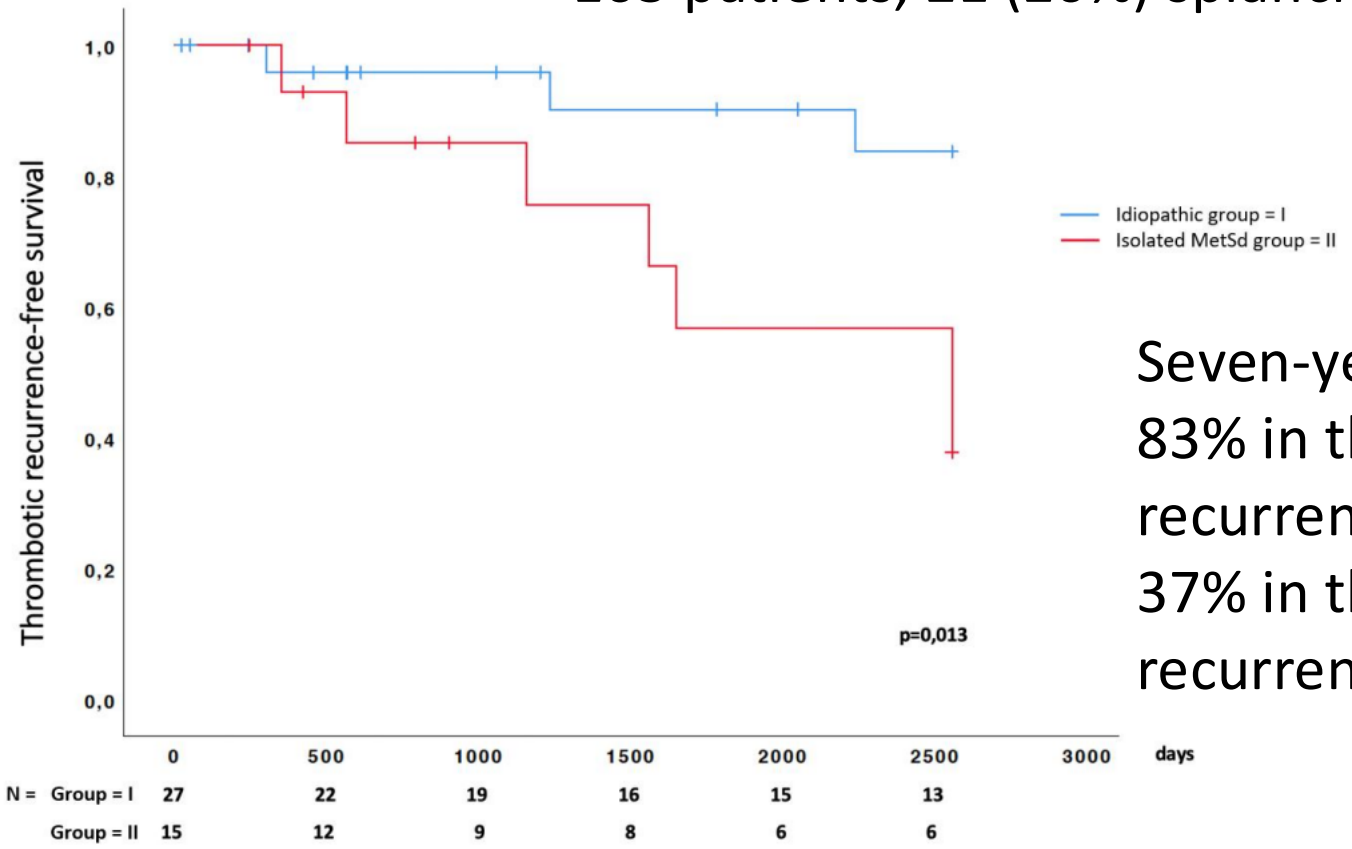
Three SARS-CoV-2-infected patients (11%) required intestinal resection for infarction 1 to 3 months after diagnosis of SVT compared to 13 (2.6%) controls (p = 0.044).

- Partial or complete recanalization of the thrombosed splanchnic vein was performed in 33% of SARS-CoV-2 patients.

Deltenre J Hep report Oct 2023

Thrombosis recurrence after ATC interruption in metabolic syndrome (N=42 patients no major risk factor for recurrence)

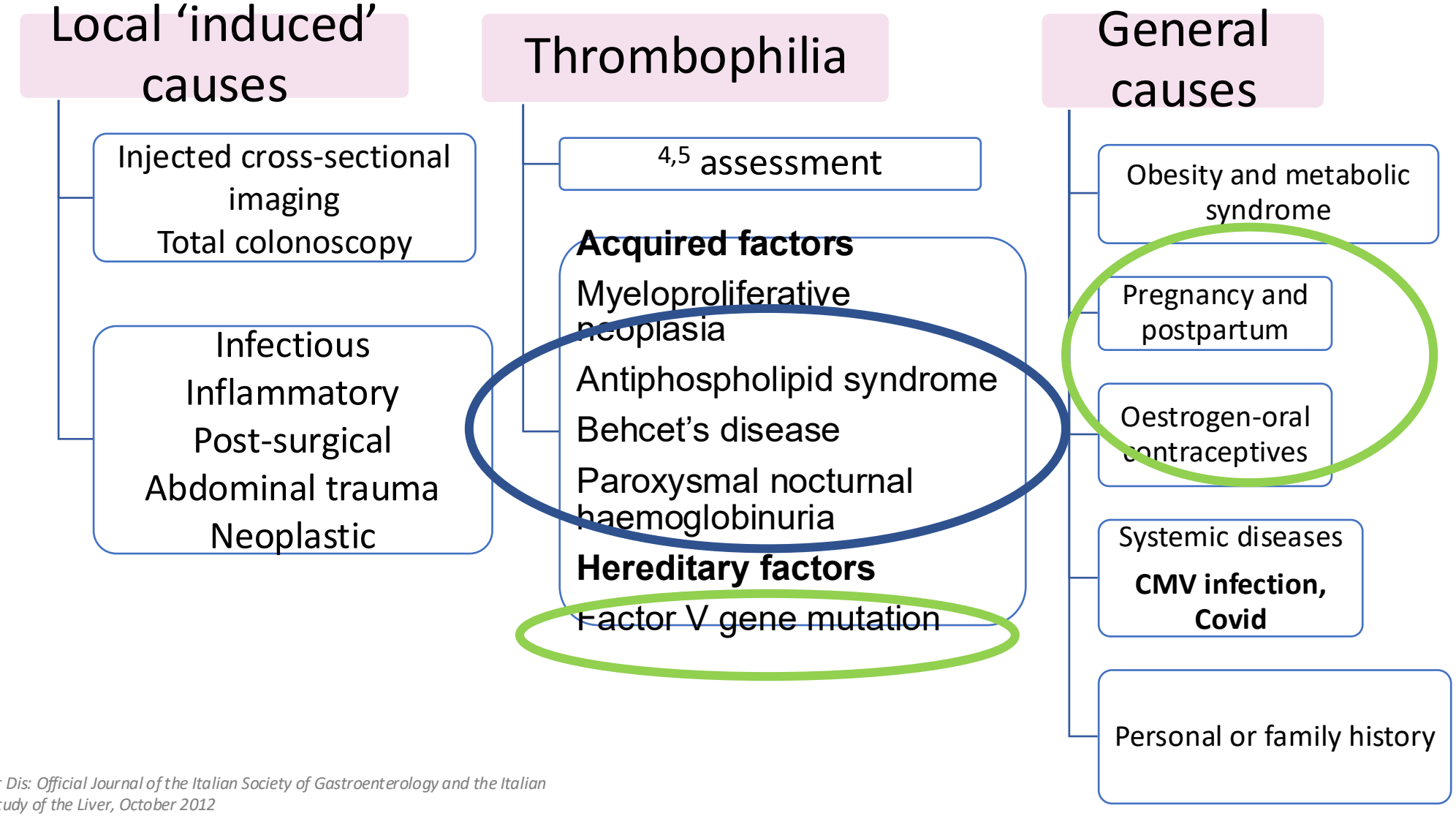
105 patients, 21 (20%) splanchnic or extra-splanchnic recurrence



Seven-year recurrence-free survival:
83% in the idiopathic group with three recurrences
37% in the isolated MetSd group with seven recurrences

Larrue EASL 2025

Risk factors for Budd-Chiari syndrome



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Diagnosis of myeloproliferative neoplasia in VLD

MPN diagnosis is based on :

241 VLD	JAK2V617F positive (n= 94)	JAK2V617F negative (n= 147)	p
Women	62%	48%	0.048
Splenomegaly	5 [0-11]	0 [0-2]	<.001
HGB	13.7	13	0.012
Neutrophils	5.2	3.7	<.001
Platelets	333	159	<.001

***JAK2* V617F** mutation

- **80%** of MPN with splanchnic thrombosis

CALR mutation

- **4%** of MPN with splanchnic thrombosis

- ***JAK2 exon 12 or MPL*** mutation*: 3%* of MPN with splanchnic thrombosis

Chait 2005 Br J Hem, Killadjian Blood 2008, Smallberg et al . Blood 2012 / Poisson et al. and Magaz J. of Hepatol. 2017, and 2021, Debureaux et al. Blood Adv, 2020

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Platelets	333	159	<.001

Spleen ≥ 16 cm
And platelets > 200/µL

***JAK2* V617F** mutation

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CALR mutation

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Chait 2005 Br J Hem, Killadjian Blood 2008, Smallberg et al . Blood 2012 / Poisson et al. and Magaz J. of Hepatol. 2017, and 2021, Debureaux et al. Blood Adv, 2020

Characteristics of VLD and PNH

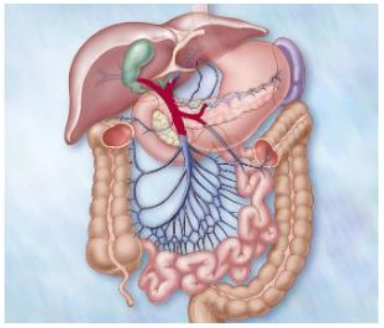
Small hepatic veins Budd-Chiari syndrome and paroxysmal nocturnal hemoglobinuria - The association of two rare entities

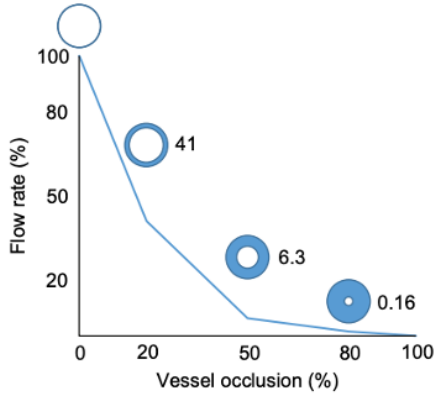
	Total
More than one imaging scan at the time of diagnosis %.	64
Delay (median years)	0.2 (0–1.7)
Other venous thrombosis %.	**40**
Cerebral venous thrombosis %.	**13**

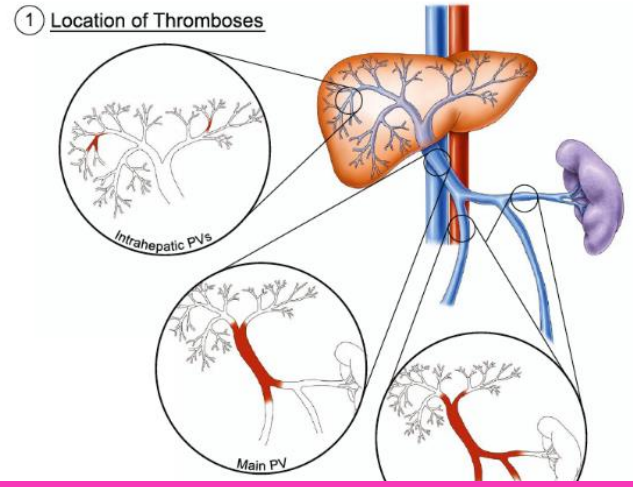
	Pnh +	Pnh -
Multiple risk factors	1 (2)	4 (3)
Haemoglobin g/dL	10 (8–11)	8.9 (7.7–10)
LDH IU	736 (482–1744)	110 (80–1500)
Platelets, g/L	101 (61–162)	249 [162–383.5]

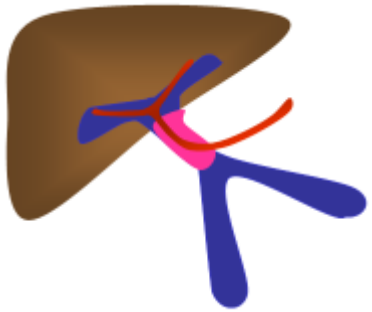
Plessier, Am J Haematology, 2022, Valdig group study gioia pathologica 2020

Rapid characterisation is required

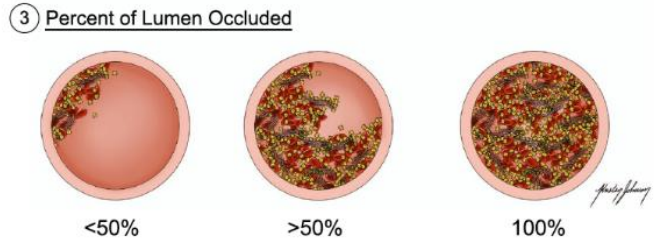


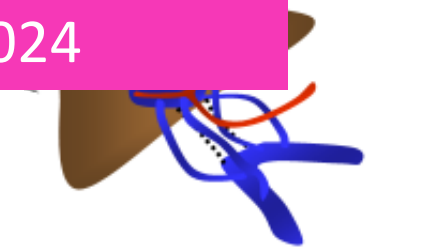






In patients with hepatic vascular disease, conduct a comprehensive clinical assessment including **risk factors**, liver morphology via imaging and measurement of liver stiffness. EASL Guidelines 2024





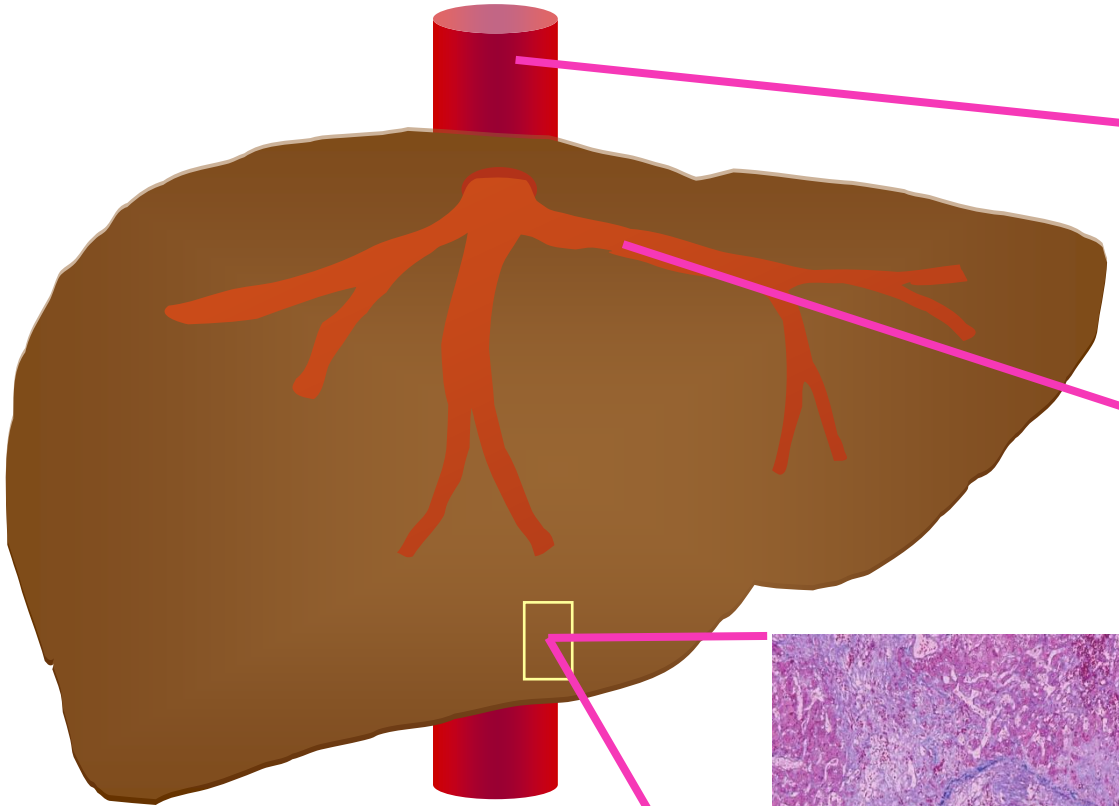
Portal cavernoma

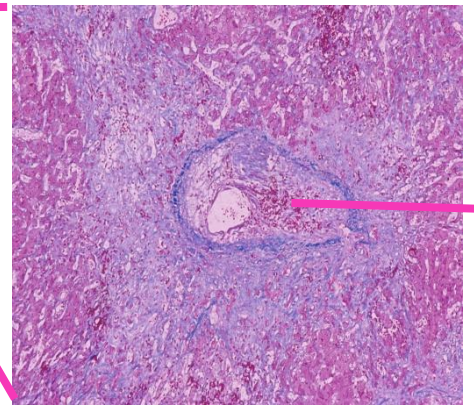
ıl. Hepatology 2021

Rapidly identify the cause

Causes	Particularities	Other venous sites	Arterial history	Veins affected
MPN	Elarged spleen contrast with high platelets	Yes cerebral	yes	Extension on Hepatic or splanchnic
PNH	Hemolytic anemia, thrombopenia	Yes cerebral	yes	Small-vessel thrombosis
Hypereosinophilia	Eosinophils > 800/mm3	Yes	Yes+++	Small-vessel thrombosis
APLS	Autoimmune diseases, pregnancy complications, prolonged activated partial thromboplastin time	Yes Catastrophic APLS	Yes ++	Small-vessel thrombosis
Behcet disease	Man, young age, mediteranean, ocular, mucocutaneous, and gastrointestinal manifestations, persisting inflammation	Yes	Yes	Inferior vena cava

Primary Budd-Chiari syndrome
Specificity of thrombotic localisation





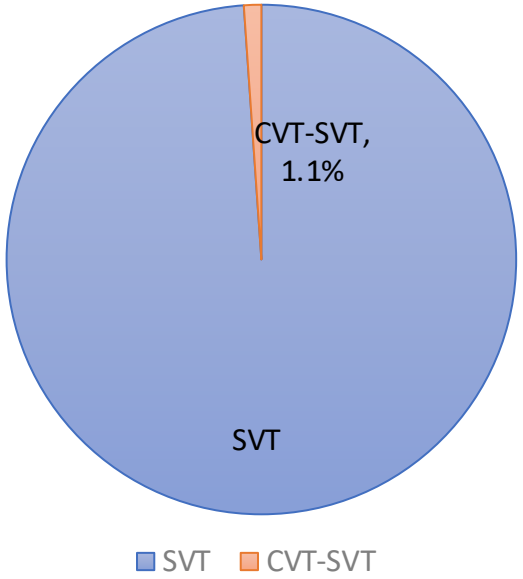
- Behcet's disease
- V Leiden

- MPN
- OCC

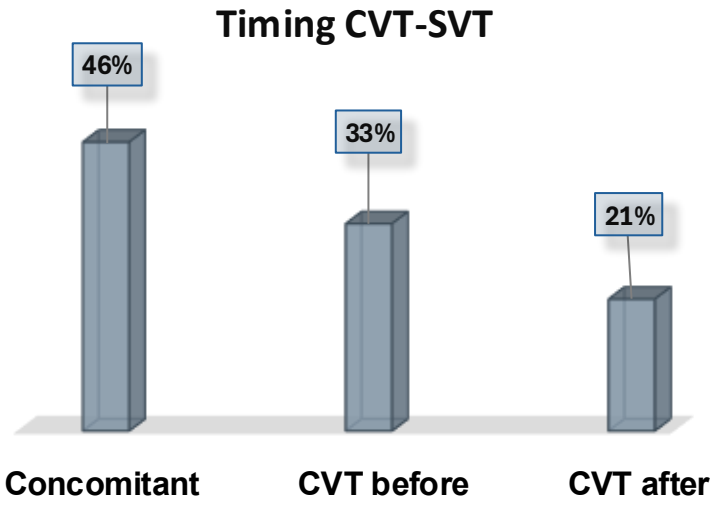
- PNH
- Covid

Valla J Hepatol 2009,
Riggio JTT 2013

Cerebral and splanchnic vein thrombosis



24/2,265
-Female (n=16; 66.7%)
-Median age: 38 y (IQR 2
56.5)
-SVT distribution:
54% NC-PVT (n=16);
46% BCS (n=11)



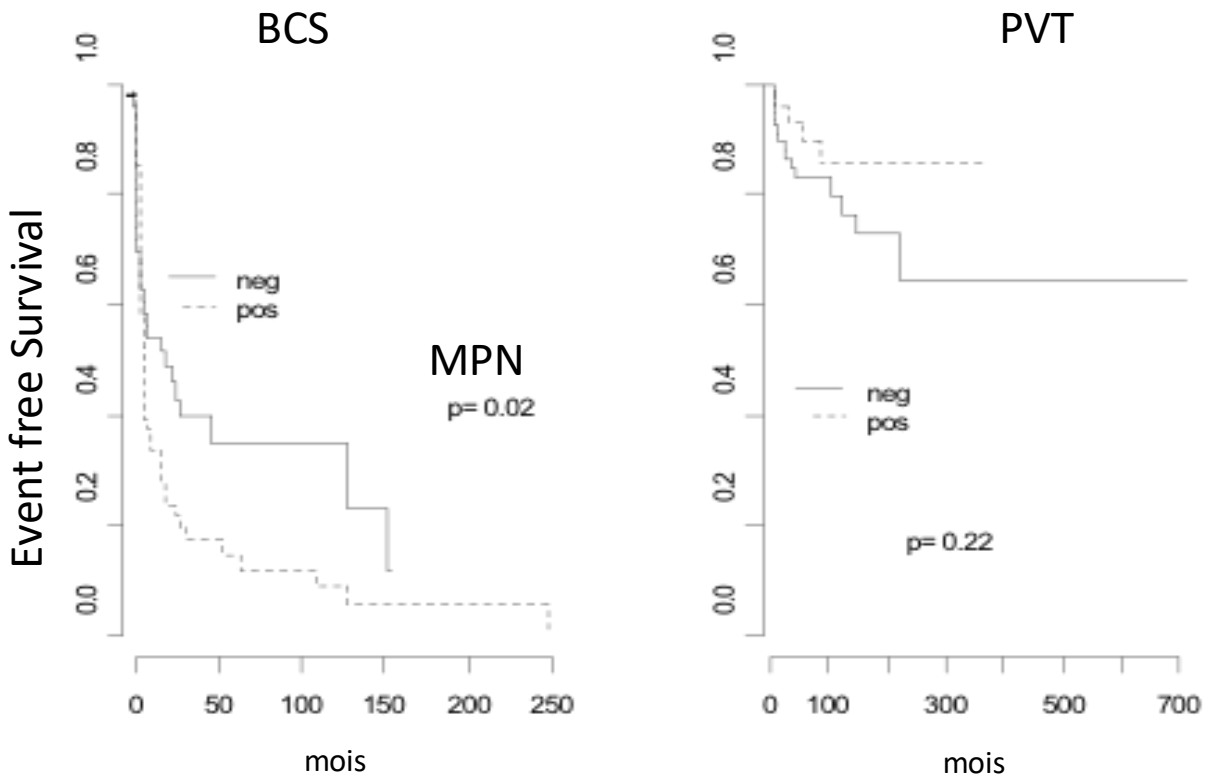
Among non-concomitant (n=13):
< 1 y: 3/13 (23.8%)
> 1 y: 10/13 (76.9%) →
6/10 (60%) > 5 y

Outcome N(%)	SVT N = 120	CVT-SVT N = 24	p-value
SVT recanalization	4 (3.4)	5 (20.8)	**0,008**
Bowel ischemia	5 (4.3)	3 (12,5)	0,136
Intestinal resection	4 (3.4)	2 (8.3)	0,270
GI bleeding Follow-up	2 (1.8)	5 (23.8)	**<0.001**
Death	9 (7.5)	3 (12.5)	0,422
Liver transplantation	2 (1.7)	0 (0.0)	>0.999

- PNH ($p < 0.001$)
- MPN ($p = 0.002$)
- 50% had ≥2 concomitant prothrombotic risk factors
- Marked and persistent prothrombotic burden over time, even during anticoagulation

Fasano, unpublished preliminary data

MPN is associated with poor survival in BCS

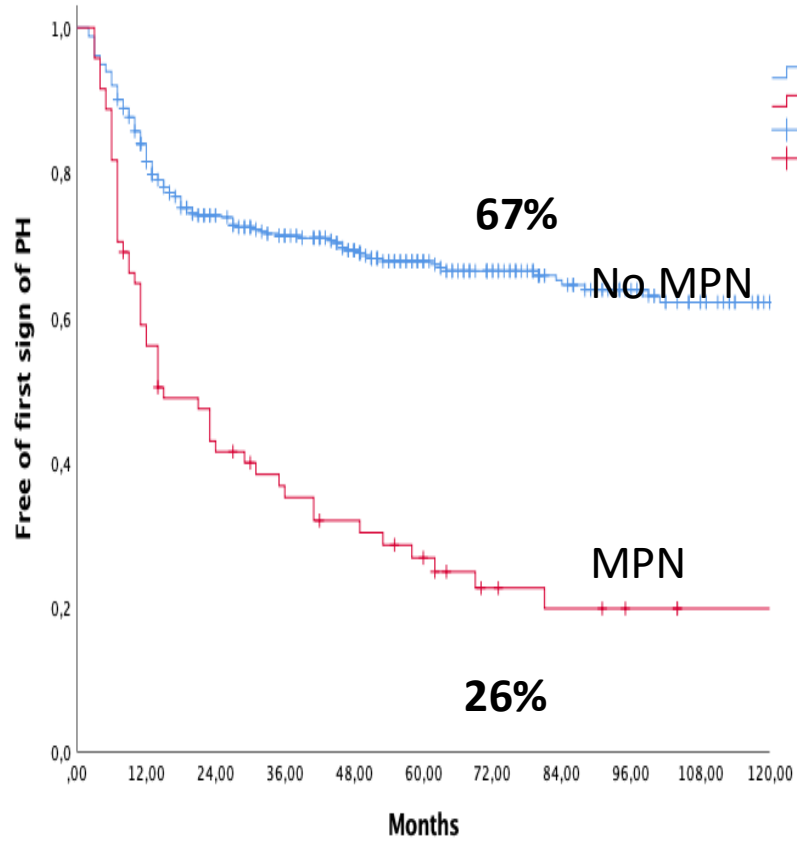


TIPS dysfunction in BCS

HR = 8,18, p = 0,017

Kiladjian JJ. *et al.* (2008). The *Blood,* 111(10) : 4922-9, Ronot radiology 2016

PHT complications and MPN in PVT



Portal hypertension free in PVT

Bartrolí-Alabau EASL 2025

JAK2 allele burden and additional NGS mutations: poor prognosis

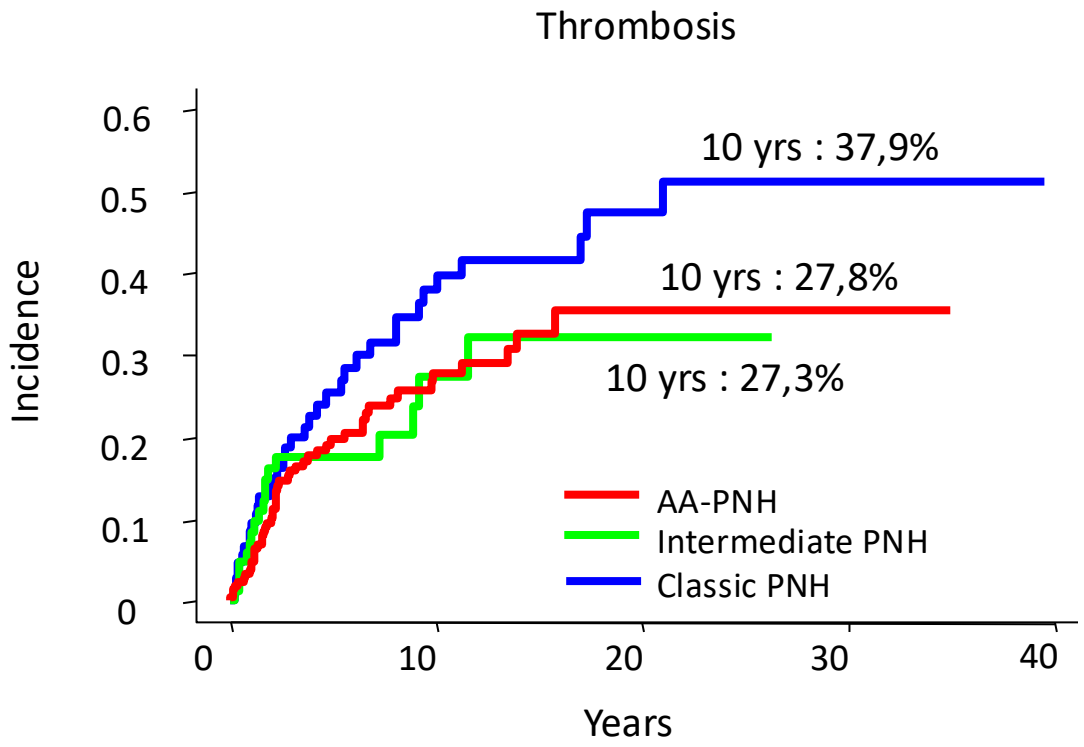
	Total (n=80)	Additional mutation (n=37)		Only a pilot mutation (n=43)
Transformation and/or deaths	10 (13%)	**8 (22%)**	p=0.04	**2 (5%)**
Secondary myelofibrosis	7 (9%)	**6 (21%)**		**1 (2%)**
Blasttransformation	2 (3%)	2 (5%)		0
Death	5 (6%)	4 (11%)		1 (2%)
Recurrence of thrombosis	12 (15%)	5 (14%)	ns	7 (16%)

NGS useful for prognosis and treatment selection

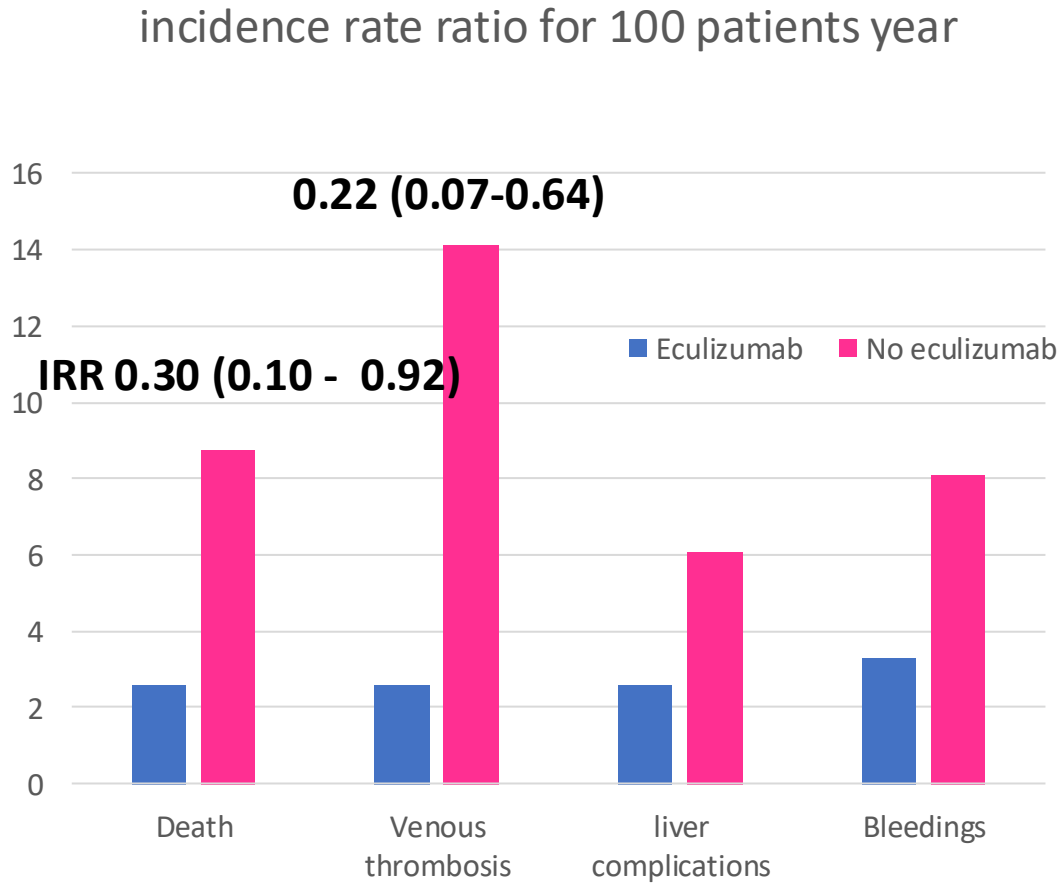
	Low risk (75%)	High risk (25%)
JAK2 allele burden	Low (< 50%)	High (≥ 50%)
Chromatin-Spliceosome-Tp53	and Absent	or Present
Secondary myelofibrosis, acute leukaemia and death.	< 5% at 10 years	>15% at 10 years

Debureaux et al. Blood Adv, 2020

Prognosis is severe when associated conditions are severe in BCS: Treating PNH improves outcomes



Peffault de Latour R. (2008). *et al. Blood,* 112(8) : 3099-3106



Plessier am J hematology, 2022, Valdig group study

Treating the risk factors impacts survival and liver complications

Treatments

- Myeloproliferative neoplasia hydroxyurea, IFN-a, anti-JAK2
- Paroxysmal nocturnal hemoglobinuria **Anti-complement anti C 5 anti C3**
- Behcet's disease Immunosuppressive : Infliximab wk 22 (94%) =complete response of vascular involvement
- Celiac disease Gluten-free diet
- Local cause: ATB and delayed surgery

Treating the cause improves survival in vascular liver disease

Prevent VLD decompensation

Chagneau AFEF, Killadjian Desbois orphanet 2014, Plessier am J haematology, 2022 De Stefano Blood Cancer J 2016 Saadoun NEJM evidence 2024

Classifying risk factors for recurrent thrombosis in VLD

Treatment strategies may vary depending on underlying risk factors for thrombosis, which may influence anticoagulant therapy. The duration of anticoagulant treatment should take into account whether these risk factors are transient or permanent.

EASL Guidelines 2025

BCS: Therapeutic anticoagulation should be initiated as soon as possible after diagnosis and continued long-term, including after LT.

PVT: The indication for long-term anticoagulation depends on the type of risk factor.

a. Long-term anticoagulation at therapeutic full dose is recommended in patients **with a permanent major risk factor** for thrombosis (LoE 3, strong).
b. In patients **without a permanent major risk factor** for thrombosis, long-term DOACs at lower dose can be considered to prevent thrombosis recurrence. (LoE 2, weak).
c. After complete resolution **of reversible risk factor**, anticoagulation discontinuation can be considered in the the absence of permanent risk factor (LoE 4, weak)

Baveno VIII

Classifying and managing risk factors for VLD

Permanent risk factors		Reversible risk factors
Major	Not major	
Myeloproliferative neoplasm Nocturnal paroxysmal hemoglobinuria Antiphospholipid syndrome Behcet's disease Homozygous or heterozygous composite thrombophilia gene mutations. Congenital antithrombin/ protein C/ protein S deficiency Active cancer Personal or 1st degree family of history deep vein thrombosis	Isolated heterozygous G20210A factor II or G1691A factor V mutation Hyperhomocysteinemia Central obesity High risk NGS variants	Local factor : - Abdominal trauma - Abdominal surgery - Abdominal inflammation/ infection Estrogen-containing contraception Pregnancy CMV infection SARS-cov2 infection SARS-cov 2 vaccination

Etiological workup should include the screening for permanent and reversible risk factors
Permanent risk factors can be further classified into major **(including thrombophilia and myeloproliferative neoplasm)** and not major risk factors depending on the risk of thrombosis recurrence. (LoE 3, strong)

Elkrief Lancet Gastroenterology and Hepatology 2024, Baveno VIII

Risk of recurrence according risk factor in PVT

	N / risk factor	Recurrence of thrombosis
Katims	APL syndrome n=34	62% recurrent thrombosis (9.5 years follow-up)
Ollivier Hourmand	PVT + local factor n=140	Major risk factor 34%
Ollivier Hourmand	Local factor n=140	No major underlying risk factor 11%
Ageno	Transient reversible risk factor n=105	6 events (6%)
Plessier RCT	111 patients without permanent major risk factor for thrombosis	19.71 per 100 person-years (95% confidence interval,7.49 to 31.92)
Ageno	Unprovoked n=163	18 events (11%)
Larrue	Idiopathic (n=27) or Met syndrome (n=15)	9 events / 42 patients (7 years follow-up) 21%
Baiges	123	33 events : 26% at 10 years)

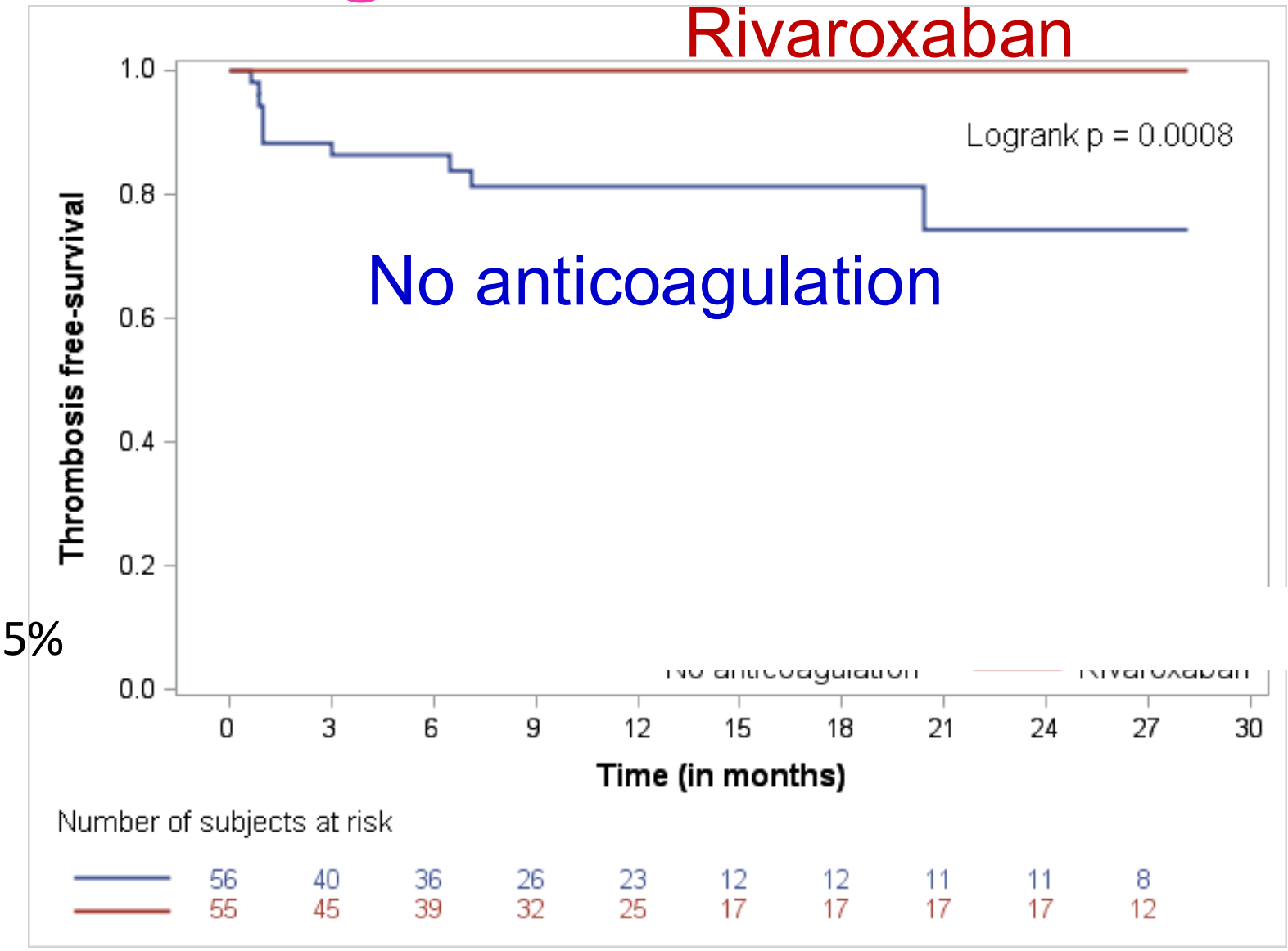
Rivaroxaban vs no anticoagulation in cases of idiopathic or low-grade risk factors

Rivaroxaban: 0/100 person-years

No anticoagulation: 19.7/100 person-years [7.5–31.9]

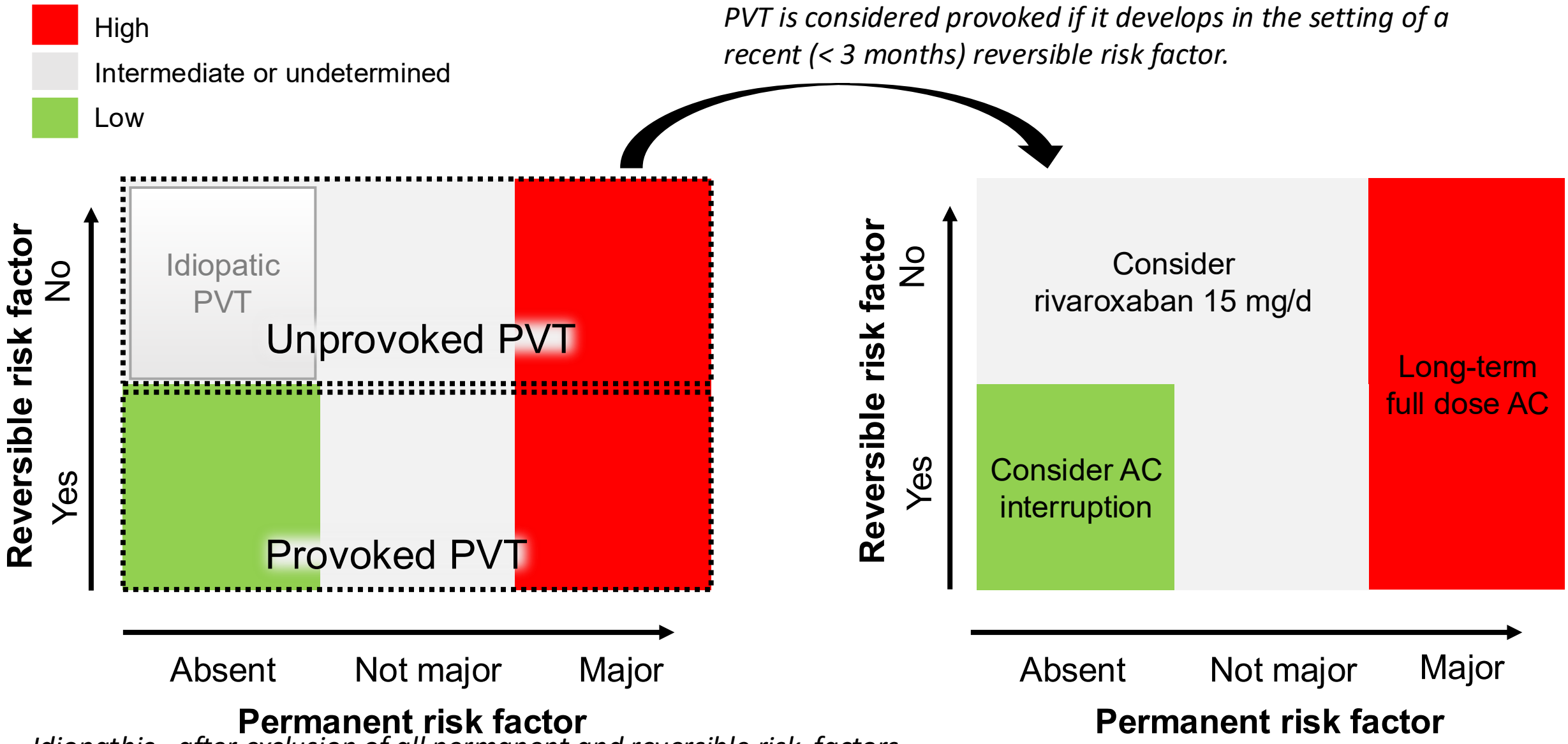
- Phlebitis 3
- pulmonary embolisms 3
- Splanchnic thrombosis 4

Median follow-up 11.8 months (95% CI [8.8–13.2])



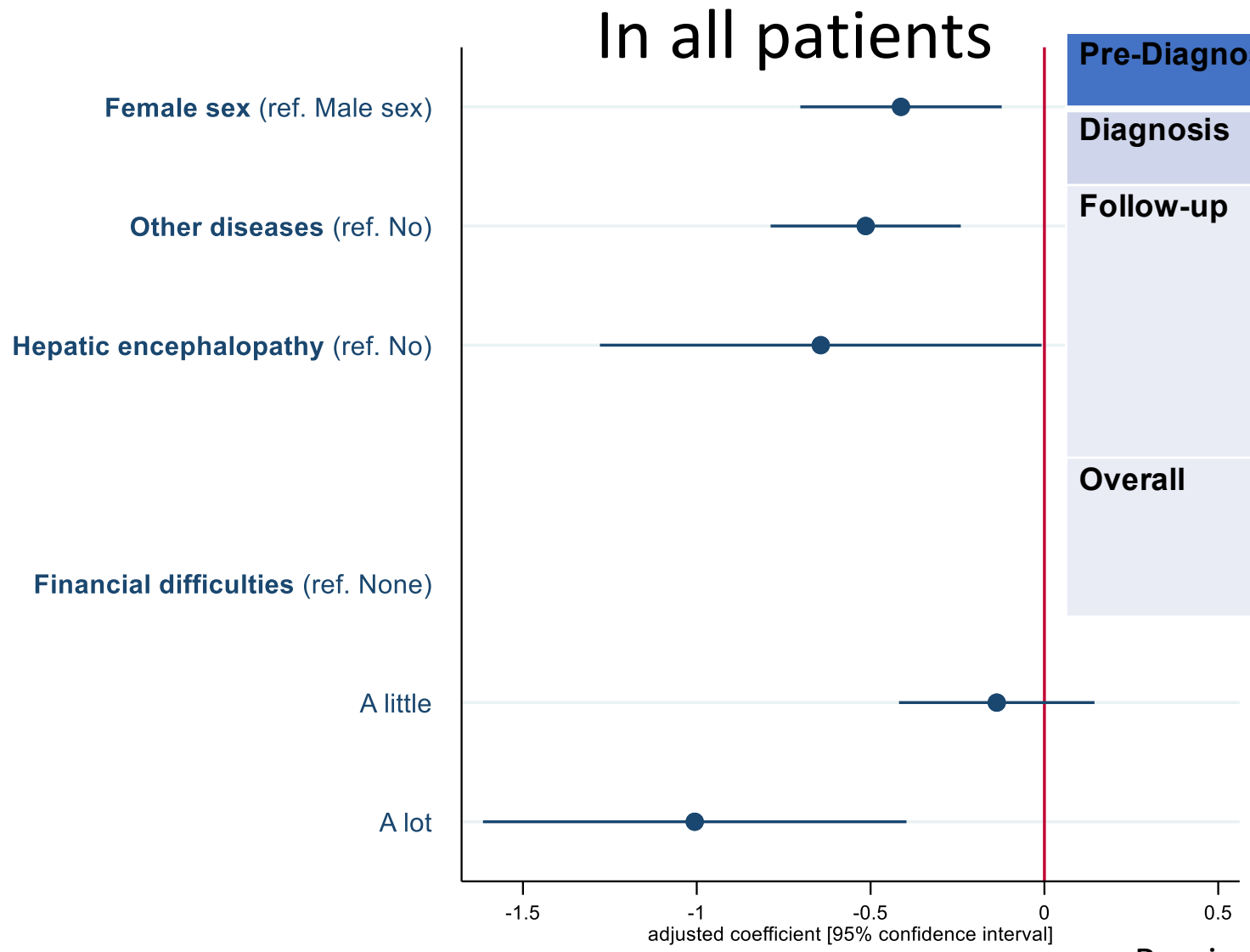
Plessier et al, NEJM Evidence 2022

Risk of recurrence of thrombosis in PVT Indication for anticoagulation in PVT



Idiopathic= after exclusion of all permanent and reversible risk factors

Factors associated with poor quality of life



Pre-Diagnosis	**Diagnosis wandering:** Patients face diagnosis wandering and **inequalities in accessing diagnosis**
Diagnosis	**Diagnosis communication:** Patients struggle to understand their disease
Follow-up	**Disease management:** Patients struggle to understand treatments and to feel in control of their condition
	Care coordination: More difficulties for patients with associated diseases or comorbidities
Overall	**All along the pathway:** Empowering patients, through peer exchange and caregiver involvement was considered essential to help them manage the disease and its broader impact on their lives.

Ramier J Hep report 2026 in press, Guilabert under review

Conclusion

- Identifying the cause is crucial in VLD
- Anticipate treating the cause
- Treat the cause
- Stratify anticoagulation according to the cause
- Empowering patients, through peer exchange, PAOs, and caregiver involvement
- Coordonate patient’s management regarding thrombophilia and vascular disease, but do not forget risk factor’s management (vaccine ,obesity….)

Networks for vascular liver diseases

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DU FOIE DE L'ADULTE ET DE L'ENFANT

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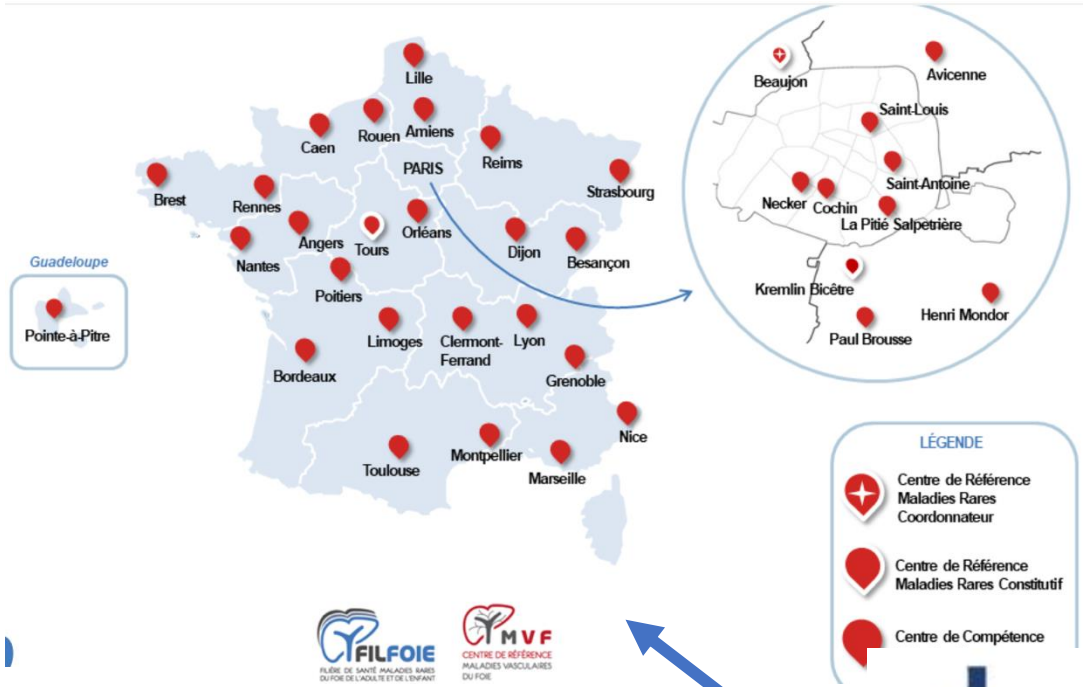
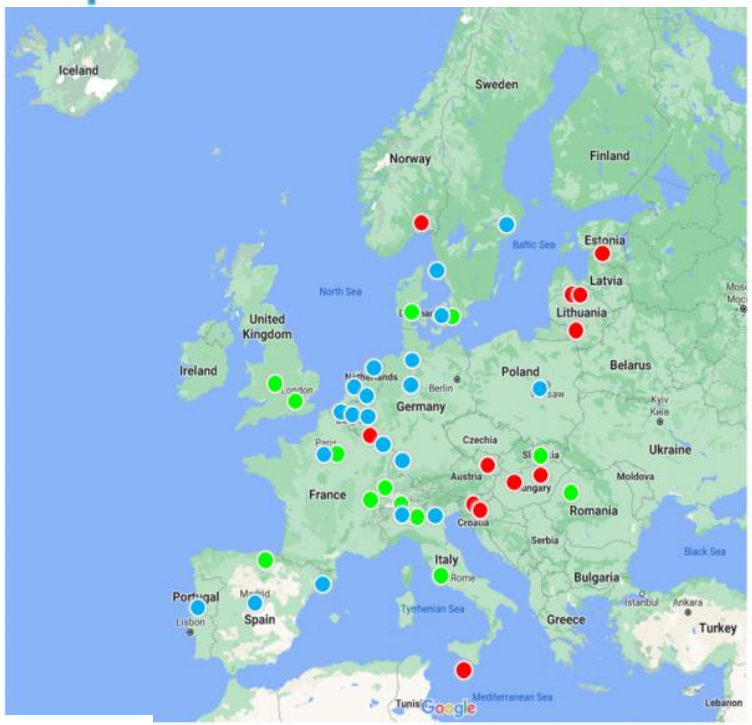


Cost Euro valdi net



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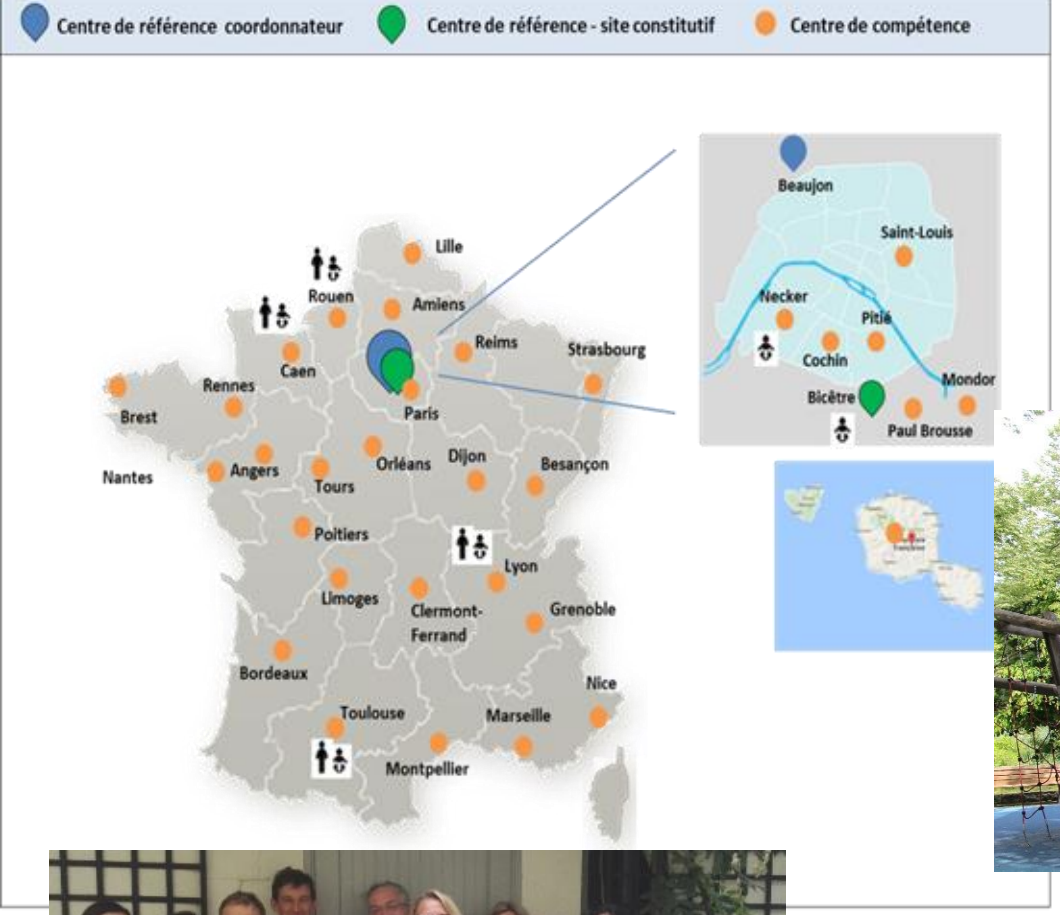

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