11th PHC
Paris, 15-16 January 2018

Vascular liver diseases
Current management - New concepts

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PHC 2018 – www.aphc.info

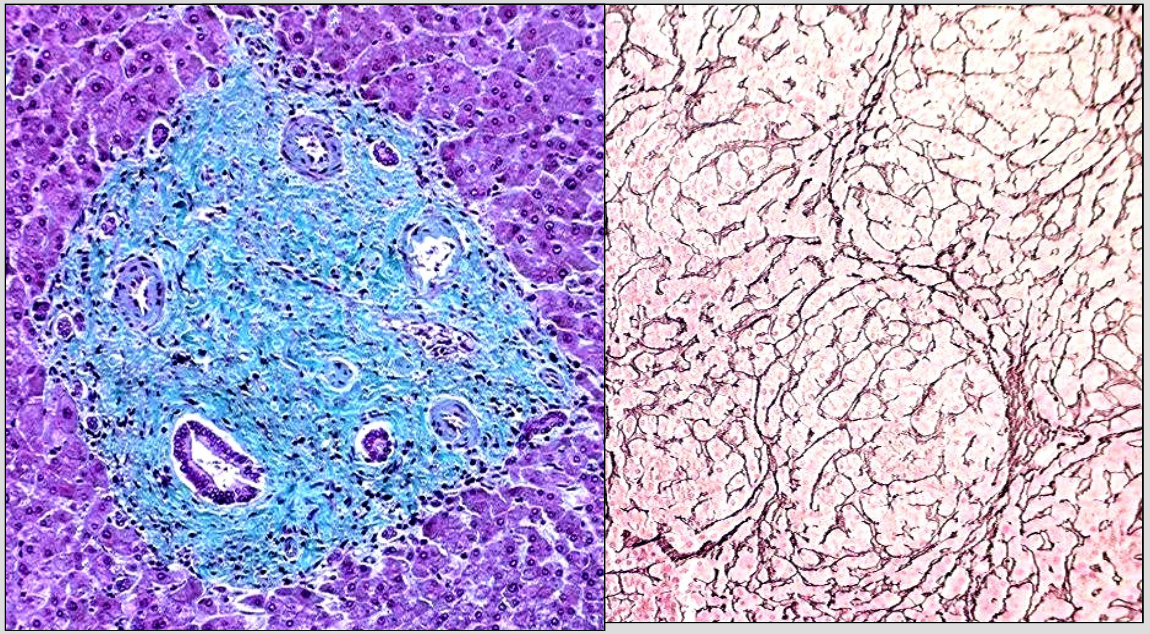
Disorders of the large or small vessels

- Hepatic arterial system
- Hepatic venous system
- Portal venous system
- Sinusoids

Obstruction
Dilatation
Fistula

Vascular liver diseases
Current management - New concepts

- Portal vein thrombosis in cirrhosis
- Vascular portosinusoidal disease

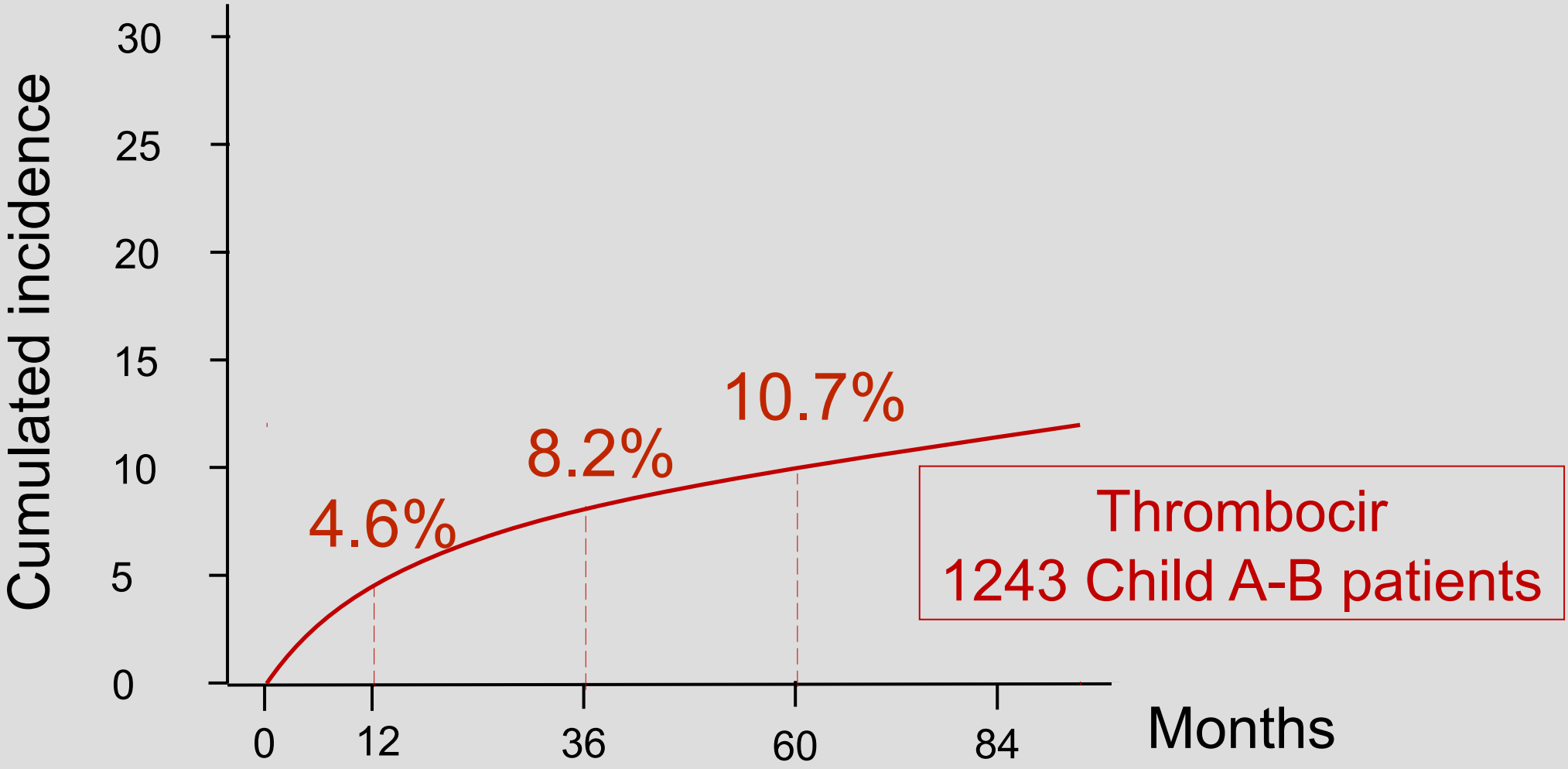


Extrahepatic portal vein thrombosis in cirrhosis

Partial	75%
Regressive	40%
Recurrent	25%

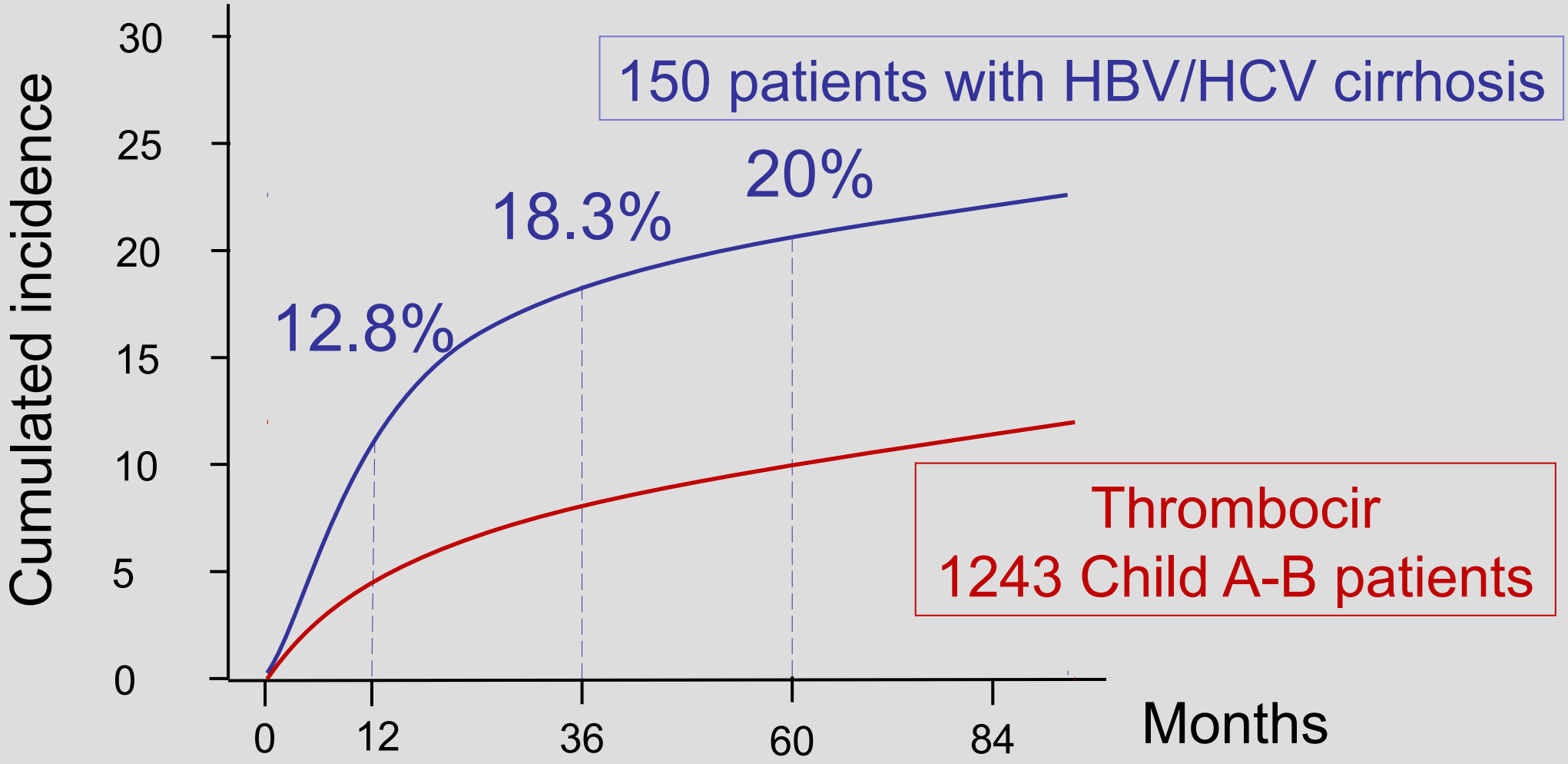
Ponziani, Transplant Rev 2014. Francoz, J Hepatol 2014. Harding, WJG 2015. Nery, Hepatology 2015

Cumulative Incidence of PVT in Cirrhosis

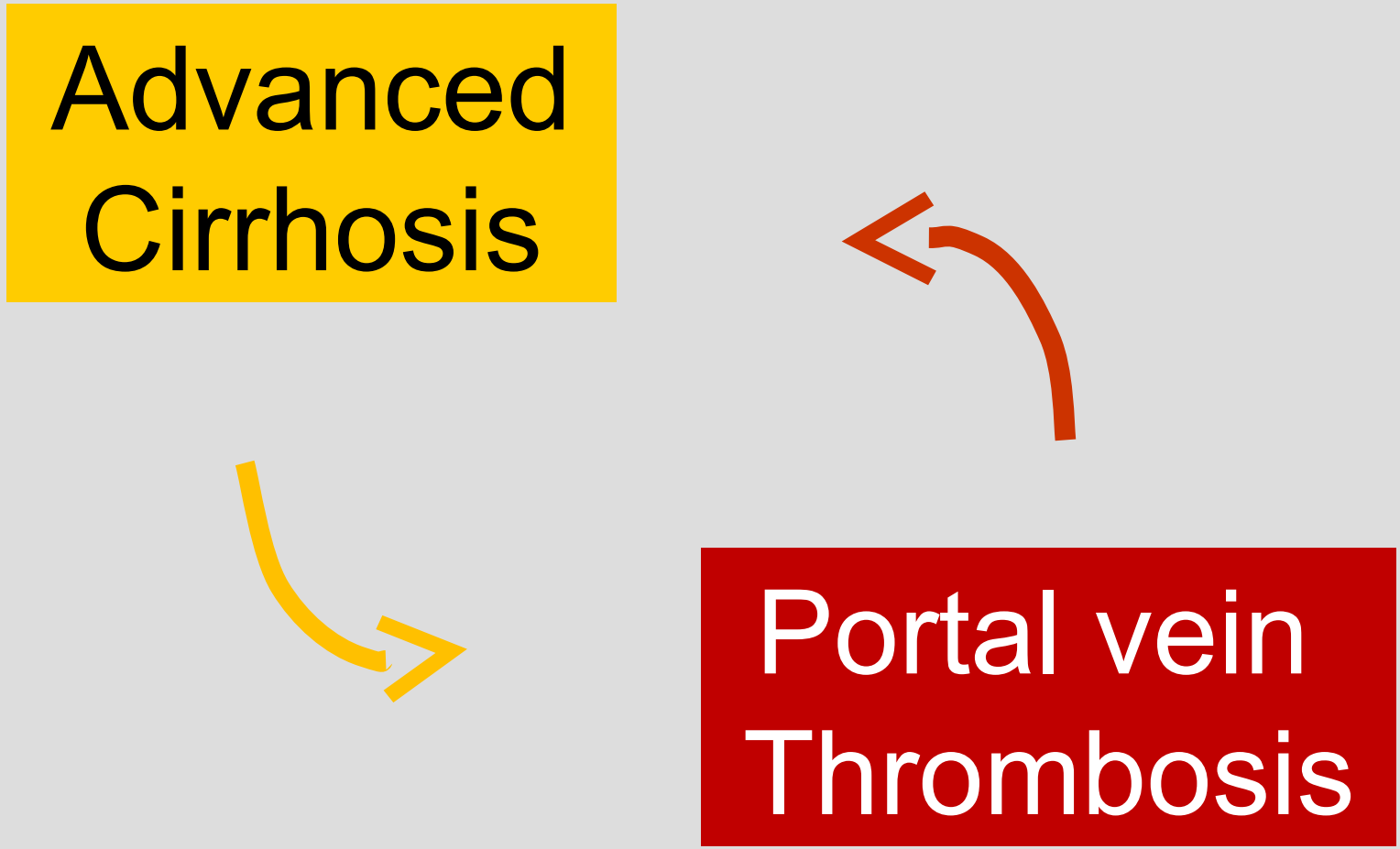


Nery, Hepatology 2015

Cumulative Incidence of PVT in Cirrhosis



Maruyama. AJG 2013


Advanced Cirrhosis
Portal vein Thrombosis

Thrombocir – Risk factors for PVT

Baseline variables	Multivariate	
	HR	*P*
Prothrombin	0.82	0.03
EV grade ≥ 2	2.14	0.004

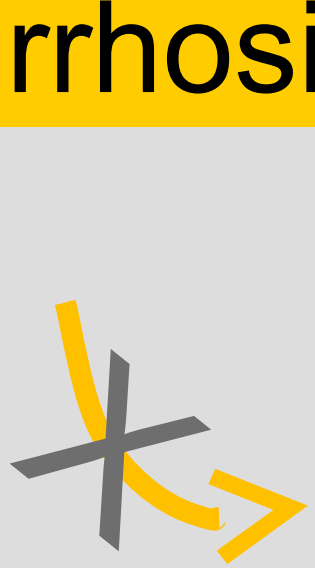
Nery, Hepatology 2015.

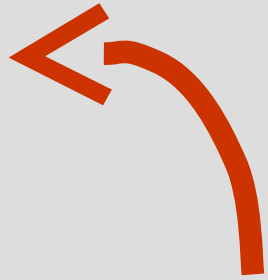
Thrombocir – Risk factors for PVT

Time dependent variables	Univariate	
	HR	*P*
Decreased PBF velocity	0.98	0.19
De novo ascites	1.81	0.01
Recent decompensation	2.11	0.007
NSBB before PVT	1.67	0.04

Nery, Hepatology 2015

Advanced Cirrhosis





Portal vein Thrombosis

Nery. Hepatology 2015

Thrombocir – Risk factors for decompensation

Baseline Variables	Multivariate	
	HR	*p*
Prothrombin	0.79	0.002
EV (≥ grade 2)	2.60	< 0.0001

Nery, Hepatology 2015

Thrombocir – Risk factors for decompensation

Time dependent variables	Univariate		Multivariate	
	HR	*p*	HR	*p*
PVT	1.61	0.058	1.37	0.44

Nery, Hepatology 2015

Thrombocir – Risk factors for death

Baseline variables	Multivariate	
	HR	*p*
EV (≥ grade 2)	2.00	0.0056
Serum bilirubin	1.15	0.038
Serum albumin (g/L)	0.96	0.02

Nery, Hepatology 2015

PVT independently associated with a decreased pretransplant mortality ?

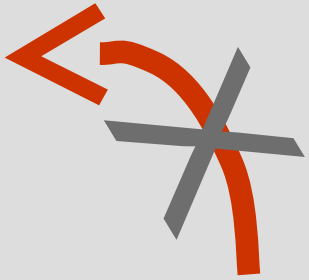
UNOS + SSDMF registries (2002-2013)

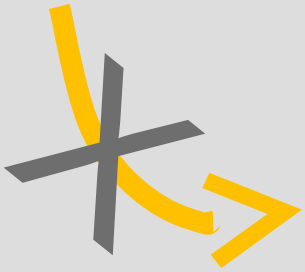
Cirrhosis without HCC	66,506
PVT at listing	2207
Adjusted HR for death	0.88 *

* 95%CI, 0.81-0.96

Berry, Clin Gastroenterol Hepatol 2015

Advanced Cirrhosis

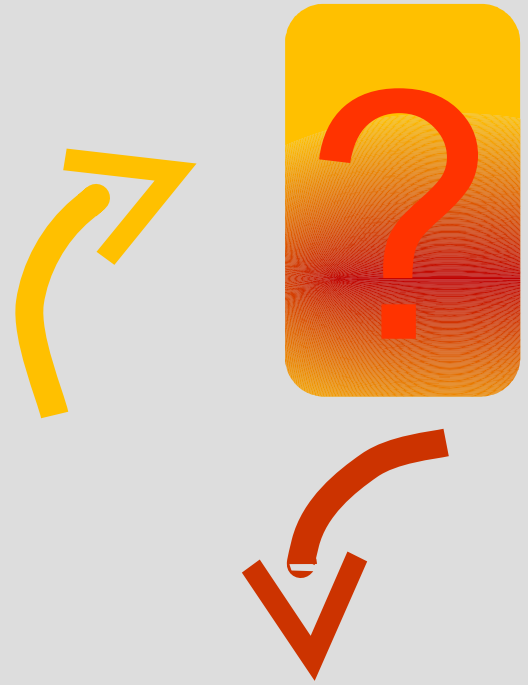




Portal vein Thrombosis

Nery. Hepatology 2015

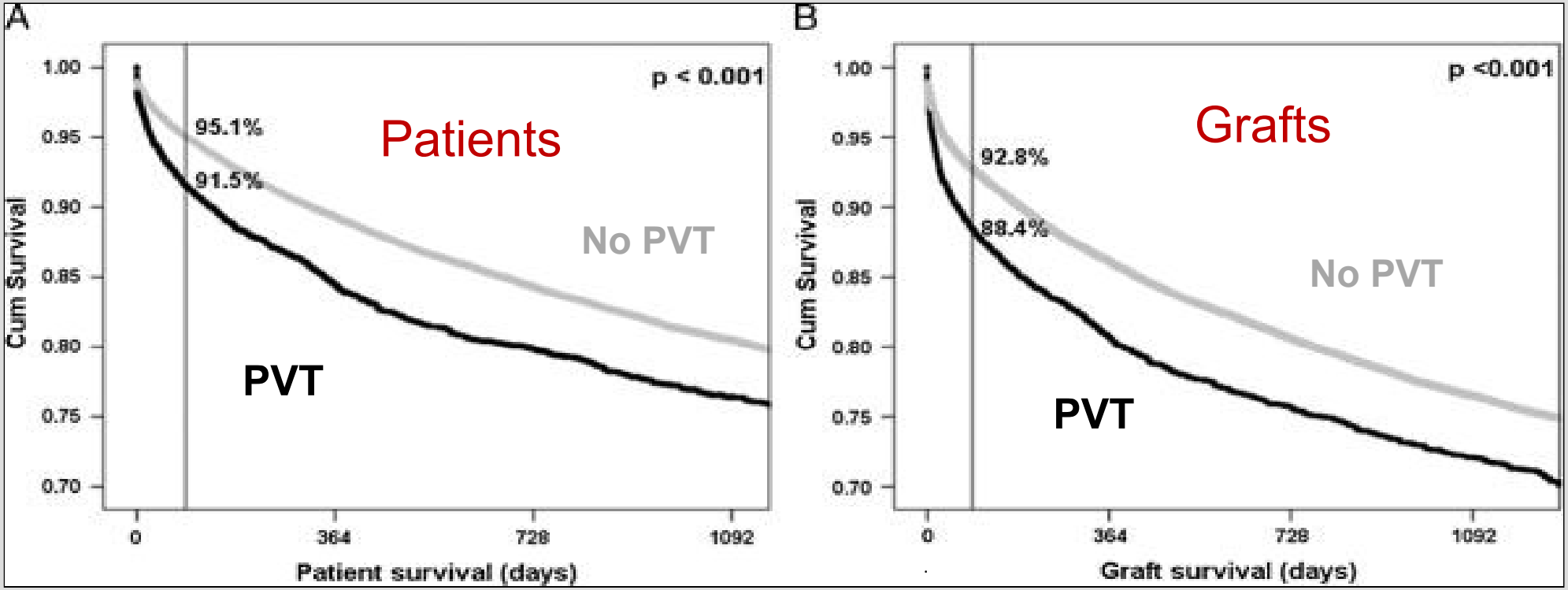
Advanced Cirrhosis



Portal vein Thrombosis

Decreased early patient and graft survival in patients with PVT at listing

OPTN registries 2002-2013



Ghabril, Transplantation 2015

Anticoagulation for Portal Vein Thrombosis in Cirrhosis

End point	OR	*P*
Complete recanalization	3.38	0.002
Thrombus progression	0.14	<0.0001
Variceal bleeding	0.23	0.04

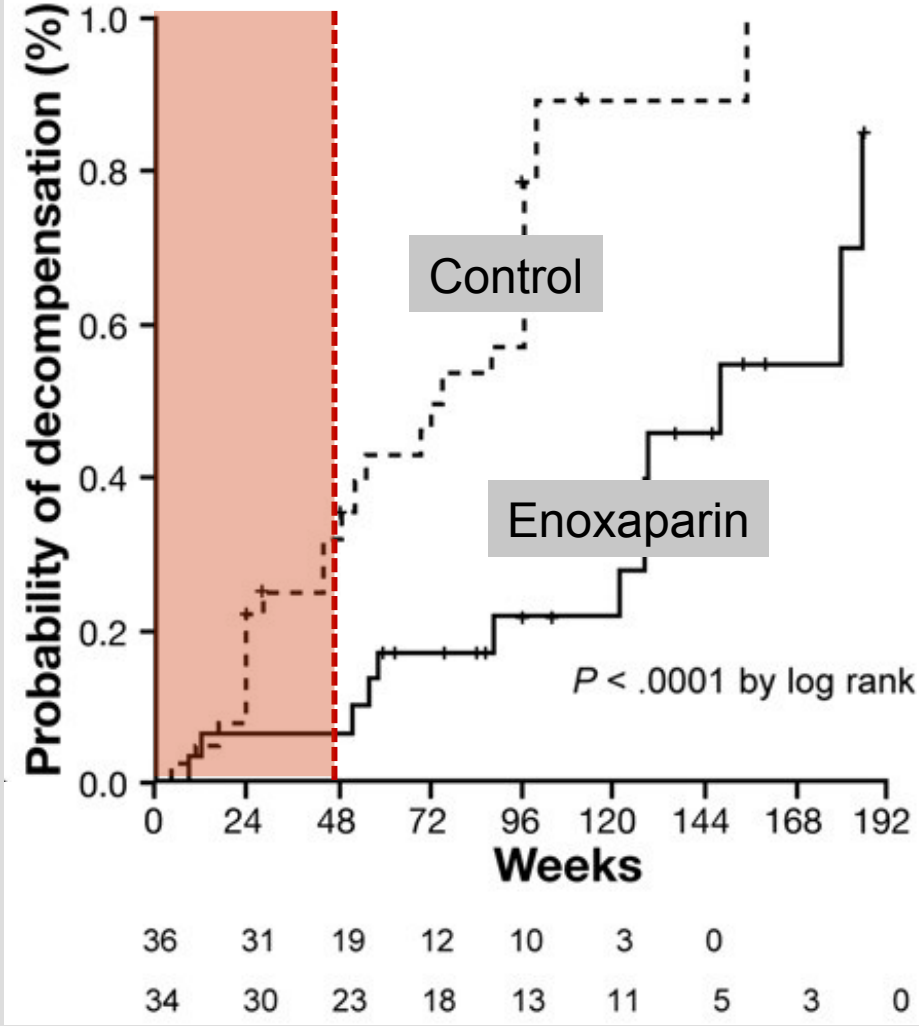
Loffredo, Gastroenterology 2017

Enoxaparin in Cirrhosis (Child-Pugh B7-C10)

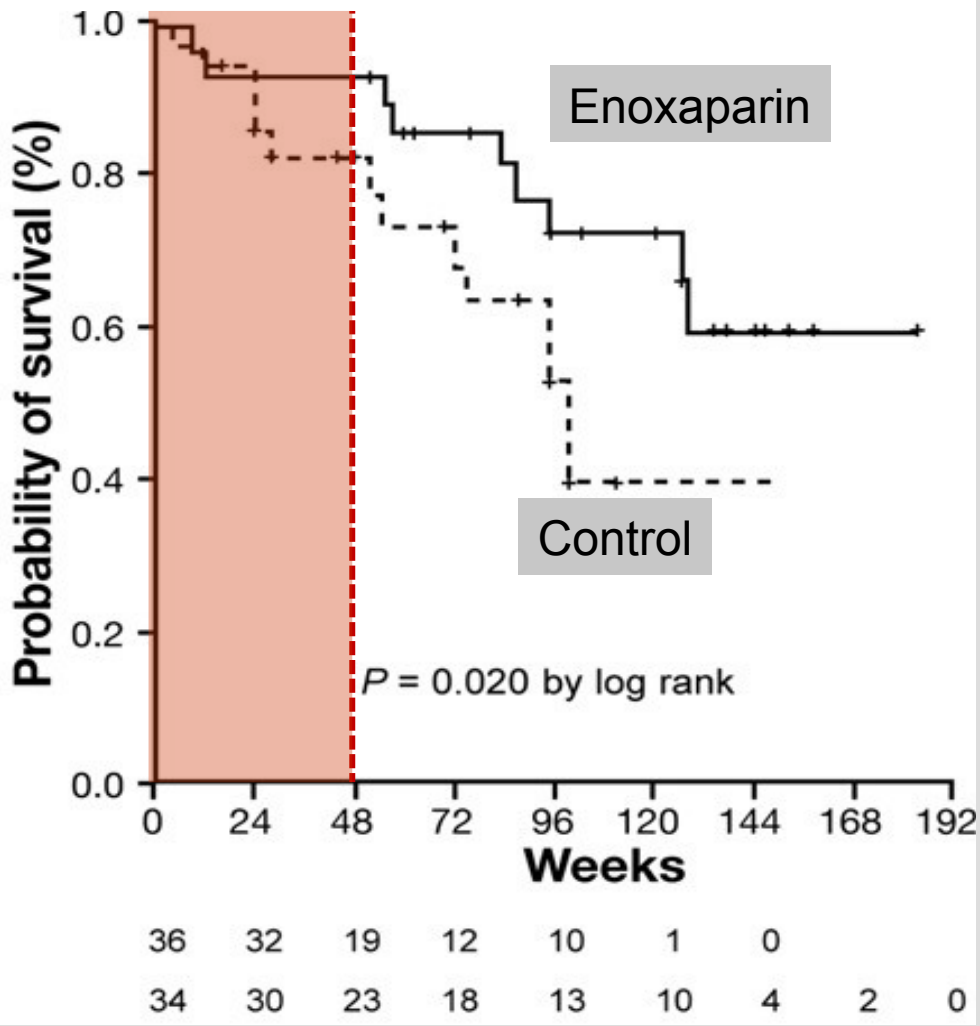
	Control	Enoxaparin
N. of patients	36	34
Partial PVT	3	0
Complete PVT	3	0
Decompensation	19	4

Villa. Gastroenterology 2012. Enoxaparin 4.000 UI/d, for 12 mo.

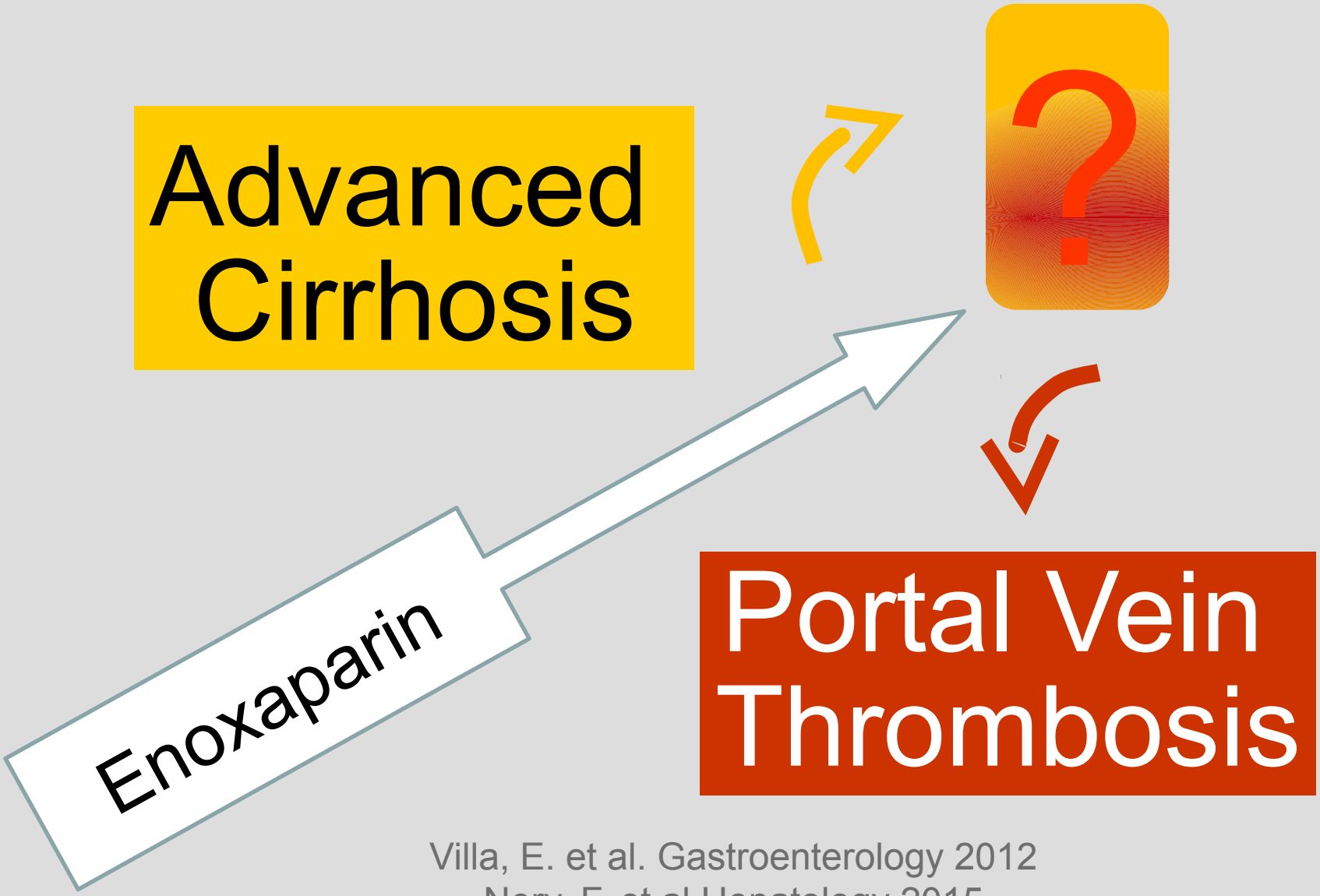
Decompensation



Survival



Villa. Gastroenterology 2012. Enoxaparin 4.000 UI/d, for 48 weeks.



Villa, E. et al. Gastroenterology 2012
Nery, F. et al Hepatology 2015

PVT in cirrhosis: Baveno consensus & EASL CPG recommendations

- Screening q. 6 mos in LTx candidates
- Anticoagulation in LTx candidates with PVT

De Franchis, J Hepatol 2016. EASL CPG, J Hepatol 2016

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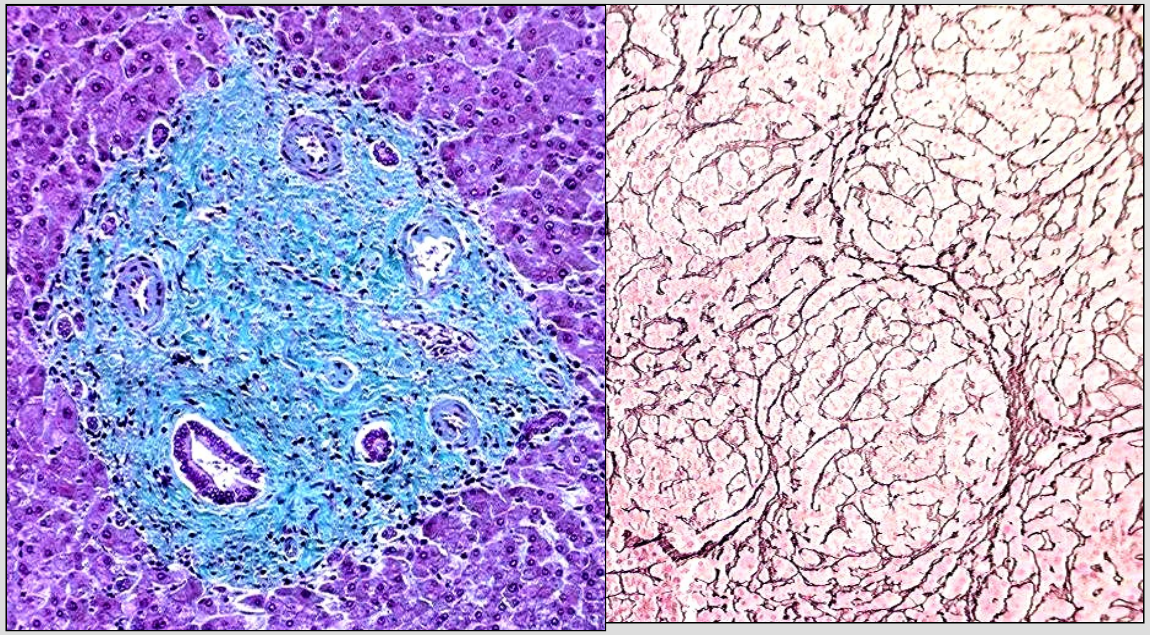
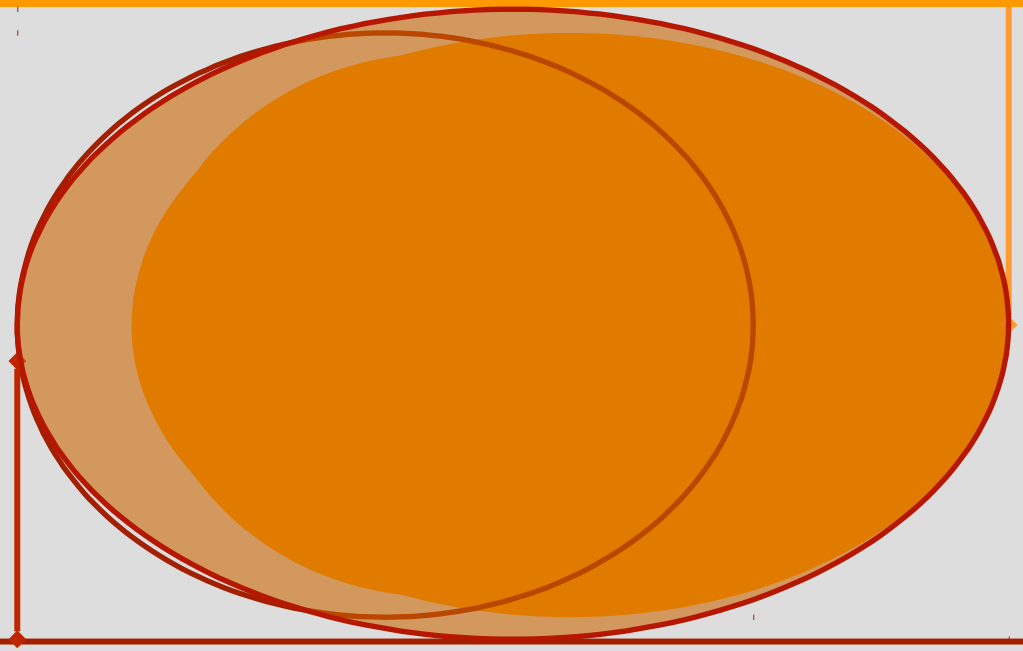


Vascular porto-sinusoidal disease

Pathology

- Obliterative portal venopathy
- Hepatoportal sclerosis
- Nodular regenerative hyperplasia

VALDIG
Ascona meeting 2017
Valdig.eu

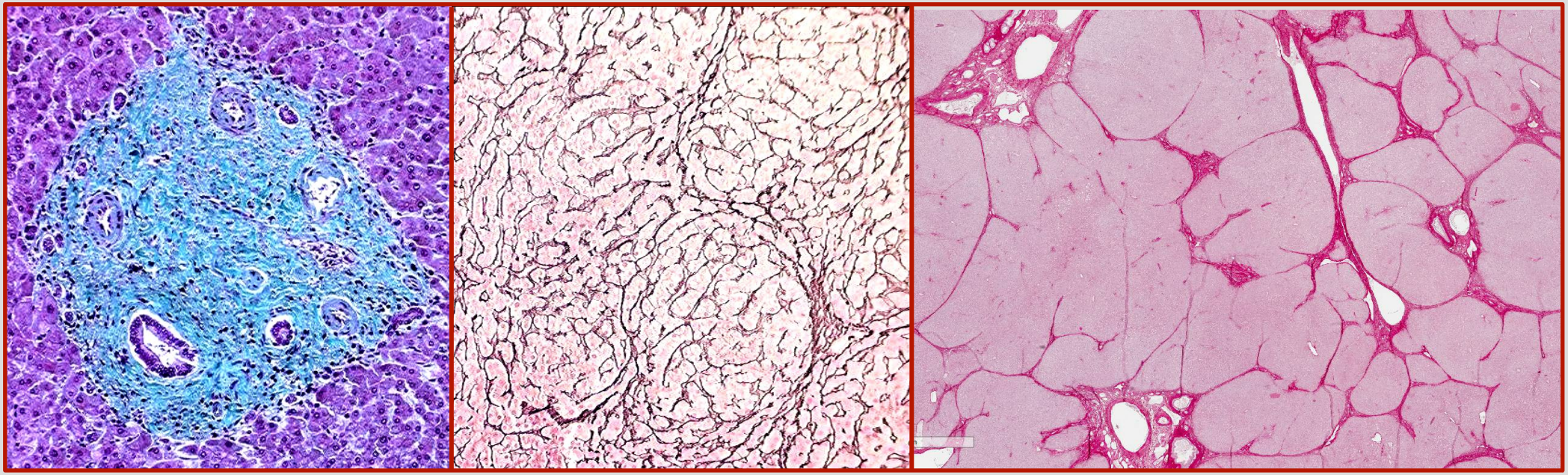


Clinics & Pathology

Idiopathic portal hypertension
Noncirrhotic intrahepatic portal hypertension

Histopathologic features of VPSD

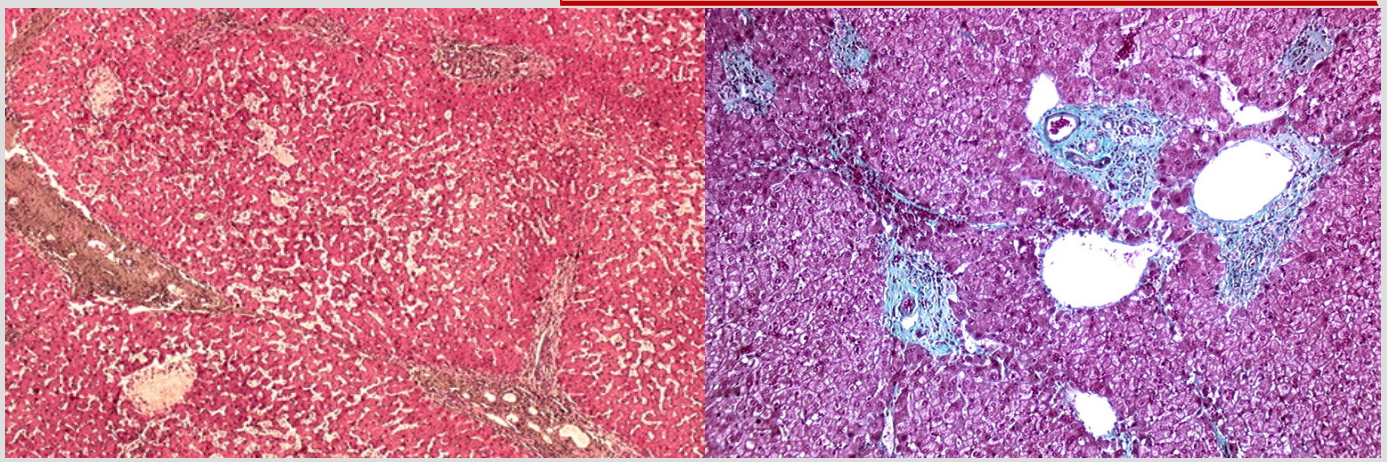
Specific
Abnormal portal venule
Nodular regenerative hyperplasia
Incomplete septal cirrhosis



Courtesy P. Bédossa, D. Cazals-Hatem

Histopathologic features of VPSD

Specific	Frequent
Abnormal portal venule	Portal Fibrosis
Nodular regenerative hyperplasia	Sinusoidal dilatation
Incomplete septal cirrhosis	Portal tract angiomatosis
	Paraportal vessels



Courtesy P. Bédossa, D. Cazals-Hatem

Clinical features of VPSD

	N	%
No clinical features of PHT	211	39 %
Initial variceal bleeding	224	30 %
Ascites	218	32 %
Encephalopathy	131	4 %
Liver failure	122	9%

Hillaire, Gut 2002. Cazals-Hatem, J Hepatol 2011. Schouten, APT 2012. Siramolpiwat, Hepatology 2014

Laboratory features of VPSD

Platelets (103/μL)	106 (27–454)
Albumin (g/l)	38 (20–52)
Bilirubin (μmol/L)	17 (5–100)
INR	1.1 (1.0–1.4)

Verheij, Histopathology 2013

Transaminases and alkaline phosphatase variably increased

Other features of VPSD

In patients with clinically significant PHT

- Hepatic venous pressure Δ < 10 mmHg*
- Smooth liver surface
- Enlarged central and atrophic peripheral liver
- Liver stiffness < 20 kPa
- Portal vein thrombosis (40%)

*Portal venous pressure > wedge hepatic venous pressure

Bissonnette, Hepatology 2016; Sarin, Gut 1987. Seijo Dig Liver Dis 2002. Glatard, Radiology 2012

VPSD – Outcome

Follow-up – *yr*	8.6 ± 7.8
Extrahepatic PVT	28%
Progression/development of PHT	46%
Liver transplantation	15%
Death	8%

59 patients with obliterative portal venopathy

Cazals-Hatem. J Hepatol 2011

Associated Conditions in 50% of VPSD Patients

Prothrombotic cond.	Myeloproliferative neoplasia, APS
Blood diseases	Lymphoproliferative neoplasia, Sickle cell disease
Disordered immunity	Immune deficiency syndromes Autoimmune disorders
Drug exposure	Purine analogs
Genetic defects	Turner, Adams-Ollivier, FOPV, etc.
None of the above	Familial and sporadic cases

Cazals-Hatem, J Hepatol 2011. Schouten, APT 2012.
Siramolpiwat, Hepatology 2014. Semela, Clin Liver Dis 2015. Jacquemain, Liver Int 2017.

VPSD – Diagnosis – VALDIG Ascona Criteria

Clinically significant PHT

- No cirrhosis

- Systemic disease/no cause for liver disease
- Mild liver dysfunction
- Stiffness < 20 kPa; HVPG < 10 mmHg

No clinically significant PHT

- No cirrhosis
- Specific histologic lesions

(http://valdig.eu/conference-ascona/)