Studi degli outcome importanti della malattia del fegato

Trombosi Portale nei pazienti che hanno eliminato HCV

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Outline

1. **Background:**
   - **Definition, prevalence, and clinical impact of portal vein thrombosis (PVT) in cirrhosis.**
   - **Special considerations regarding PVT and alterations of coagulation in HCV-related cirrhosis.**

2. **PITER-based project:**
   - **Specific aims.**
   - **Study design.**
   - **Preliminary results.**

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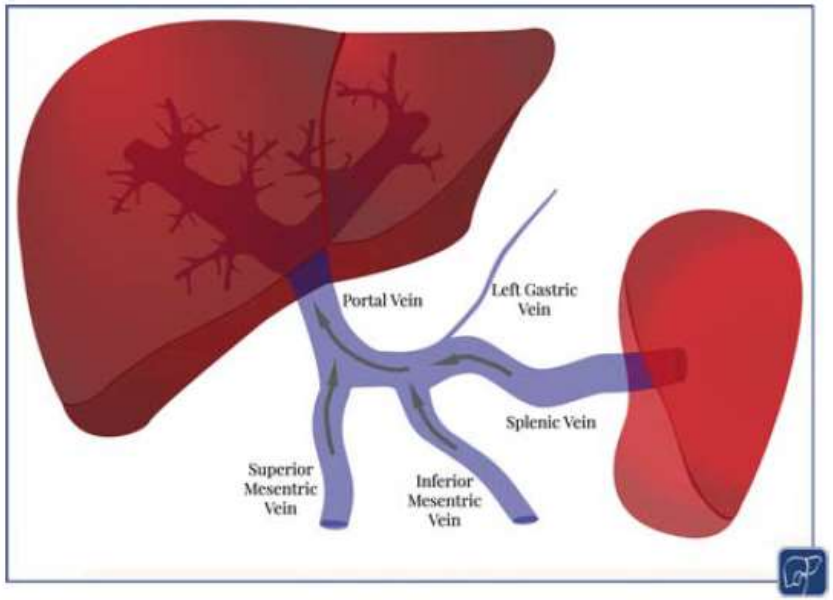
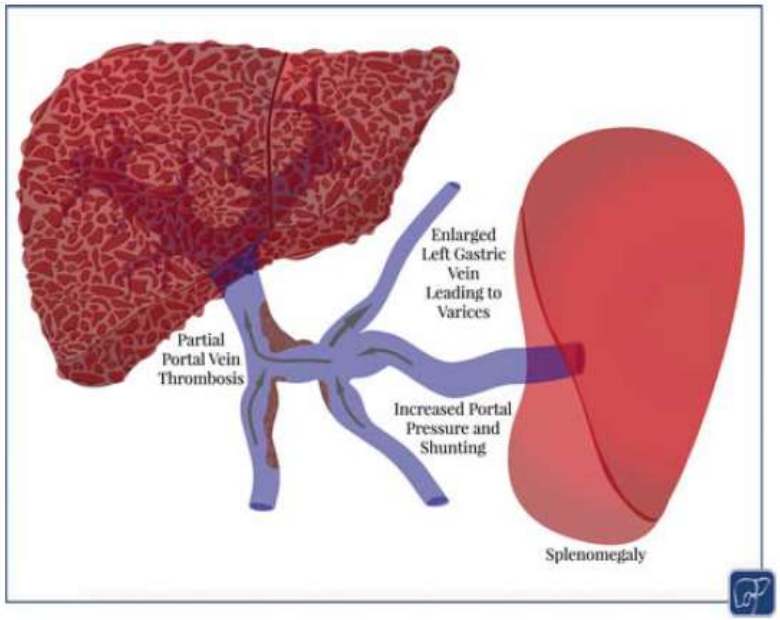
Portal vein thrombosis

- **PVT** is defined as the **presence** of a **thrombus in the lumen of** the **main portal vein**, which can **extend into intra or extrahepatic venous branches.**

Normal portal venous anatomy



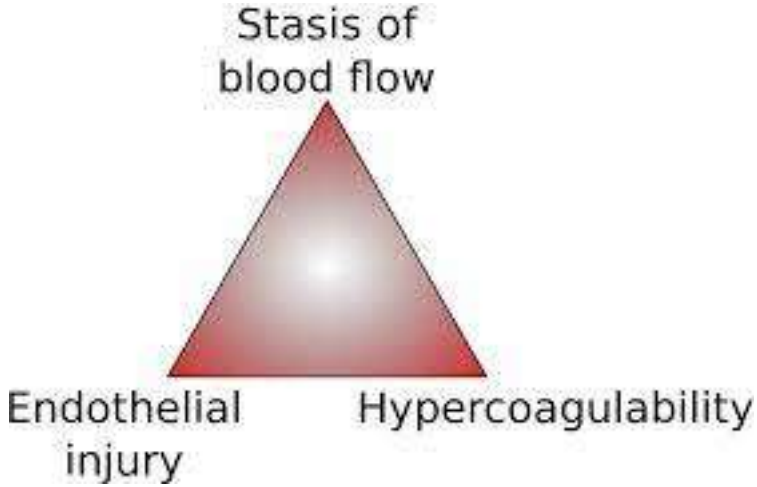
Partially occlusive PVT



Scotts M, Semin Liv Dis 2021

Pathophysiology of PVT in cirrhosis

- **Venous thrombosis is promoted by a triad of pathophysiological factors (Virchow's triad) :**



Turon F, J Hep 2021
Senzolo M et al J Hep 21

PVT is the most common thrombotic complication in cirrhosis

- The **prevalence** of PVT in cirrhosis **increases in parallel** with **disease severity**:
  - **5%-10%** in Child **A** ("compensated").
  - **15-20%** in Child **B/C** ("decompensated").
  - Up to **26%** in **liver transplant candidates**.

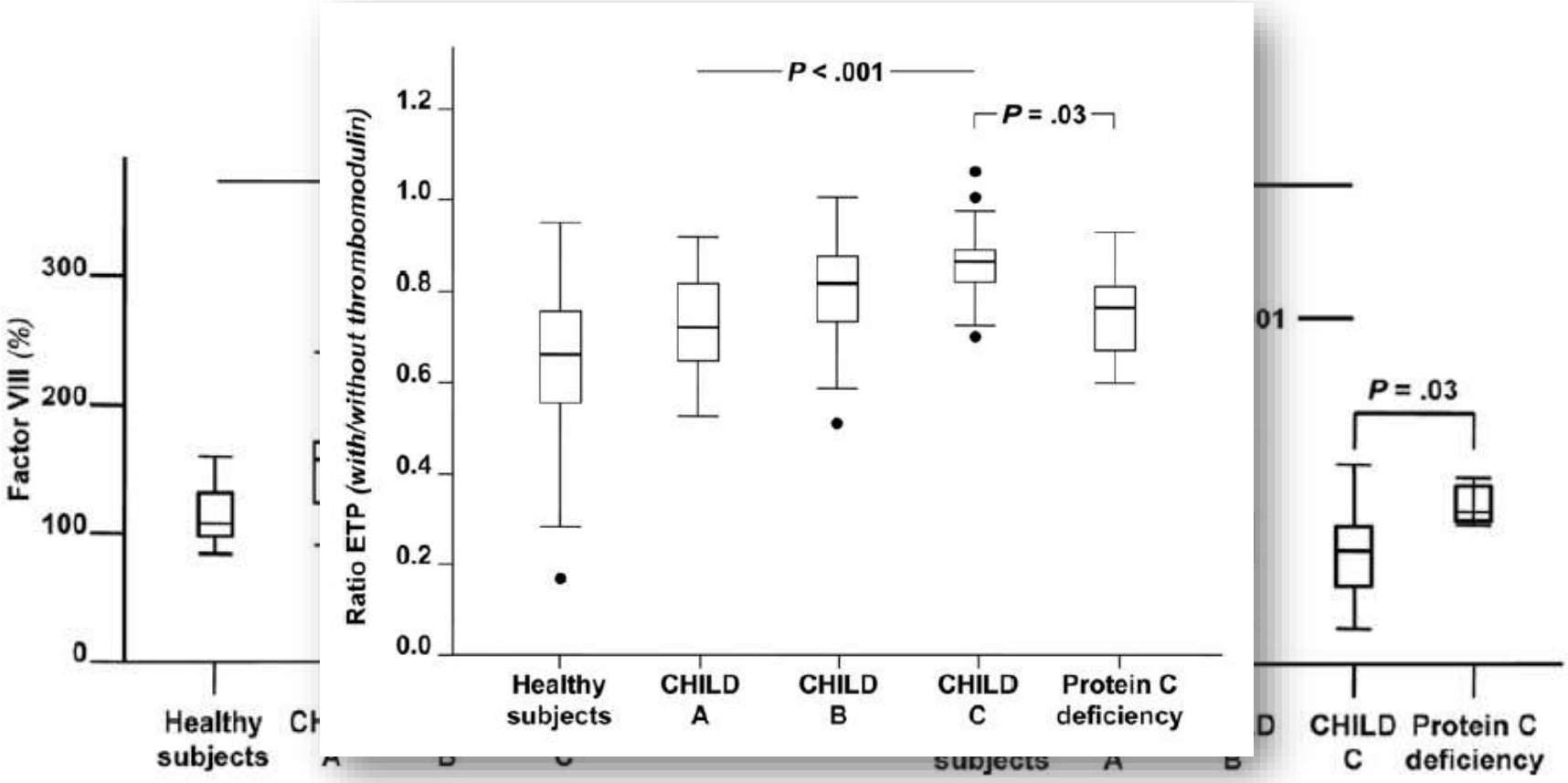
- **1-year incidence** ranges between **~4%** and **~24%,** with **lower risks** in cohorts including mostly **compensated patients**.

Nery F, HEPATOLOGY 2014
Zanetto A, DLD 2017

An Imbalance of Pro- vs Anti-Coagulation Factors in Plasma From Patients With Cirrhosis

ARMANDO TRIPODI,* MASSIMO PRIMIGNANI,‡ VEENA CHANTARANGKUL,* ALESSANDRA DELL'ERA,‡ MARIGRAZIA CLERICI,* ROBERTO DE FRANCHIS,‡ MASSIMO COLOMBO,§ and PIER MANNUCCIO MANNUCCI*

**Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Department of Internal Medicine and Medical Specialties, and ‡Third Division and §First Division of Gastroenterology, University and IRCCS Ospedale Maggiore, Mangiagalli and Regina Elena Foundation, Milano, Italy*



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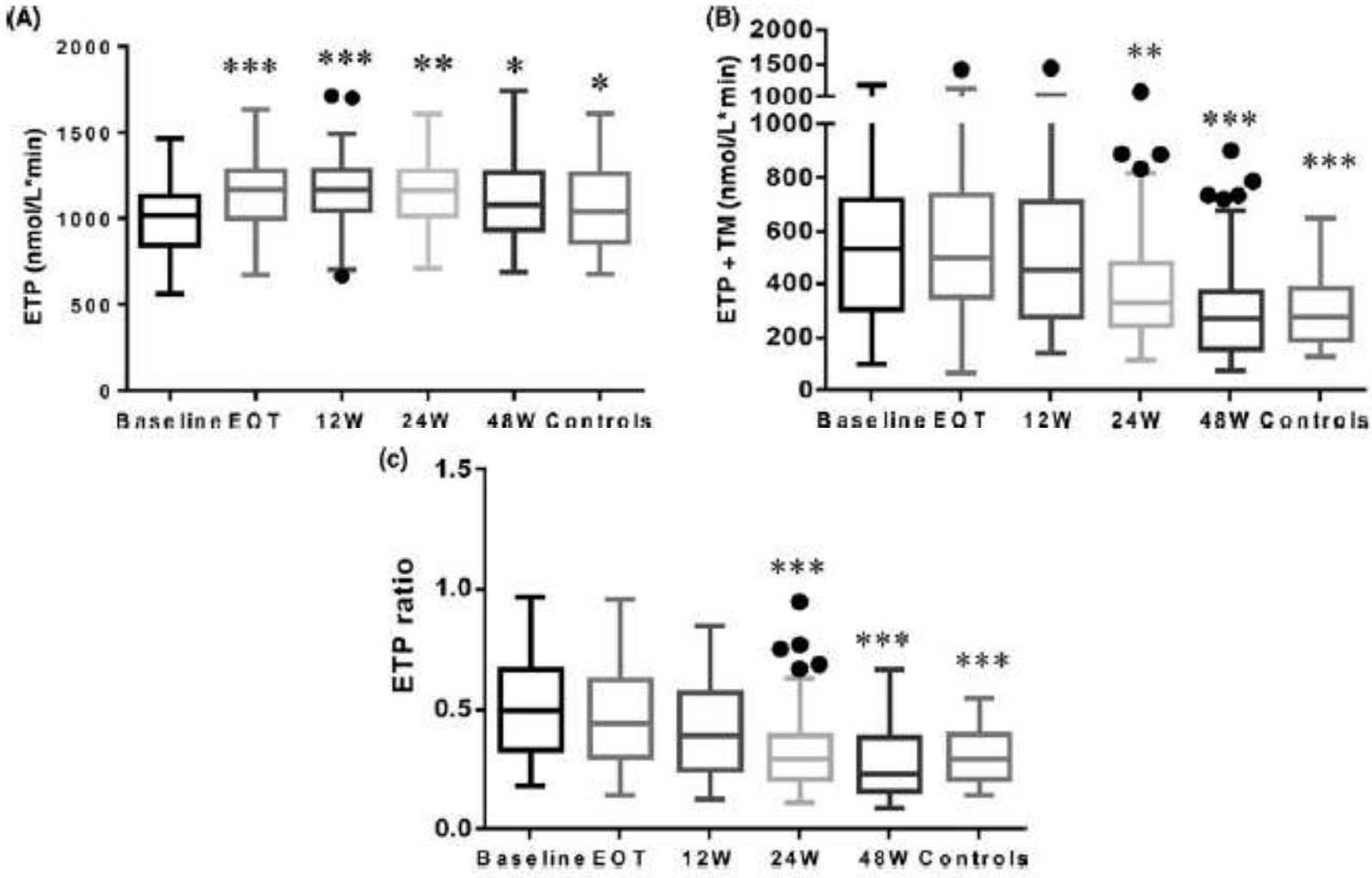
Achievement of SVR is associated with significant amelioration of cirrhosis hyper-coagulability



Russo FP and Zanetto A, Liver International 2018

Hepatic benefit of HCV cure: don't forget coagulation!

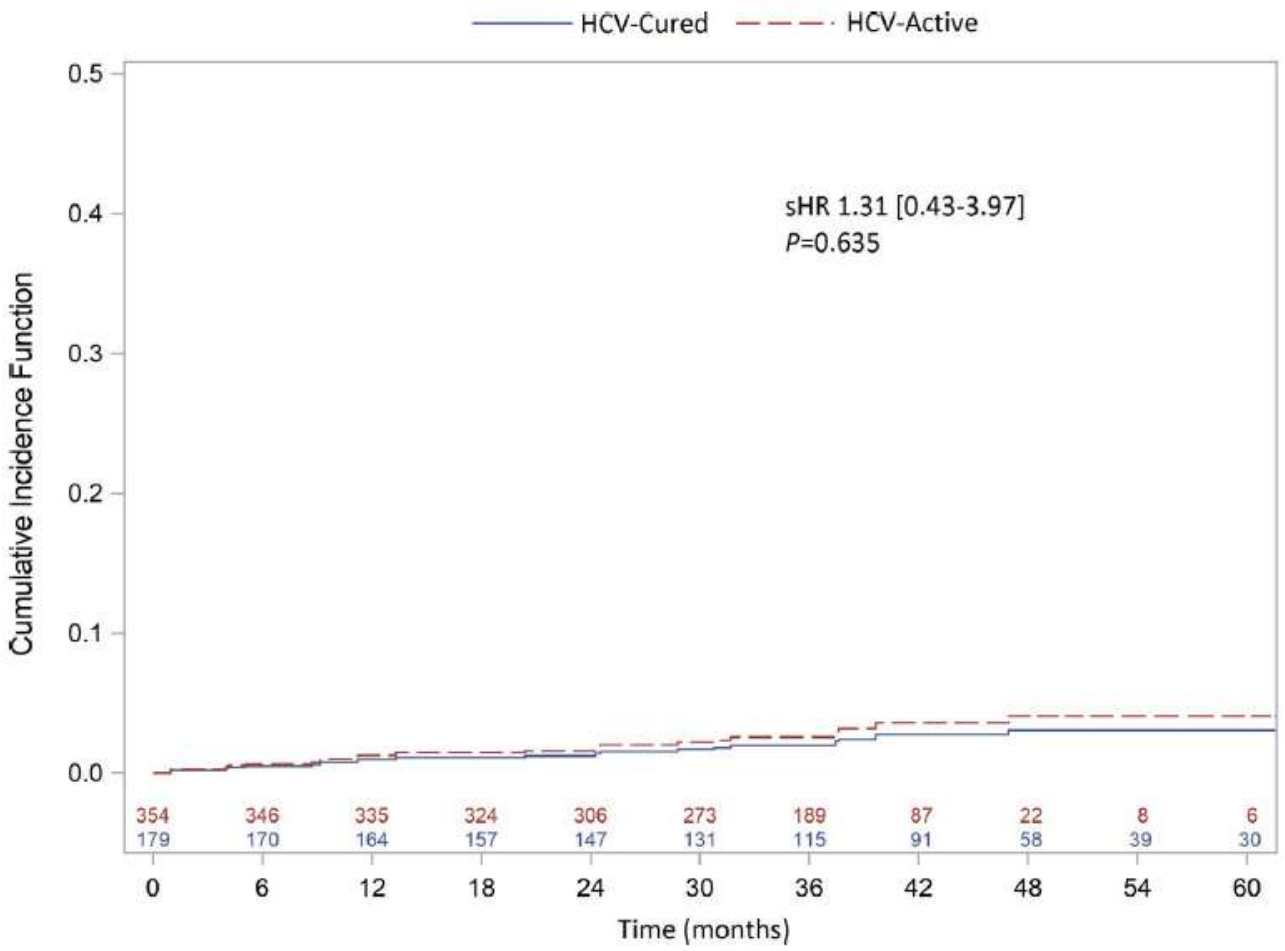
- **Hypercoagulability** may be **implicated not only** in **macrovascular thrombosis**, such as PVT, **but also in microvascular, sinusoidal thrombosis.**

- **Micro-thrombosis** may **lead to parenchymal extinction** and **cirrhosis progression**.

- Therefore, **by reverting the hypercoagulable state associated with HCV-related cirrhosis**, one could potentially **improve patient's outcome**.

Zanetto A, Simioni P, Russo FP, J Hep 2020

Whether and how this translates into reduced risk of PVT in unclear



Mandorfer M & Turon F, Liver International 2021

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PITER-based study

Carmine Coppola, Daniela Caterina Amoruso, Anna Linda Zignego, Monica Monti, Giovanni Raimondo, Roberto Filomia, Giuseppina Brancaccio, Maurizia R Brunetto, Barbara Coco, Gloria Taliani, Elisa Biliotti, Donatella Ieluzzi, Alfredo Di Leo, Andrea Iannone, Salvatore Madonia, Marco Cannizzaro, Liliana Chemello, Luisa Cavalletto, Massimo Puoti, Filomena Morisco, Valentina Cossiga, Francesco Barbaro, Federico Alessandro, Dallio Marcello, Anna Licata, Adele Rosaria Capitano, Alessia Giorgini, Pierluigi Blanc, Piera Pierotti, Antonio Craxì, Vincenza Calvaruso, Gabriella Verucchi, Lorenzo Badia,Rumi Mariagrazia, Marcello Persico, Mario Masarone, Gasbarrini Antonio, Pompili Maurizio, Ciancio Alessia, Piscaglia Fabio , Serio Ilaria, Luchino Chessa, Martina Loi, Pietro Invernizzi, Antonio Ciaccio, Morsica Giulia, Giacometti Andrea, Brescini Lucia, Andreone Pietro, Margotti Marzia, Benedetti Antonio, Cucco Monica, Teresa Santantonio, Serena Rita Bruno, Gentile Ivan Baiocchi Leonardo, Grassi Giuseppe, Ferrari Carlo, Diletta Laccabue, Coppola Nicola, Sagnelli Caterina Mastroianni Claudio M, Nardone Gerardo, Sgamato Costantino

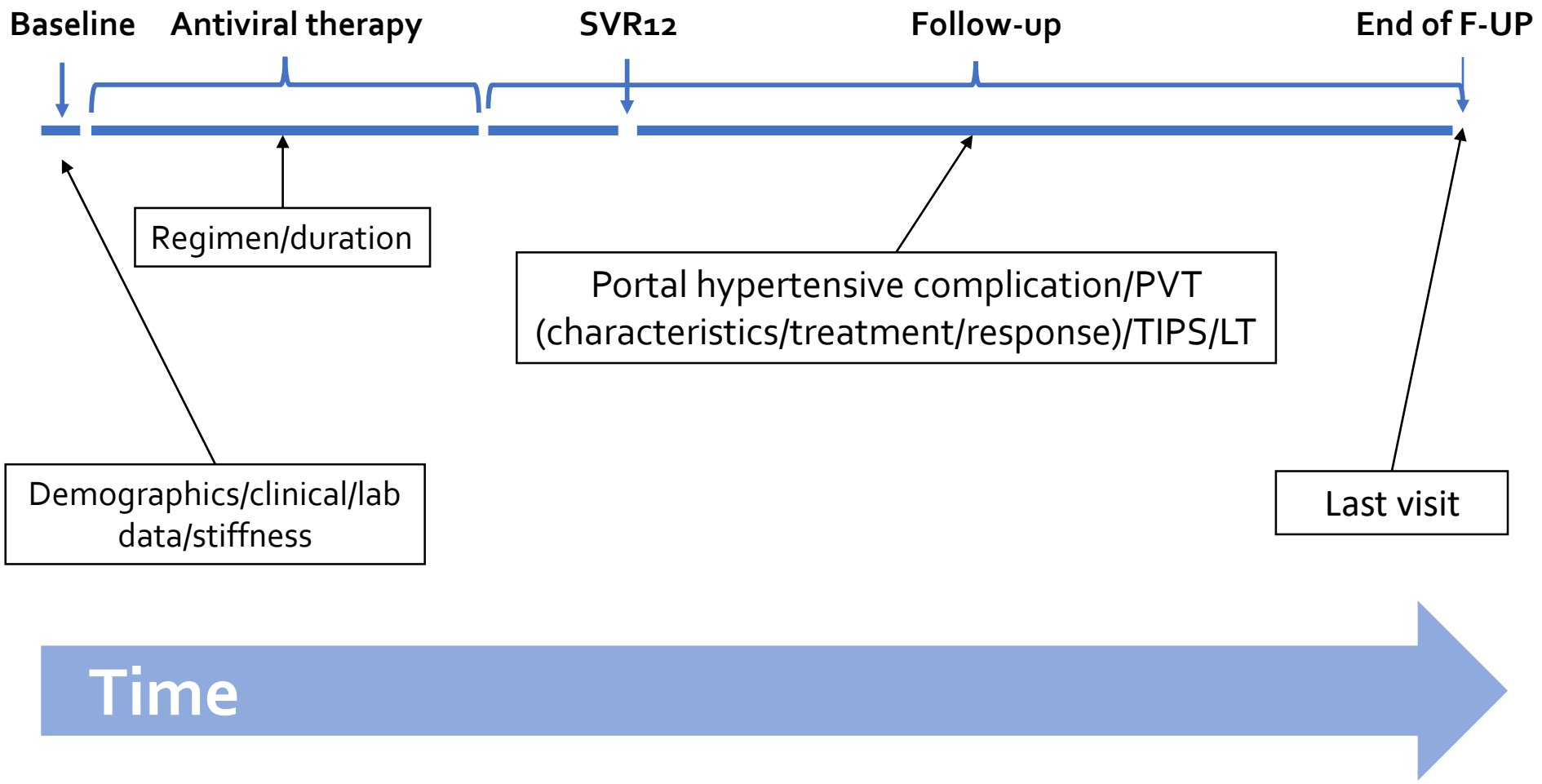
Loreta Kondili, MariaGiovanna Quaranta

Luigina Ferrigno, Alberto Zanetto

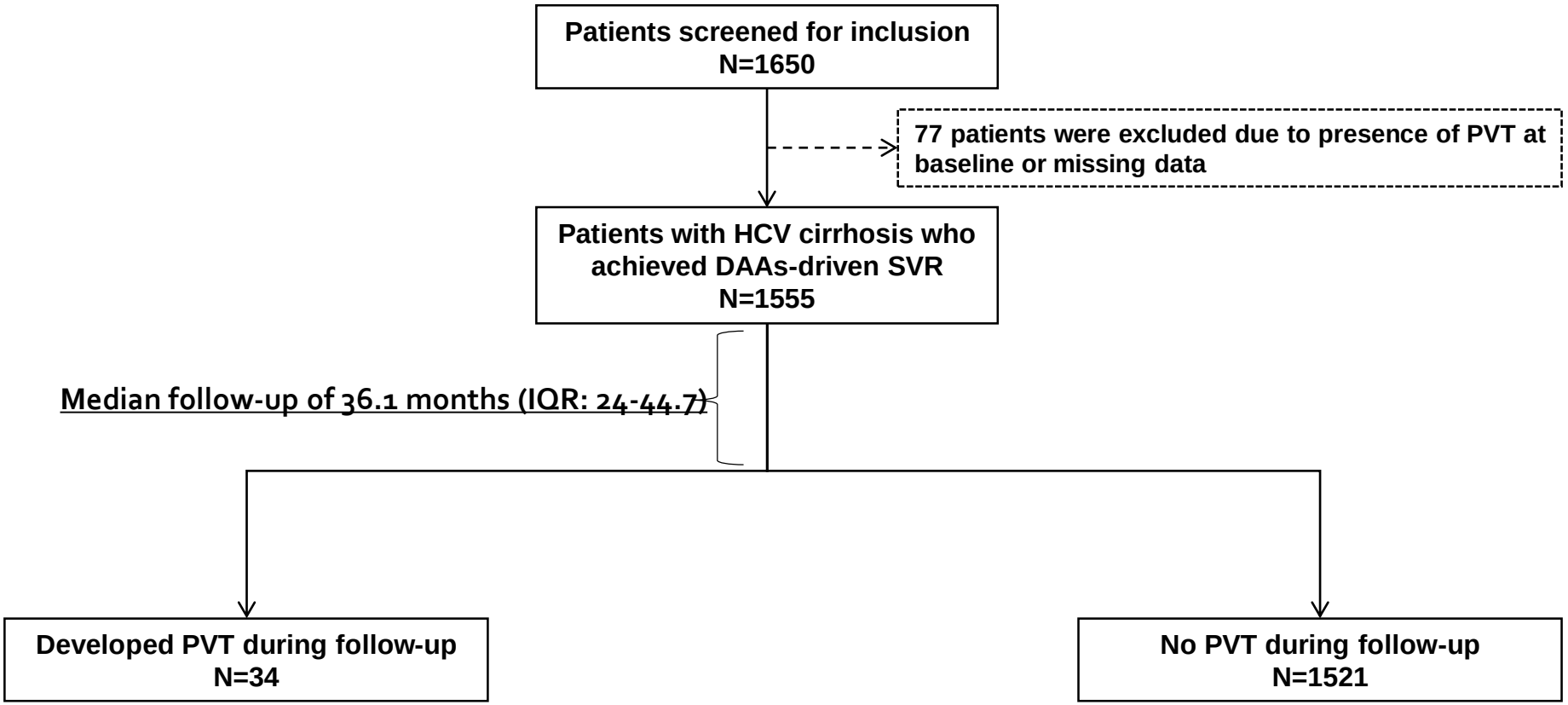
Specific aims

1. To assess the **incidence of PVT** in a **large**, real-world **cohort** of **patients** with **HCV cirrhosis** who **achieved SVR** after **DAAs**.
2. To **investigate predictive factors** for **development of PVT** in these patients.
3. To **prospectively investigate** the **impact of PVT** on the **natural history of HCV-related cirrhosis** after SVR.

Study design



Results



Examined population SVR (N=1555)	N.	%
No thrombosis	1521	97.8
Thrombosis post-therapy	34	2.2
Incidence rate:	0.8 x 100 person-years	

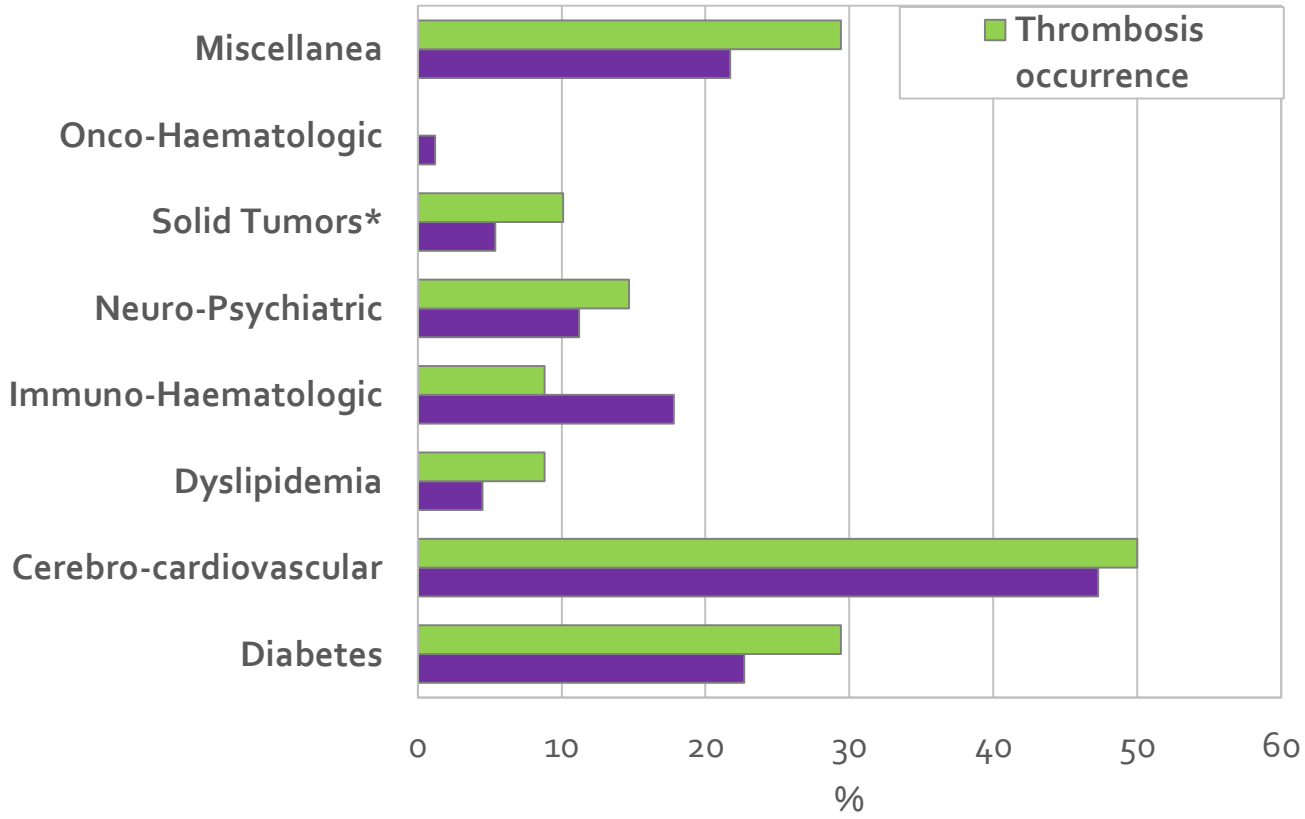
Epidemiological features in patients who developed PVT vs. those who did not

		No thrombosis (N=1521*)		Thrombosis occurrence (N=34*)			TOTAL (N=1555*)	
Epidemiological features		Median (IQR)		Median (IQR)		p**	Median (IQR)	
		N.	%	N.	%	p***	N.	%
HCC	Yes	120	7.9	7	20.6	**0.007**	127	8.2
	No	1401	92.1	27	79.4		1428	91.8

Clinical features in patients who developed PVT vs. those who did not

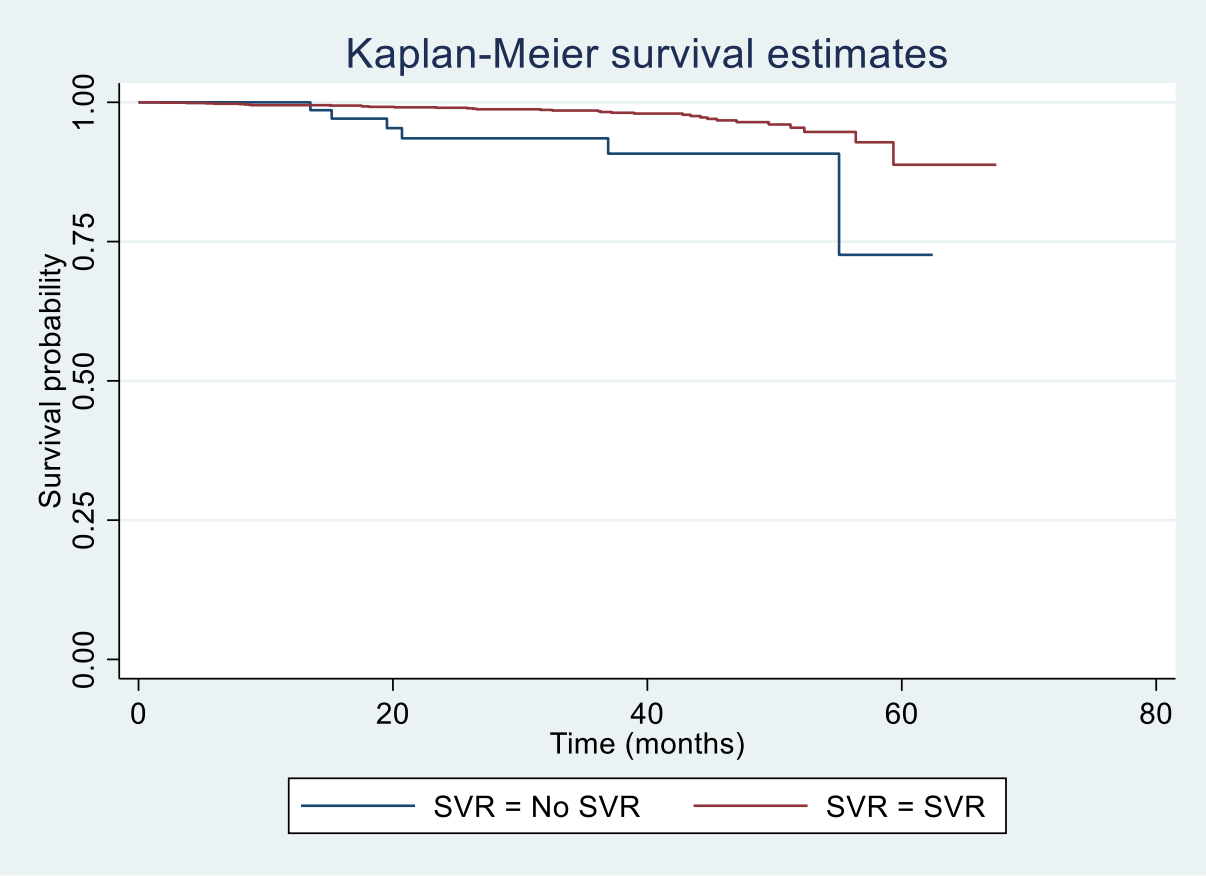
Clinical features		N.	%	N.	%	p***	N.	%
Platelets count	≤ 150,000/µL	1075	71.3	33	97.1	**0.001**	1108	71.9
	> 150,000/µL	432	28.7	1	2.9		433	28.1
Albumin (g/dL)	≤ 3.5	346	24.1	21	61.8	< **0.001**	367	25.0
	> 3.5	1088	75.9	13	38.2		1101	75.0
Bilirubin (mg/dL)	≥ 1.1	460	31.3	24	70.6	< **0.001**	484	32.1
	< 1.1	1012	68.8	10	29.4		1022	67.9
FIB4	> 3.25	1025	68.5	29	85.3	**0.037**	1054	68.9
	≤ 3.25	471	31.5	5	14.7		476	31.1
Child-Pugh Class	A	1305	85.8	23	67.7	**0.003**	1328	85.4
	B	216	14.2	11	32.4		227	14.6
Ascites	Yes	108	7.1	6	17.7	**0.020**	114	7.3
	No	1413	92.9	28	82.4		1441	92.7
Esophageal varices	Yes	335	22.0	27	79.4	< **0.001**	362	23.3
	No	1186	78.0	7	20.6		1193	76.7
Esophageal varices grade	F1	220	70.5	10	43.5	**0.024**	230	68.7
	F2	81	26.0	11	47.8		92	27.5
	F3	11	3.5	2	8.7		13	3.9
History of bleeding	Yes	35	2.3	5	14.7	< **0.001**	40	2.6
	No	1486	97.7	29	85.3		1515	97.4
Previous decompensations	Yes	159	10.5	11	32.4	< **0.001**	170	10.9
	No	1362	89.6	23	67.7		1385	89.1

Comorbidities in patients who developed PVT vs. those who did not



* p value Chi-square test = 0.032. For all the other groups appeared a not significant p-value.

Survival



Log-rank test p = 0.002

Events happened during the follow-up of cirrhotic patients successfully treated with DAA

		No thrombosis (N=1521*)		Thrombosis occurrence (N=34*)			TOTAL (N=1555*)	
Events		N.	%	N.	%	p***	N.	%
Death	Yes	72	4.7	10	29.4	**< 0.001**	82	5.3
	No	1449	95.3	24	70.6		1473	94.7
HCC	Pre-therapy	120	7.9	7	20.6	**< 0.001**	127	8.2
	Post-therapy	78	5.1	11	32.4		89	5.7
	No	1323	87.0	16	47.1		1339	86.1
Decompensation	Pre-therapy	88	5.8	2	5.9	**< 0.001**	90	5.8
	Pre/Post-therapy	71	4.7	9	26.5		80	5.1
	Post-therapy	74	4.9	15	44.1		89	5.7
	No	1288	84.7	8	23.5		1296	83.3

Expected results/future perspective

1. Improved risk stratification regarding the risk of PVT in patients with HCV cirrhosis who achieve DAAs—driven SVR.

2. Assessment of the impact of PVT on the residual risks of decompensation after the achievement of SVR in HCV-related cirrhosis.

3. By comparing these results with historical data from patients treated with PEG-IFN based therapy, evaluation of thrombotic risk in DAA-driven SVR compared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Dank U
Merci
mahalo
Köszi
спасибо
Grazie
Thank you
mauruuru
Takk
Gracias
Dziękuję
Děkuju
danke
Kiitos