

# HBV : clinical case

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# Disclosures

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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 <sup>7</sup> IU/ml	10 <sup>4</sup> -10 <sup>7</sup> IU/ml	<2,000 IU/ml <sup>oo</sup>	>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

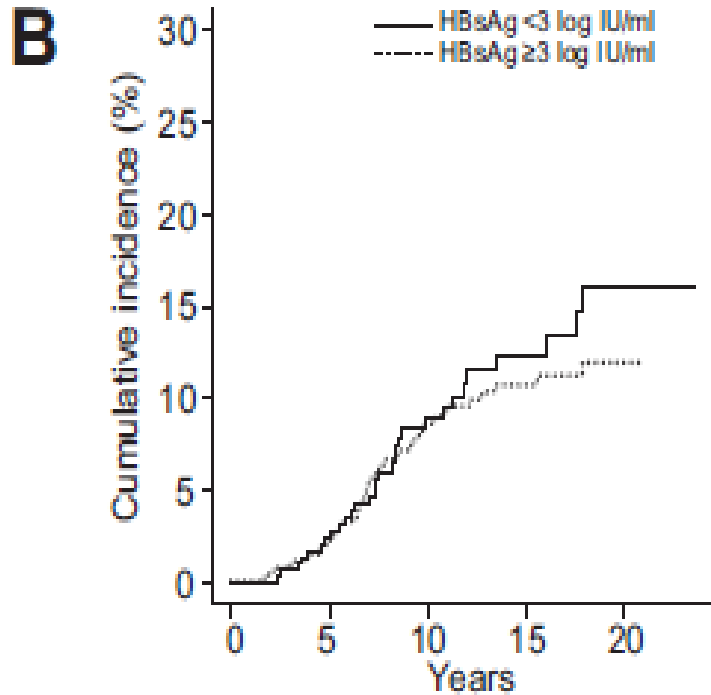
# Diagnostic performance of qHBsAg

N = 1 529

Predictive Criteria	HBV DNA <2000 IU/mL and HBsAg <1000 IU/mL		
	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

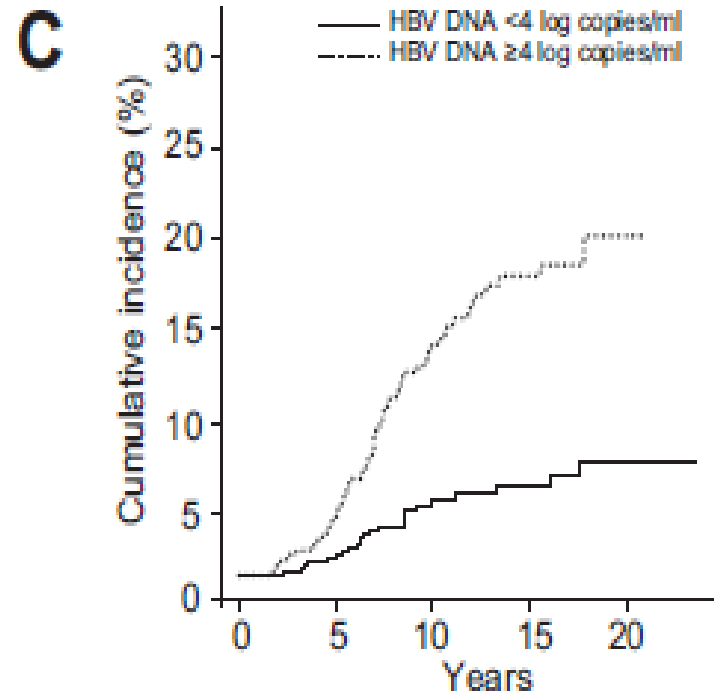
\*Inactive carriers versus all active CHB.

# Pronostic performance of qHBsAg



Number at risk

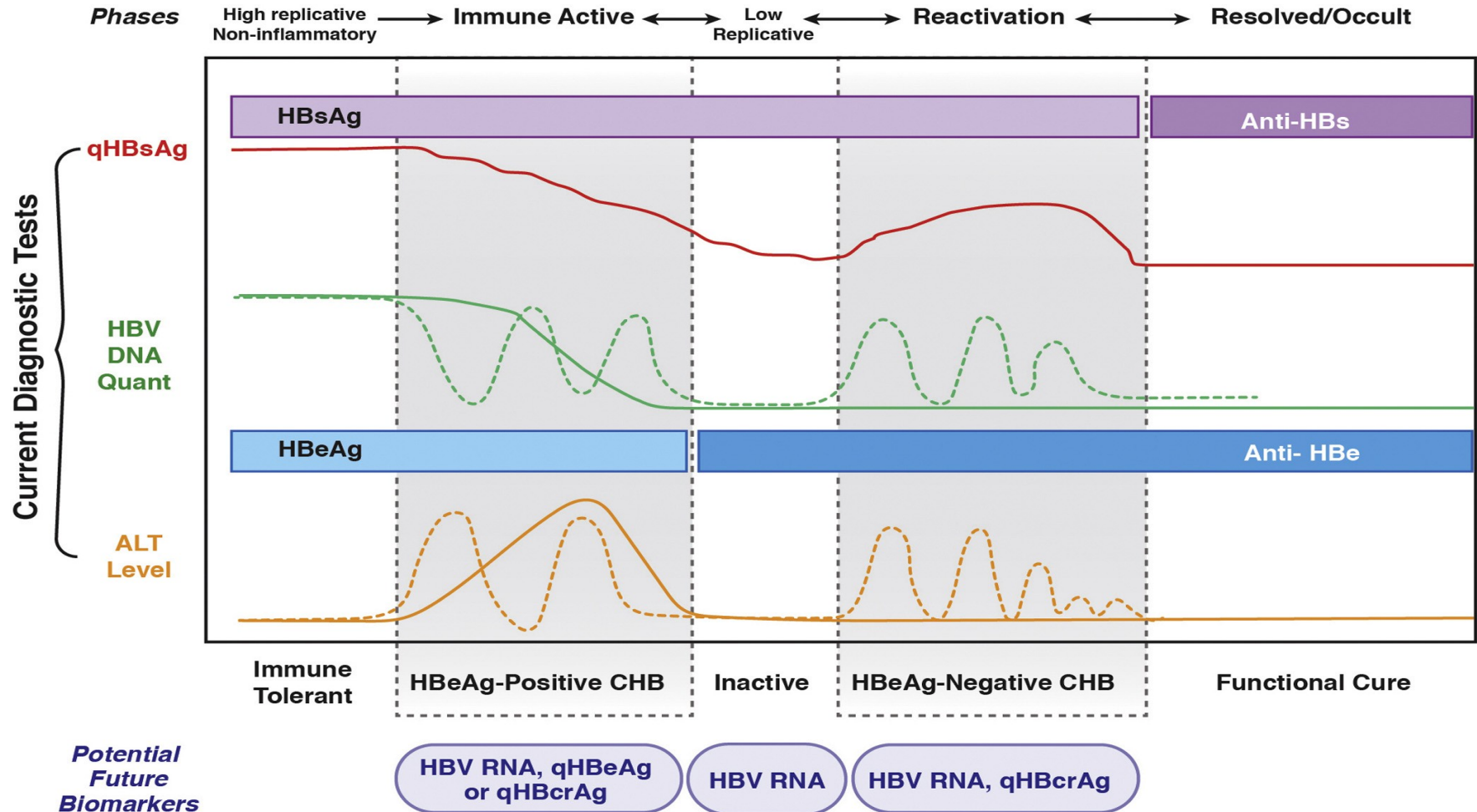
HBsAg <3 log IU/ml	359	271	162	90	37
HBsAg ≥3 log IU/ml	606	485	305	183	73



Number at risk

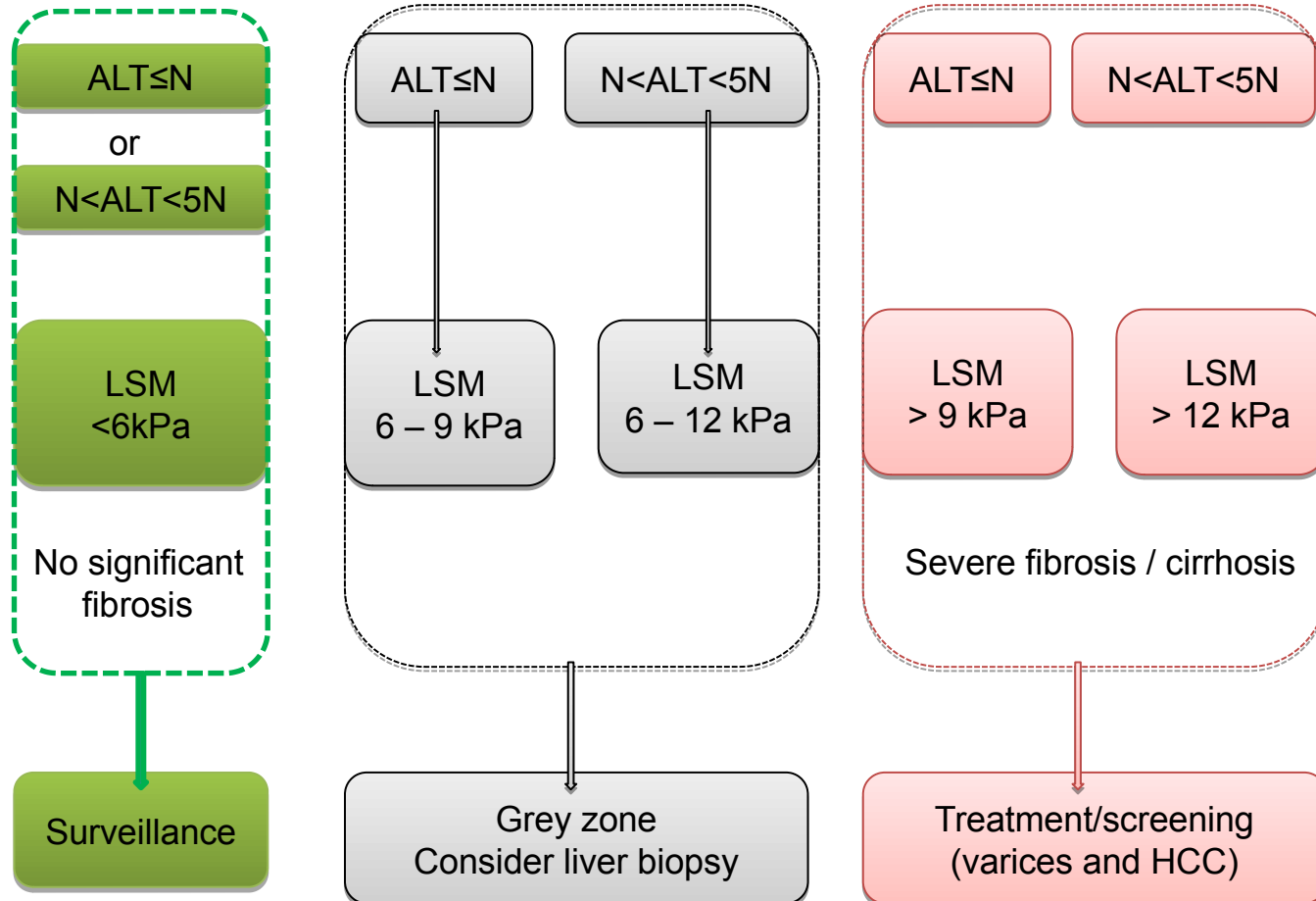
HBV DNA <4 log copies/ml	582	463	289	168	74
HBV DNA ≥4 log copies/ml	449	346	218	133	53

# Phases of HBV infection





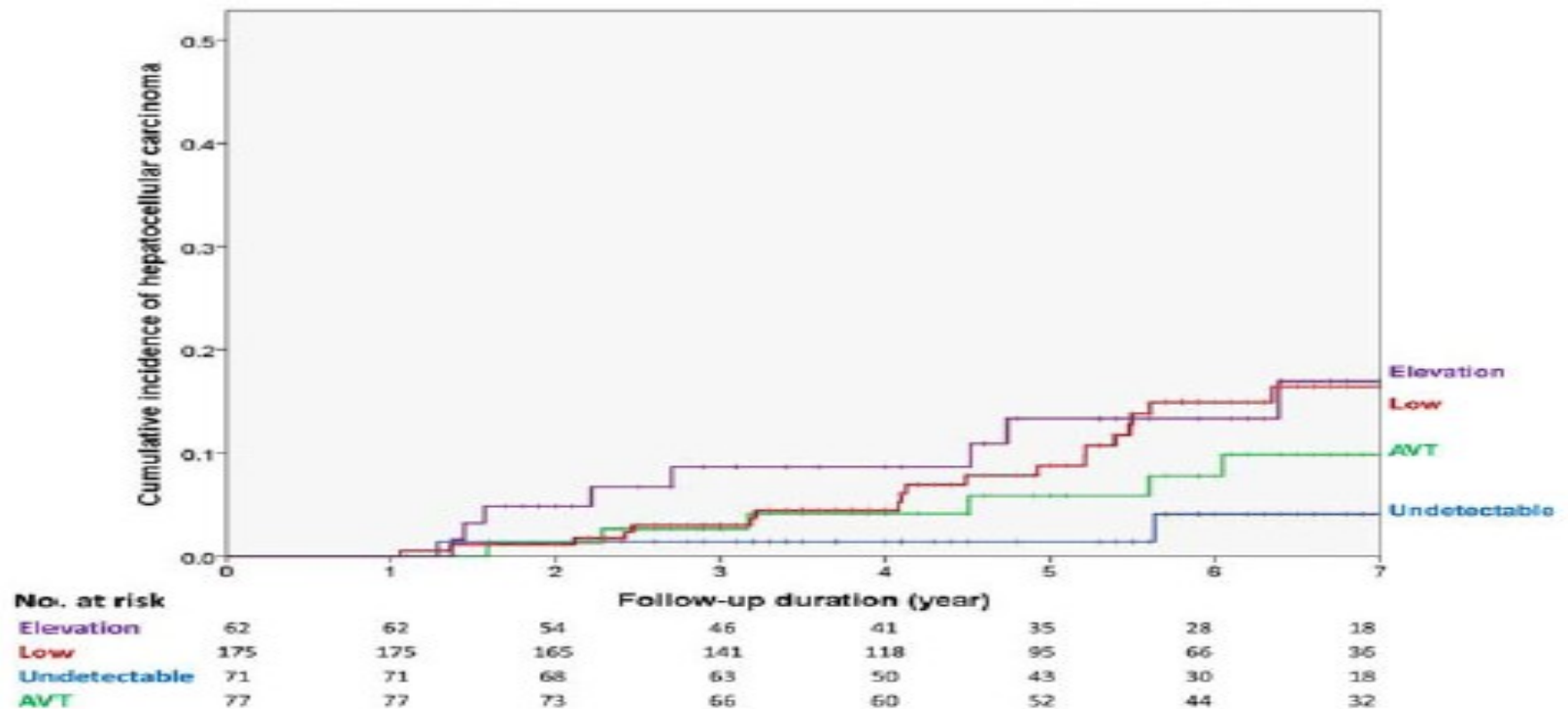
# Performance of transient elastography



# Inactive cirrhosis should be treated

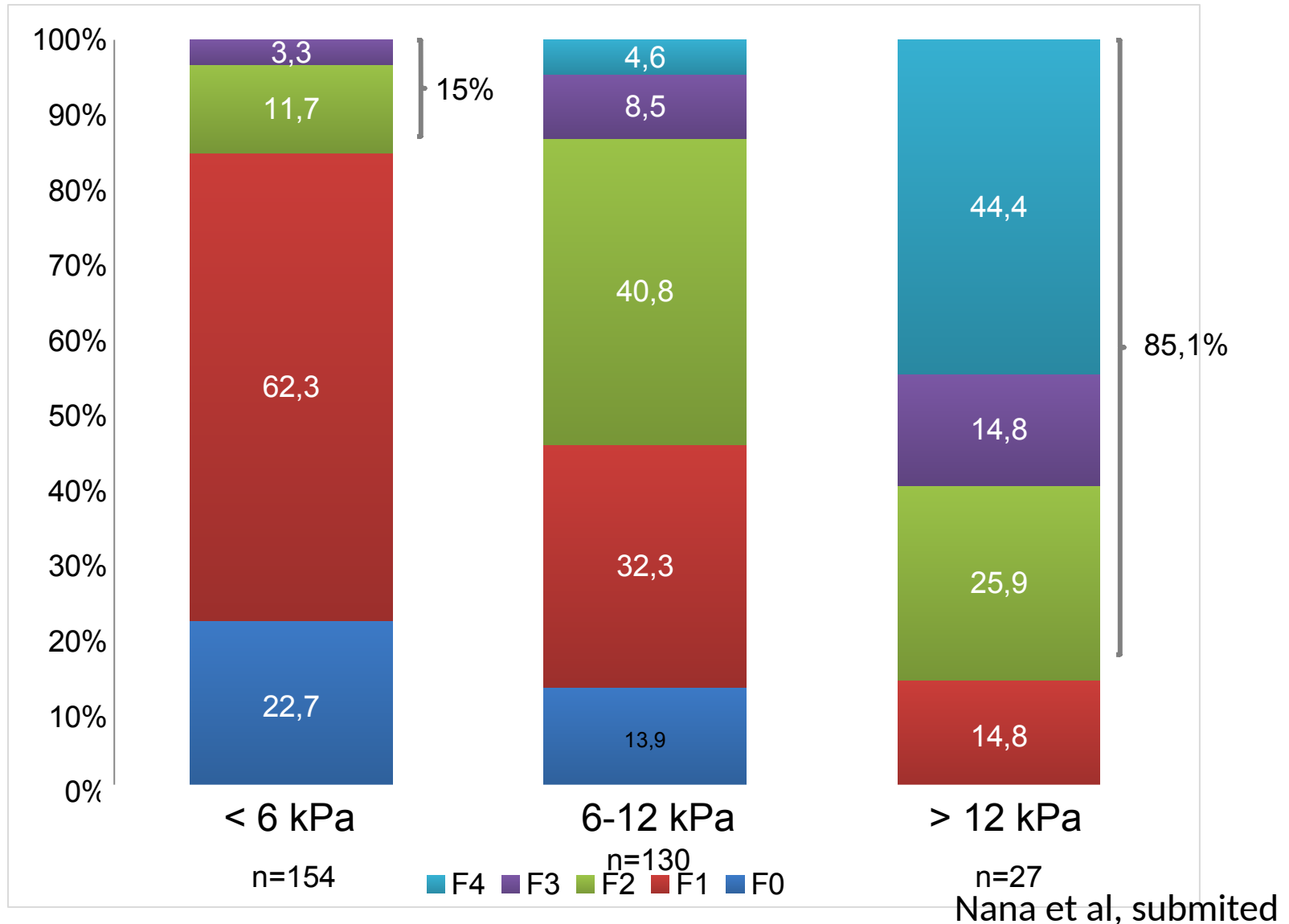
385 patients with cirrhosis and HBV DNA < 2 000 IU/ml

Median follow-up : 5.8 years



# Prevalence of fibrosis stages according to EASL

$N < ALT < 5N$



# 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**

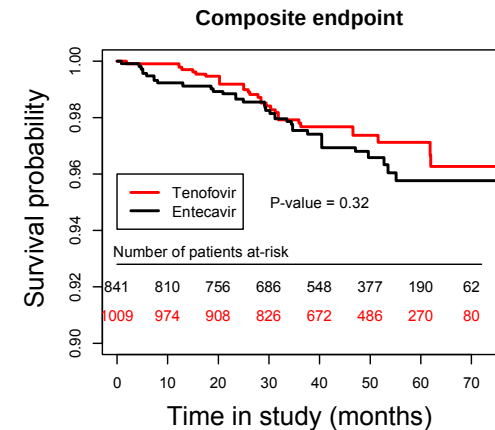
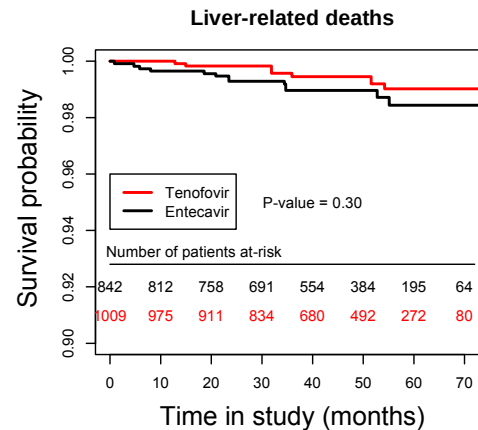
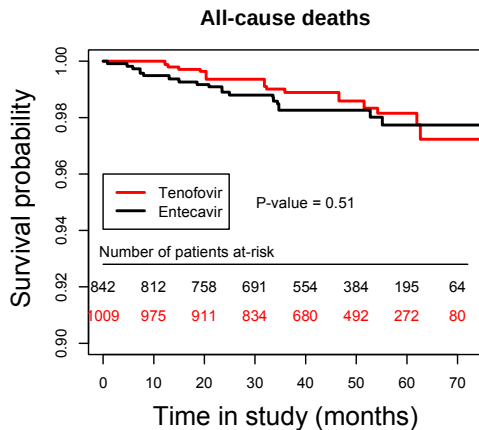
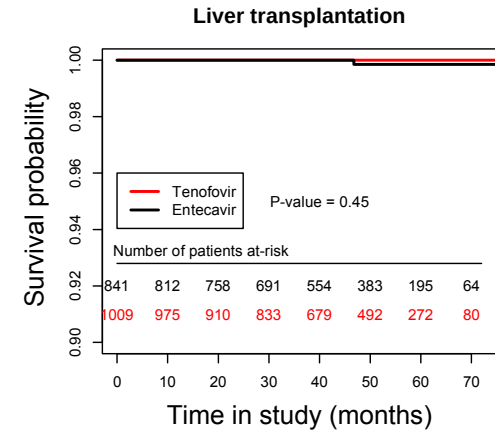
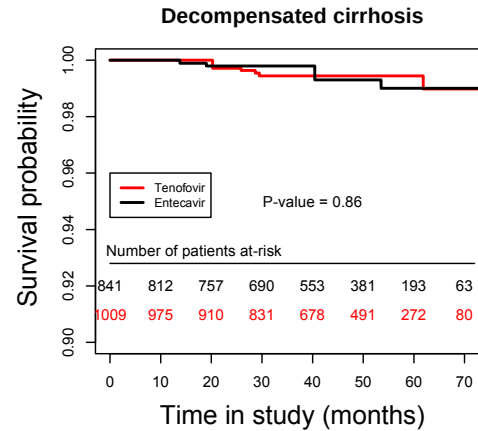
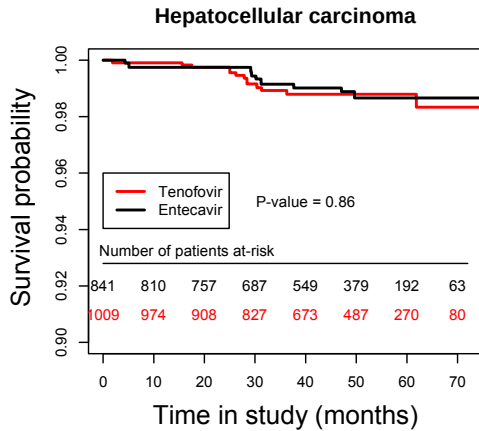
**2. Switch to TDF**

**3. Add IFN**

**4. Stop NUC therapy**

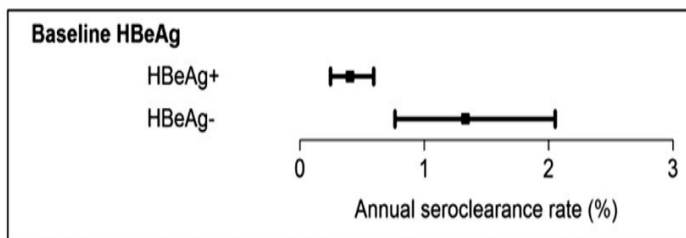
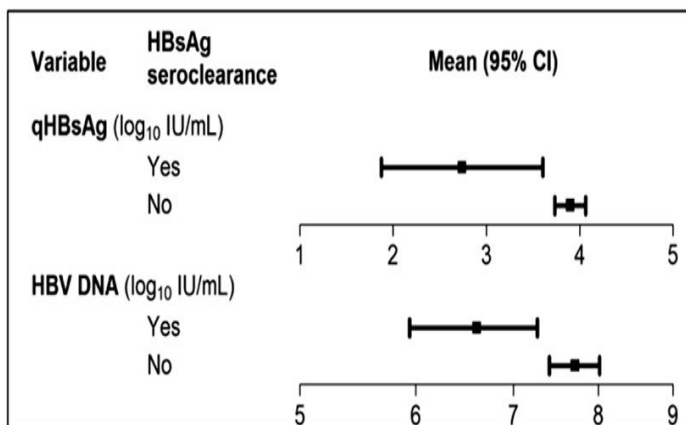
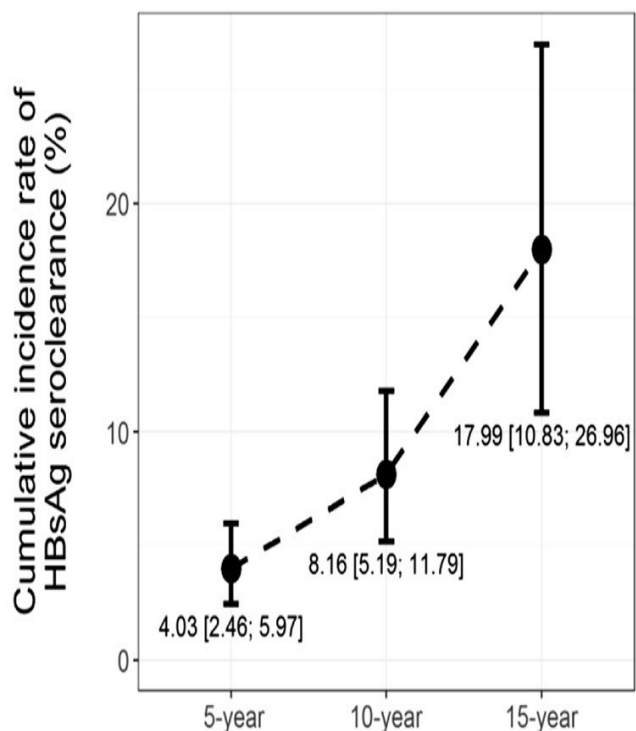
# ETV vs TDF : is there a difference?

Data from the HEPATHER cohort

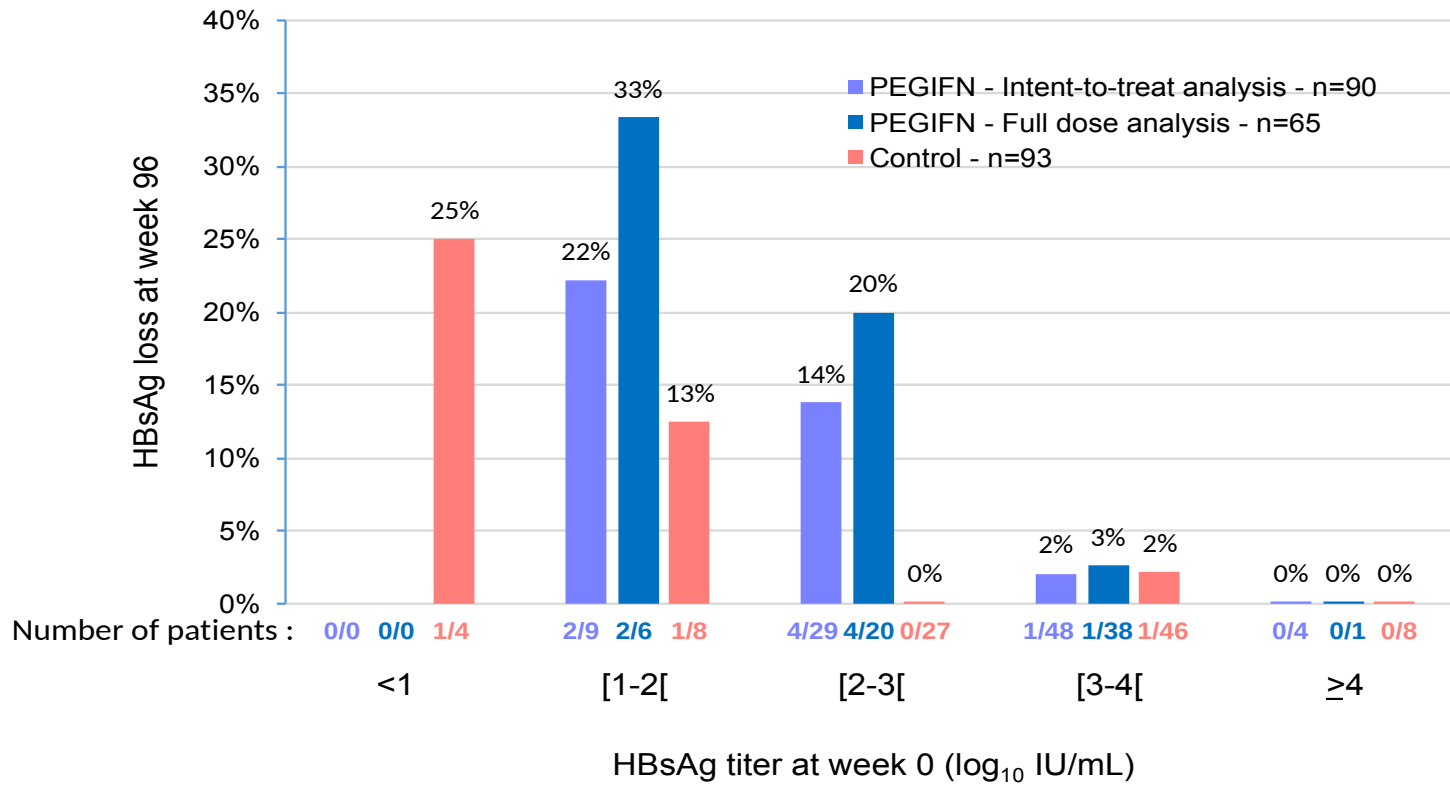


# Baseline qHBsAg predicts HBsAg clearance

- **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.



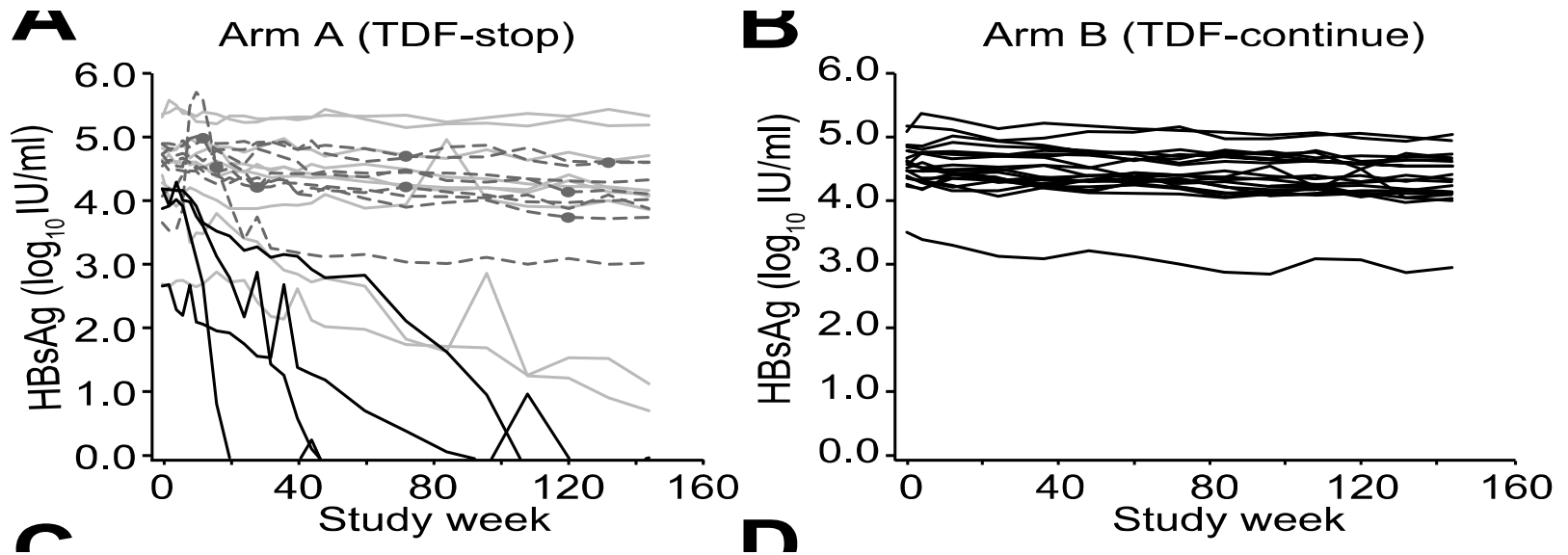
# Sequential NUC + IFN strategy





# NUC cessation strategy

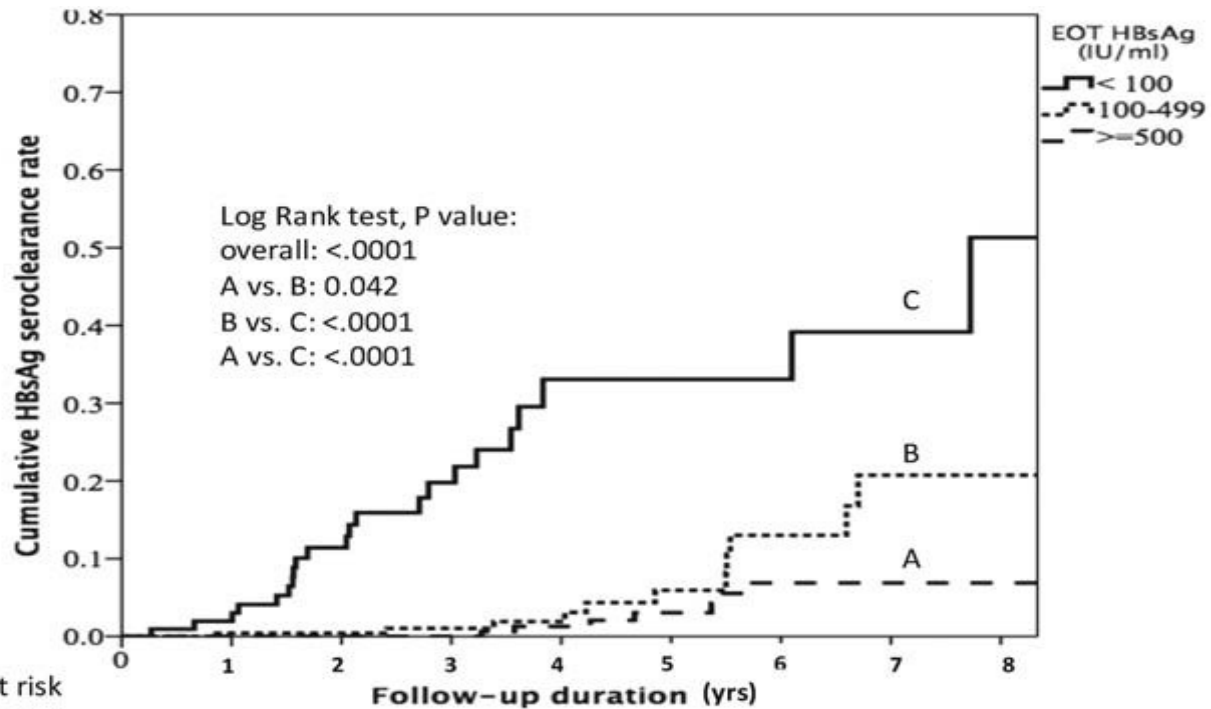
Randomized study in 42 patients with not detectable HBV DNA on TDF (3.5 years)



HBsAg loss in 19% of patients

# NUC cessation strategy

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



Patient at risk		0	1	2	3	4	5	6	7	8
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

# Patient case

**Biopsy : METAVIR F3 : TDF started in 2014**

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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?

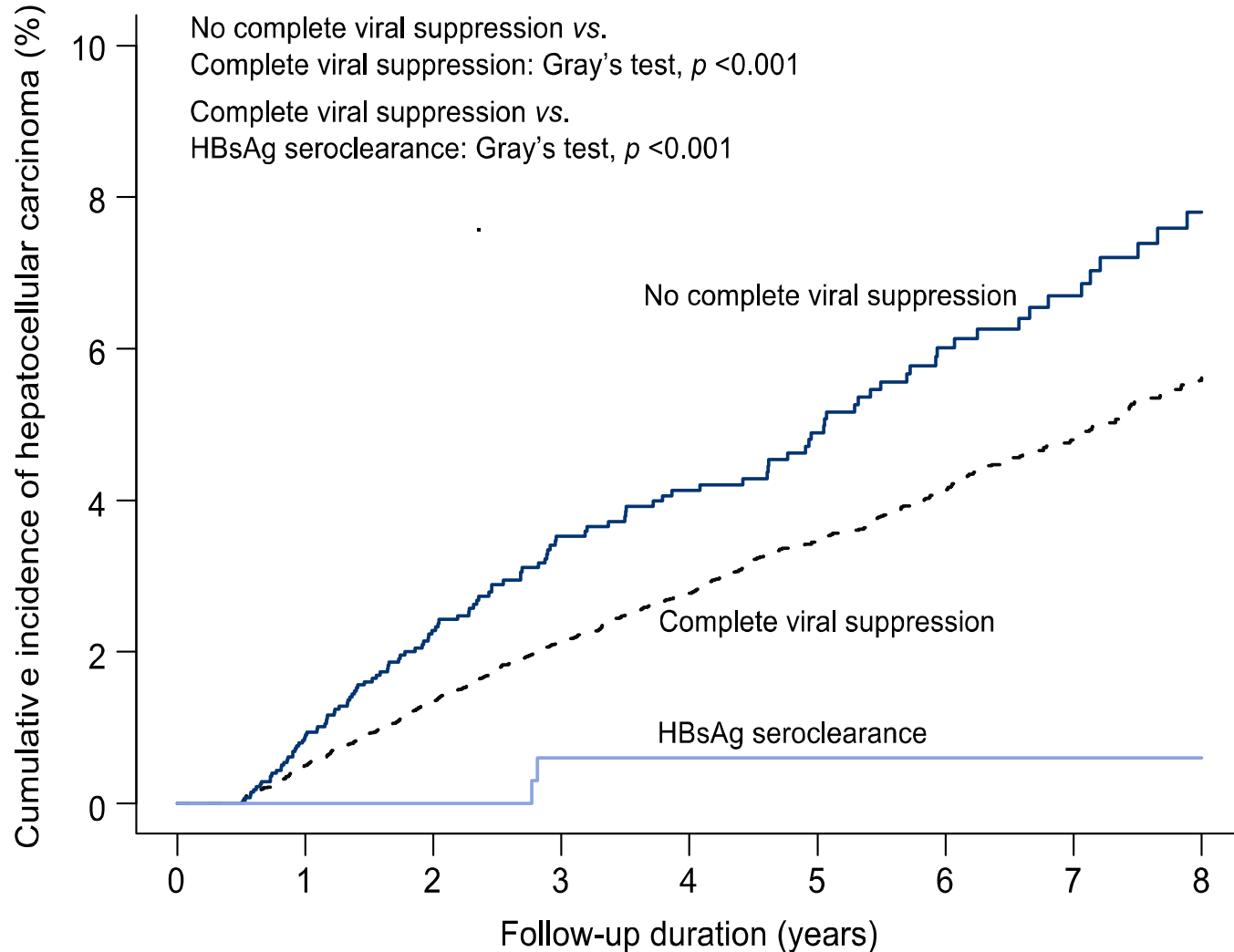
**1. Continue ETV**

**2. Stop ETV now**

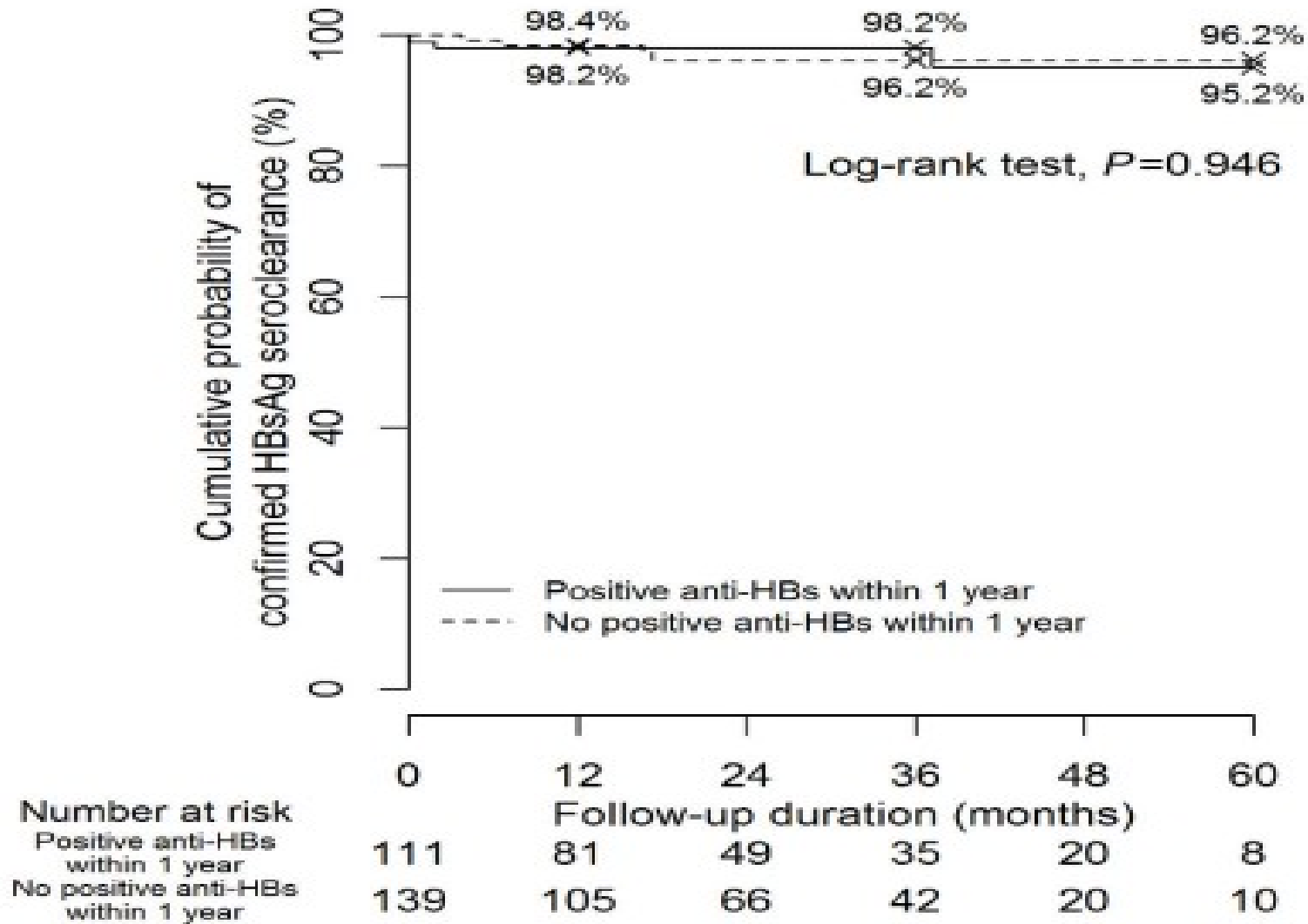
**3. Stop ETV after 6 months of consolidation**

**4. Stop ETV after HBs sero-conversion**

# HBsAg clearance is associated with a better prognosis



# No impact of HBs sero-conversion



# 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 ( $\geq 3$  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).