HBV : clinical case

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Disclosures

BMS : Speaker symposium, board , research support

MSD : speaker symposium , board

Gilead : speaker symposium, board

Janssen : speaker symposium, board

Abbvie : speaker symposium, board

Echosens : speaker symposium

Intercept : speaker symposium, board, soutien recherche

Patient case

Age / Gender	58-years / male
HBV diagnosed	2015 (HIV, HCV, HDV -)
Route of transmission	Mother-to-child
ALT	32 IU/ml
Hbe Ag	Negative
HBV DNA	894 IU/ml
qHBs Ag	578 IU/ml
Platelets	158 IU/ml
Liver stiffness	8.6 kPa
Ultrasound	Normal

How do you manage this patient?

1. Inactive carrier : monitor every 3 months

2. Inactive carrier : monitor every year

3. Hbe (-) hepatitis with fibrosis : treatment

4. Indication for liver biopsy

New EASL classification

	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	$>10^7$ IU/ml	10^4-10^7 IU/ml	<2,000 IU/ml°°	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

EASL guidelines 2017

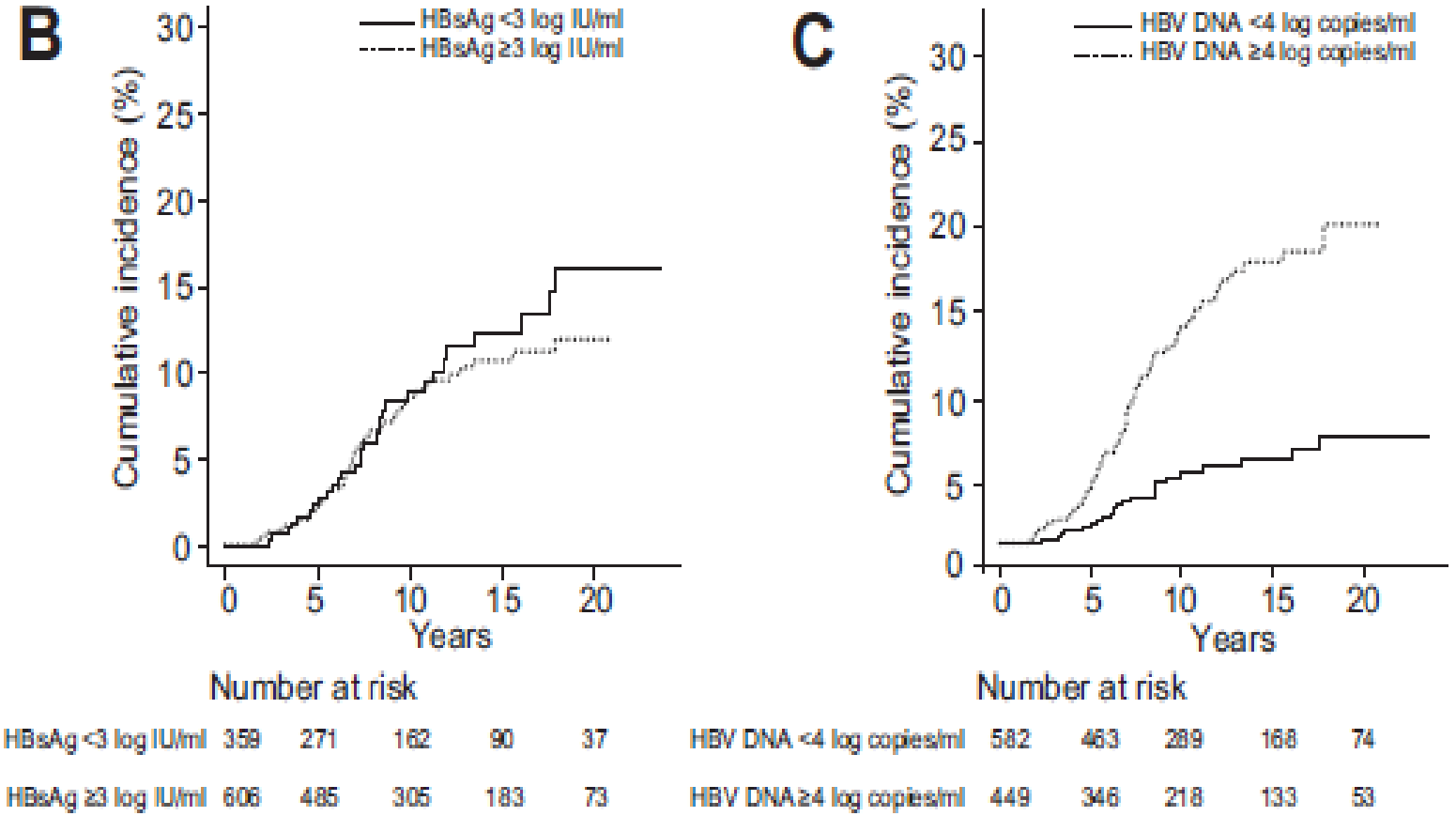
Diagnostic performance of qHBsAg

	N = 1 529		
Predictive Criteria	HBV DNA <2000 IU/mL	HBsAg <1000 IU/mL	HBV DNA <2000 IU/mL and HBsAg <1000 IU/mL
Sensitivity	1.0	0.71	0.71
Specificity	0.73	0.50	0.85
Positive predictive value	0.79	0.59	0.83
Negative predictive value	1.0	0.63	0.74
Diagnostic accuracy	0.87	0.61	0.78

*Inactive carriers versus all active CHB.

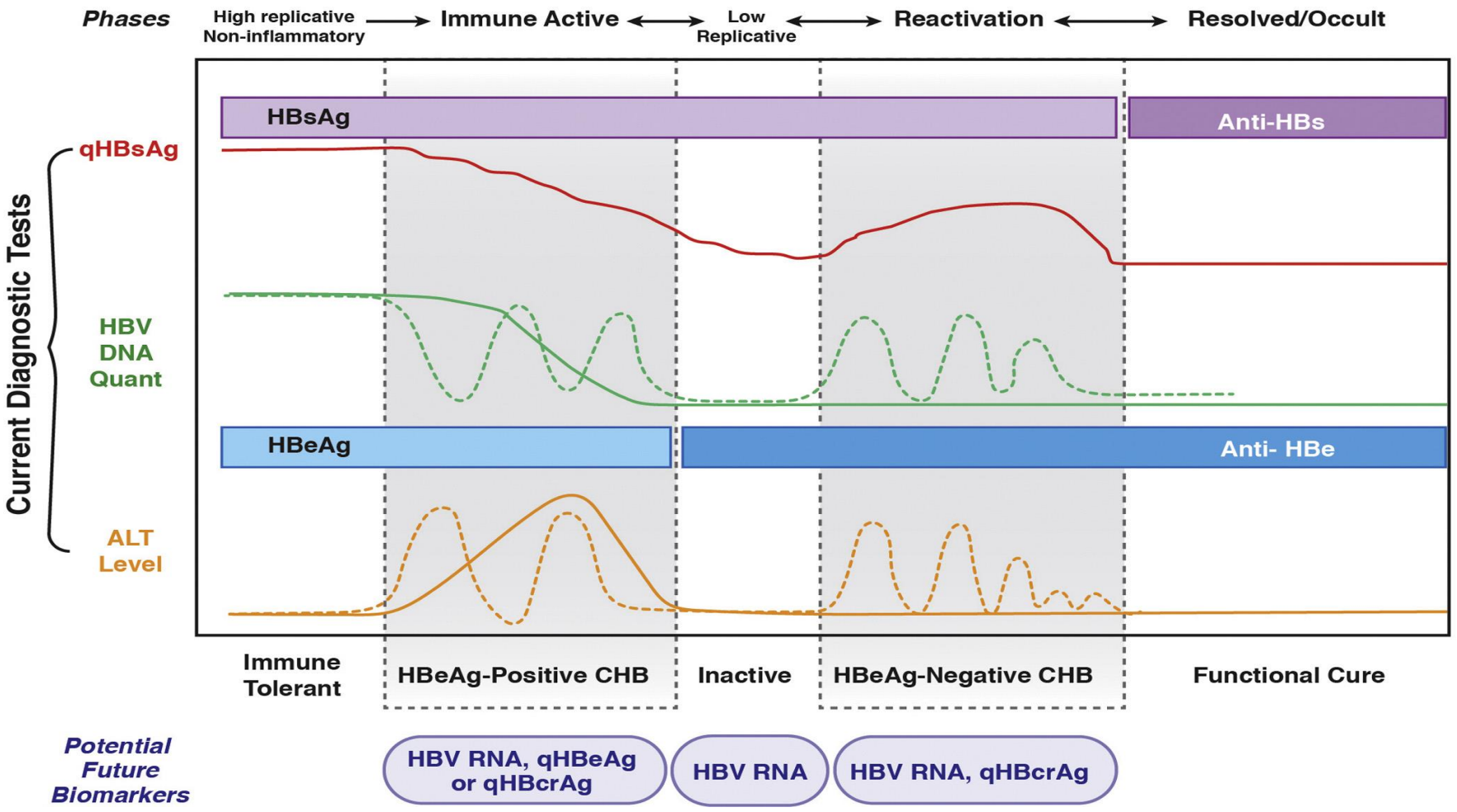
Liu et al, Hepatology 2016

Pronostic performance of qHBsAg



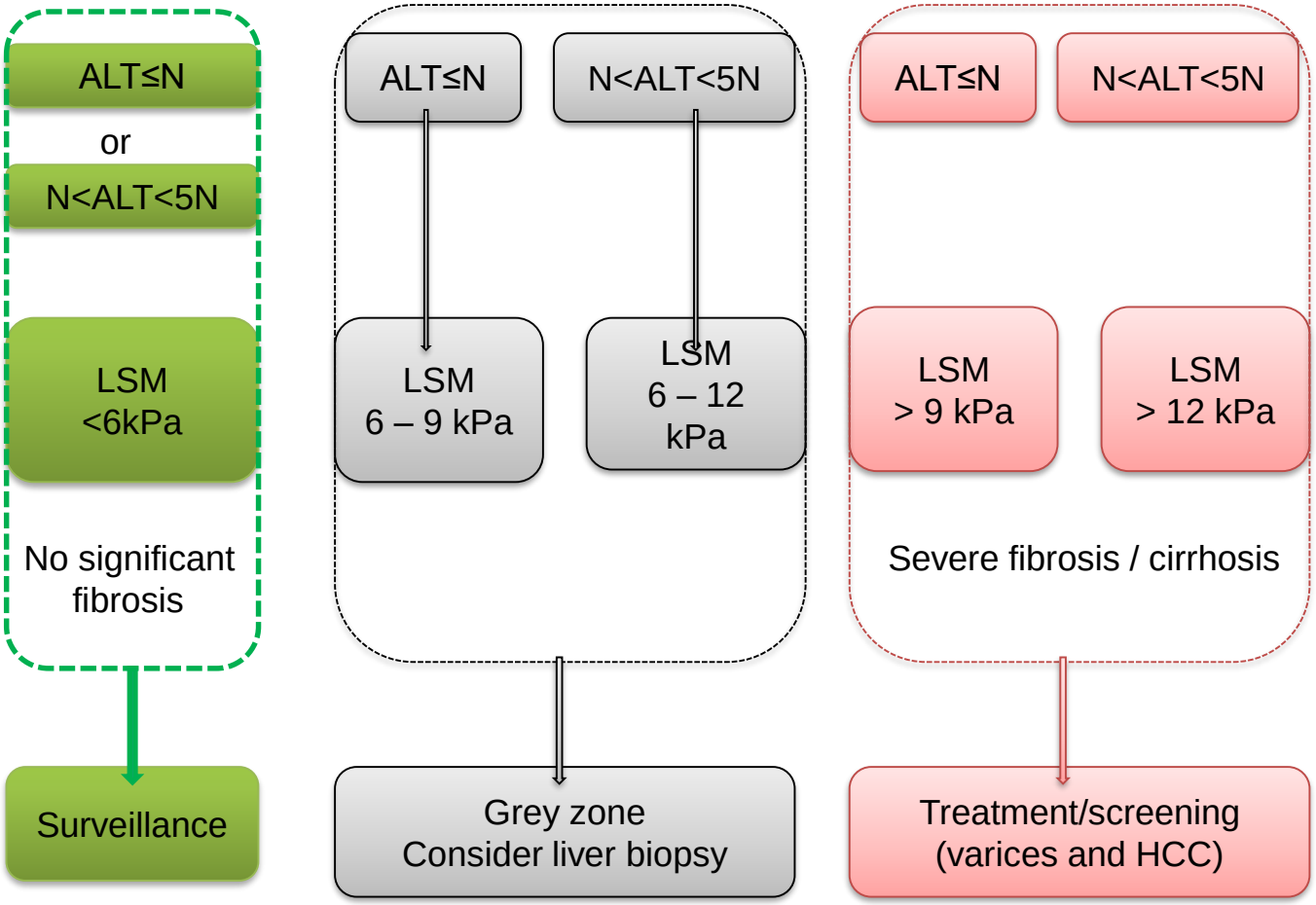
Tada et al, J Hepatol 2016

Phases of HBV infection



Terrault et al, Gastroenterology 2019

Performance of transient elastography

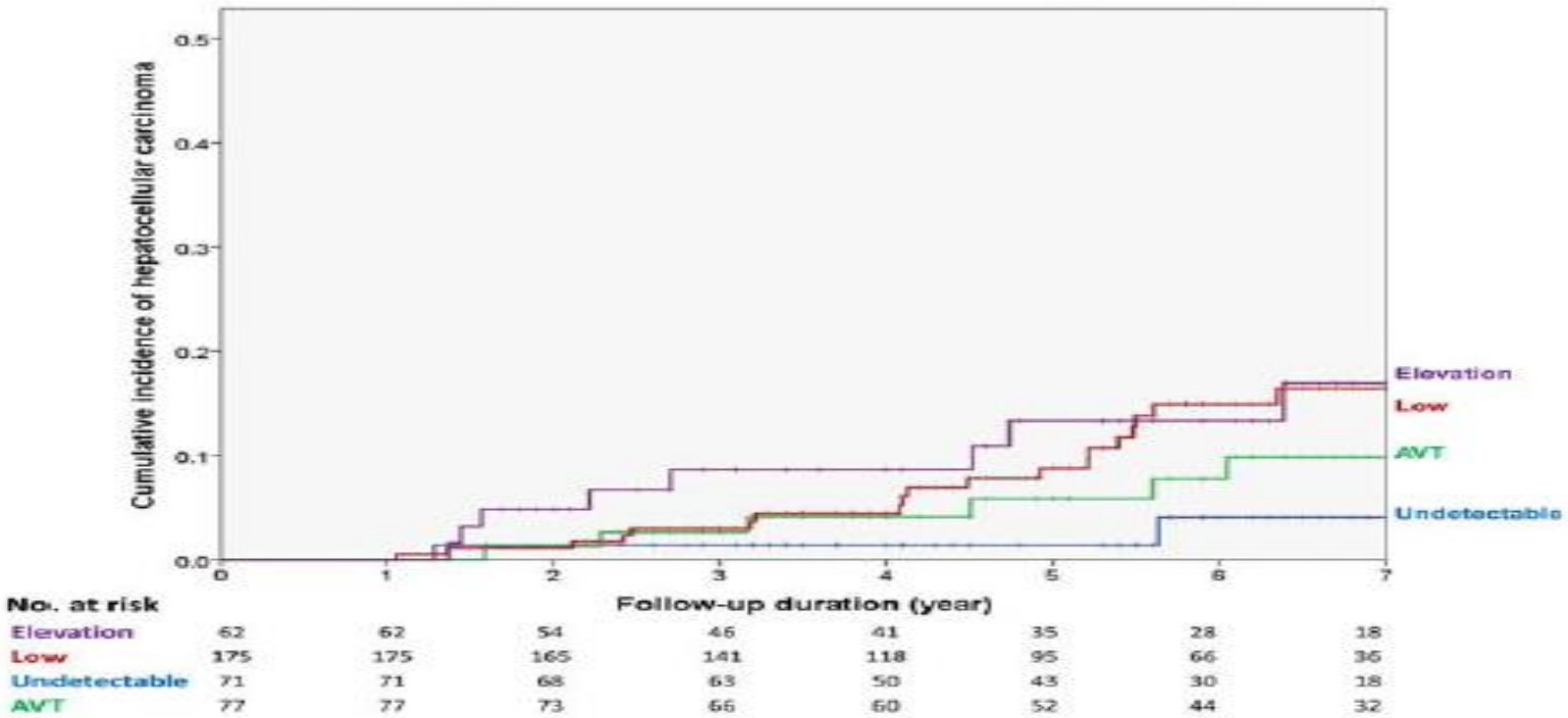


EASL-ALEH Clinical Practice Guidelines. J Hepatol 2015;63:237–264

Inactive cirrhosis should be treated

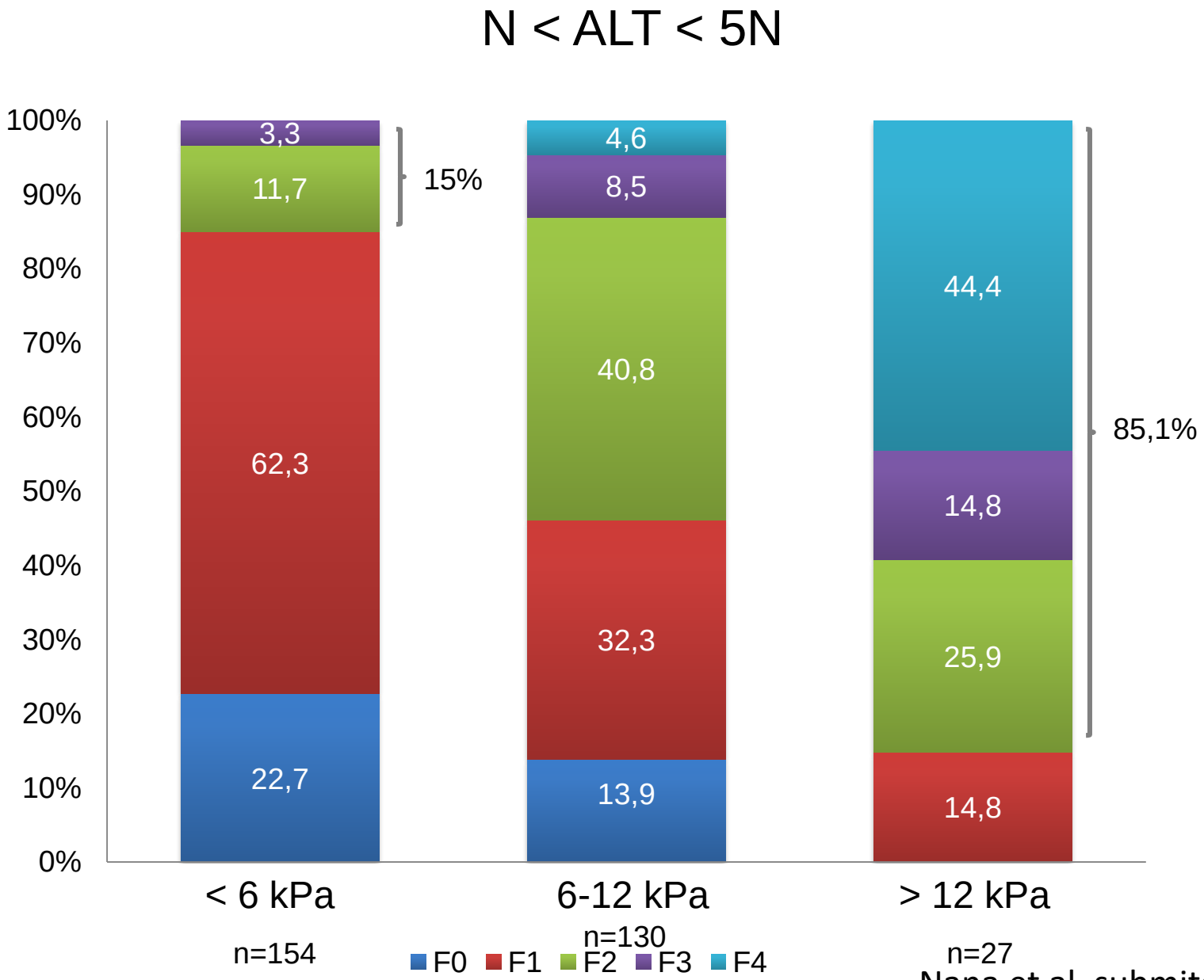
385 patients with cirrhosis and HBV DNA < 2 000 IU/ml

Median follow-up : 5.8 years



Sin et al, Hepatology 2015

Prevalence of fibrosis stages according to EASL



Nana et al, submited

Patient case

Biopsy : METAVIR F3 : TDF started in 2014

	M6	M12	M18	M24	M30	M36
ALT (IU/L)	32	24	22	25	25	21
HBV DNA (IU/ml)	<12	< 12	< 12	< 12	<12	<12
qHBsAg	672	423	204	98	74	59
Platelets	152	166	167	170	171	169
LS (kPa)	-	9.4	-	6.2	-	7.1
US	Normal	Normal	Normal	Normal	Normal	Normal

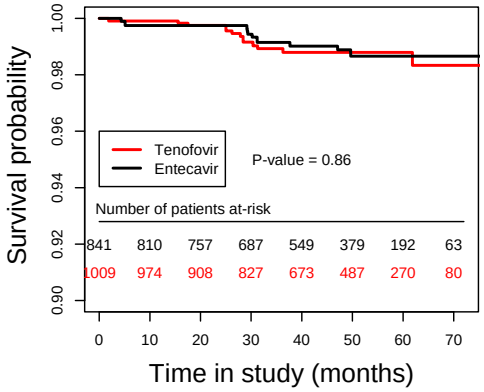
How do you manage this patient?

1. Continue ETV
2. Switch to TDF
3. Add IFN
4. Stop NUC therapy

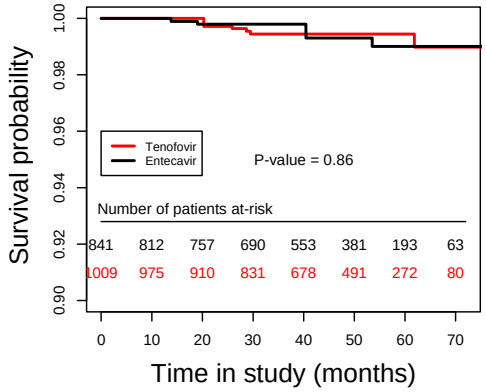
ETV vs TDF : is there a difference?

Data from the HEPATHER cohort

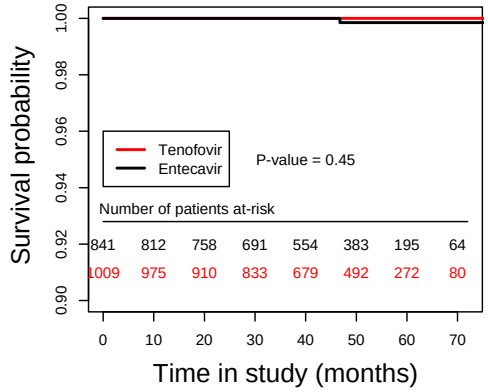
Hepatocellular carcinoma



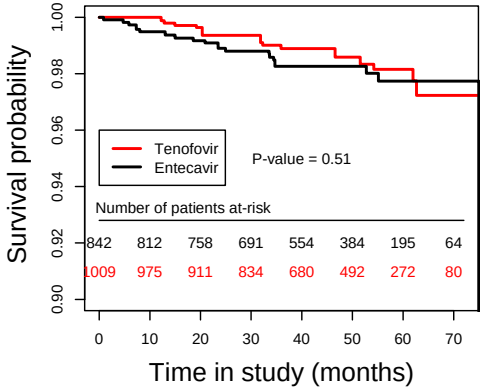
Decompensated cirrhosis



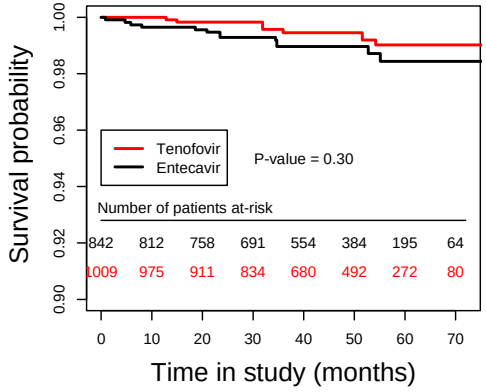
Liver transplantation



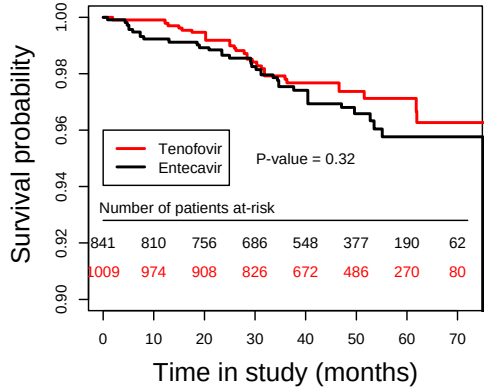
All-cause deaths



Liver-related deaths



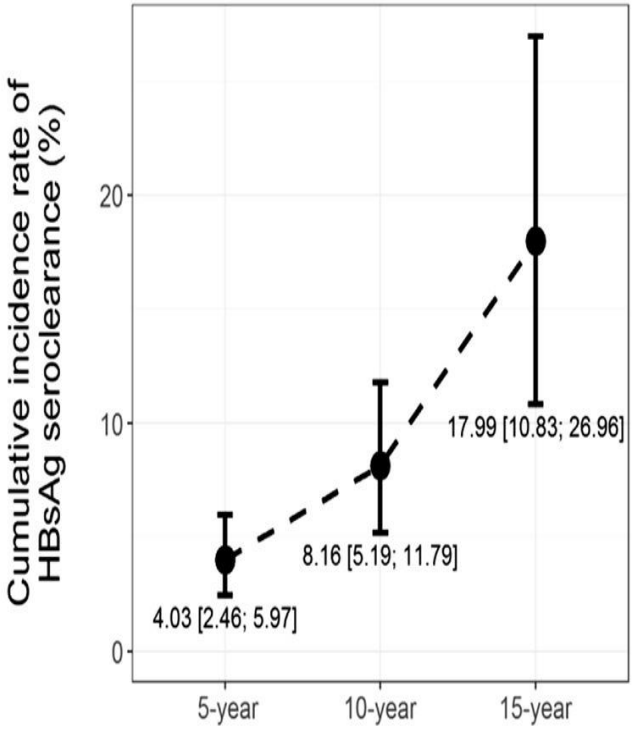
Composite endpoint

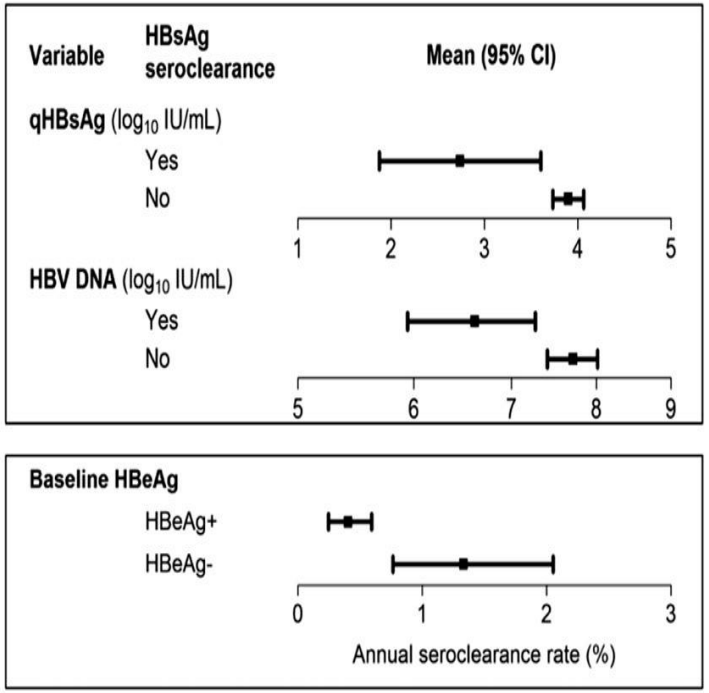


Pol et al, submited

Baseline qHBsAg predicts HBsAg clearance

- **Study purpose & design:** A systematic review and meta-analysis to determine the annual, 5-, 10-, and 15-year cumulative HBsAg seroclearance rate using data from 42,588 HBsAg positive treated and untreated persons in 34 studies.
- **Results:** The annual HBsAg seroclearance rate was 1.02% (95%CI: 0.79-1.27). Low baseline HBV DNA, quantitative HBsAg, and negative HBeAg were associated with a significantly higher HBsAg seroclearance rate.

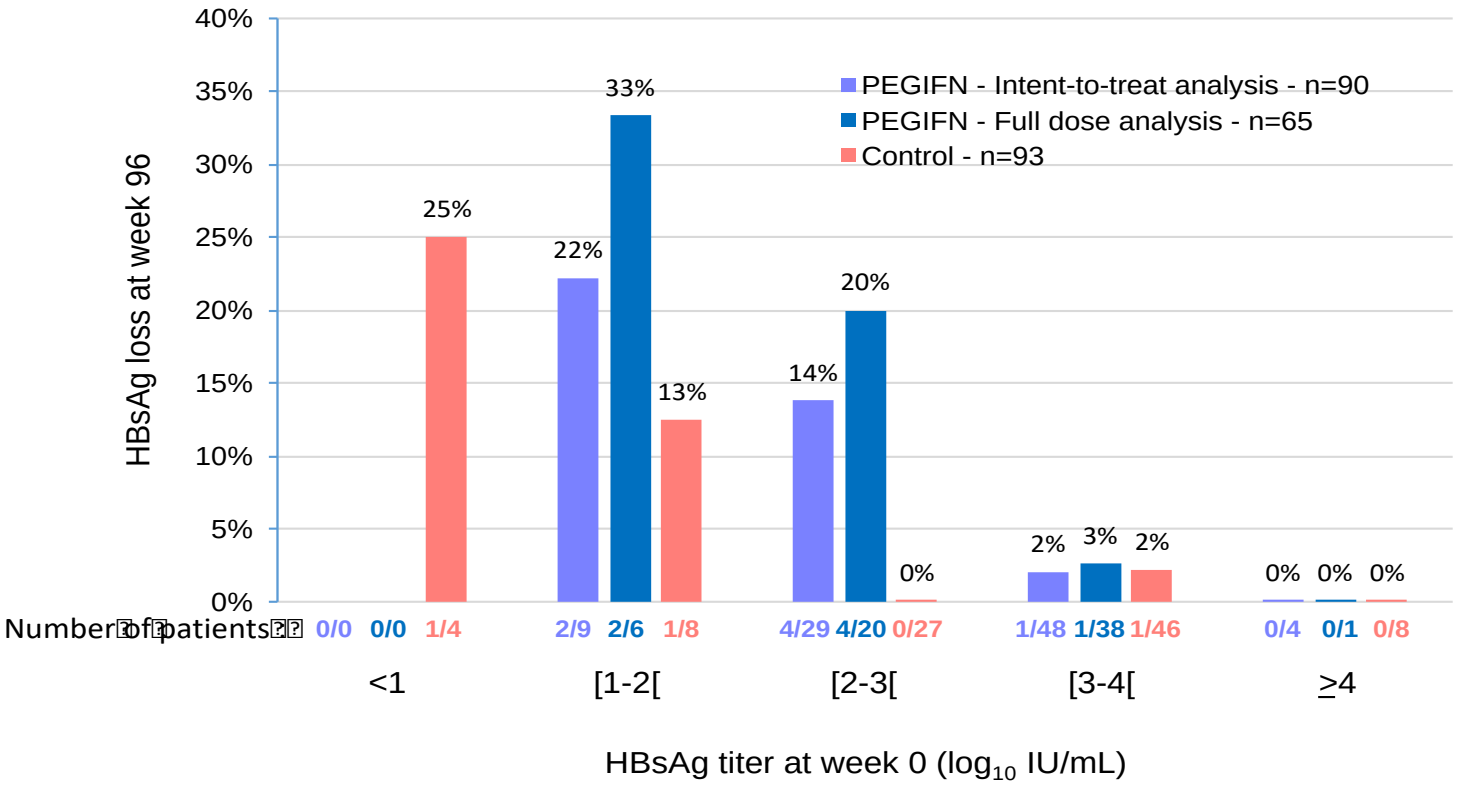




Gastroenterology

Yeo et al. Gastroenterology 2019

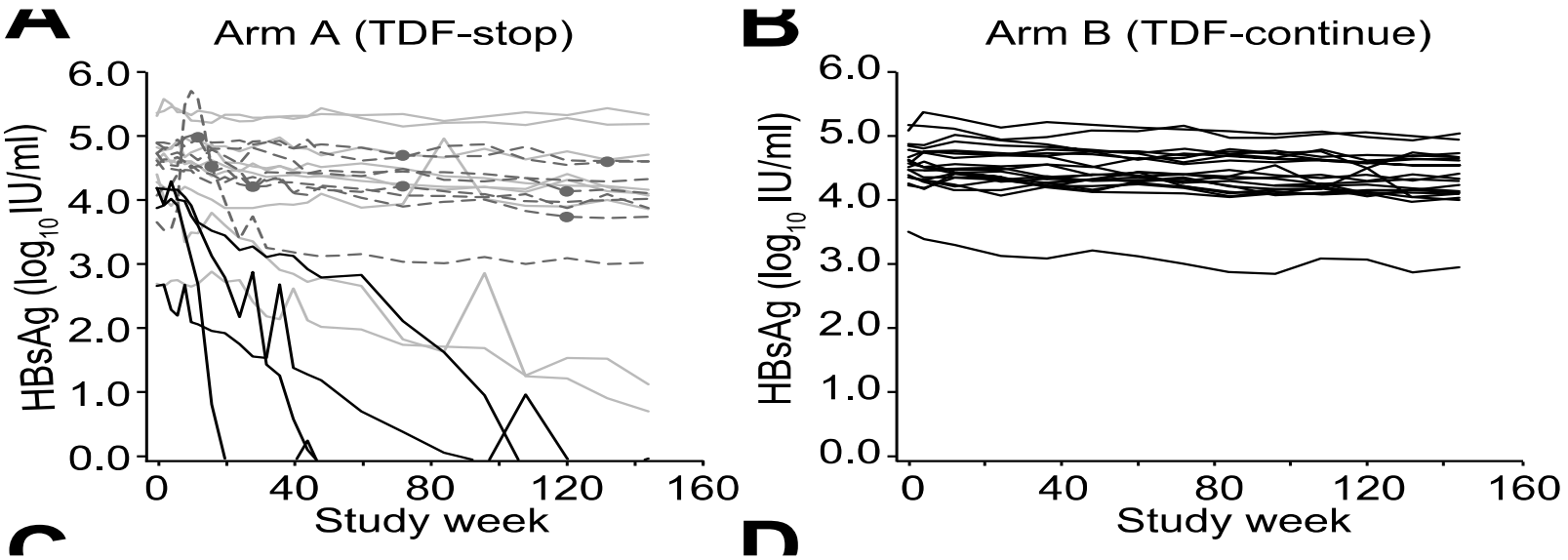
Sequential NUC + IFN strategy



Bourlière et al, Lancet Hepatogastro 2016

NUC cessation strategy

Randomized study in 42 patients with not detectable HBV DNA on TDF (3.5 years)

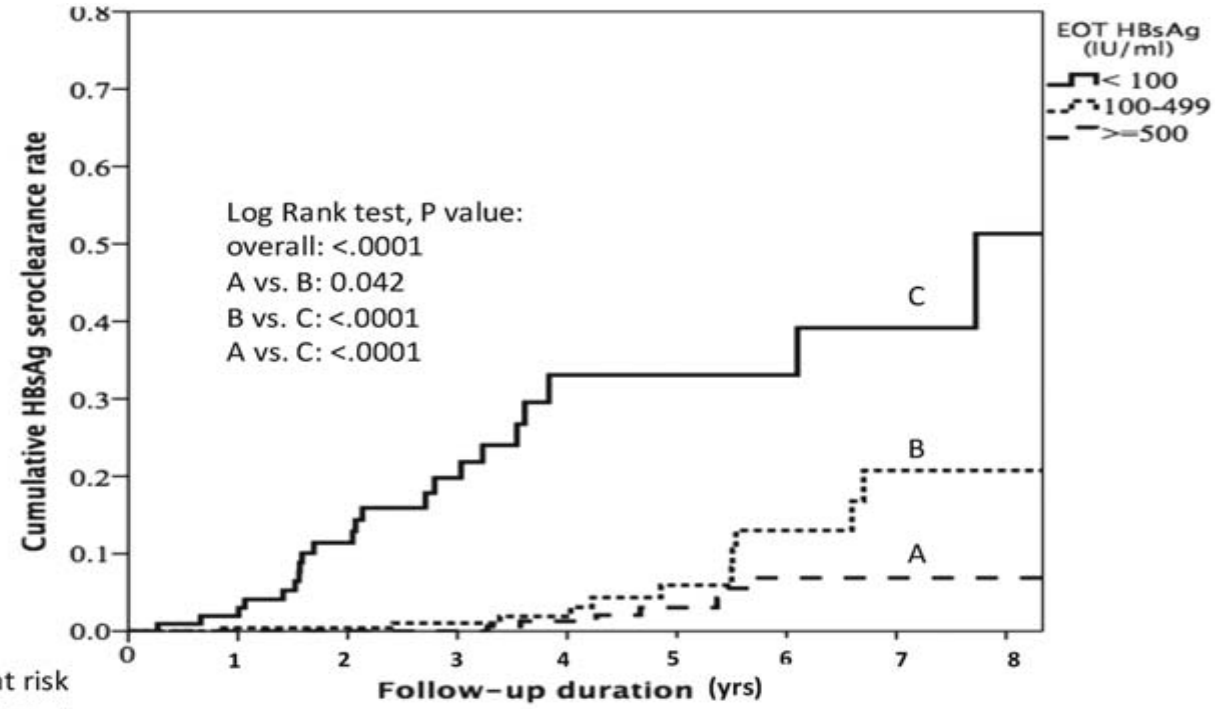


HBsAg loss in 19% of patients

Berg et al, J Hepatol 2017

NUC cessation strategy

Cohort study in 691 patients (cirrhosis : 44%) according to APASL rules



Patient at risk

	EOT HBsAg (IU/ml)									
A	>=500	303	92	61	39	17	14	12	8	4
B	100-499	274	232	185	129	86	52	30	18	8
C	<100	114	92	61	39	17	13	12	8	4

Jeng et al, Hepatology 2018

Patient case

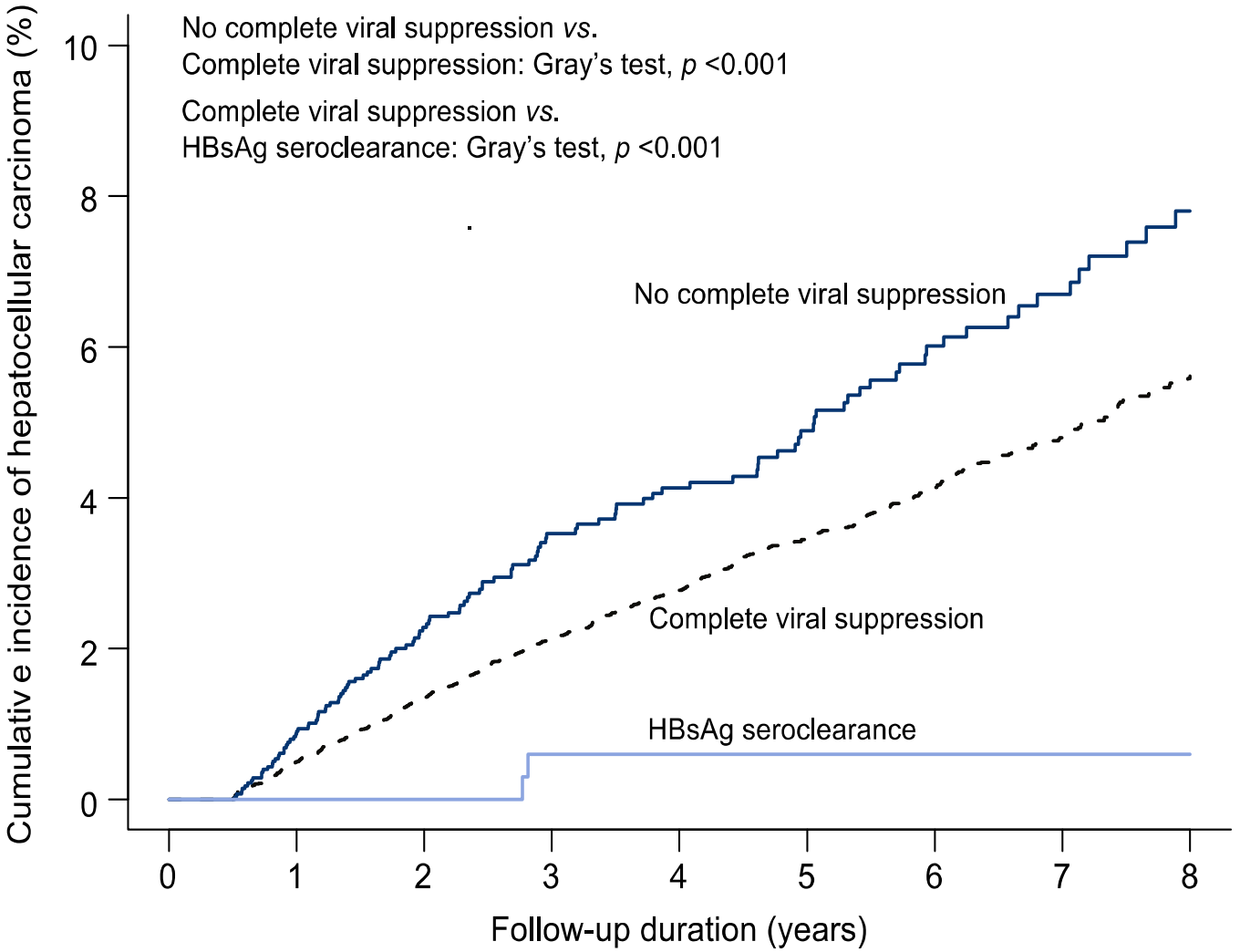
Biopsy : METAVIR F3 : TDF started in 2014

	M6	M12	M18	M24	M30	M60
ALT (IU/L)	32	24	22	25	25	21
HBV DNA (IU/ml)	<12	< 12	< 12	< 12	<12	<12
qHBsAg	672	423	204	98	74	negative
Platelets	152	166	167	170	171	175
LS (kPa)	-	9.4	-	6.2	-	6.4
US	Normal	Normal	Normal	Normal	Normal	Normal

How do you manage this patient?

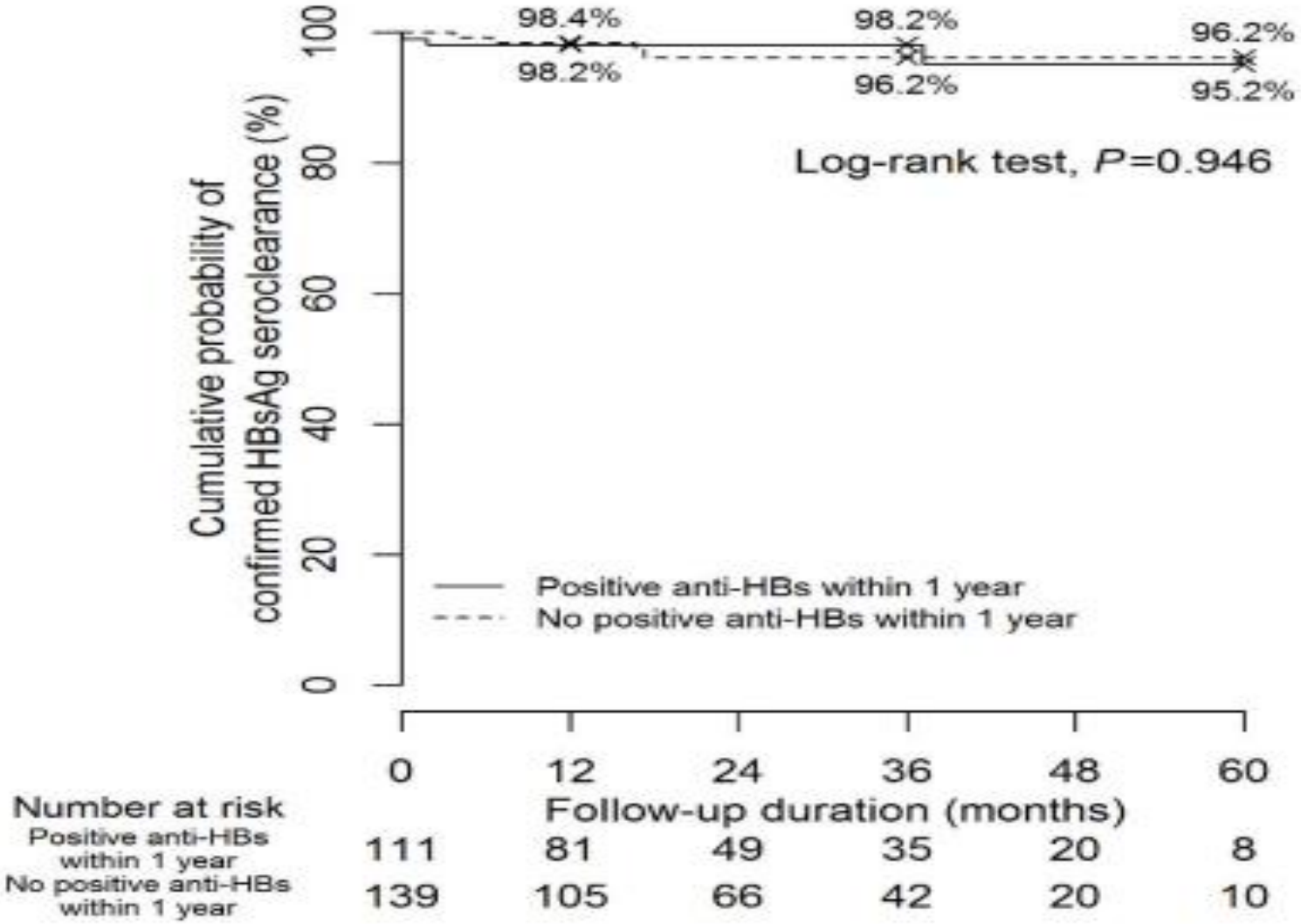
1. Continue ETV
2. Stop ETV now
3. Stop ETV after 6 months of consolidation
4. Stop ETV after HBs sero-conversion

HBsAg clearance is associated with a better prognosis



Yip et al, J Hepatol 2018

No impact of HBs sero-conversion



Yip et al, J Hepatol 2017

EASL guidelines on NUC cessation

- NAs should be discontinued after confirmed HBsAg loss, with or without anti-HBs seroconversion (Evidence level II-2, grade of recommendation 1).
- NAs can be discontinued in non-cirrhotic HBeAg-positive CHB patients who achieve stable HBeAg seroconversion and undetectable HBV DNA and who complete at least 12 months of consolidation therapy. Close post-NA monitoring is warranted (Evidence level II-2, grade of recommendation 2).
- Discontinuation of NAs in selected non-cirrhotic HBeAg-negative patients who have achieved long-term ($\geqslant$3 years) virological suppression under NA(s) may be considered if close post-NA monitoring can be guaranteed (Evidence level II-2, grade of recommendation 2).