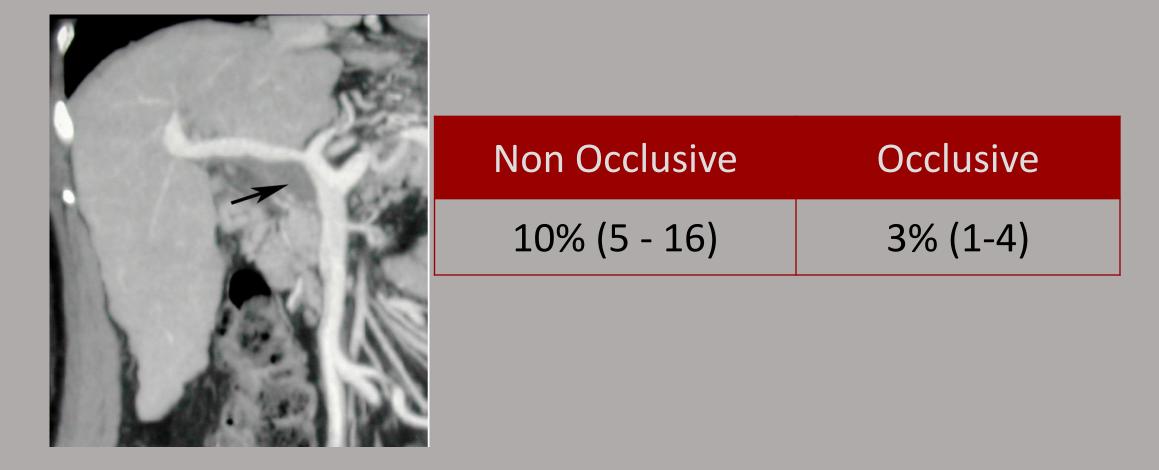
#### Portal Vein Thrombosis in Patients with Cirrhosis

#### Dominique Valla

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#### **Extrahepatic Portal Vein Thrombosis in Cirrhosis**



Nery, Hepatology 2014. Maruyama, Am J Gastro 2013. Luca, Radiology 2012. Senzolo & Garcia-Pagan. JHEP 2021

## **Extrahepatic Portal Vein Thrombosis in Cirrhosis**



Non-Occlusive	75%
Transient	40%
Recurrent	25%

Trends for spontaneous recanalization

- Occlusion < 50% of lumen occupancy
- Child A vs Child B-C

Nery, Hepatology 2014. Maruyama, Am J Gastro 2013. Luca, Radiology 2012. Senzolo & Garcia-Pagan. JHEP 2021

#### Portal Vein Thrombosis in Patients with Cirrhosis

• Whom to treat?

How to treat?

• How long to treat

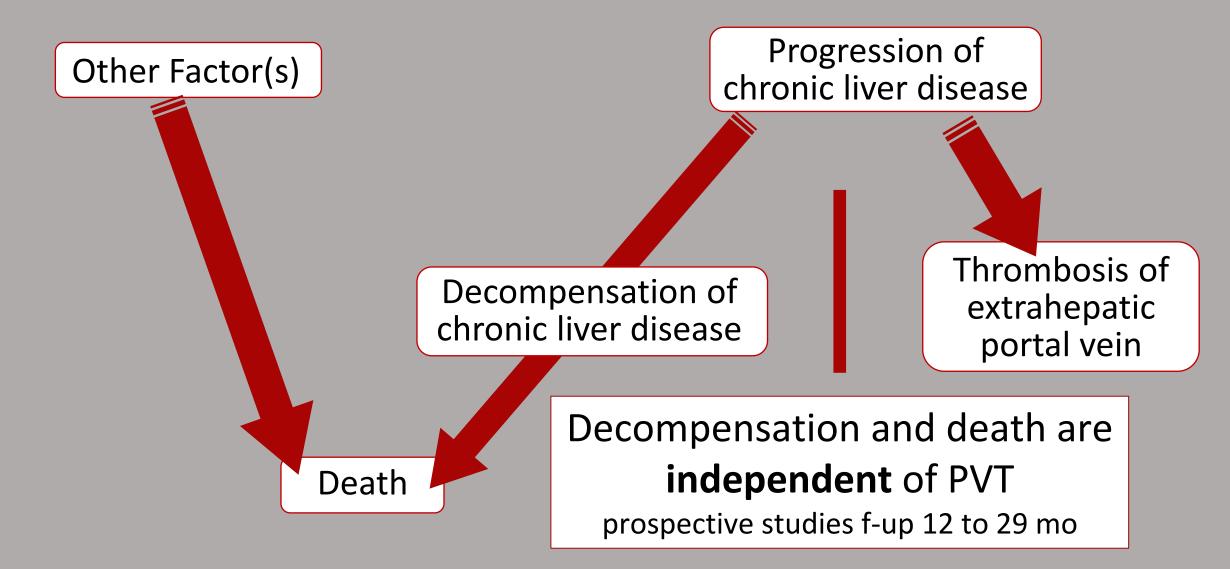
• Who is at risk?

• What are the consequences?

Risk increases with the severity of portal hypertension and liver dysfunction

Nery, Hepatology 2015. Turon, J Hepatol 2021

#### PVT is NOT associated with Excess Mortality/Morbidity before LT



Nery Hepatology 2014. Noronha. Liver Int 2019. Luca. Radiology 2012. Senzolo. Clin Transl Gastroenterol 2018.

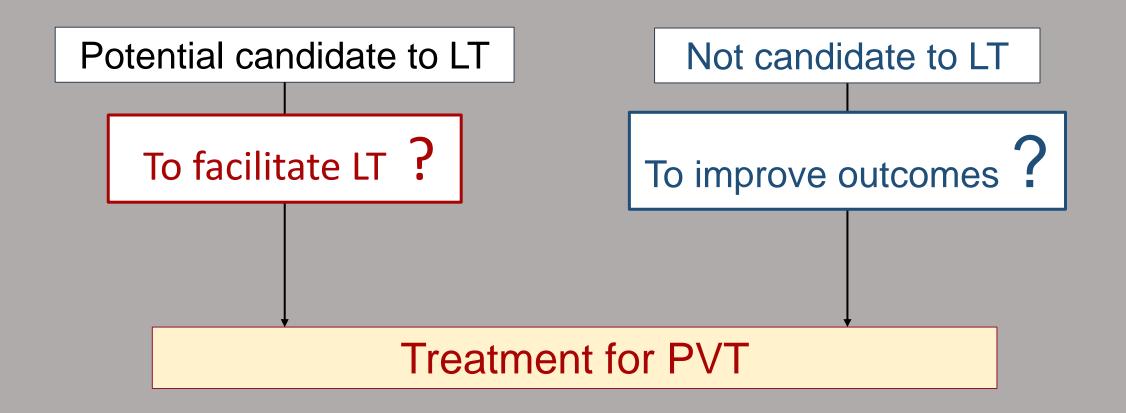
#### PVT is Associated with an Excess Mortality after LT

ľ		Experim	ental	Cont	rol		Odds Ratio		Odds Ratio	
	Study or Subgroup	Events		Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl	
	Gayowski 1996	4	23	8	65	0.9%	1.50 [0.41, 5.55]			
	Lerut 1997	10	38	63	288	2.5%	1.28 [0.59, 2.77]			
	Figueras 1997	2	14	19	119	0.6%	0.88 [0.18, 4.24]			
	Yerdel 2000	21	63	123	779	4.6%	2.67 [1.53, 4.66]	2000	I	
	Molmenti 2002	13	85	232	1546	4.0%	1.02 [0.56, 1.88]	2002		
	Dumortier 2002	6	38	61	468	1.8%	1.25 [0.50, 3.12]	2002		
	Shi L 2003	5	19	89	433	1.4%	1.38 [0.48, 3.93]	2003		
	Gimeno 2005	20	83	18	83	2.8%	1.15 [0.56, 2.37]	2005		1
	Bertelli 2005	9	64	111	657	2.8%	0.80 [0.39, 1.68]	2005		∣ 1-yr Mo
	Lendoire 2007	10	26	55	281	2.1%	2.57 [1.11, 5.97]	2007		
	Wu 2009	3	24	18	170	0.9%	1.21 [0.33, 4.45]	2009		OR 1.5
	Tao 2009	9	42	52	221	2.3%	0.89 [0.40, 1.97]	2009		
	Pan 2009	34	253	261	2508	9.0%	1.34 [0.91, 1.96]	2009	+	
	Gao 2009	11	46	51	262	2.7%	1.30 [0.62, 2.73]	2009		
	Doenecke 2010	5	24	34	169	1.4%	1.04 [0.36, 3.00]	2010		
	Englesbe 2010	10	30	143	574	2.4%	1.51 [0.69, 3.30]	2010		
	Suarez 2010	14	48	94	569	3.4%	2.08 [1.07, 4.03]	2010		
	Shi 2010	11	48	45	356	2.7%	2.05 [0.98, 4.32]	2010		
	Ravaioli 2011	14	91	112	798	4.0%	1.11 [0.61, 2.04]	2011		
	D'Amico 2013	10	51	71	396	2.7%	1.12 [0.53, 2.33]	2013		
	Hlbi 2014	36	174	157	1205	8.3%	1.74 [1.16, 2.61]			
	Ghabril 2015	282	3321	2217	45249	36.7%	1.80 [1.58, 2.05]	2015	-	
	Total (95% CI)		4605		57196	100.0%	1.55 [1.37, 1.75]		•	
	Total events	539		4034						
	Heterogeneity: Tau <sup>2</sup> =		= 22.75		(P = 0.3)	6) <sup>,</sup> I <sup>z</sup> = 8%				Zanet
	Test for overall effect:	•		•	η = 0.0i	oy, i = 0 x			0.2 0.5 1 2 5	
	, correr everall ellever.	2 - 0.07 (	0.00						PVT non PVT	

1-yr Mortality after LT OR 1.55 (1.37-1.75)

Zanetto. Transpl Int 2018

### Indications of Treatment for Cirrhosis with PVT



Baveno VII. de Franchis. J Hepatol 2022

#### Portal Vein Thrombosis in Patients with Cirrhosis



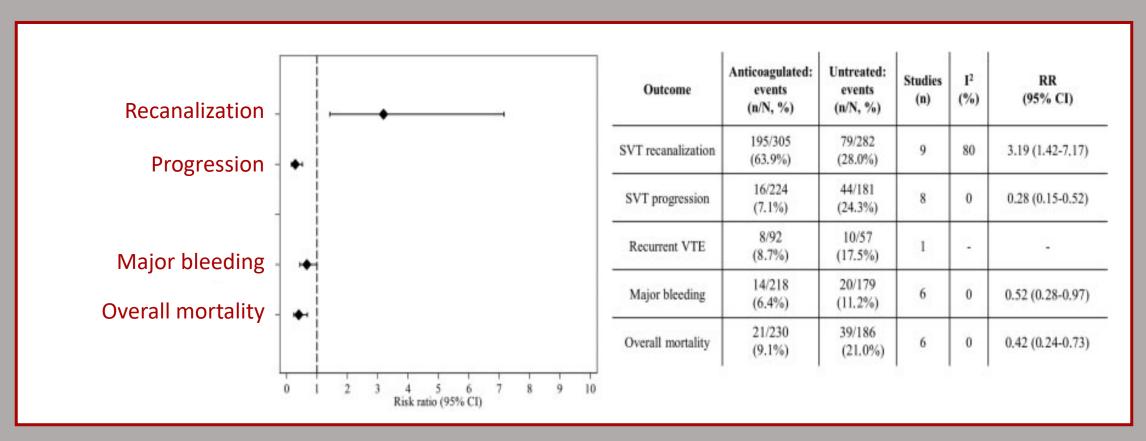
• How to treat?

How long to treat

- Anticoagulation?
- TIPS & Recanalization?

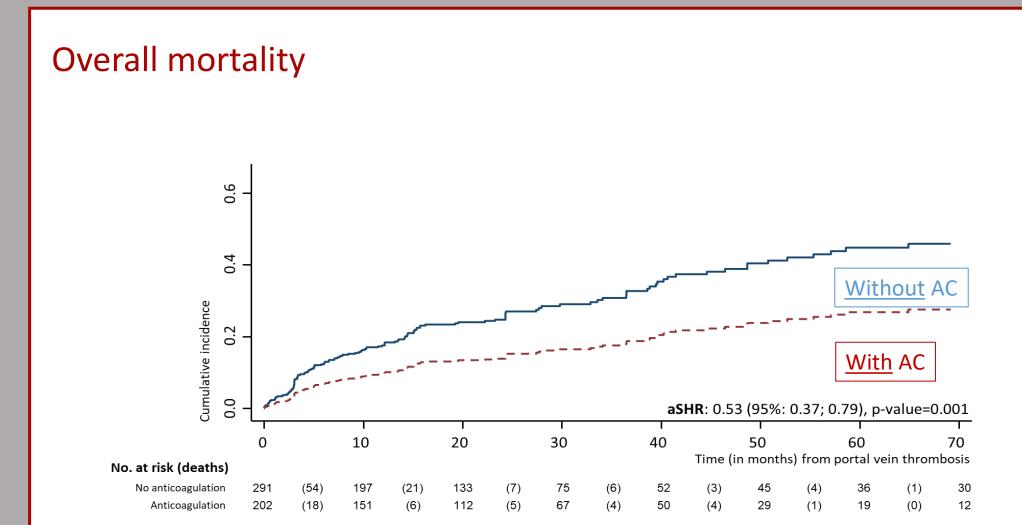
#### Efficacy and Safety of Anticoagulation In Patients with Cirrhosis and PVT

Meta-analysis, 26 studies, 1475 patients, -2019



E Valeriani. Throm Haemost 2021

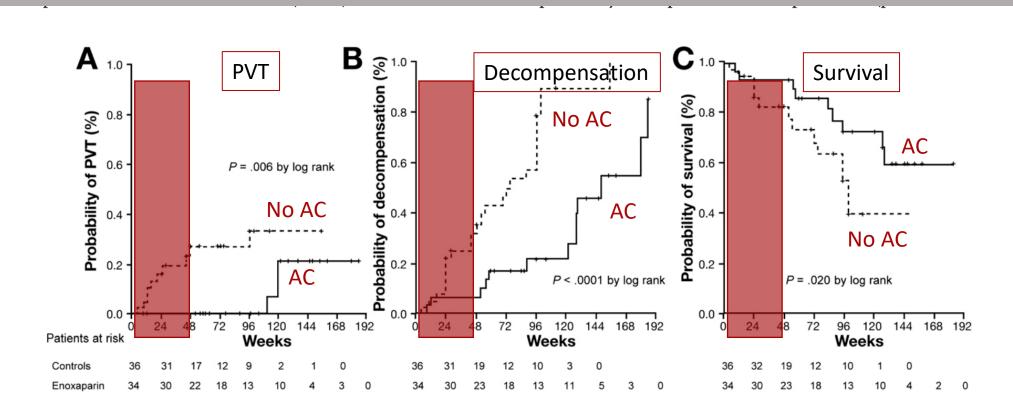
## Anticoagulants Improve Outcome of Cirrhosis with PVT



Sub-hazard ratio adjusted (aSHR) by age at diagnosis, etiology, Child, thrombosis extension and localization and variceal prophylaxis

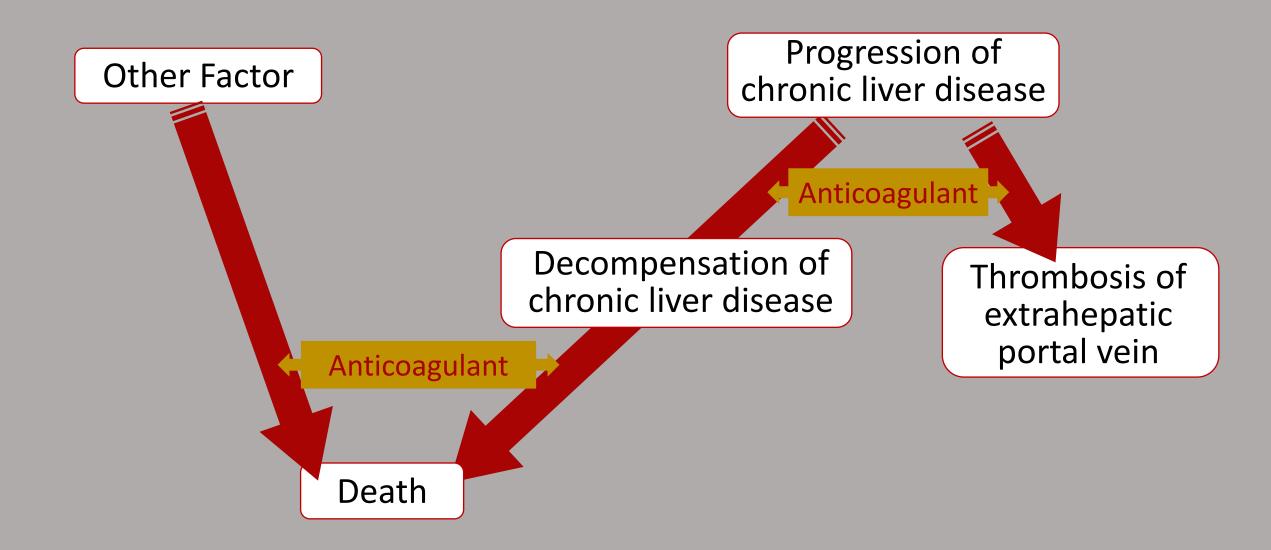
Guerrero et al. J Hepatol 2022

# Anticoagulants Improve Outcome of Cirrhosis without PVT

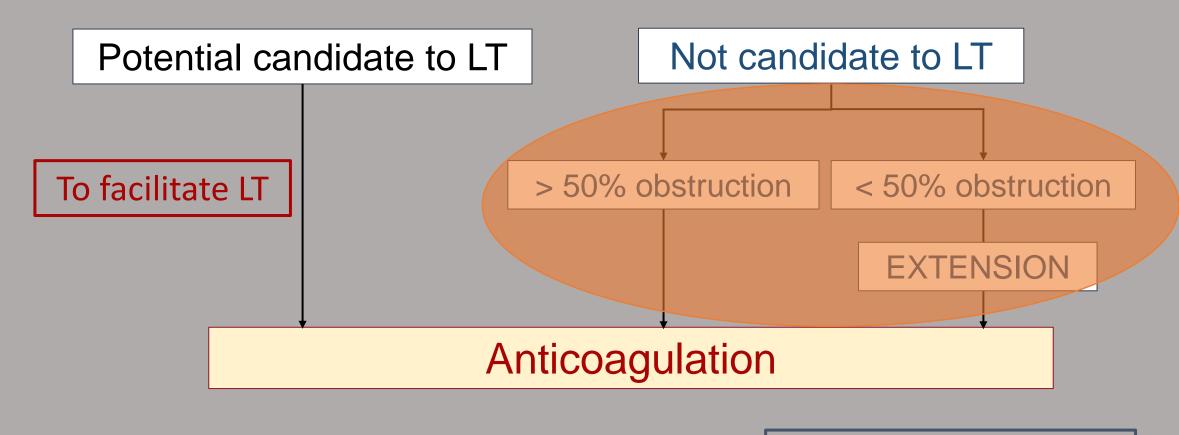


**Figure 1.** Actuarial probability of developing PVT or hepatic decompensation, and probability of survival according to treatment group. Probability of remaining free from (A) PVT, (B) hepatic decompensation, and (C) probability of survival. Dashed line: controls; continuous line: enoxaparin-treated patients.

Villa et all. Gastroenterology 2012



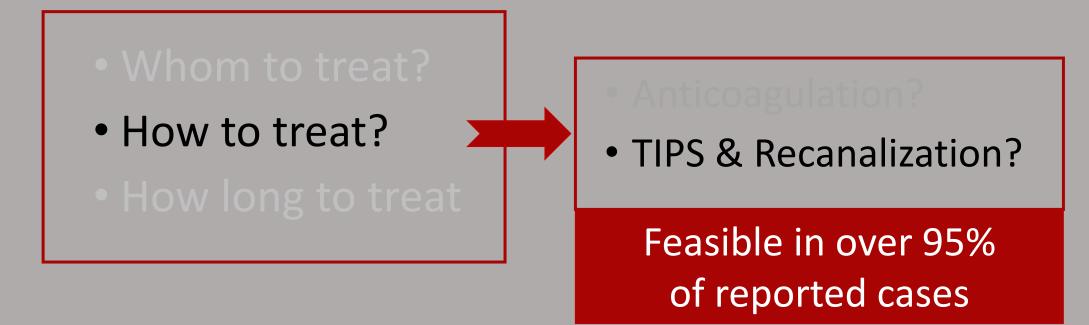
#### Anticoagulation for the Treatment of Cirrhosis with PVT



To improve outcomes

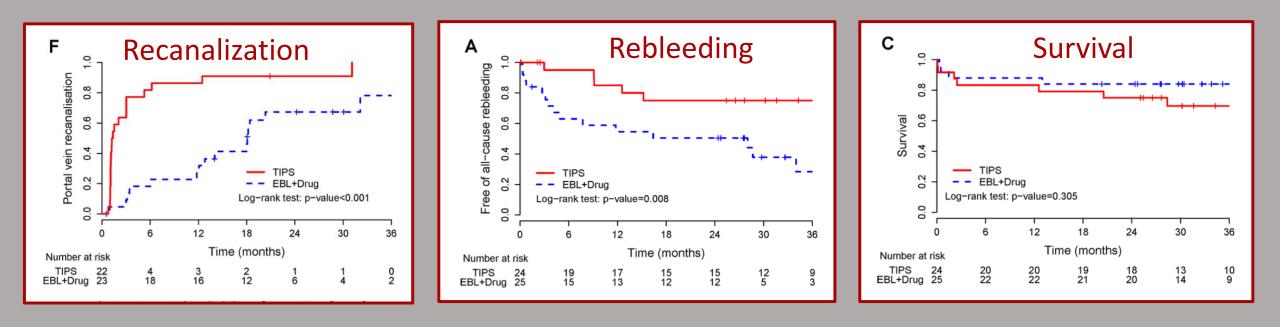
Baveno VII. de Franchis. J Hepatol 2022

#### Portal Vein Thrombosis in Patients with Cirrhosis

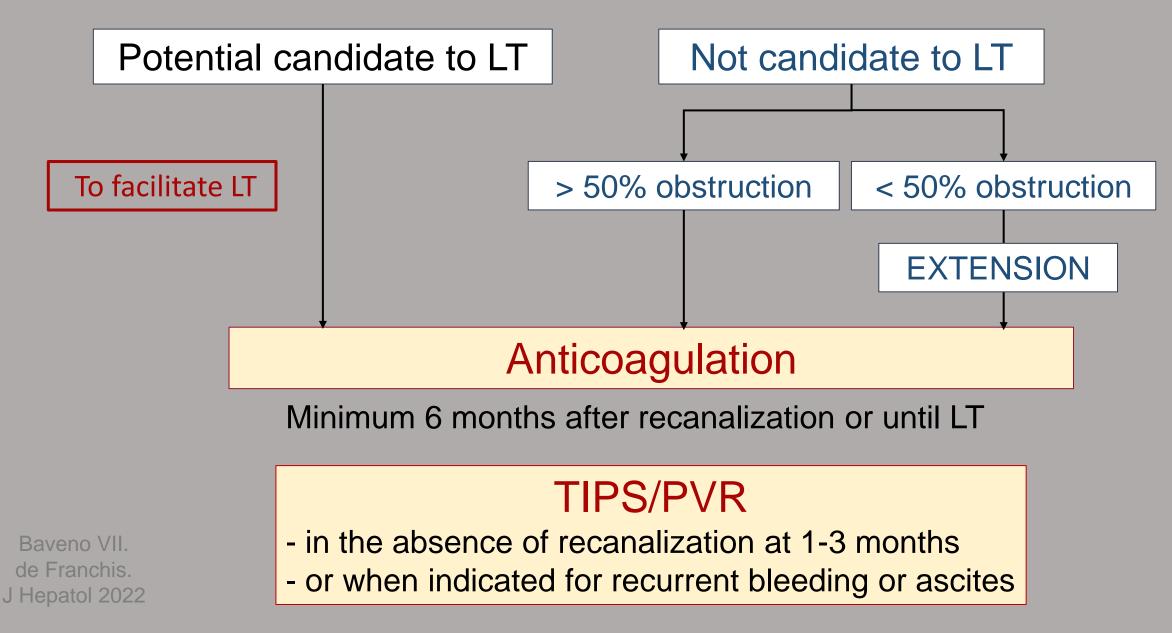


Rodriguez. APT 2018 Thornbul. J Vasc Interv Radiol 2017

#### **TIPS For PVT in Patients with Cirrhosis**



## TIPS for the Treatment of Cirrhosis with PVT



## Portal Vein Thrombosis in Patients with Cirrhosis

- Whom to treat?
- How to treat?
- How long to treat

• Recurrence is frequent after recanalization and interruption of AC

• AC improve the outcome of cirrhosis independent of PVT

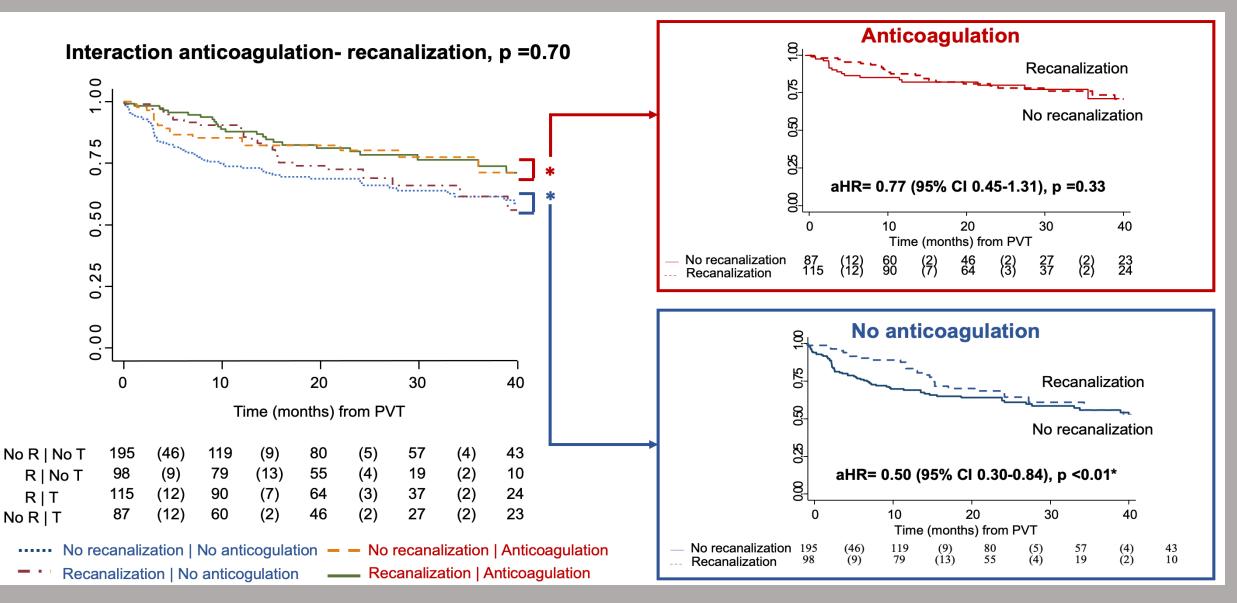
•TIPS improve recanalization withput impacting survival.

Le Wang et al. Adv Ther 2021

Guerero. J Hepatol 2022 Villa. Gastroenterology 2012

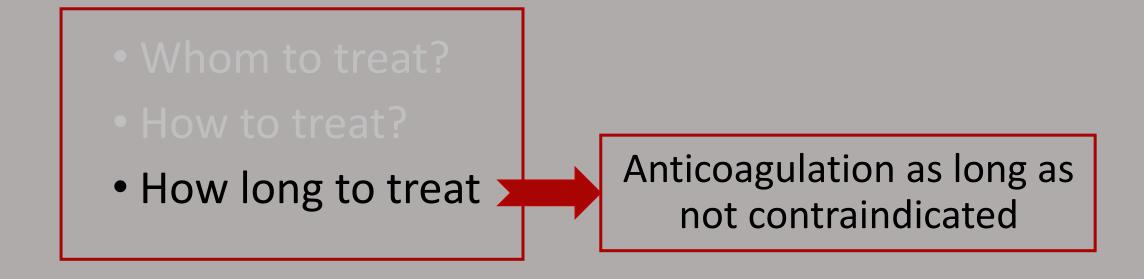


#### **IMPORTAL: Overall survival and PVT recanalization**



Guerrero et al. EASL ILC 2019

## Portal Vein Thrombosis in Patients with Cirrhosis



Recurrence is frequent after recanalization and interruption of AC
AC improve the outcome of cirrhosis independent of PVT

•TIPS improve recanalization withput impacting survival.

Le Wang et al. Adv Ther 2021

Guerero. J Hepatol 2022 Villa. Gastroenterology 2012

Lv. Gut 2017

## Conclusions

# Portal Vein Thrombosis in Patients with Cirrhosis

- Whom to treat?
- How to treat?
- How long to treat

Most patients with PVT

#1- Anticoagulants

#2- TIPS/recanalization pre-LT

AC as-long-as not contraindicated





Service d'hépatologie, Hôpital Beaujon, circa 1994

AASLD annual meeting, Boston, 2002

#### EASL Governing Board and Office, 2011



#### EASL Masterclass, Milan-Pavia, 2015







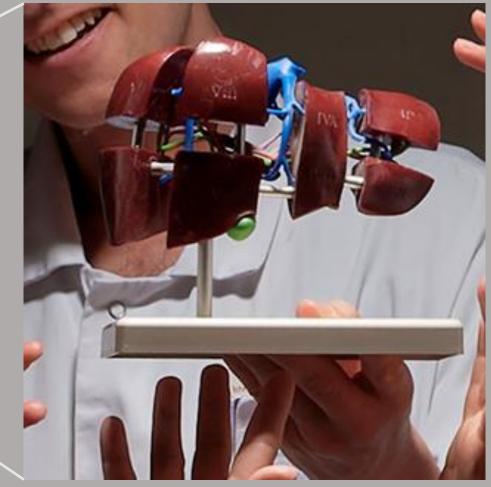
#### ILC, Vienna, 2023. VALDIG Meeting



Welcome and introduction (PE Rautou) Steering committee composition and ERN re Finances (PE Rautou) VALDIG website (PE Rautou) VALDIG-ERN activities (A Plessier); Castor of VALDIG publications: new publications and n Updates about ongoing/planned studies (V H VALDIG educational activities (F Nery) VALDIG social network activities (A Shukla) VALDIG meetings (Paris, L Elkrief; Padova, COST action proposal (PE Rautou)

sing remarks (Virginia Hernandez-Gea)





CRMVF\* Resourcing Team Session 2020

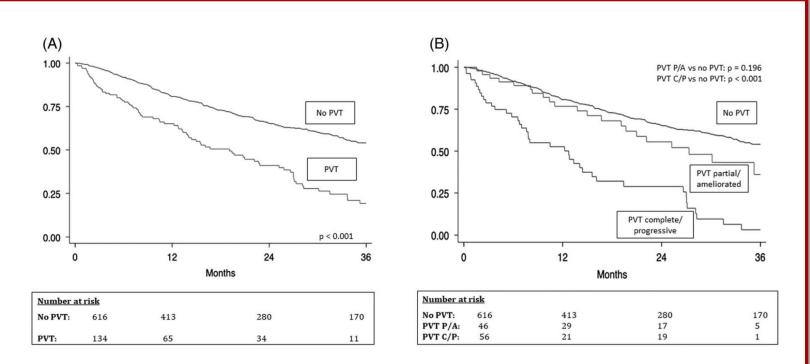
\*Centre National de Référence des Maladies Vasculaires du Foie

## Meta-Analysis: Anticoagulants and Cirrhosis with PVT

Study name	5	Statistics fo	or each stu	idy	Events / total Odds ratio and 95% C					95% CI		
	Odds ratio	Lower limit	Upper limit	P-value	Anticoagulant treatment	No treatment						Relative weight
Senzolo	0,094	0,010	0,873	.038	1/35	5/21		_	<u> </u>	1	1	39,28
Chung	0,310	0,012	8,292	.485	0 / 14	1 / 14						18,06
Wang	1,033	0,062	17,282	.982	1/31	1/32				<u> </u>		24,57
cai	0,164	0,006	4,358	.280	0/5	2/6	←			-		18,10
	0,232	0,058	0,939	.041	2/85	9/73						
							0,01	0,1	1	10	100	

Loffredo. Gastroenterology 2017

# Portal vein thrombosis in patients with HCC



**FIGURE 2** Kaplan-Meier estimates of survival probabilities according to the presence of PVT (A) and according to the presence of PVT and its evolution pattern (B). Abbreviations: C/P, complete/progressive; PVT, portal vein thrombosis; P/A, partial/ameliorated evolution pattern.

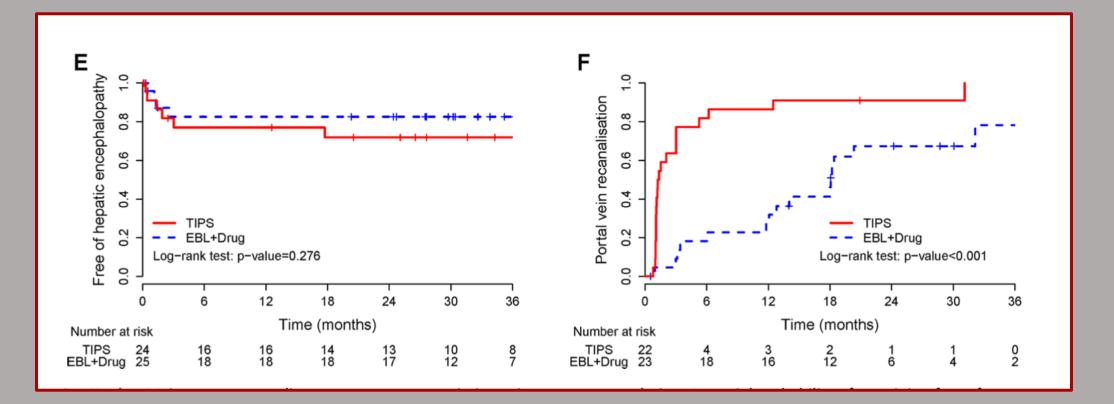
PVT independently associated with tumor volume and portal hypertension

PVT, particularly when complete or progressive, independently associated with lower survival

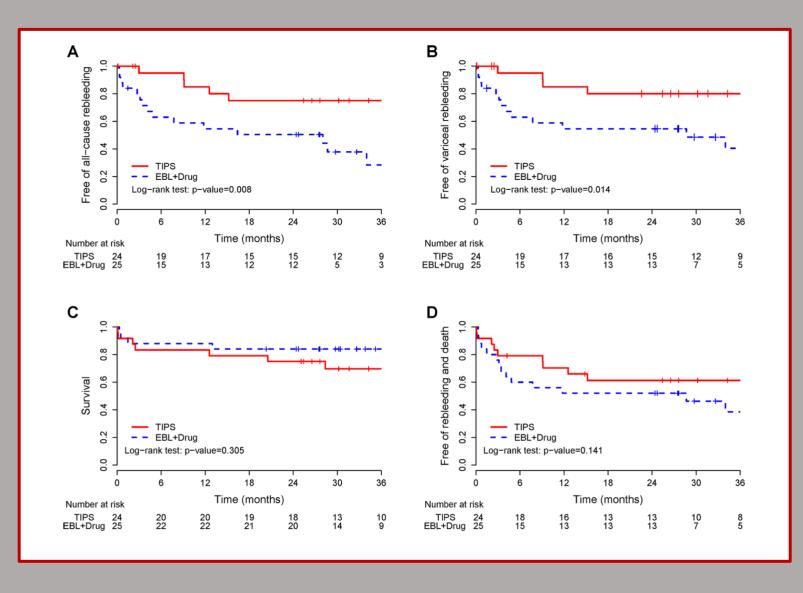
# Which anticoagulant?

Low molecular weight heparins	<ul> <li>Largest experience, including RCTs</li> <li>half-life ~ 4h, dose-independent elimination</li> <li>renal excretion</li> <li>90% biodisponibility</li> <li><i>but</i> injection</li> </ul>
Vitamin K antagonists	<ul> <li>oral administration</li> <li><i>but</i> unreliability of INR in cirrhosis</li> </ul>
Direct oral anticoagulants	<ul> <li>- increasing amount of data</li> <li>- oral administration</li> <li>- greater efficacy and safety than Vit. K antagonists</li> <li>- <u>but</u> contraindicated in advanced cirrhosis</li> </ul>

#### **TIPS For PVT in Patients with Cirrhosis**



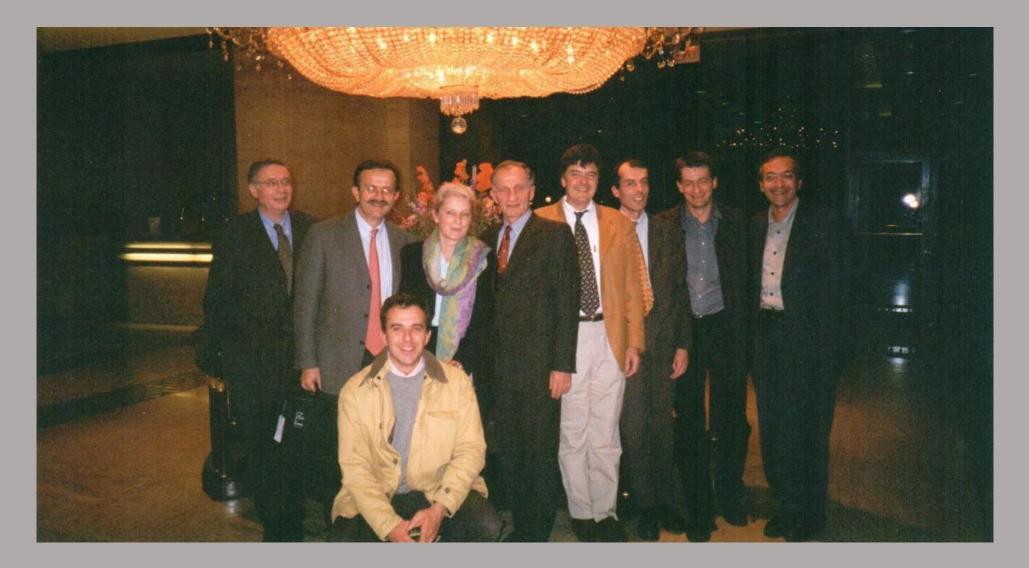
#### **TIPS For PVT in Patients with Cirrhosis**



Lv. Gut 2017



#### Service d'hépatologie, Hôpital Beaujon, circa 1994



#### AASLD annual meeting, Boston, 2002



#### EASL Masterclass, Milan-Pavia, 2015



ILC, Vienna, 2023. VALDIG