PVT in patients with cirrhosis
Impact of treating the cause of cirrhosis

Mattias Mandorfer, M.D. Ph.D.

Vienna Hepatic Hemodynamic Lab,

Division of Gastroenterology and Hepatology,

Department of Internal Medicine III,

Medical University of Vienna, Vienna, Austria

Panel 3/session 2, part 2 – "Impact of aetiological therapies in the course of cirrhosis"

- B6: "Aetiological treatment of the underlying liver disease may reduce portal hypertension and prevents complications in patients with established cirrhosis (1b;A)."

- **B7: "Removal/suppression of the primary aetiological factor leads to potentially meaningful decreases in HVPG in the majority of patients and substantially reduces the risk of hepatic decompensation. (A1)"**

- Comment: We are preferring the wording "removal/suppression of the primary aetiological factor". The updated statement accounts for the increasing body of evidence for beneficial effects on HVPG and clinical endpoints.

Panel 3/session 2, part 2 – "Impact of aetiological therapies in the course of cirrhosis"

- **B7: "Removal/suppression of the primary aetiological factor includes sustained virological response (SVR) in patients with HCV infection, viral suppression in the absence of HDV coinfection in patients with HBV infection, and long-term abstinence from alcohol in patients with alcohol-related liver disease (ALD). (A1)"**

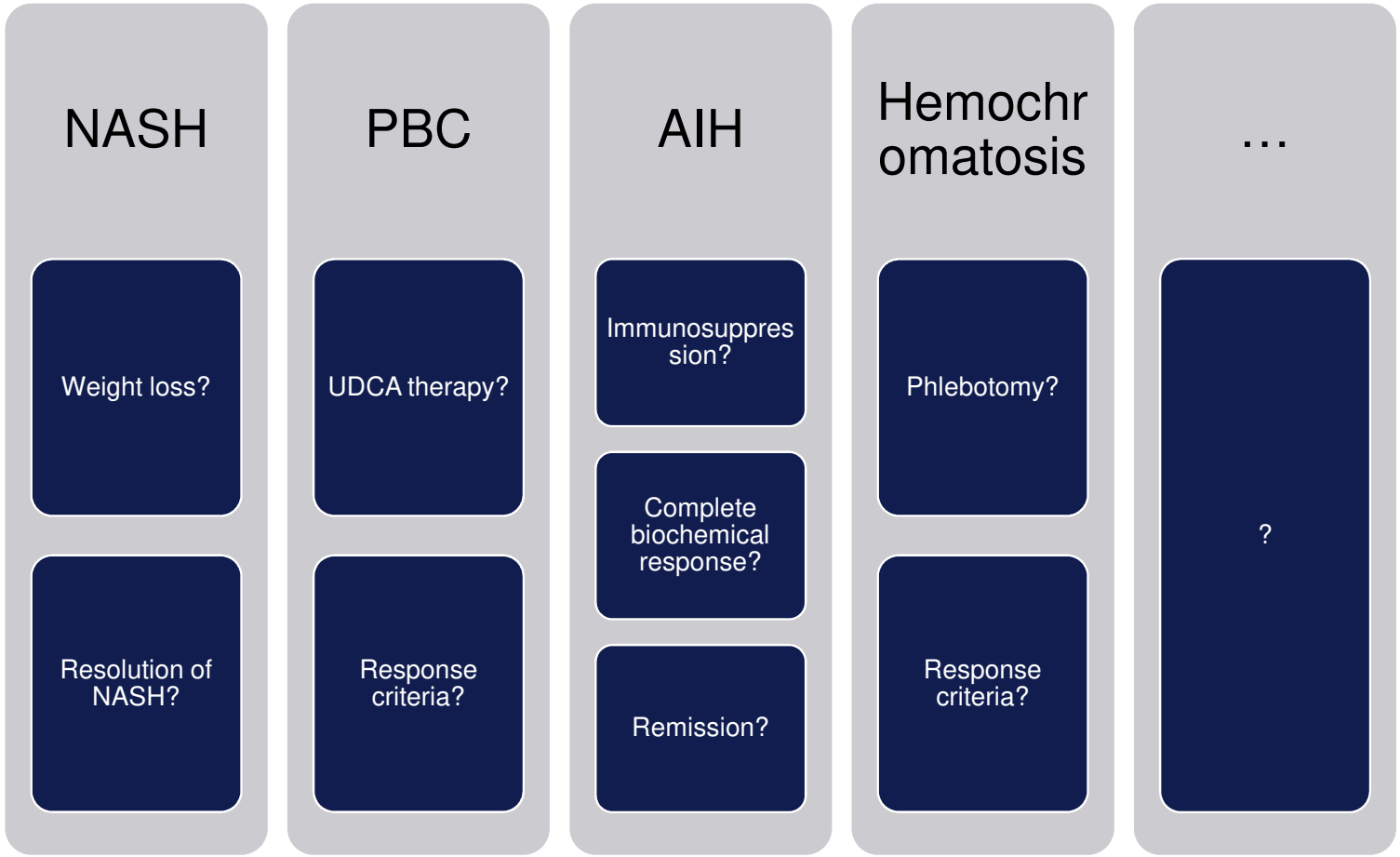
- Comment: This new statement reflects the results of our literature review, the individual patient data meta-analysis for HCV (uploaded), the meta-analysis for HBV, and the responses to our survey (uploaded).

Panel 3/session 2, part 2 – "Impact of aetiological therapies in the course of cirrhosis"

- **B7: "The definition and impact of the removal/suppression of the primary aetiological factor in other ACLD is less well established. (A1)"**

- Comment: This new statement reflects the results of our literature review.

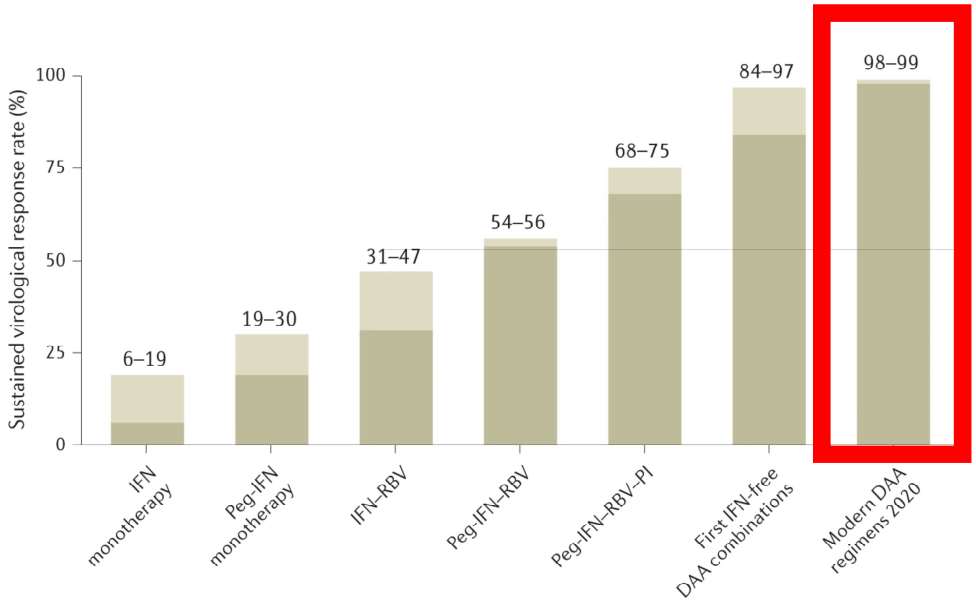
Other aetiologies?



HCV-cure

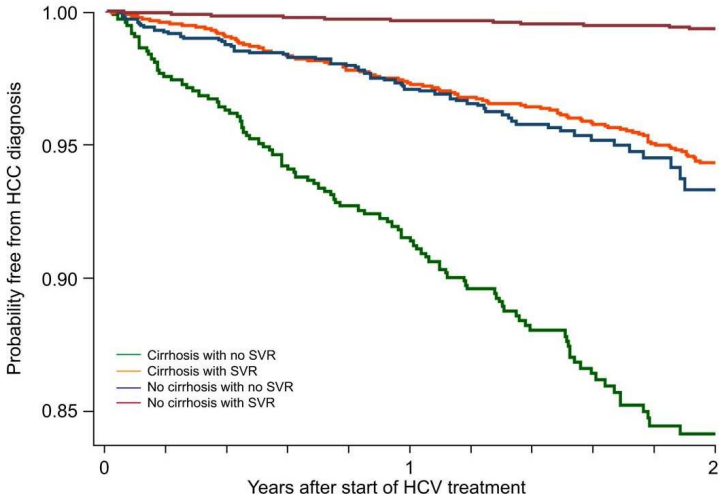
Unprecedented opportunity to study the impact of ‘removal of the primary aetiological factor’

- Chronic HCV infection is common
- Treatment is nearly universally effective
- Thus, the probability of achieving virological response is largely uncoupled from patient characteristics
- Reduces the risk of bias



Manns et al. Nat Rev Gastroenterol Hepatol 2022

Model: HCV-cure in patients with ACLD



#1 clinical challenge post SVR

Ioannou et al. J Hepatol 2018; Semmler and Lens et al. J Hepatol 2022;
modified from Intagliata et al. Gastroenterology 2019; Nery et al. Hepatology 2015

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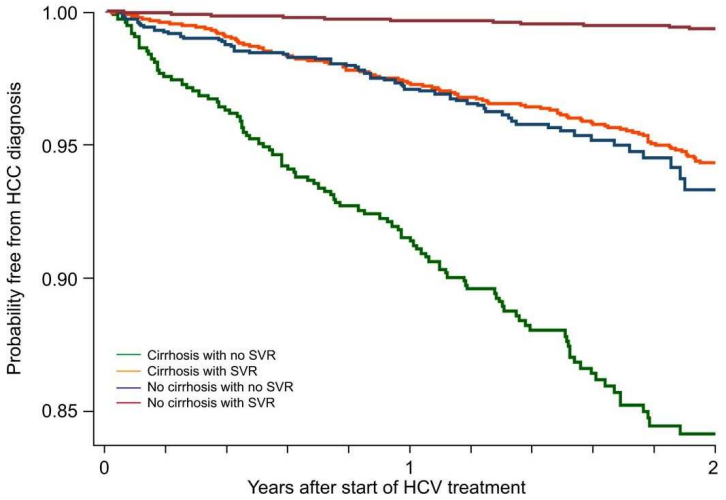

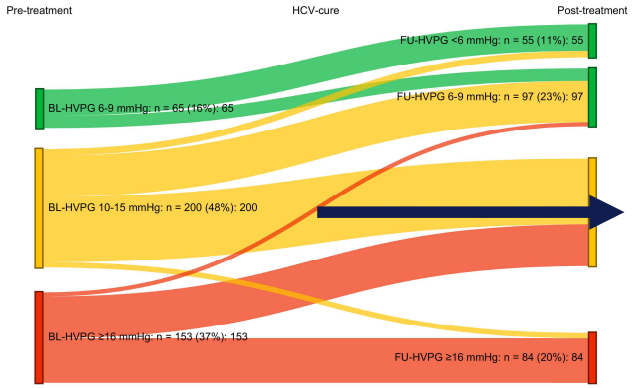

↓ Sinusoidal PH / ↑ liver function

↓ Hepatic decompensation

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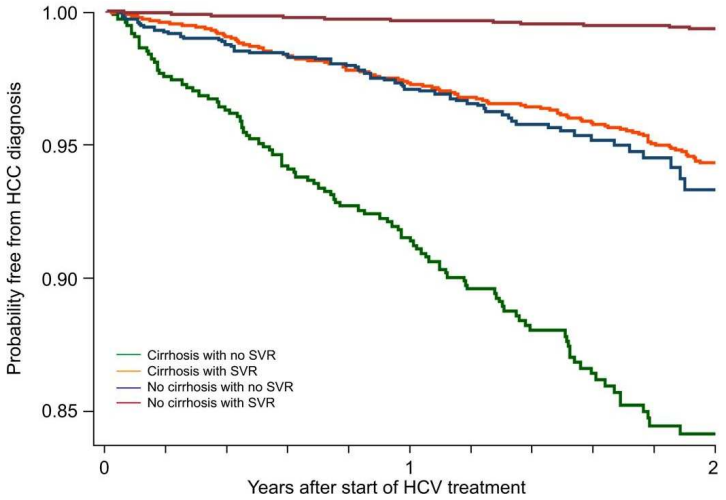

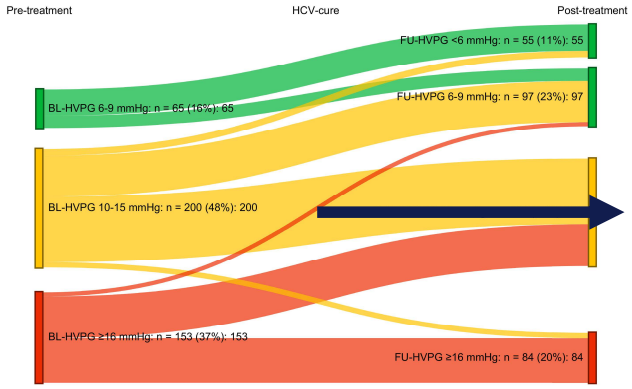

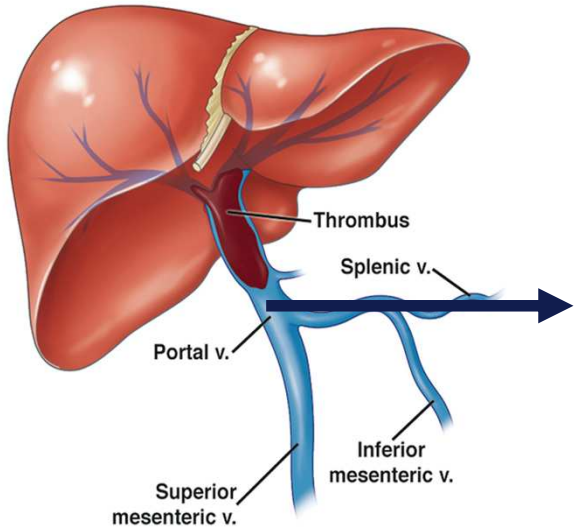

↓ Sinusoidal PH/↑ liver function

↓ Hepatic decompensation

Prehepatic portal hypertension

?Hepatic decompensation?

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Source: NASA

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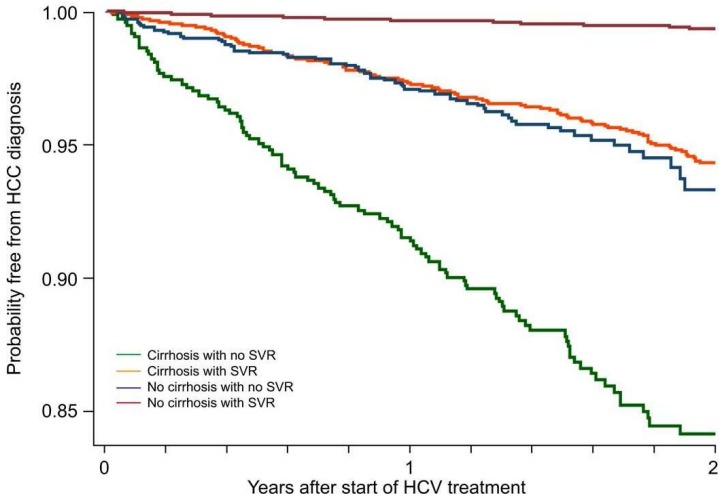

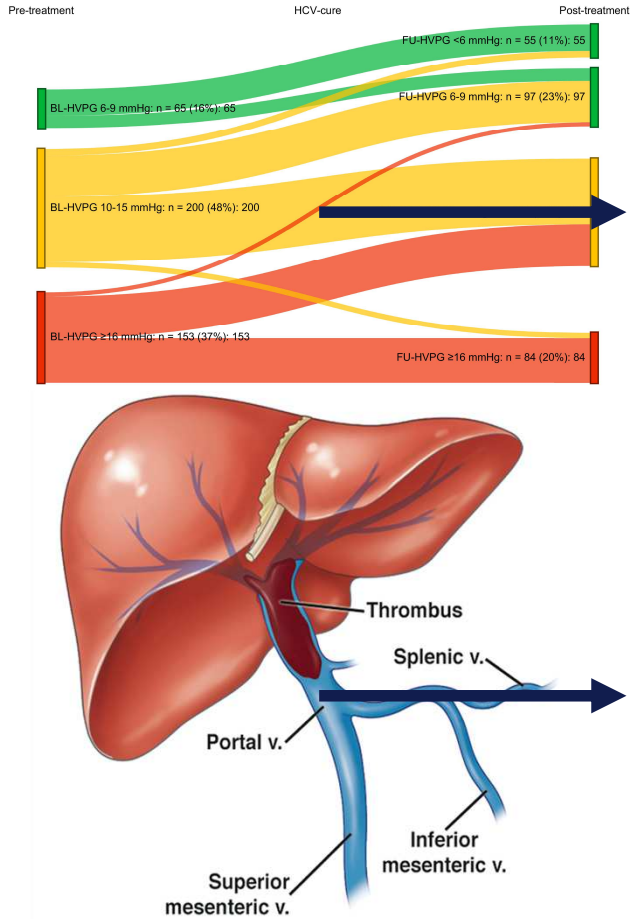

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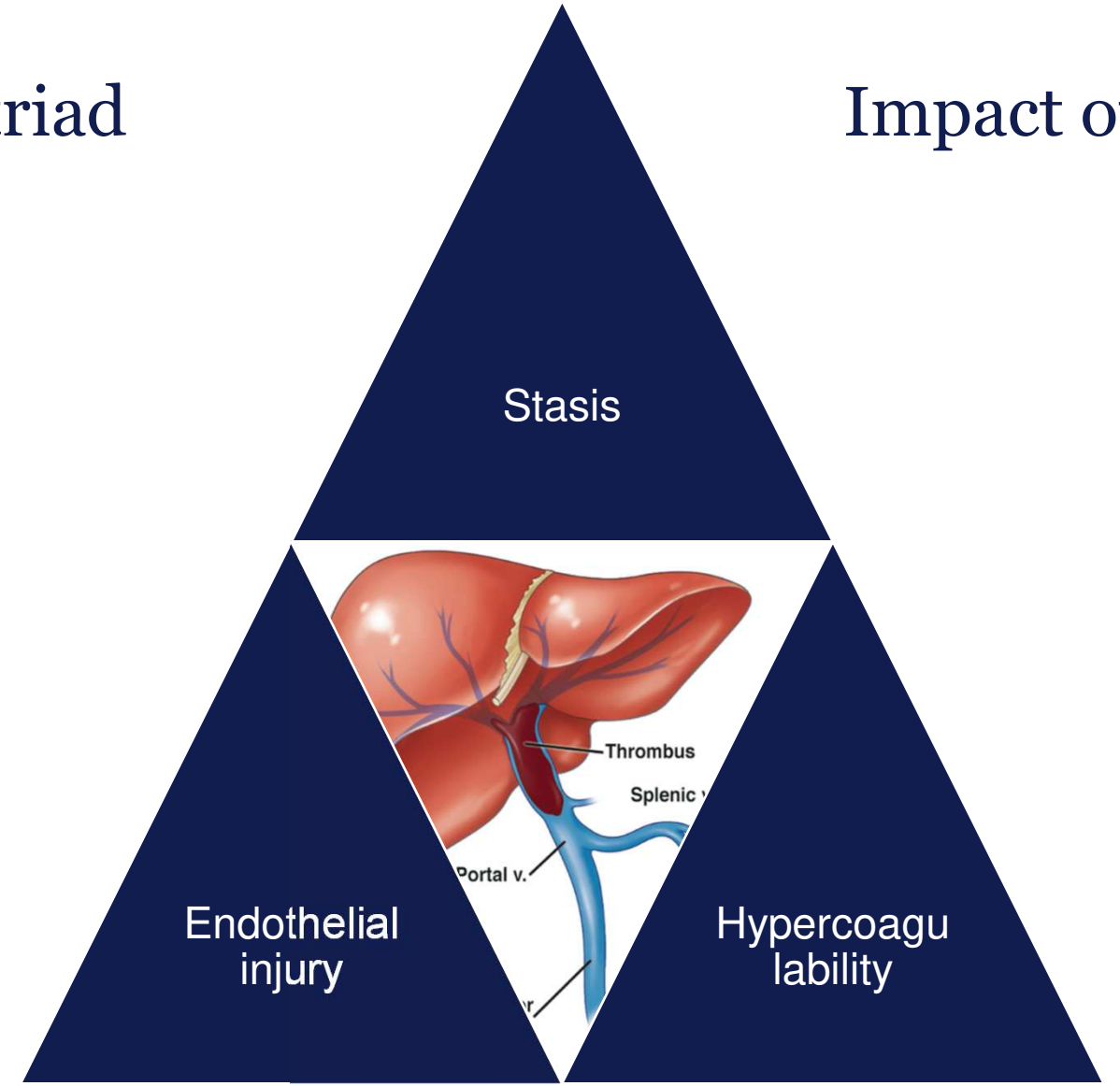
Virchow's triad

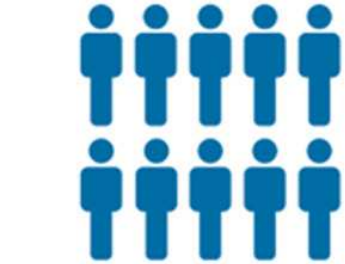
Impact of HCV-cure



↓ Bacterial translocation (LBP and IL-6)
↓ VWF

↑ PLT – ↓ VWF
↑ Pro- and anticoagulants – more stable balance?
Reversal of hypercoagulability (ETP ratio)

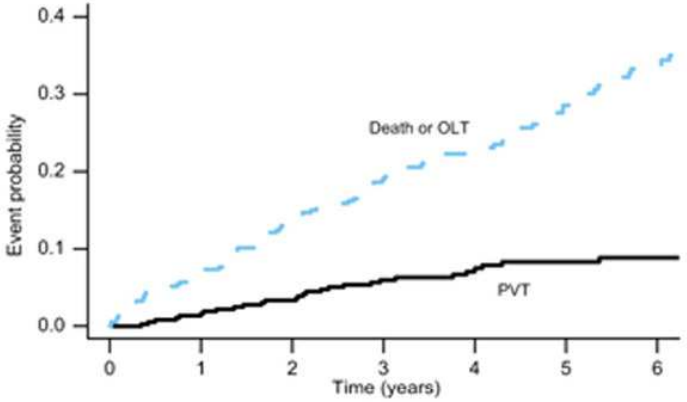
Semmler and Lens et al. J Hepatol 2022; Mandorfer et al. Hepatology 2020; Bauer et al. Dig Liver Dis 2022; Bradley et al. Eur Radiol 2019; Faheem et al. Egypt Liver J 2022; Sayyar et al. Liver Int 2019; Tripodi et al. Liver Int 2017; Russo et al. Liver Int 2018



369 cirrhotic patients without PVT

Prospective follow-up 48 ± 27 months

29 patients developed PVT



Independent risk factors for PVT

Platelet count	0.98 (0.97-0.99)	**0.002**
PBFV <15 cm/sec	2.28 (0.99-5.26)	**0.05**
Variceal bleeding	2.52 (1.06-5.99)	**0.036**

Subgroup of 310 patients (23 PVT): hemostatic/inflammatory evaluation

Spleen length	1.23 (1.10-1.40)	**0.002**
PBFV <15 cm/sec	2.66 (1.07-6.61)	**0.035**
Factor X	0.97 (0.94-0.99)	**0.036**

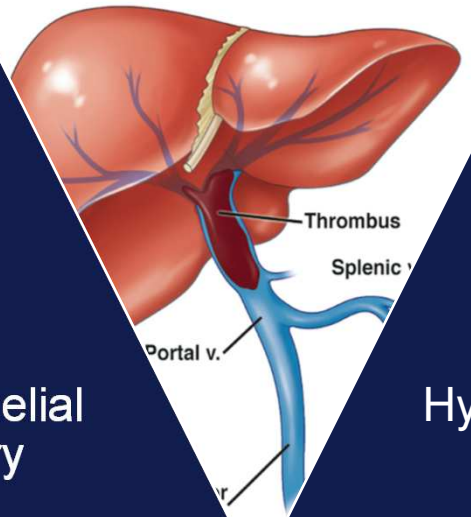
Turon et al. J Hepatol 2021

Virchow's triad

Impact of HCV-cure

↓ HVPG – intrahepatic resistance

Stasis



Endothelial injury

Hypercoagu lability

↓ *Bacterial translocation (LBP and IL-6)*
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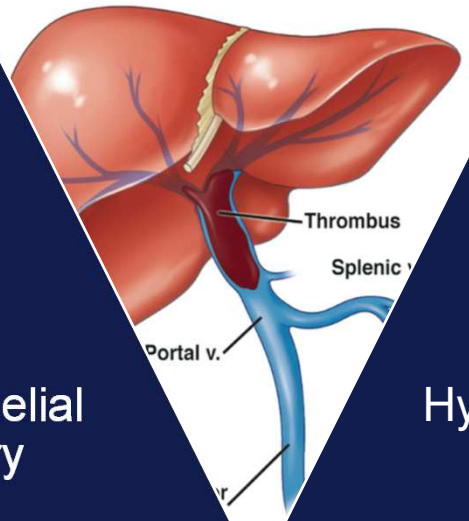
Virchow's triad

Impact of HCV-cure

Stasis

↓ HVPG – intrahepatic resistance

Portal blood flow velocity
= (PC-MRI)/↑ (US)



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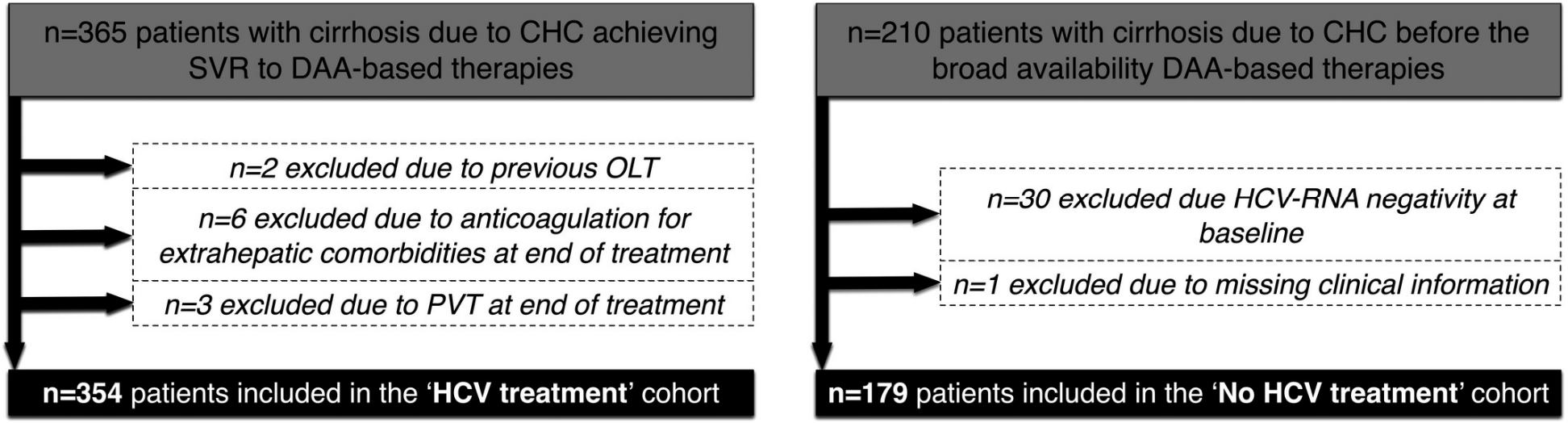
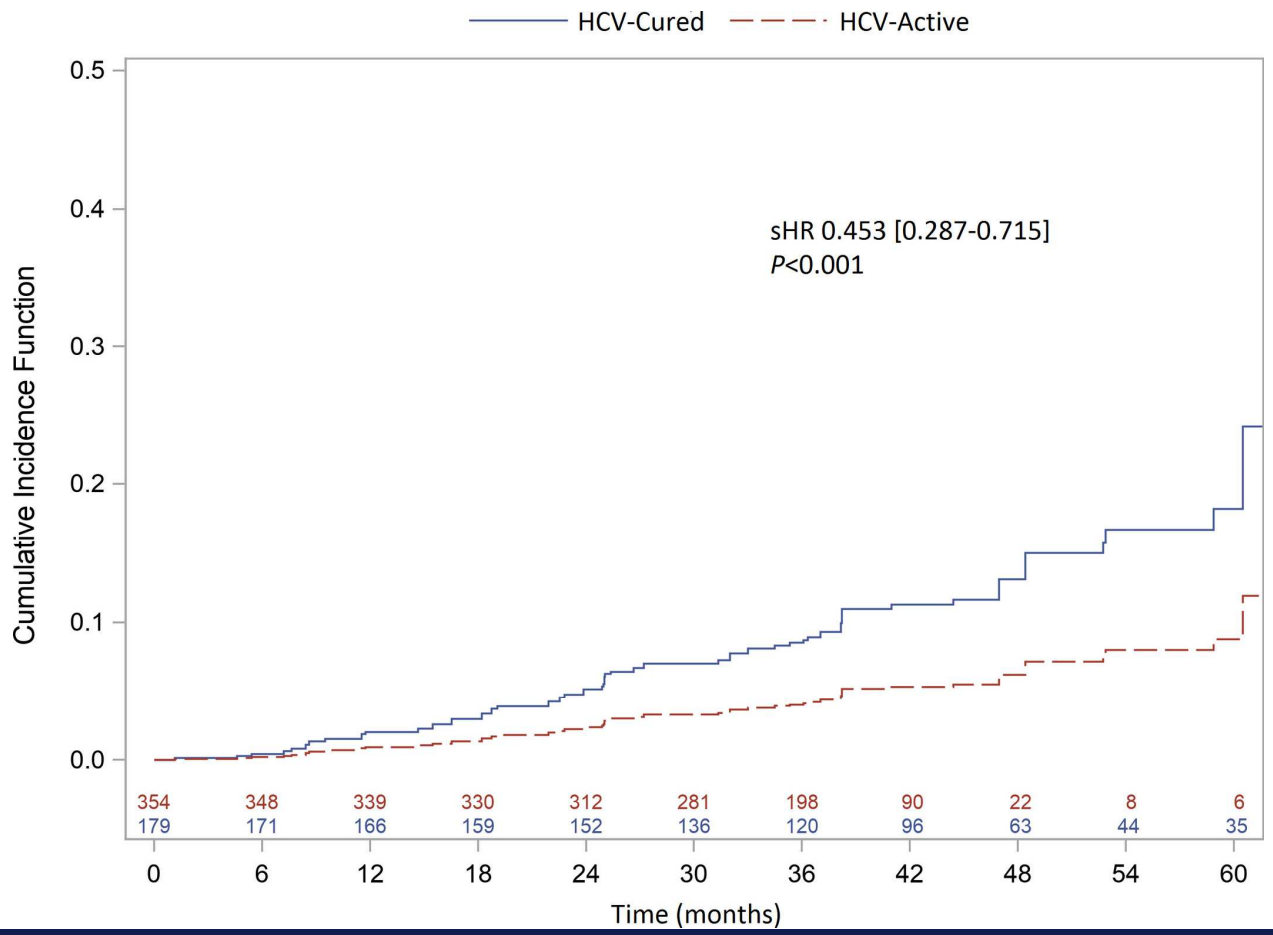
Impact of HCV-cure



Mandorfer and Turon et al. Liver Int 2021

Impact of HCV-cure on mortality



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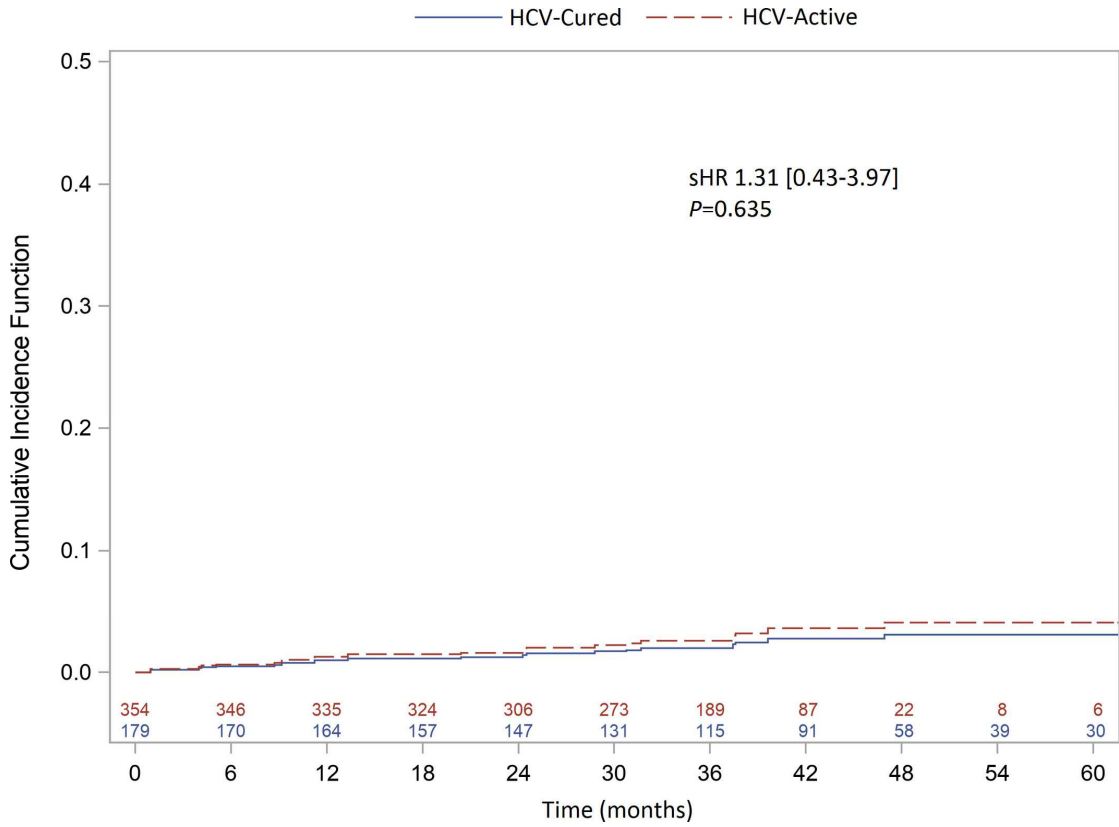
Impact of HCV-cure on non-tumoural PVT

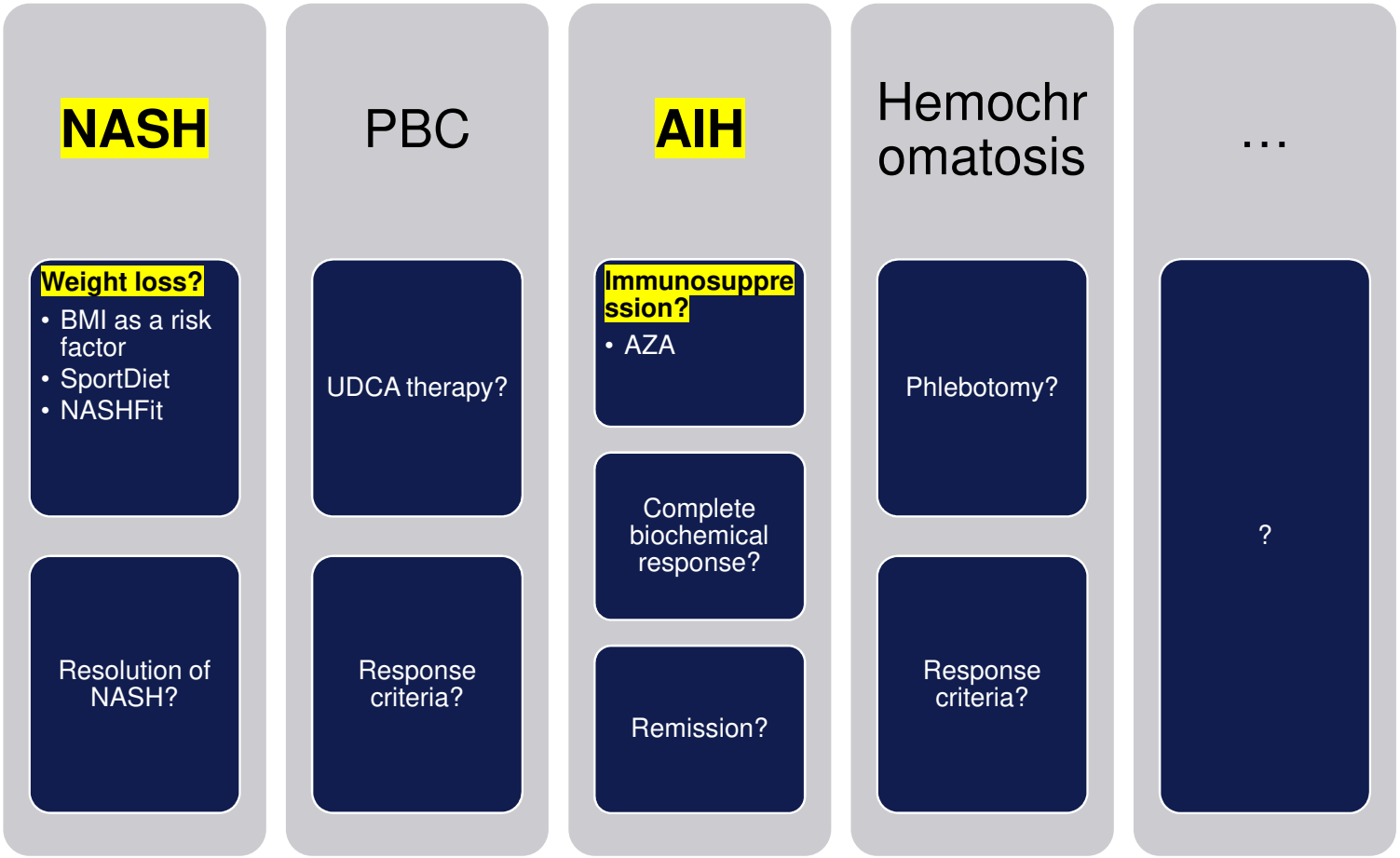
Cumulative incidences of non-tumoural PVT: HCV-Cured vs. HCV-Active

- Year 1: 1.4% vs. 1.7%
- Year 2: 1.7% vs. 2.3%
- Year 3: 2.7% vs. 3.5%
- Year 4: 3.9% vs. 5.4%
- Year 5: 3.9% vs. 5.4%



Mandorfer and Turon et al. Liver Int 2021

Other aetiologies?



Bureau et al. J Hepatol 2016; Berzigotti et al Hepatology 2016; Stine et al. Hepatology 2022; De Gottardi et al. J Hepatol 2022

Summary & research agenda

- **Removal of the primary aetiological factor modifies** several components of the **Virchow's triad**:
  - ↓ Endothelial injury
  - ↓ Biomarkers of hypercoagulability
  - Portal blood flow velocity?
- **No evidence for a ↓ in PVT risk** after HCV-cure
- Liver disease severity remains the **main determinant of non-tumoural PVT development**
- Knowledge gaps:
  - Removal/suppression of the primary aetiological factor reduces PVT risk by ameliorating liver disease progression during long-term follow-up?
  - Other aetiologies than HCV?

Thank you for your attention!