Clinical cases

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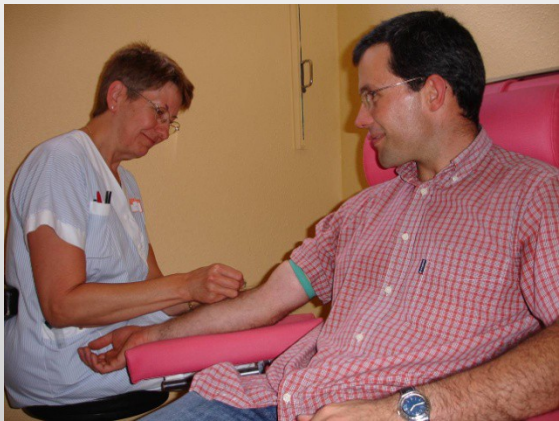
Diagnosis of liver fibrosis

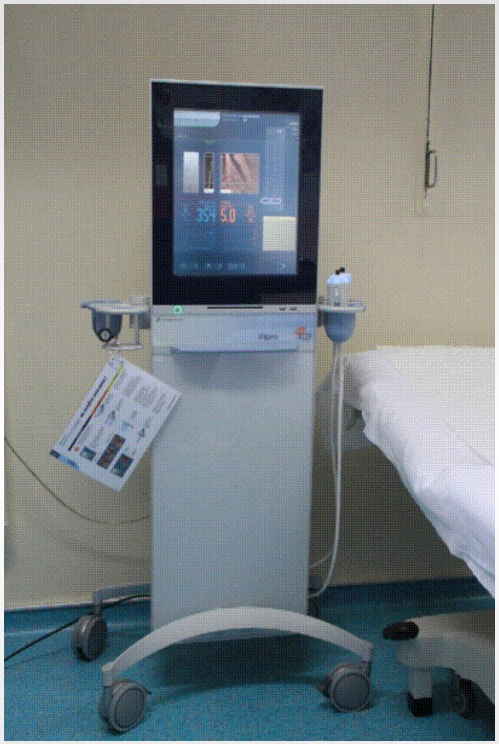
- Liver biopsy
- Blood markers
- Liver stiffness

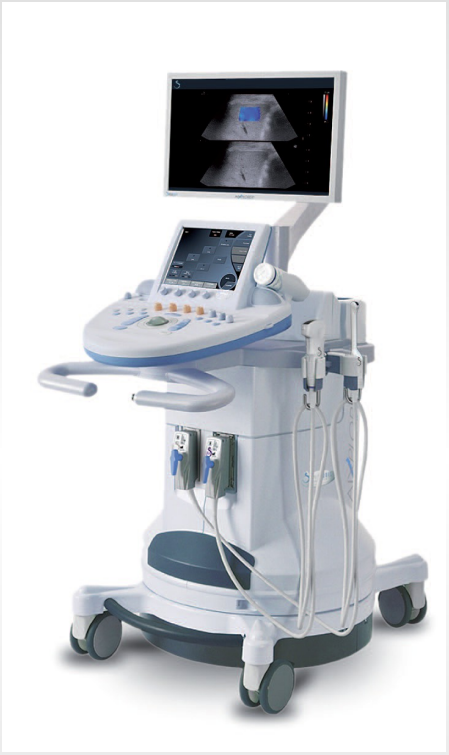
Blood markers

- Hepascore
- Fibrotest
- Fibrometer
- ELF
- APRI
- FIB4



Liver stiffness measurement

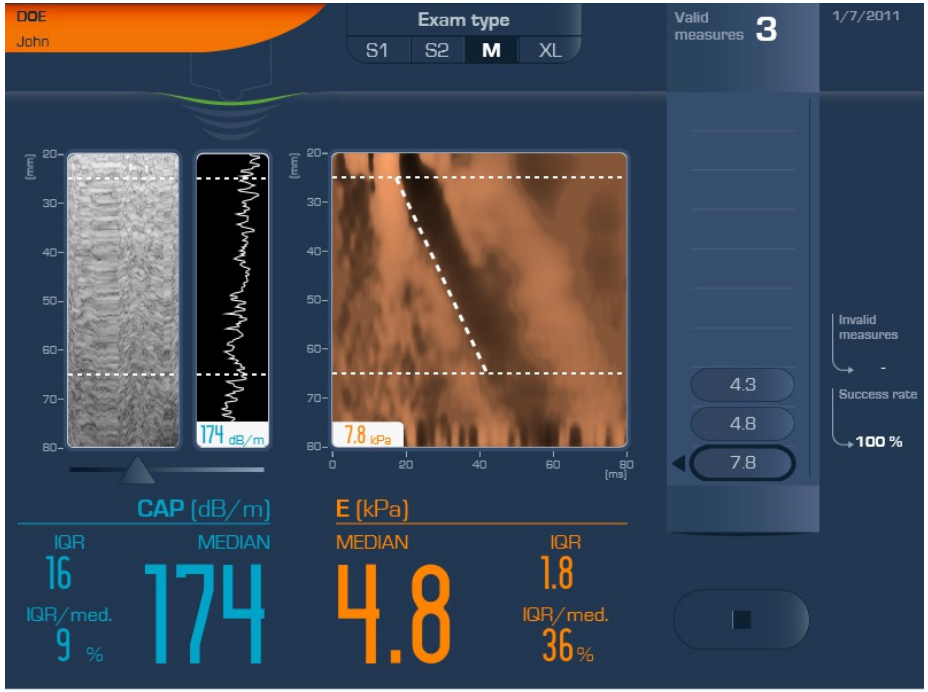




FibroScan – ARFI - SSI

FibroScan

FibroScan examination: screen



CAP : 100 to 400 dB/m

E : 2 to 75 kPa

Case 1. Female, 47 yrs, manager

- HBV infection
- BMI 27 kg/m²
- No alcohol
- « inactive carrier » since 2004
- HBV-DNA between 614 & 2712 IU/ml
- Liver stiffness between 3.8 & 7 kPa
- November 2011
  - Normal ALT level
  - HBV-DNA 7538 IU/ml
  - Liver stiffness 4.5 kPa

What do you think?

1. LB to be performed
2. New evaluation in 6 months
3. Fibrotest or Fibrometer

What do you think?

1. LB (EASL guidelines)

Case report

- LB in March 2012
  - 29 mm
  - A1F0
  - Steatosis < 5%
  - NAS 1
- Liver stiffness 5.9k Pa

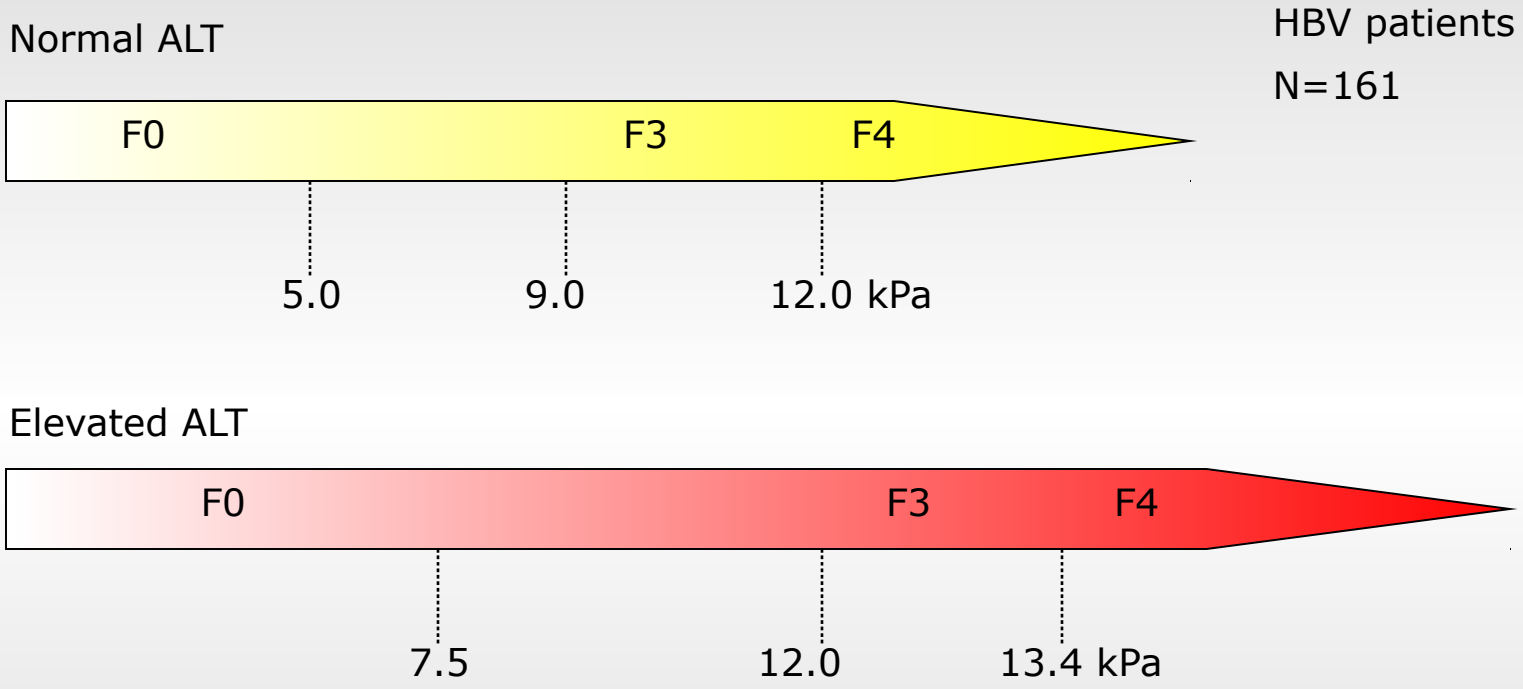
Cut-offs according to the disease (significant fibrosis)

	Cutoff (kPa)	Sensitivity	Specificity	PPV	NPV	AUROC
HCV	≥7.1	.68	.89	.88	.70	.86
HBV	≥7.2	.74	.88	.82	.82	.86
PBC	8.8	.67	1.00	1.00	.75	.91
PSC	8.6	.72	.89	.85	.78	.84
NAFLD	7	.76	.80	.75	.78	.80
HCV+HIV	7.2	.88	.66	.75	.88	.83

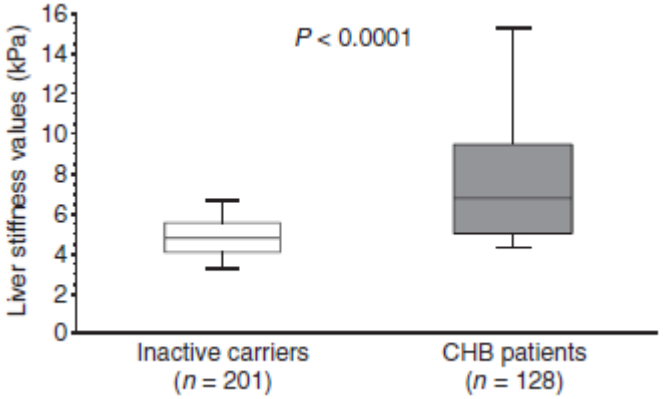
Abbreviatons: NPV, negative predictive value; PBC, primary biliary cirrhosis; PPV, positive predictive value; PSC, primary sclerosing cholangitis.

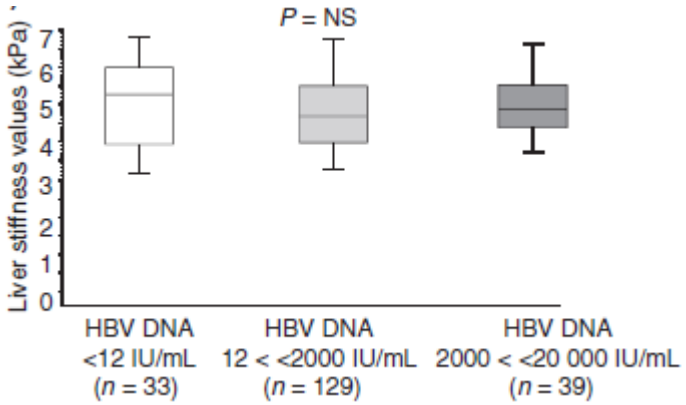
Patel K et al. Clin Liver Dis 2014;4:97-100

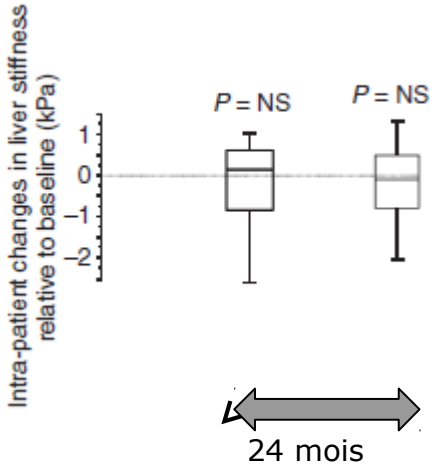
Interpretation



Liver stiffness in inactive carriers





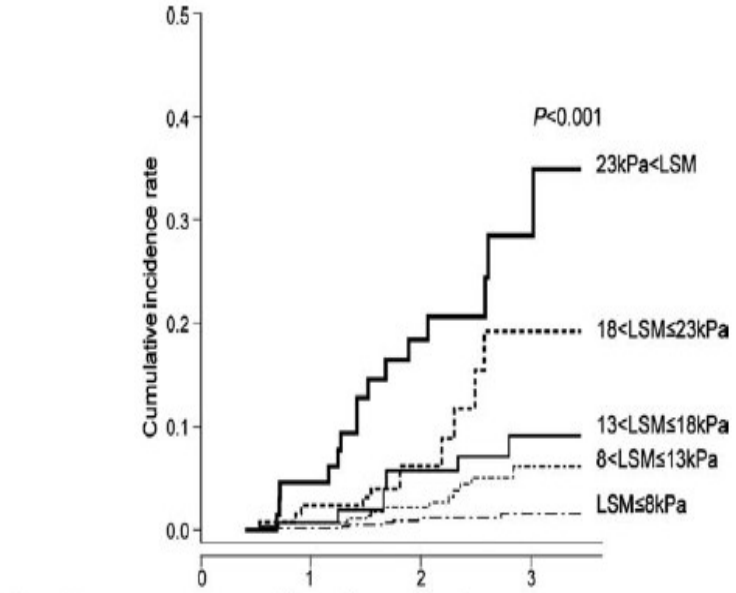


Castera L, de Lédinghen V. Aliment Pharmacol Ther 2011;33:455-65

Liver stiffness and risk of HCC

- Incidence HCC
- 1 130 HBV patients
- Follow-up 31 months

N=1130



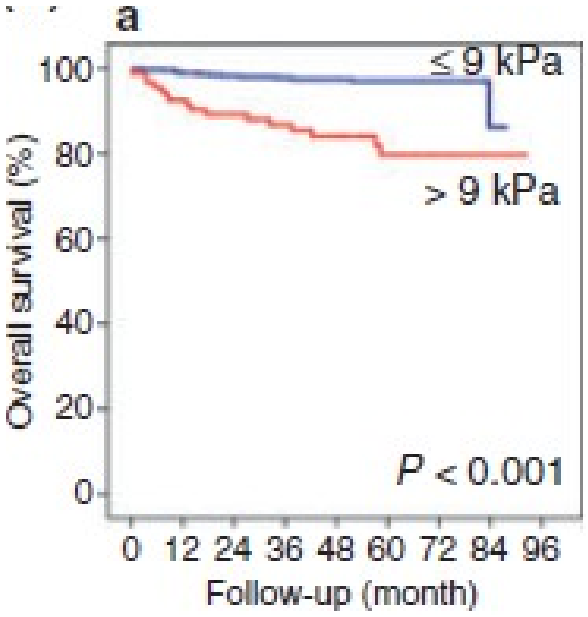
No. at risk				
LSM ≤ 8kPa	595	594	589	588
8 < LSM ≤ 13kPa	285	282	278	272
13 < LSM ≤ 18 kPa	130	126	122	120
18 < LSM ≤ 23 kPa	53	53	49	45
23 kPa < LSM	67	64	56	53

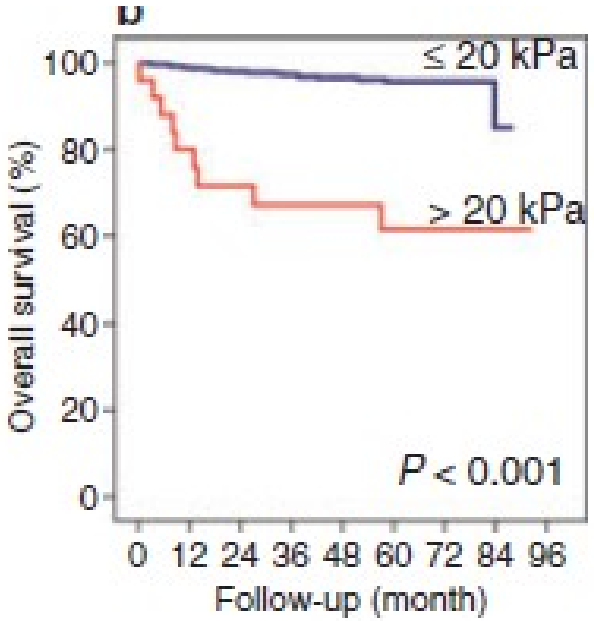
Jung KS et al. Hepatology 2011; 53: 885-94

Non-invasive tests for fibrosis and liver stiffness predict 5-year survival of patients chronically infected with hepatitis B virus

V. de Lédinghen*,†, J. Vergniol*, C. Barthe*, J. Foucher*,‡, F. Chermak*, B. Le Bail†,§, W. Merrouche* & P.-H. Bernard‡

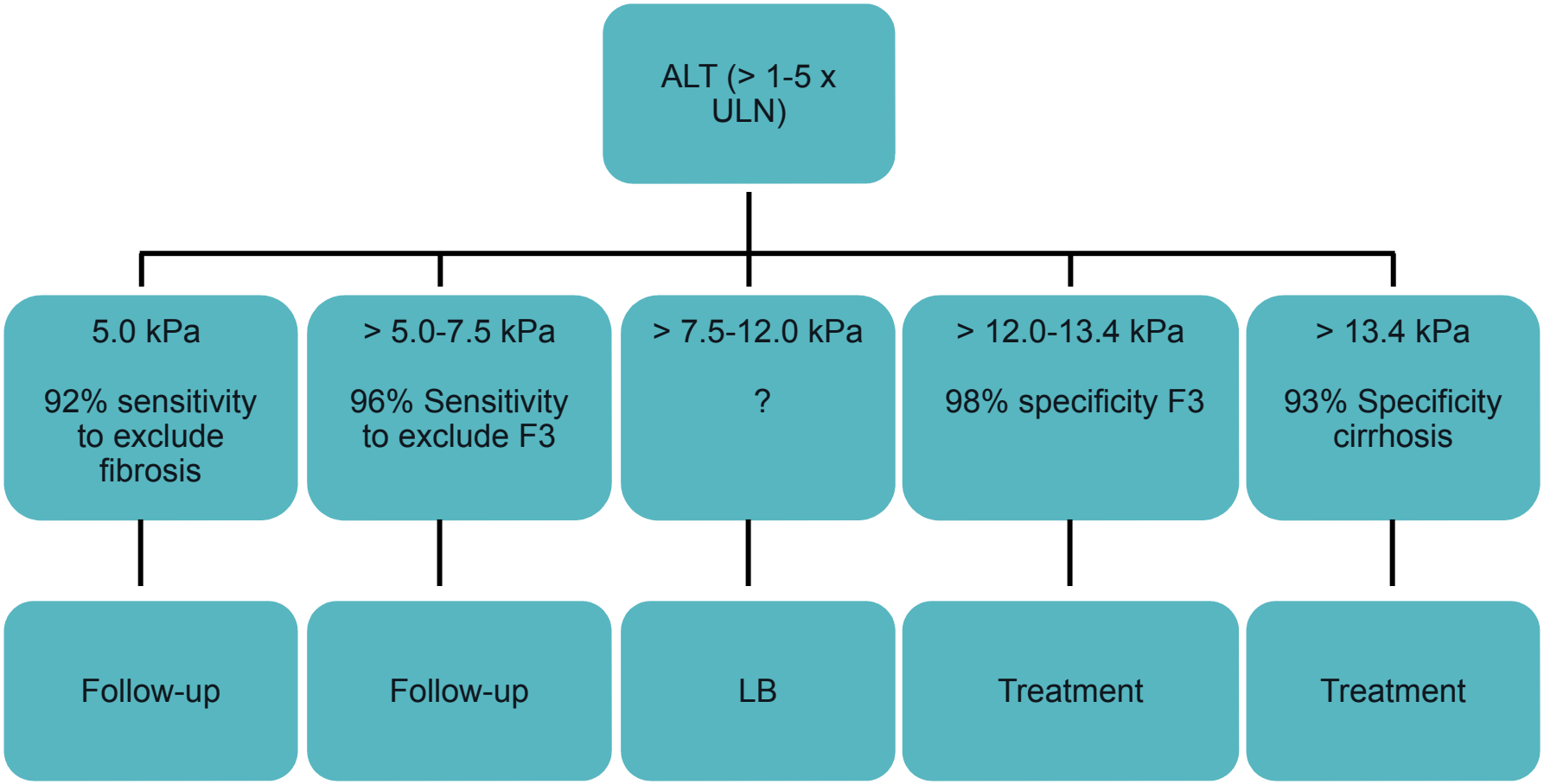
- 600 HBV patients
- Follow-up 50 months





Aliment Pharmacol Ther 2013; 37:977-88

Liver stiffness and elevated ALT level



Chan HL, et al. J Viral Hepat. 2009;16:36-44.

Take home message

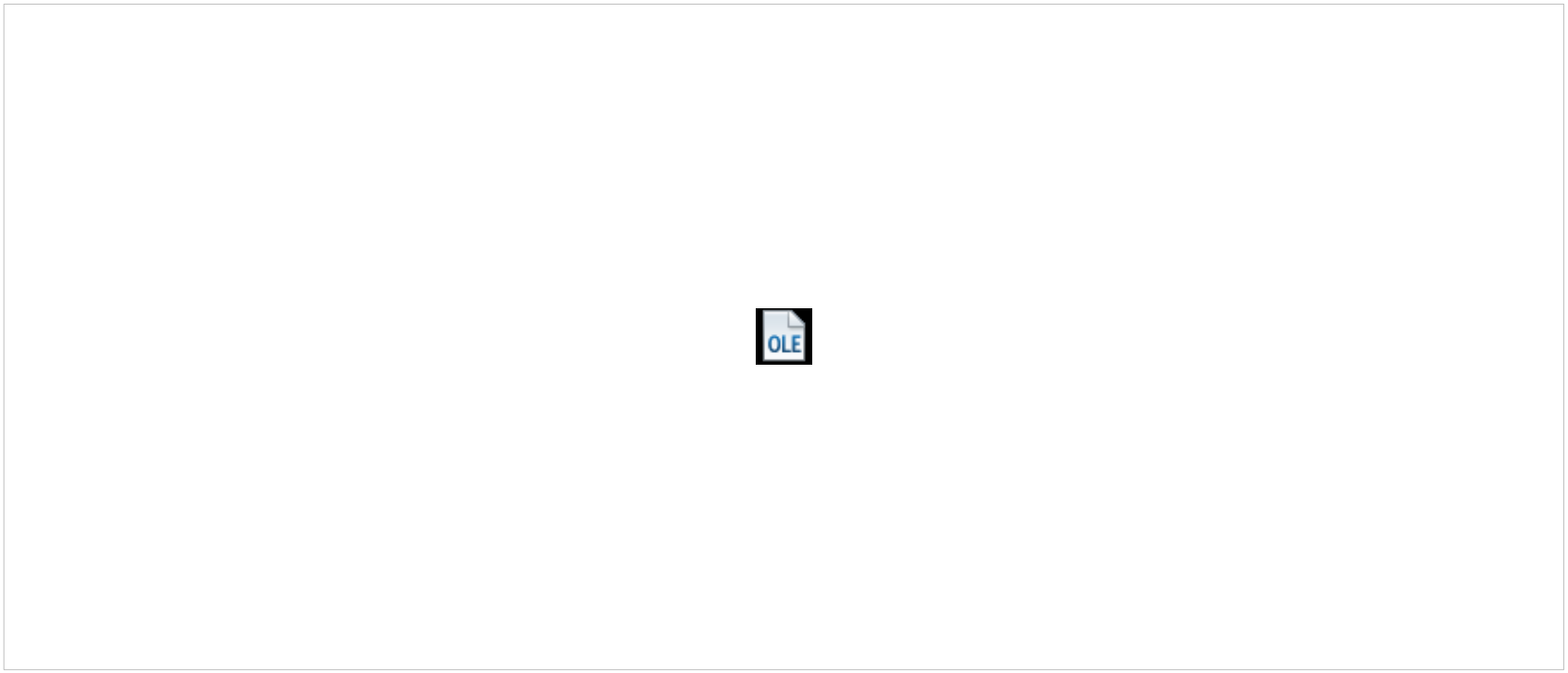
- Liver stiffness is associated with inflammation
- Not compare cut-offs between HCV and HBV infection
- Inactive carrier must have normal values

Case 2. Henri, 60 years old

- Genotype 1b HCV infection
- Contamination: transfusion 1984
- 91 kg 1.73 m (BMI 30 kg/m²)
- Hypertension (bisoprolol)
- No alcohol
- Liver biopsy (2002) : A2F2
- No response to PEG-IFN + Ribavirin treatment

Evolution of liver stiffness

kPa



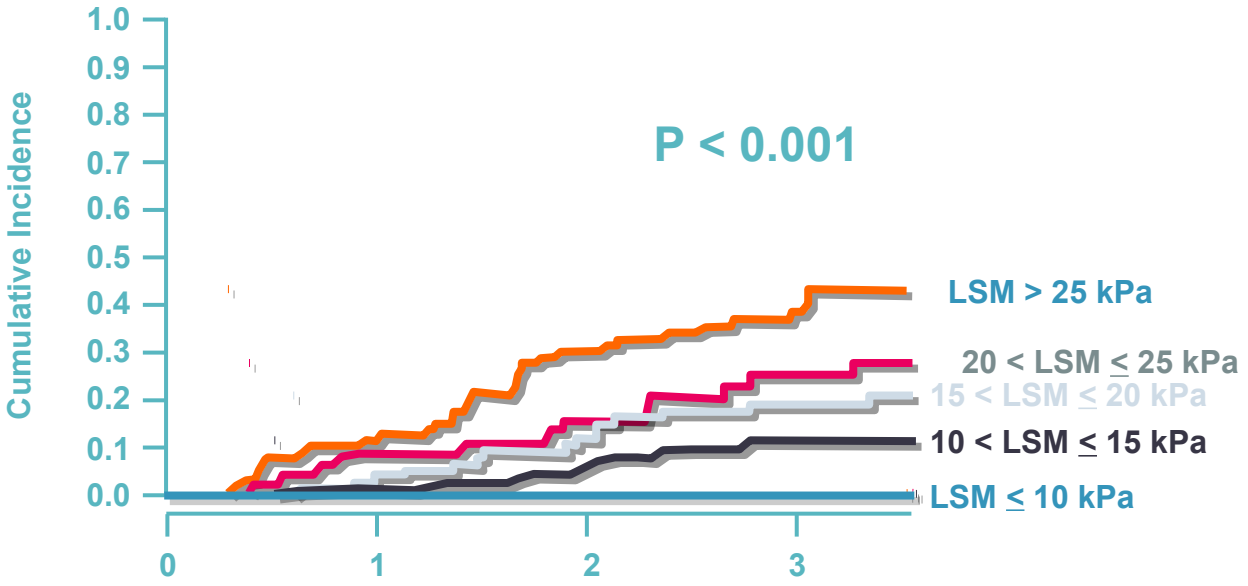
Suspensive treatment

What do you think?

1. There is a cirrhosis.
2. No need for an endoscopy. He does not have any oesophageal varices (liver stiffness < 20 kPa).
3. No need for HCC screening. He does not have a cirrhosis.

Liver stiffness and hepatocellular carcinoma

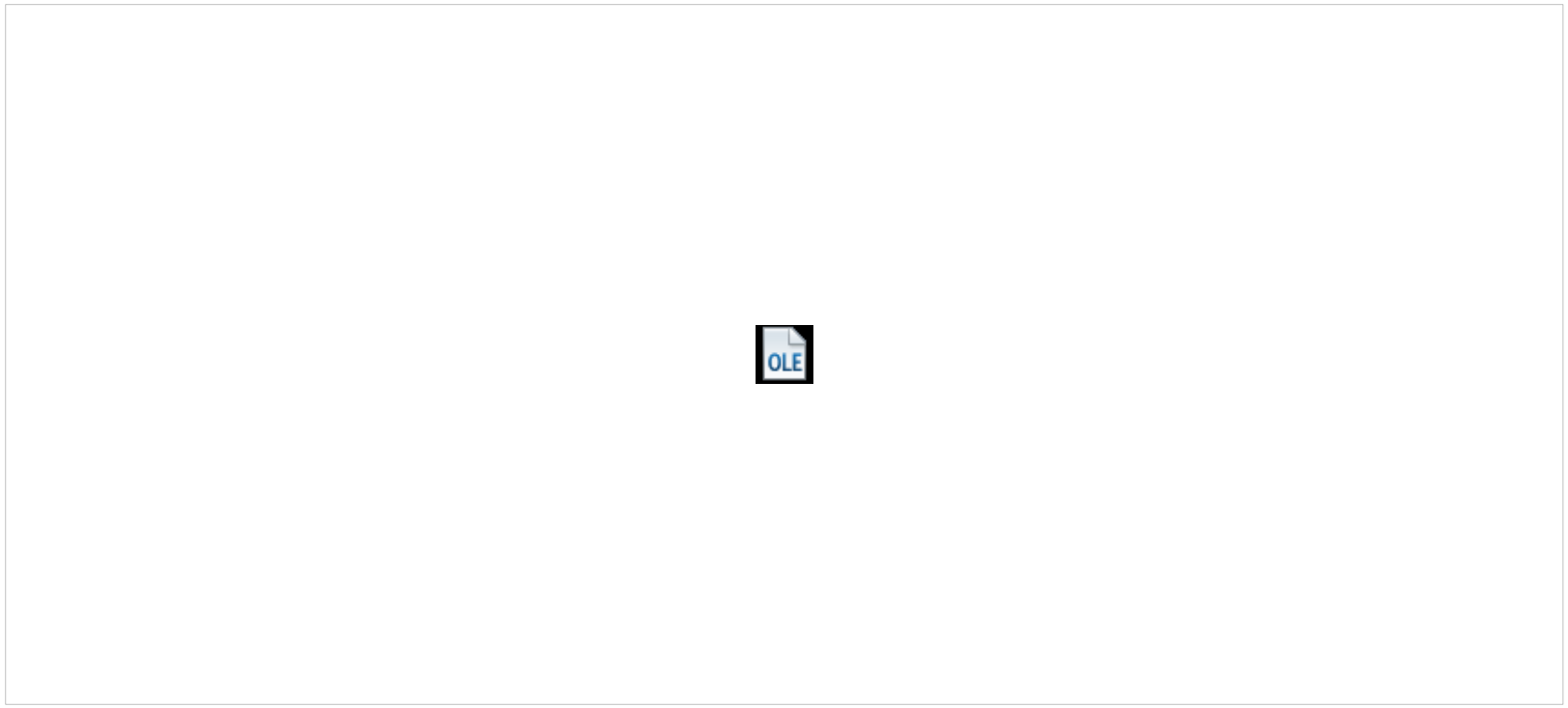
- 866 patients with HCV infection, 3-year follow up
- Hepatocellular carcinoma during follow-up: 77



No. At risk				
< 10 kPa	511	501	476	427
10.1 – 15 kPa	142	130	111	94
15.1 – 20 kPa	79	76	63	51
20.1 – 25 kPa	47	41	36	29
> 25 kPa	87	75	54	41

Masuzaki R et al, Hepatology 2009;49:1954-61

Evolution of Fibrotest

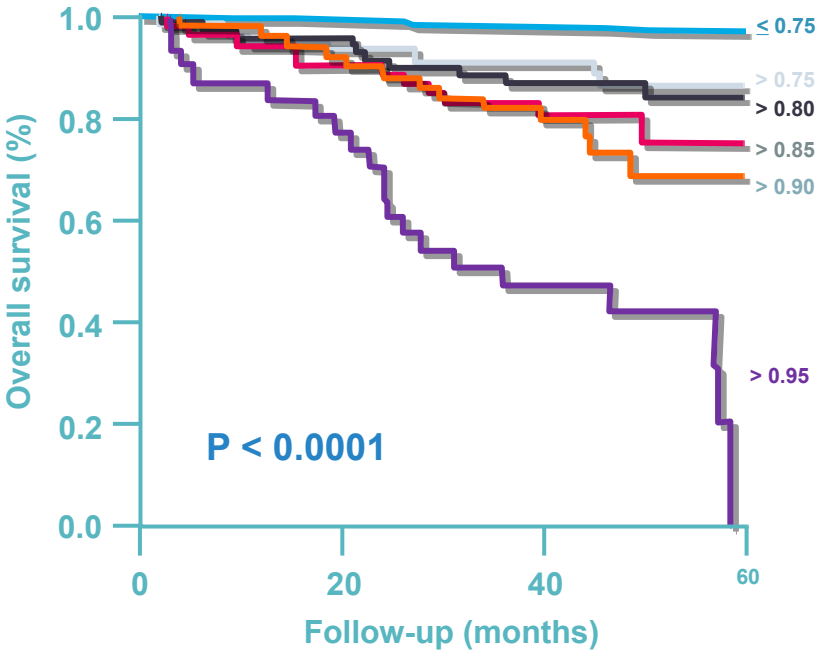


Suspensive treatment

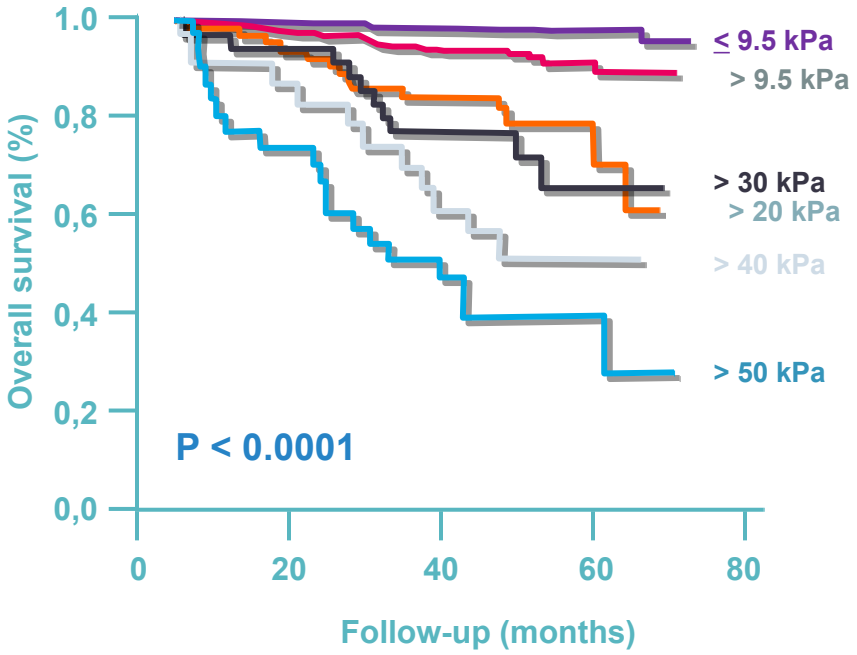
Liver stiffness and survival

- 1457 HCV patients; Follow-up: 5 years
- Overall survival: 91.7%

Fibrotest

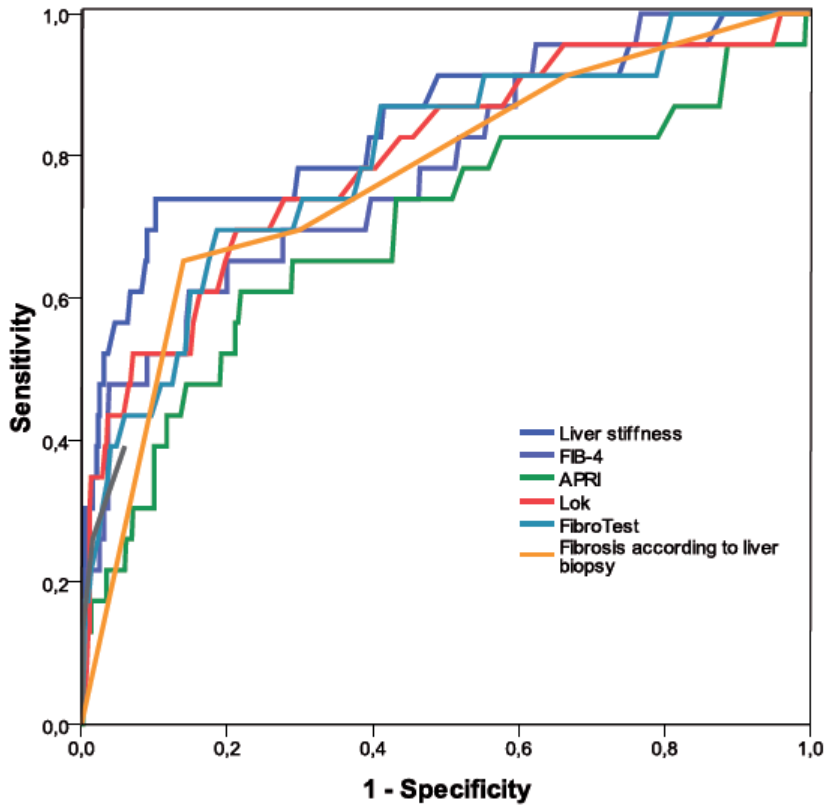


FibroScan



Vergniol J, et al. Gastroenterology 2011;140:1970–9

Prediction of overall survival



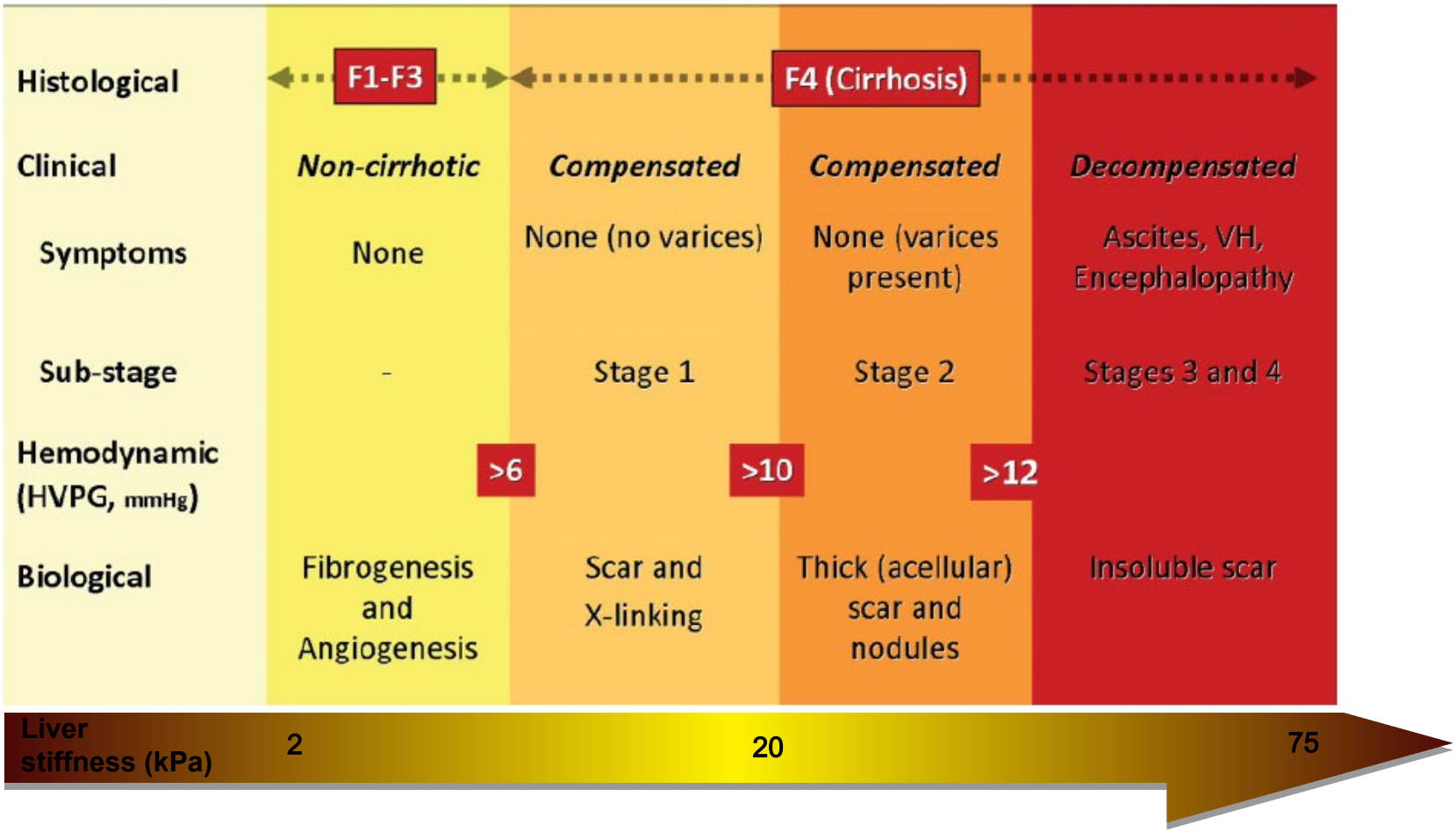
AUROCS

Liver stiffness	0.82
FibroTest	0.80
Liver biopsy	0.76

FibroScan and Fibrotest are better predictors than liver biopsy

Vergniol J, et al. Gastroenterology 2011;140:1970–9

Natural history of liver fibrosis



Garcia-Tsao G et al. Hepatology 2010;51:1-5

Foucher J, et al. Gut 2006;55:403–8

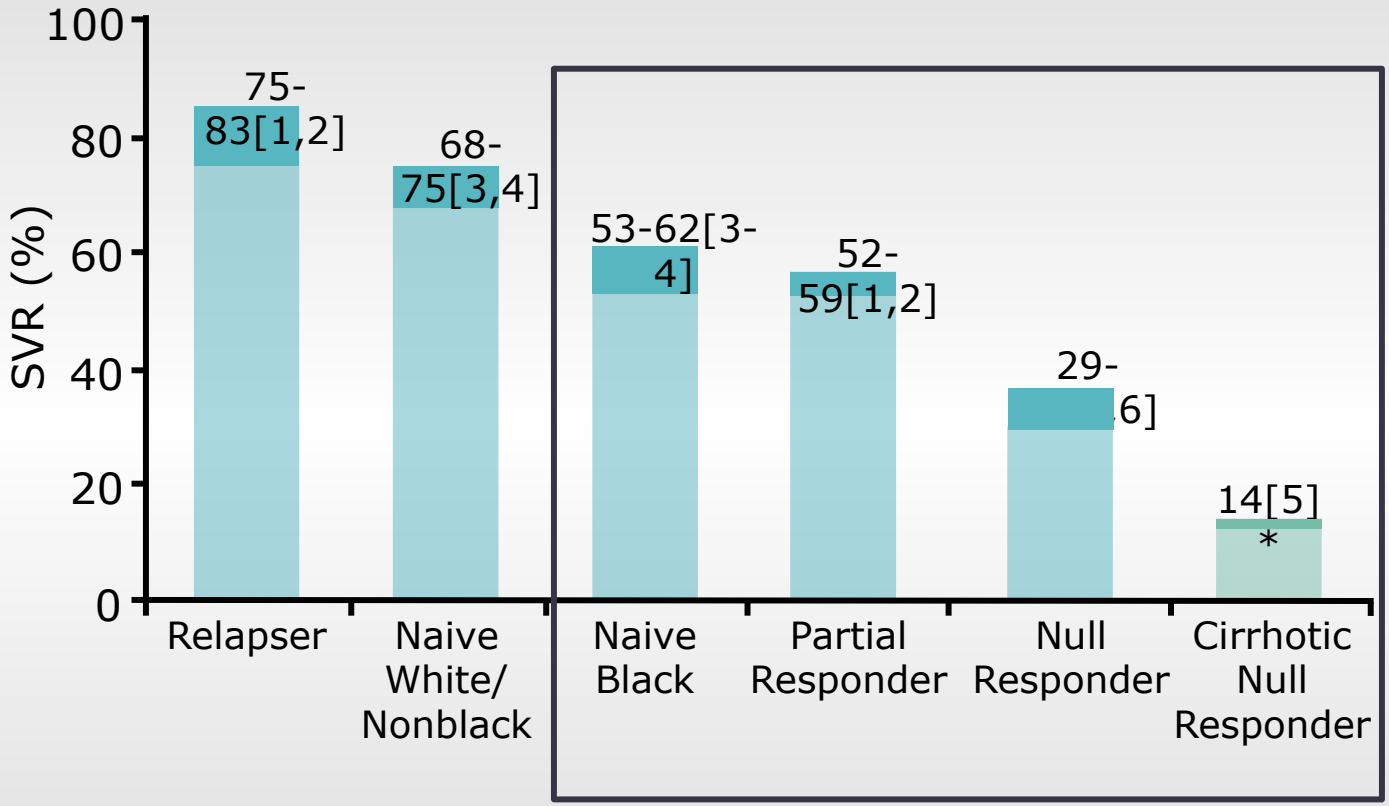
Henri, May 2011

- Liver stiffness: 15.1 kPa
- No oesophageal varices
- No hepatocellular carcinoma
- Child A
- HCV-RNA: 6,426,000 UI/ml

- Do we need Telaprevir?

What do we expect?

Telaprevir and Boceprevir SVR by Patient Type



*Pooled TVR arms of REALIZE trial.

1. Zeuzem S, et al. N Engl J Med. 2011;364:2417-2428. 2. Bacon BR, et al. N Engl J Med. 2011;364:1207-1217. 3. Jacobson IM, et al. N Engl J Med. 2011;364:2405-2416. 4. Poordad F, et al. N Engl J Med. 2011;364:1195-1206. 5. Zeuzem S, et al. EASL 2011. Abstract 5. 6. Vierling JM, et al. AASLD 2011. Abstract 931.

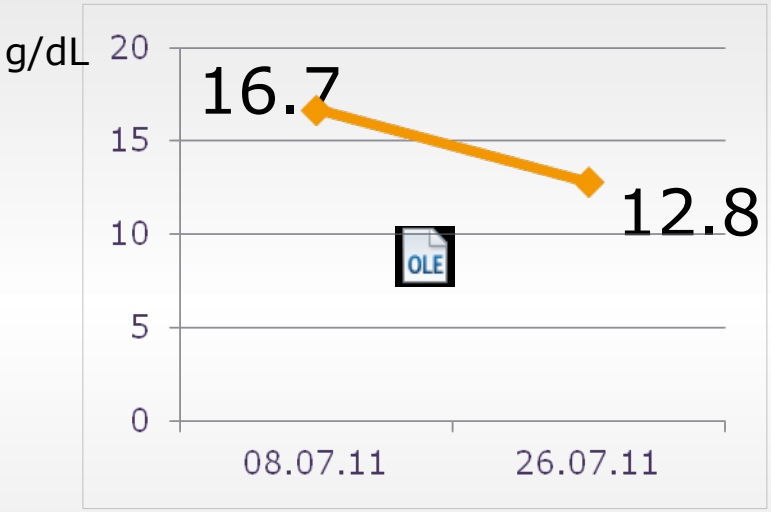
July 8th, 2011

- Henri starts the treatment
  - Pegasys® 180 µg per week
  - Ribavirin 1200 mg per day
  - Telaprevir 750 mg every 8 hours

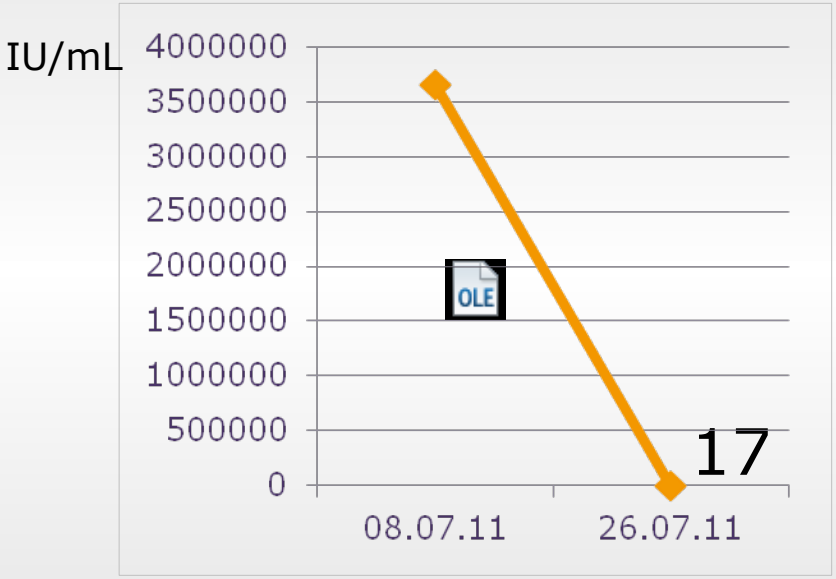
July 26th (day 18)

- Fatigue
- Irritability
- Dyspnea

Blood sample (day 18)



Hemoglobin



HCV-RNA

What is your decision?

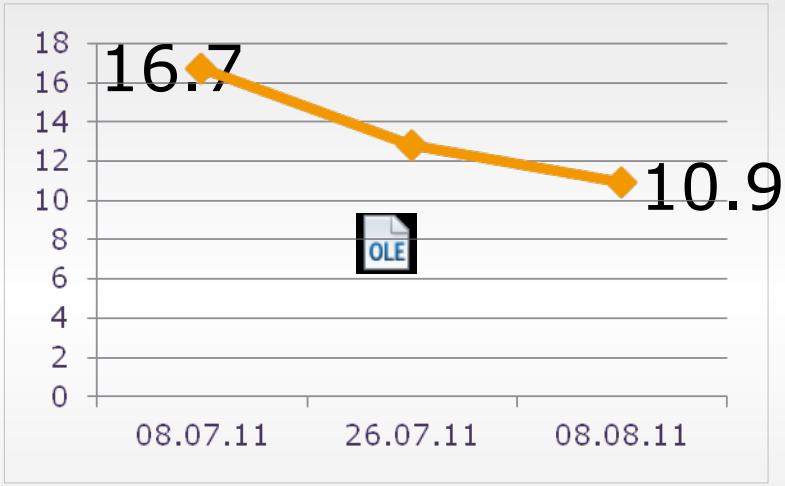
1. No change
2. Stop Ribavirin
3. Decrease Ribavirin dose
4. Stop Telaprevir

No change….
August 8th (week 4)

- Fatigue
- Headache
- Dyspnea
- Diarrhea

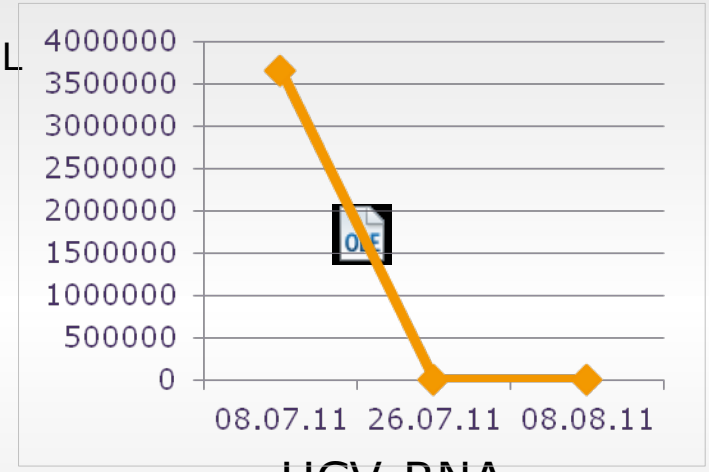
Blood sample at week 4

g/dL



Hemoglobin (g/dL)

IU/mL



HCV-RNA

Neutrophils 1650/mm3
Platelets 109 G/L

What is your decision?

1. No change
2. Decrease Ribavirin dose
3. EPO (epoetin alfa)
4. Stop Telaprevir

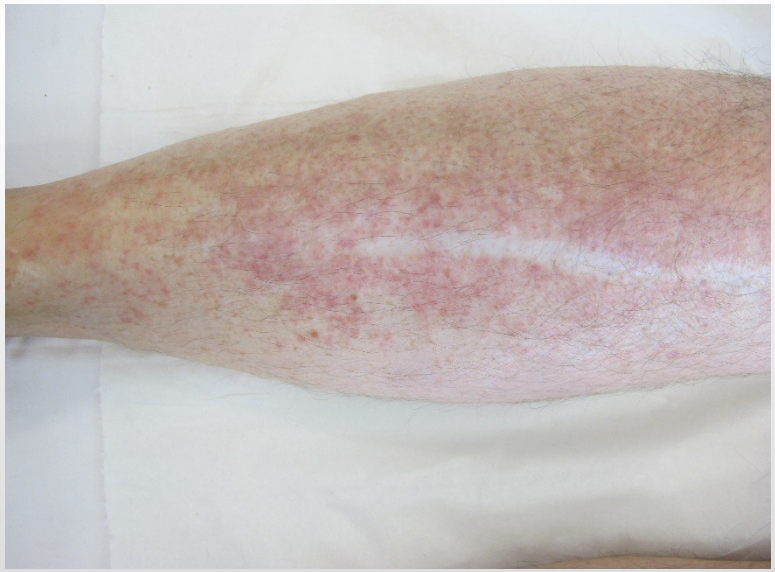
Henri at week 4

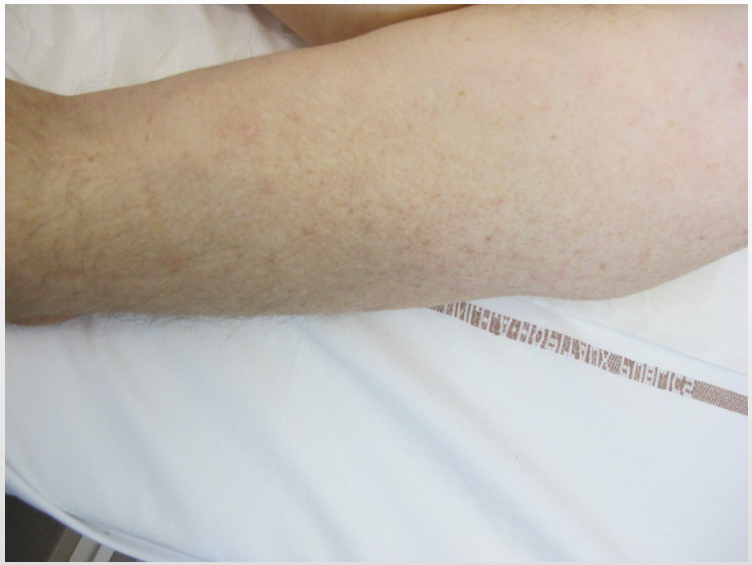
- EPO started

- A week 8
  - Fatigue
  - Dyspnea
  - Cought
  - Anorectal symptoms

Anal pruritus well managed.
At week 8

- Rash for 7 days
- Legs and arms





What do you do?

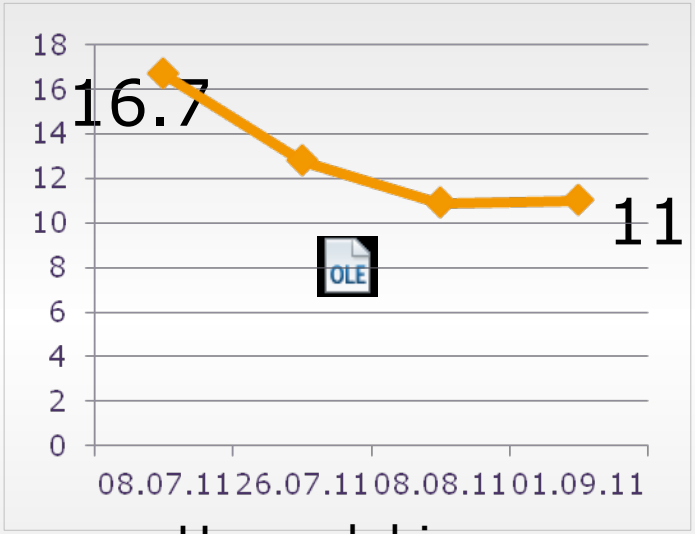
1. Stop Telaprevir
2. Ask a dermatologist to see him next week
3. Emollients, anti-histamines and topical corticosteroids

Treatment of Henri at week 8

- Emollient
- Topical steroidal ointment: betamethasone
  - Twice daily, 10 days
  - Once daily, 10 days
  - Once every other day, 10 days
- Desloratadine (non-prohibited systemic antihistamine)
- Triple therapy was continued

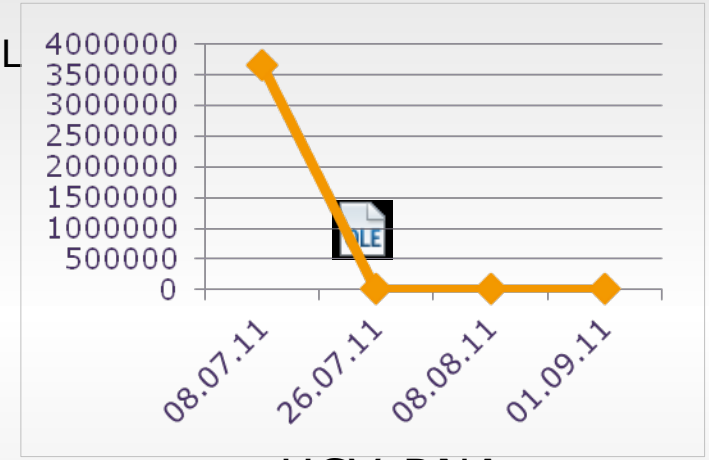
At week 8

g/dL



Hemoglobin

IU/mL



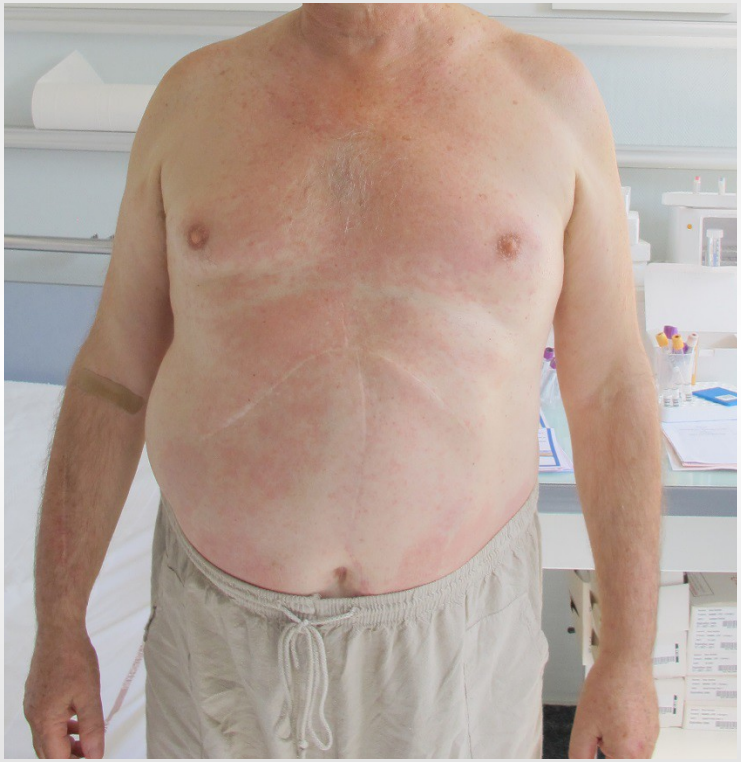
HCV-RNA

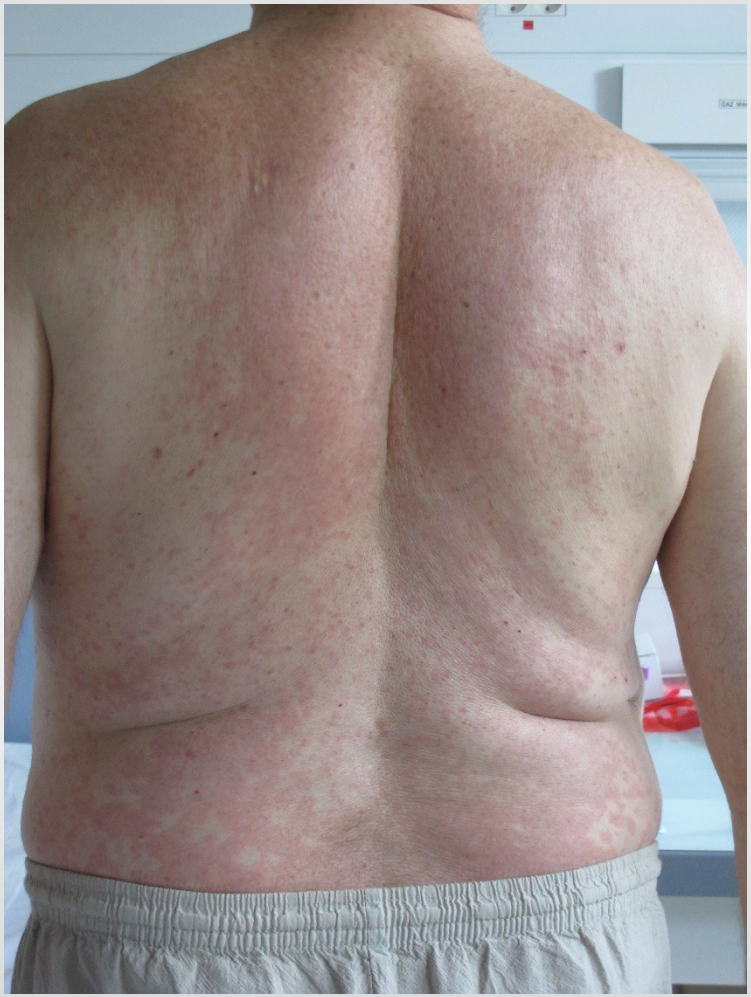
Neutrophils 2150/mm3
Platelets 166 G/L

At week 8, Henri is busy….

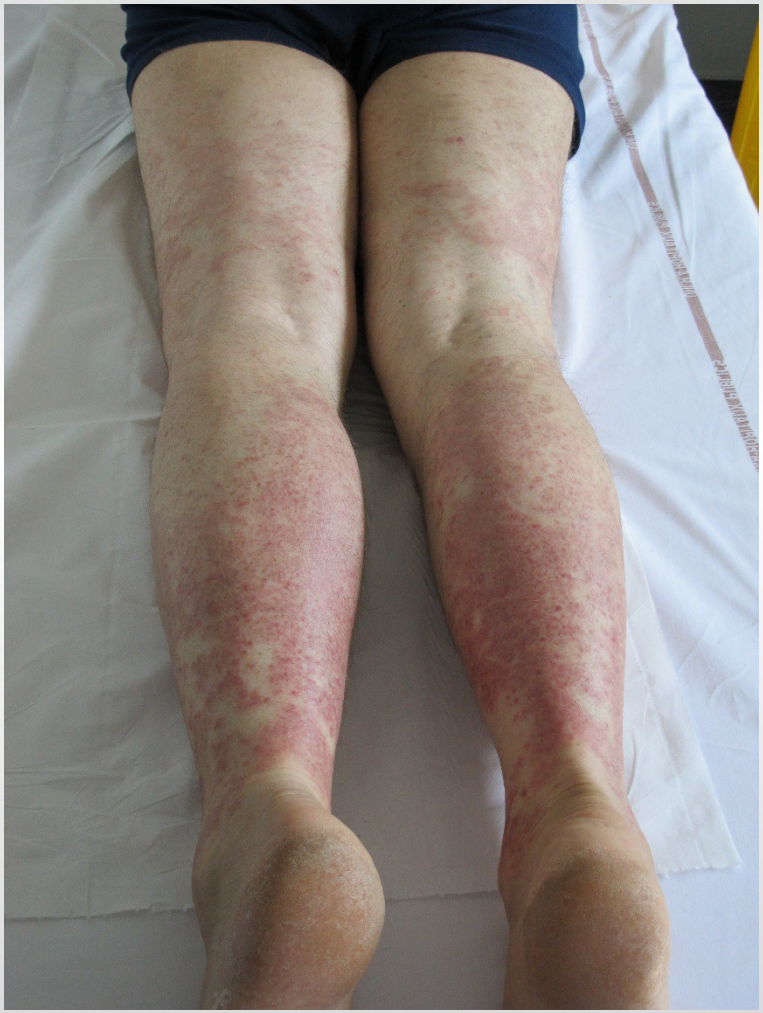
- PEG-IFN
- Ribavirin
- Telaprevir
- EPO
- Treatment of anal pruritus
- Treatment of rash

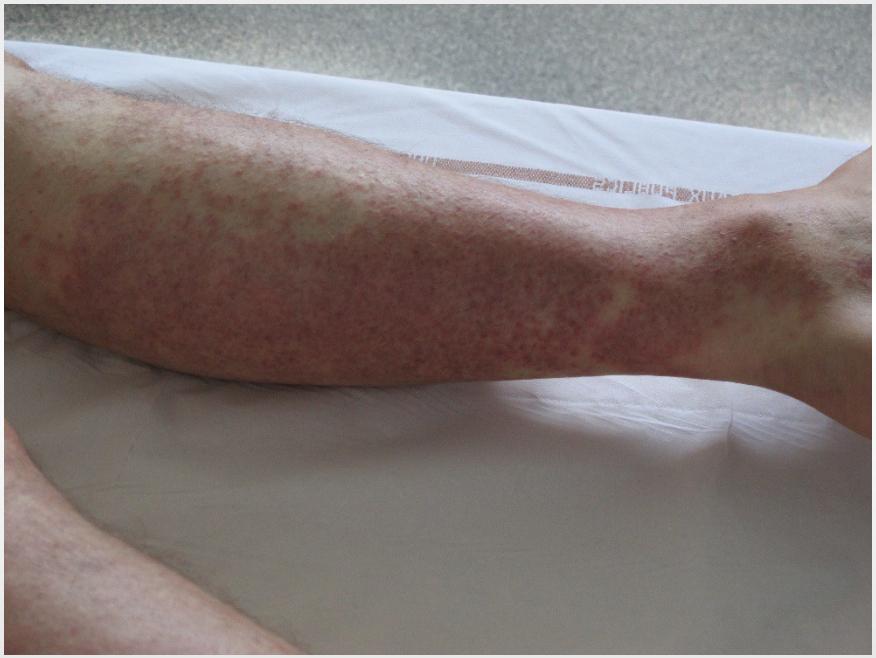
At week 10, emergency….





Week 10





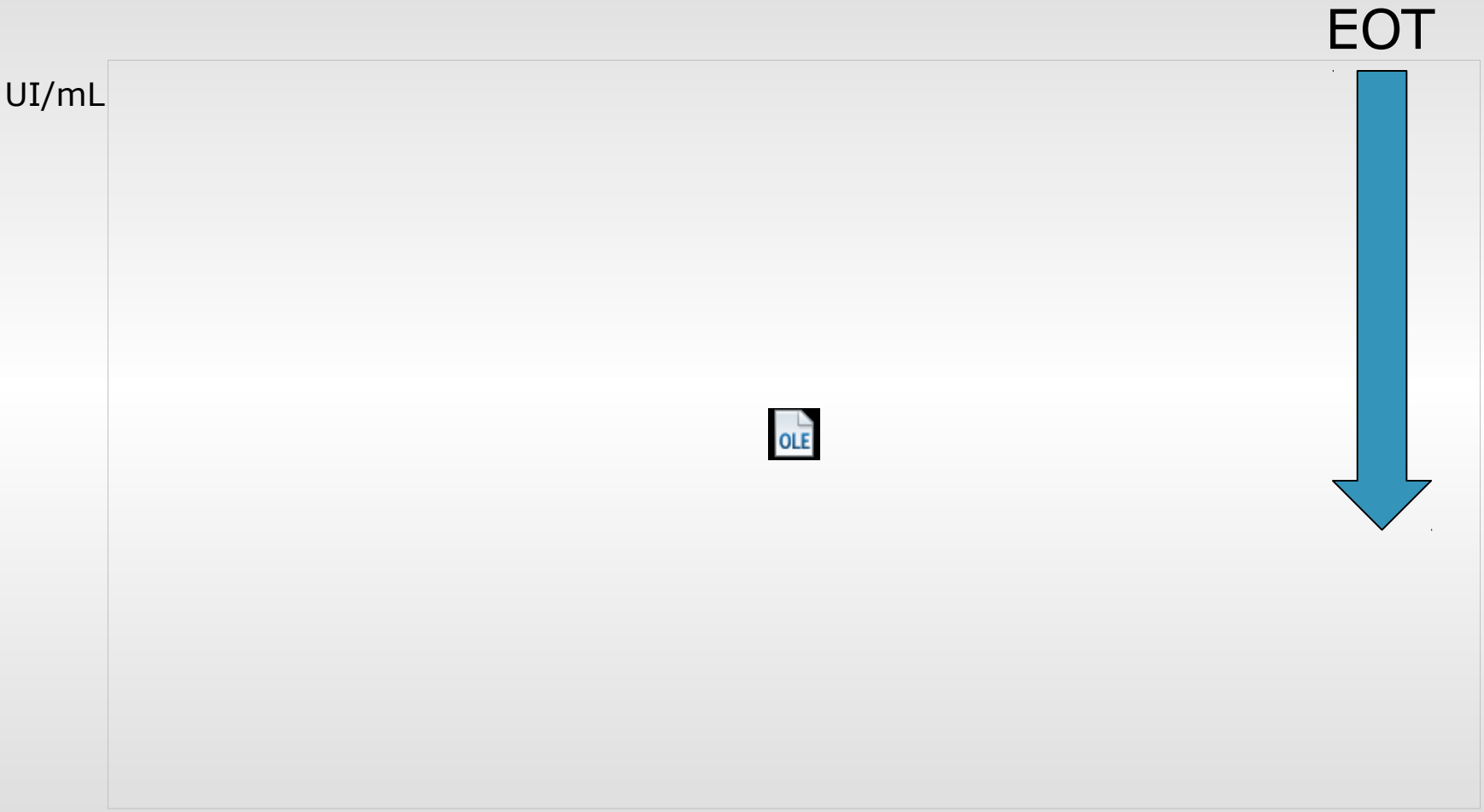
What do you do?

1. Hospitalization in dermatology unit
2. Same treatment for rash
3. Stop Telaprevir
4. Stop Telaprevir and PEG-IFN and Ribavirin

At week 10, Telaprevir stopped.

- During the follow-up:
  - Resolution of rash
  - Resolution of anal pruritus
  - EPO always needed
- PEG-IFN + ribavirin until 08-Jun-2012

HCV-RNA evolution

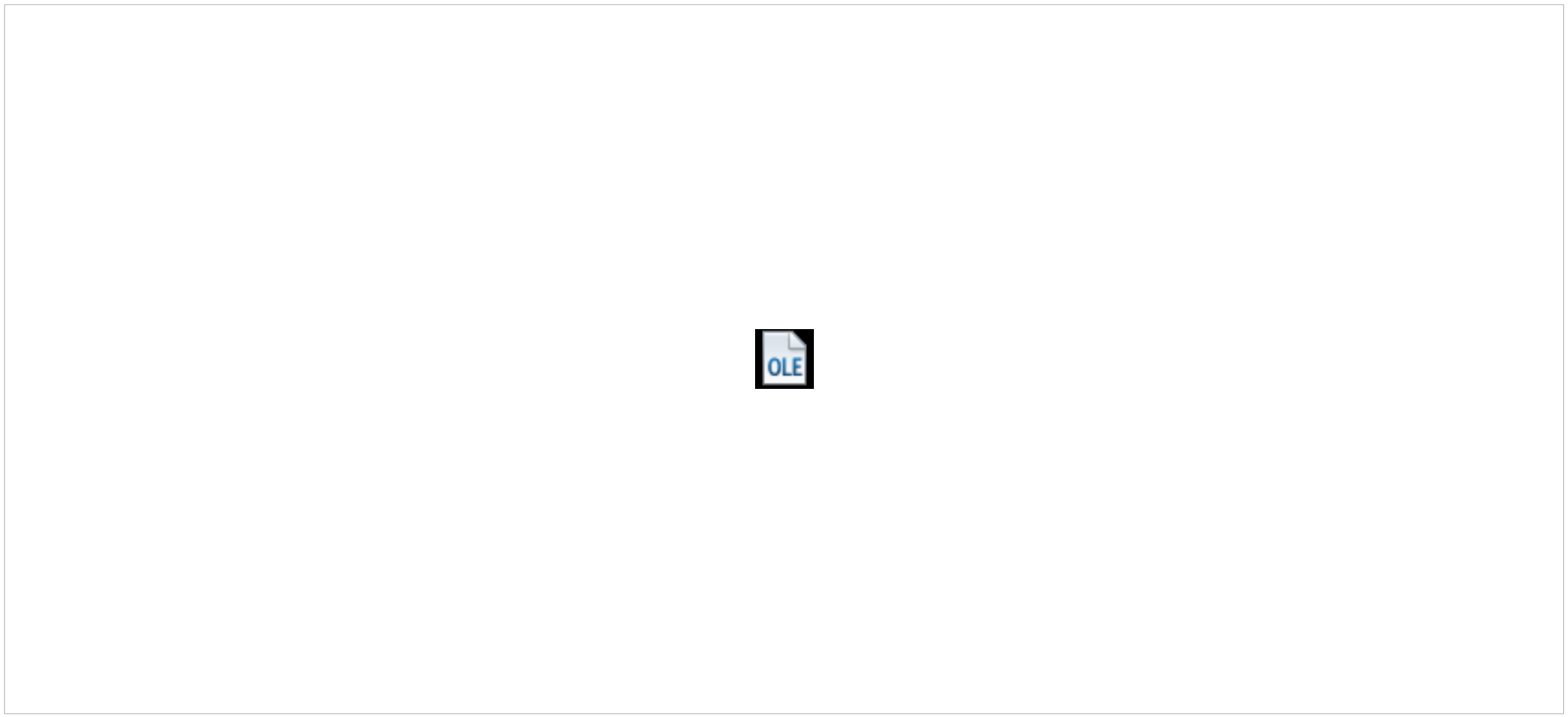


Henri, end of 2012

- Virological relapse.....
- Sofosbuvir is not available….
- Wait… and see!

Evolution of liver stiffness

kPa

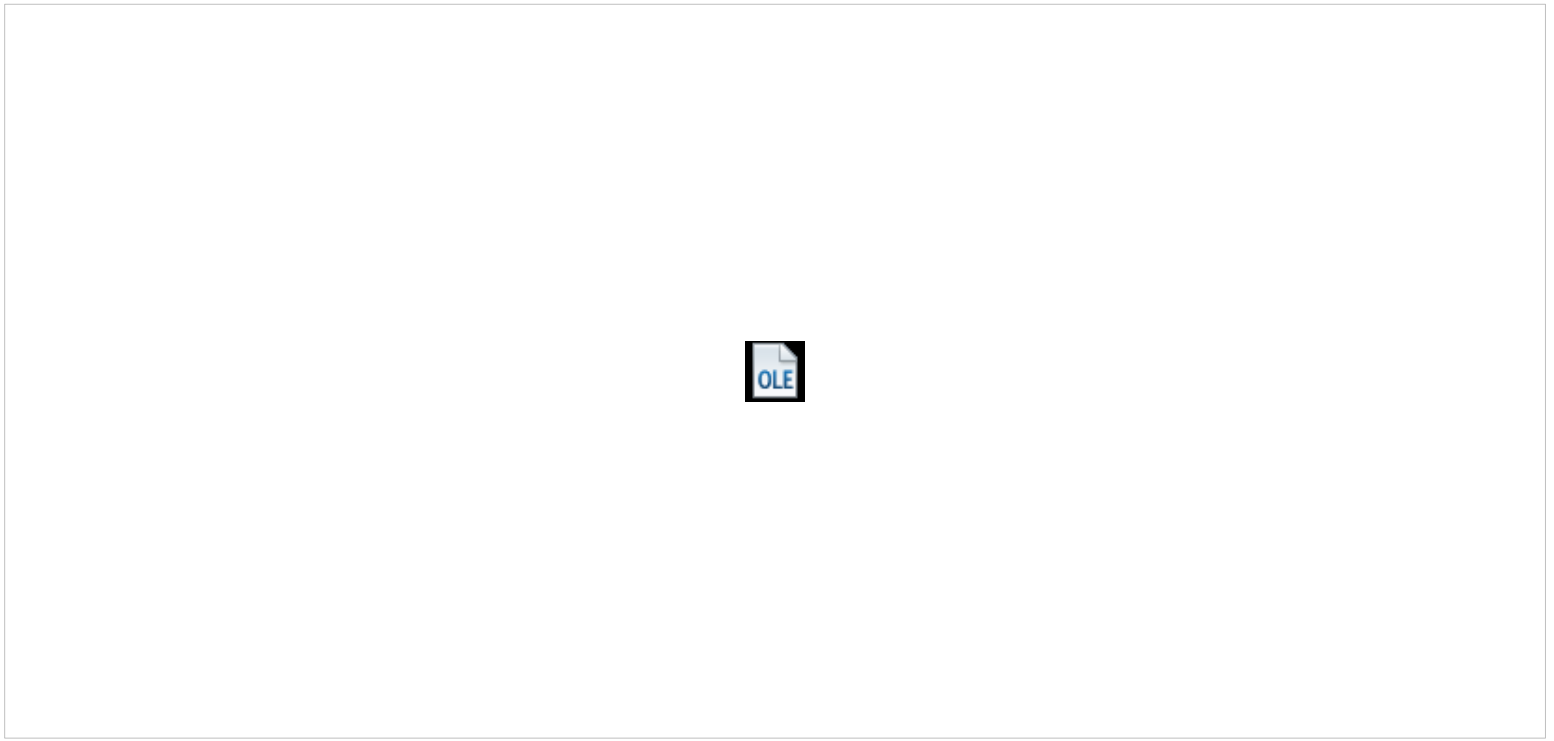


Henri, oct 2013

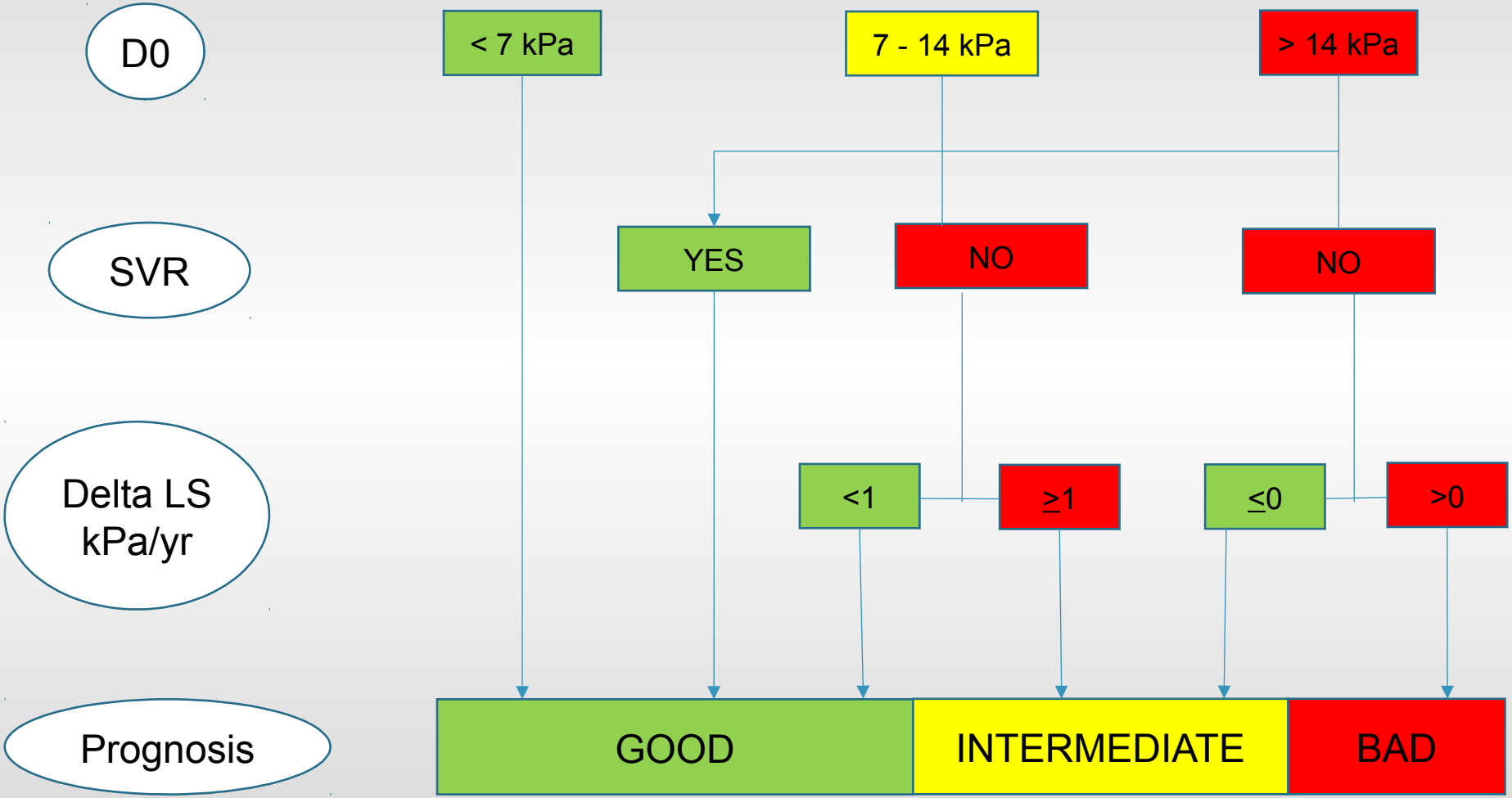
- Clinical Trial
- SIRIUS study
- Sofosbuvir + Ledipasvir: 21-Oct-2013 to 07-Apr-2014
- SVR…

Evolution of liver stiffness

kPa



Liver stiffness and SVR in HCV patients



Vergniol J et al. Hepatology 2014

Take home message

- Liver stiffness is associated with the severity of cirrhosis
- Liver stiffness offers a mean for rapid discrimination of different steps of progression within the stage of compensated cirrhosis.
- SVR and no increase of LS are associated with good prognosis

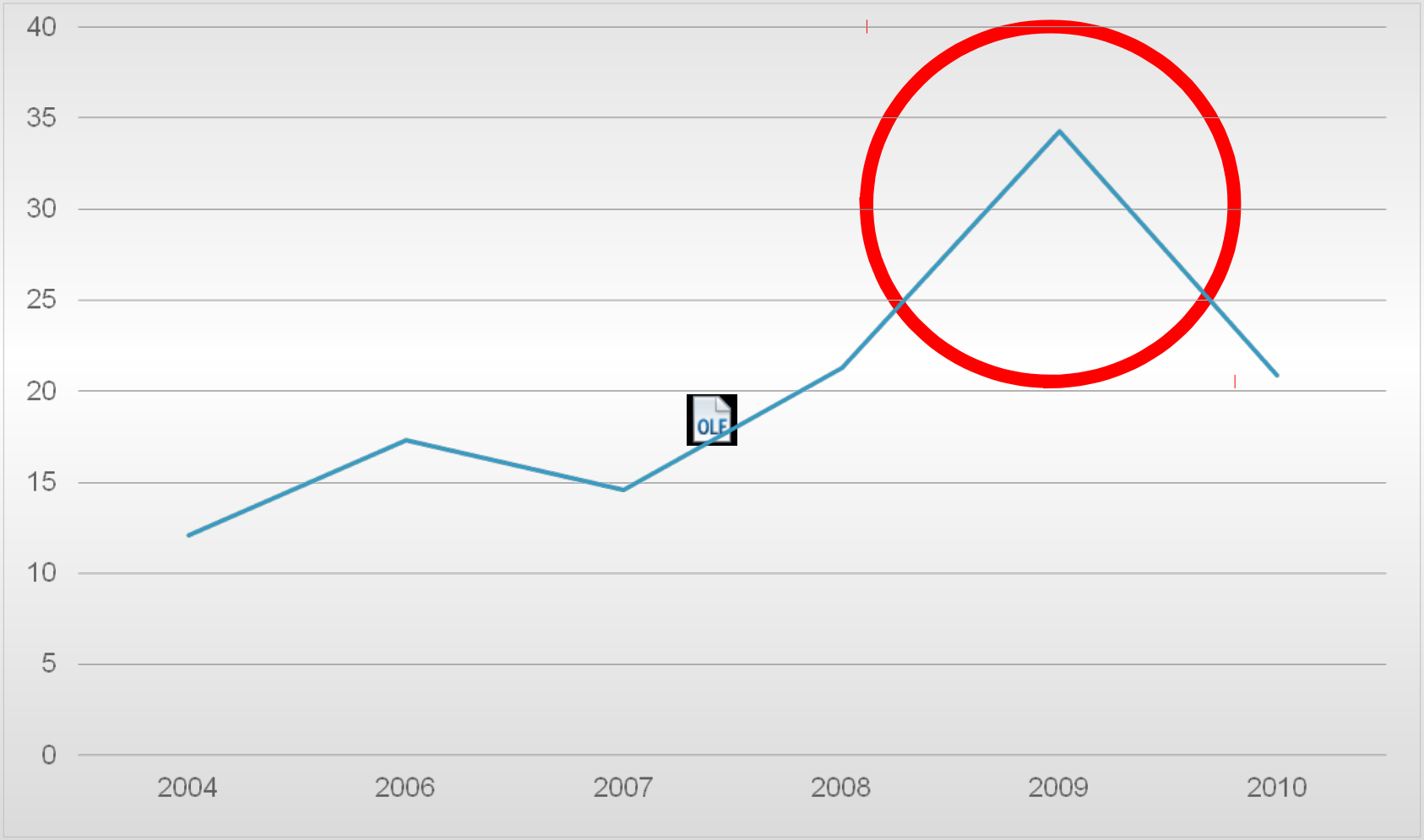
Case 3. Anne

- Birthdate: sept 1945
- BMI 33 kg/m²
- HCV infection, Genotype 1b
- Transfusion
- Diagnosis: 2004
- No alcohol
- Endoscopy: oesophageal varices 2 (Propranolol)
- US: no CHC

Anne

- Treatement PEG-IFN + ribavirin (Jul 2005 – Jan 2006)
  - No response
- Follow-up using liver stiffness until 2010

Anne – Liver stiffness

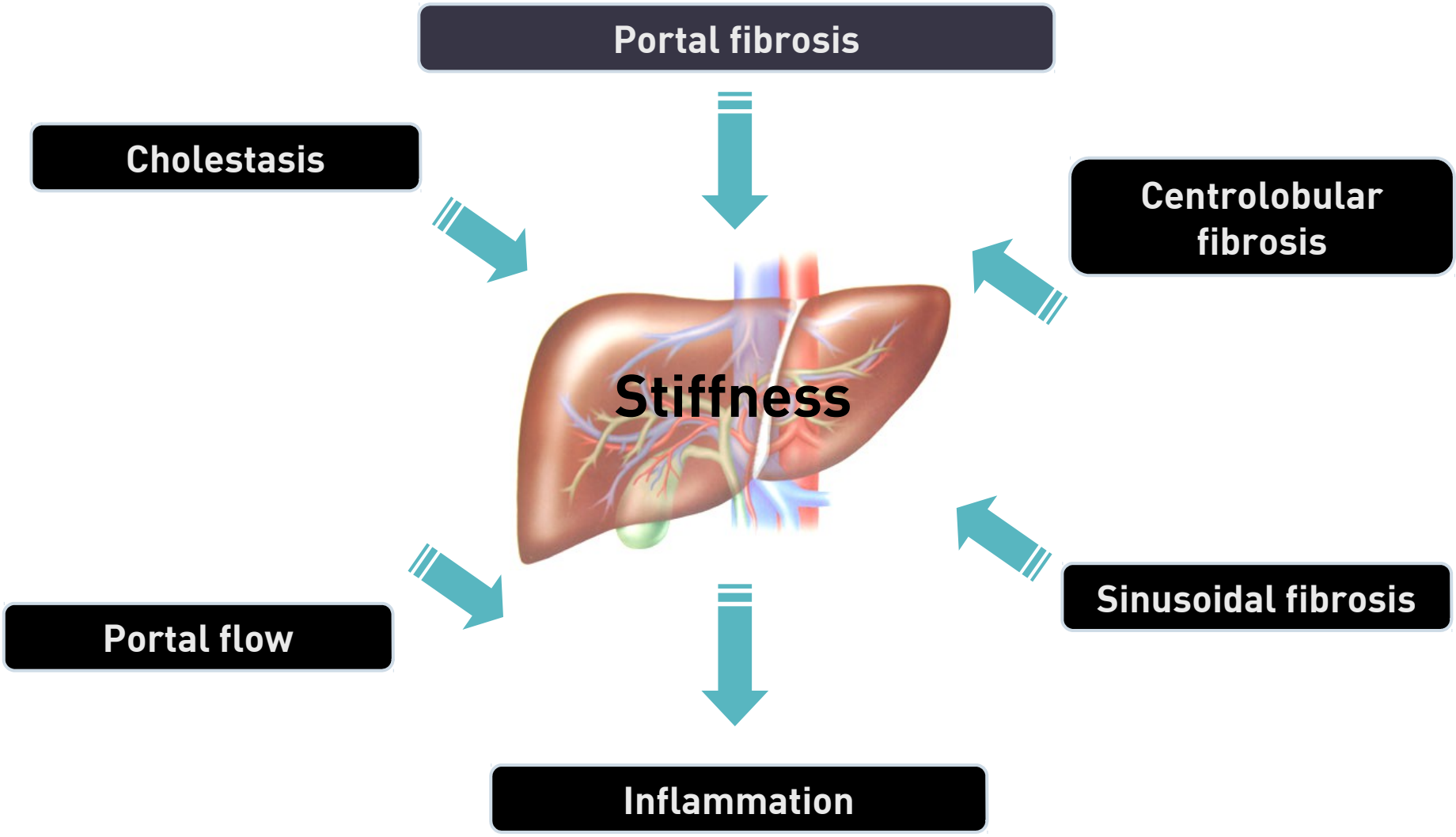


Fibroscan interpretation

		LSM (kPa)		
		< 7.1	7.1 – 12.5	≥ 12.5
IQR/LSM	≤ 0.10	Excellent		
	0.10 – 0,30	Moderate		
	> 0.30		Bad	

Lucidarme D et al. Hepatology 2009;49:1083-9.
Boursier J et al. Hepatology 2012

Factors associated with Liver Stiffness



Anne

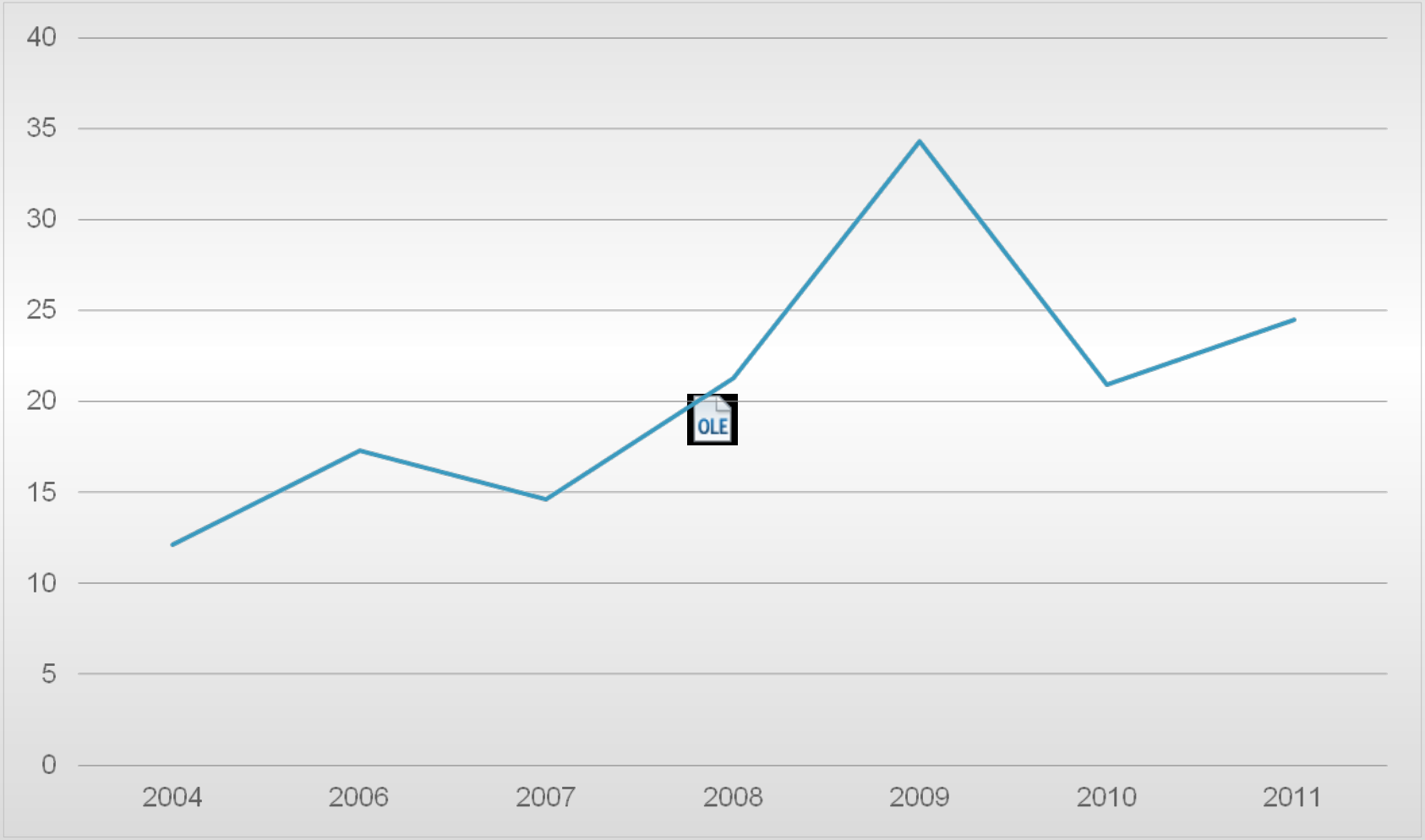
- Sept 2010: HCC 3 cm
  - Treatment by radiofrequency

Anne – 2nd treatment

- Child B cirrhosis
- PEG-IFN + ribavirin (18-Mar-2011 to 28-Apr-2011)
- Then Boceprevir added
- Intolerance to treatement
- Stop treatment 07-May-2011

- November 2011 : new nodule 13 mm
- AFP: 18 ng/mL
- Waiting for liver transplantation

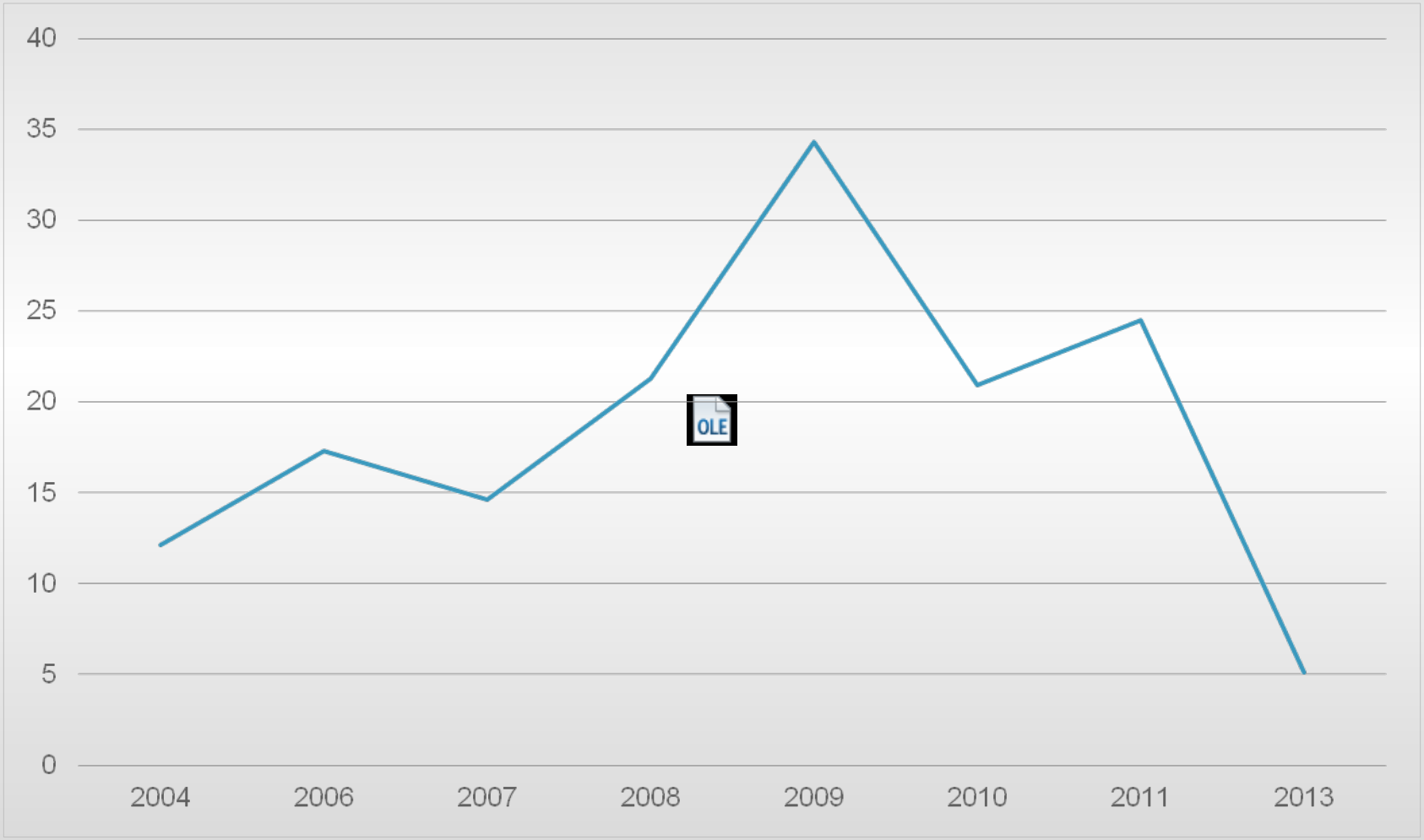
Anne – Liver stiffness



Anne – Liver transplantation 11-Nov-2011

- Treatment
  - Tacrolimus
  - Mycophenolate
  - Hypertension treatment

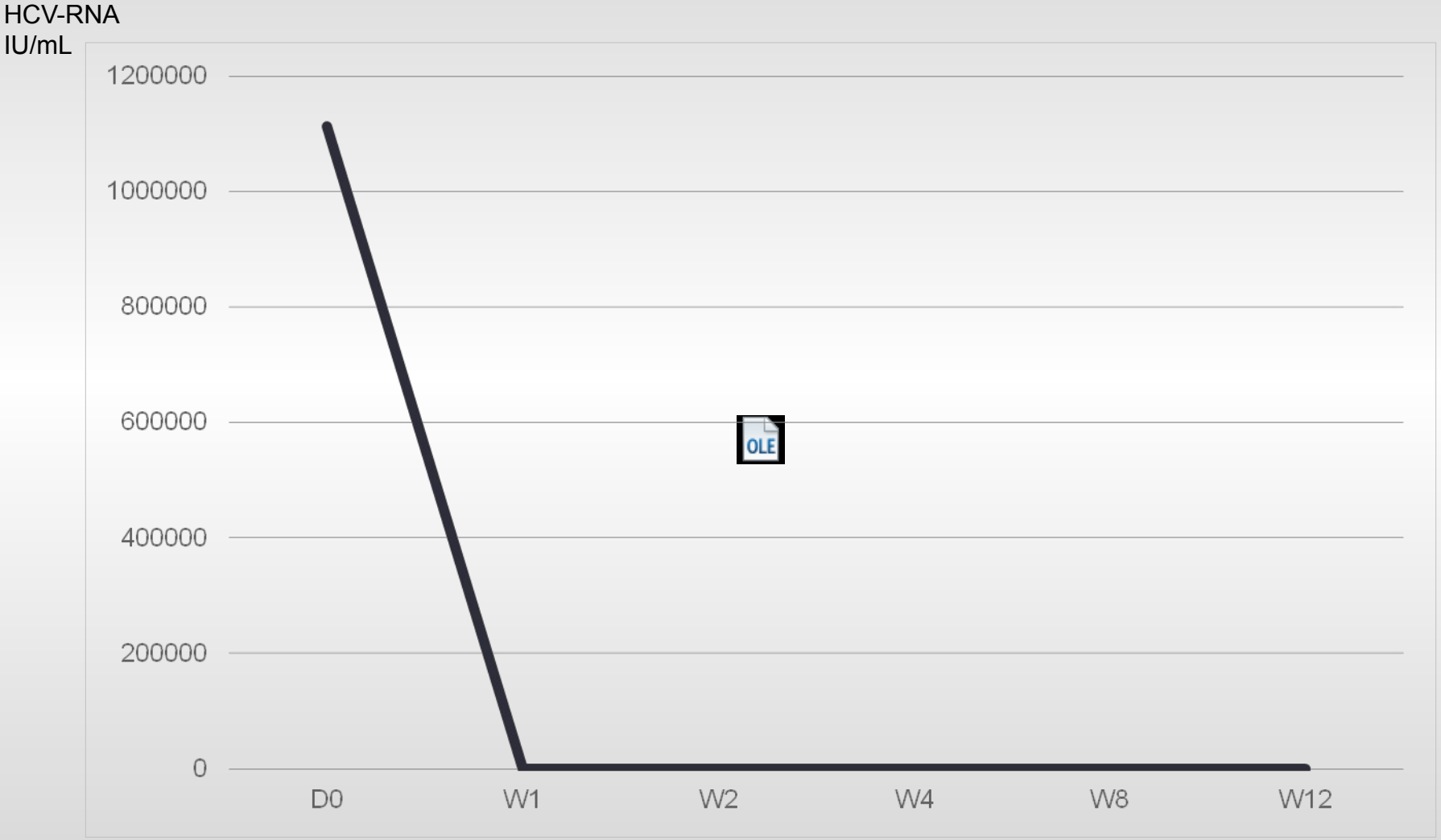
Anne – Liver stiffness



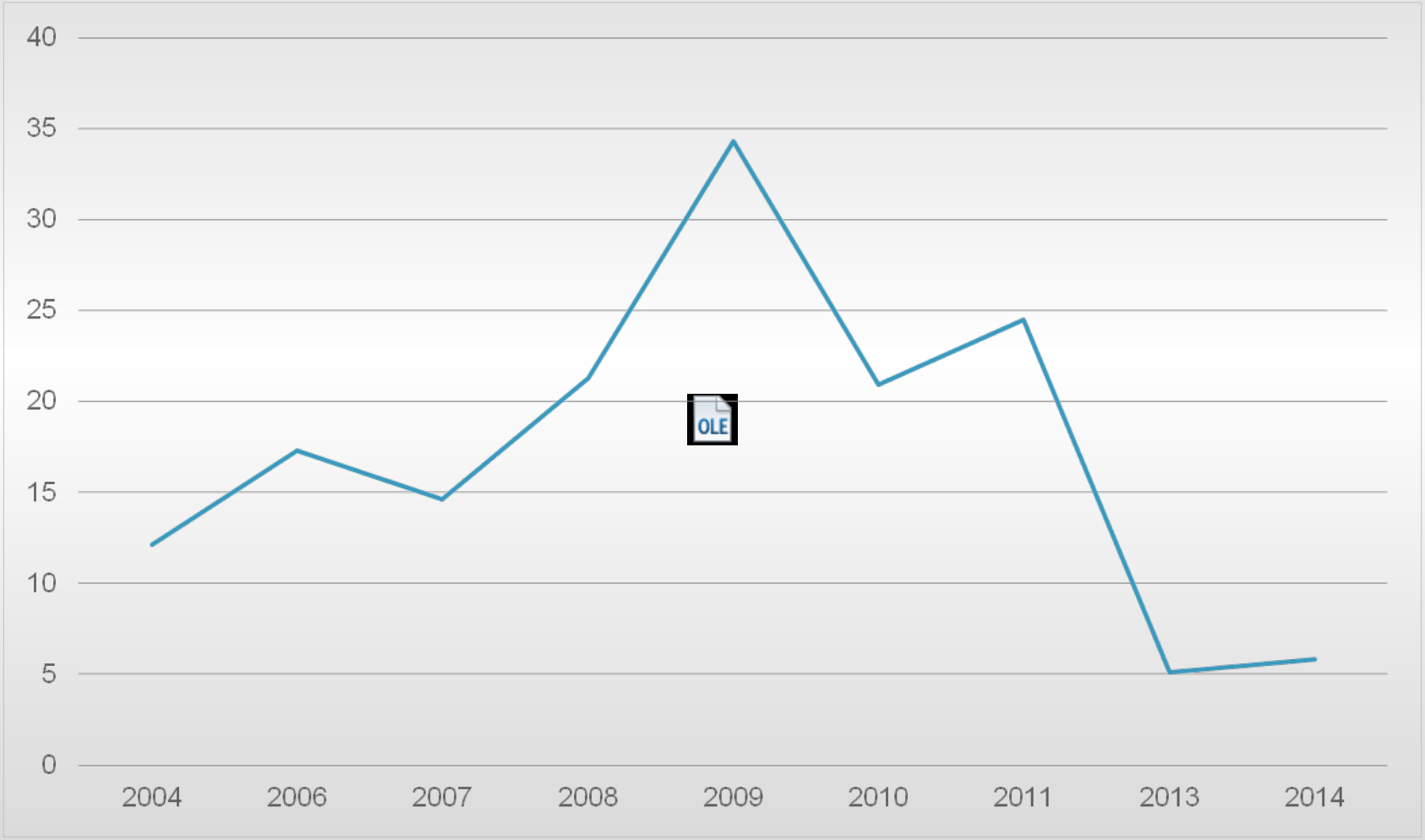
Anne – 3rd treatment

- HCV recurrence after liver transplantation
- Sofosbuvir + Daclatasvir
  - 23-Sep-2014 to 16-Dec-2014

Anne – Viral load with SOF-DCV



Anne – Liver stiffness



Anne – Follow-up…

- FU4 scheduled on 13-Jan-2015….

Take home message

- Adequate liver stiffness measurement
  - 10 measurements
  - IQR/LS < 30%
- Interaction HCV NASH?

What the clinician needs to know…

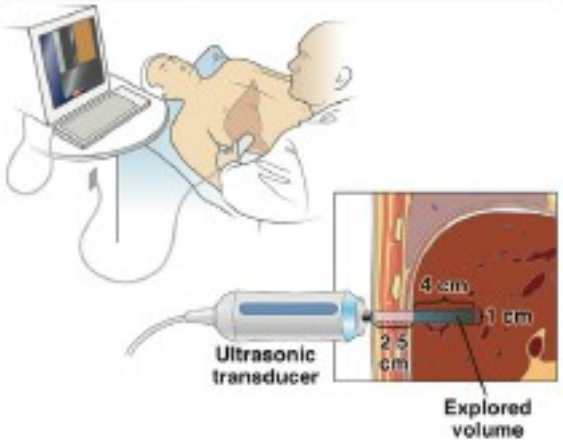
Chronic Hepatitis C
- Cutoffs to know:
  - 7.3 kPa suggests significant fibrosis
  - 12.5 kPa suggests cirrhosis

Chronic Hepatitis B
- Must know: HBV DNA
- Cutoffs to know:
  - 11.7 kPa suggests cirrhosis
  - If normal ALT: consider treating at 9.0 kPa

NAFLD
- Cutoff to know:
  - 10.3 kPa suggests cirrhosis
- Consider performing CAP assessment
- Consider XL probe for obese patients

Transient elastography: what the clinician needs to know

1. What is the underlying disease?
2. Other evidence of advanced liver disease? (e.g., perform a physical exam and check serological tests for fibrosis)
3. What can affect the test?
   a. Is the patient fasting?
   b. What is the body mass index?
   c. What is the burden of inflammation? (e.g., check ALT)
   d. Is the patient actively drinking alcohol?
   e. Is there evidence of cholestasis?



Alcoholic liver disease
- Must also know: drinking status
- Cutoffs to know:
  - 22.7 kPa suggests cirrhosis if drinking
  - 12.5 kPa suggests cirrhosis if abstinent

Biliary liver disease
- Must also know: alkaline phosphatases
- Cutoff to know:
  - 17.9 kPa suggests cirrhosis

Portal hypertension in cirrhotic patients
- Cutoffs to know:
  - 20.0 kPa suggests HVPG ≥ 10
  - 50.7 kPa suggests high risk of variceal bleeding

Tapper EB et al. Clin Gastroenterol Hepatol 2015;13:27-36

Thanks


Modifiez les styles du texte du masque
Deuxième niveau
Troisième niveau
Quatrième niveau
Cinquième niveau