

The Differences in Antiviral Agents in the Treatment of Hepatitis B

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EASL HBV Guidelines

- ◆ **EASL Consensus Conference 2002 (Geneva)**
J Hepatol 2003
- ◆ **Clinical Practice Guidelines 2008**
J Hepatol 2009
- ◆ **Actualized Clinical Practice Guidelines 2012**
J Hepatol 2012

WHO TO TREAT EASL Guidelines

1. Same indications for:

HBeAg+ and HBeAg-

2. Indication depends on:

- HBV DNA
- ALT
- Liver biopsy

WHO TO TREAT

EASL Guidelines

HBeAg + or HBeAg -

WHO TO TREAT EASL Guidelines

HBeAg + or HBeAg -

**HBV DNA < 2000 UI
ALT = N
No liver biopsy**

WHO TO TREAT

EASL Guidelines

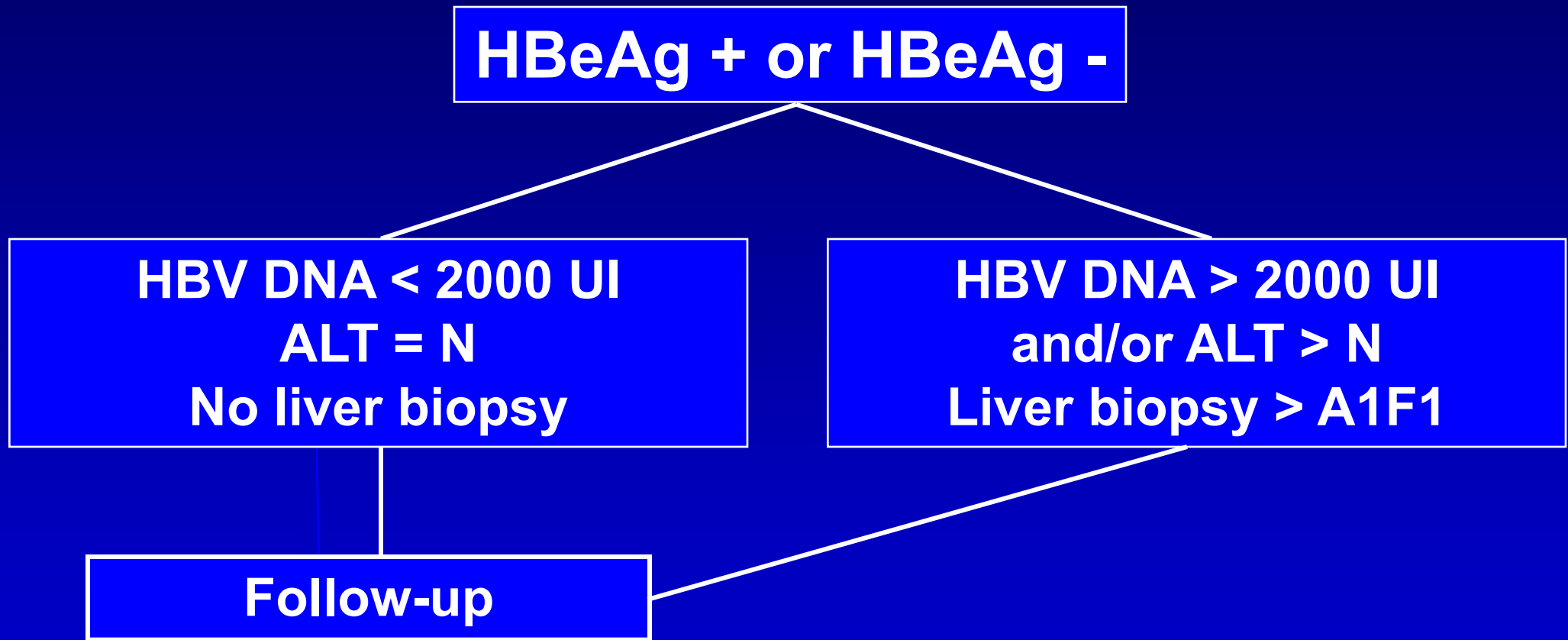
HBeAg + or HBeAg -

**HBV DNA < 2000 IU
ALT = N
No liver biopsy**

Follow-up

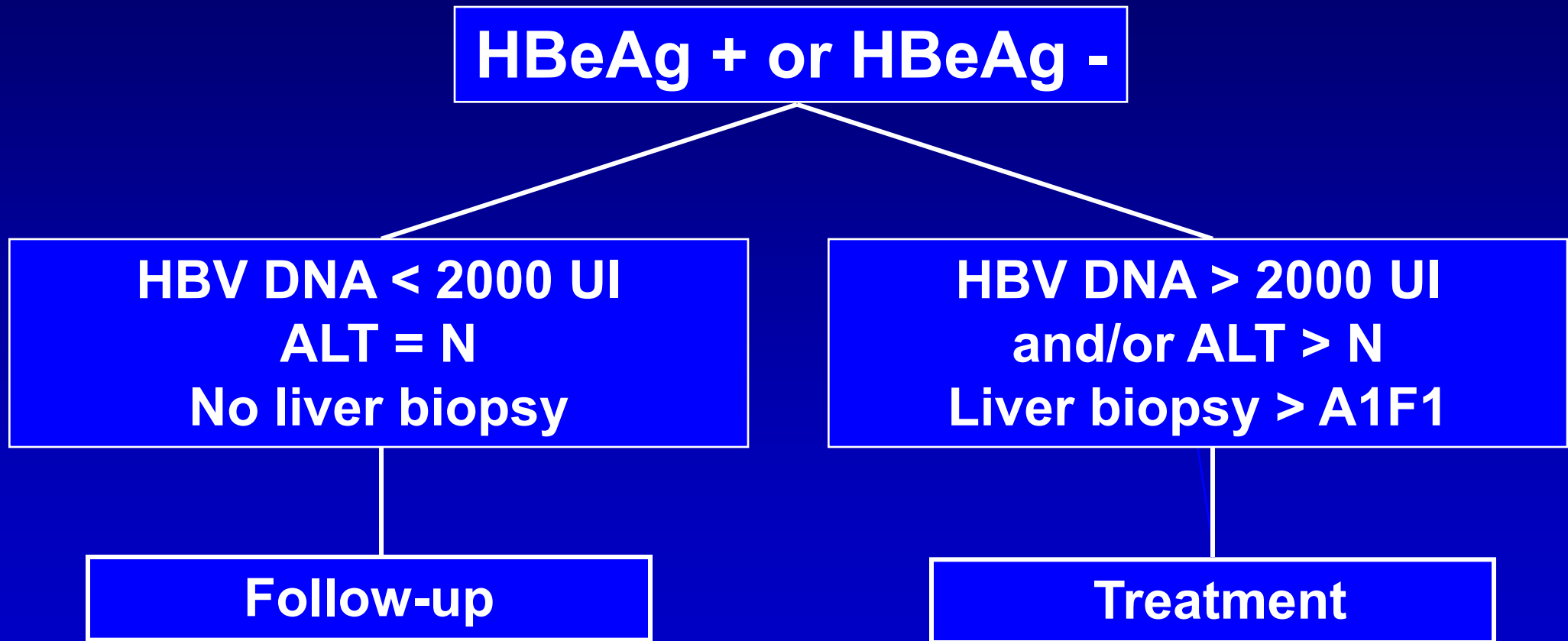
WHO TO TREAT

EASL Guidelines



WHO TO TREAT

EASL Guidelines



Special groups

- ◆ **Immunotolerant patients**
 - ◆ No treatment
- ◆ **Inactive carriers (HBV DNA < 20 000 UI and ALT N)**
 - ◆ No treatment
- ◆ **Patients with mild chronic hepatitis B**
 - ◆ No treatment
- ◆ **Patients with compensated cirrhosis**
 - ◆ Treatment
- ◆ **Patients with decompensated cirrhosis**
 - ◆ Urgent treatment

HOW TO TREAT EASL Guidelines

HBeAg + or HBeAg -

HOW TO TREAT EASL Guidelines

HBeAg + or HBeAg -

PEG IFN

HBV DNA < 8 log

ALT > 2N

HOW TO TREAT EASL Guidelines

HBeAg + or HBeAg -

PEG IFN

HBV DNA < 8 log

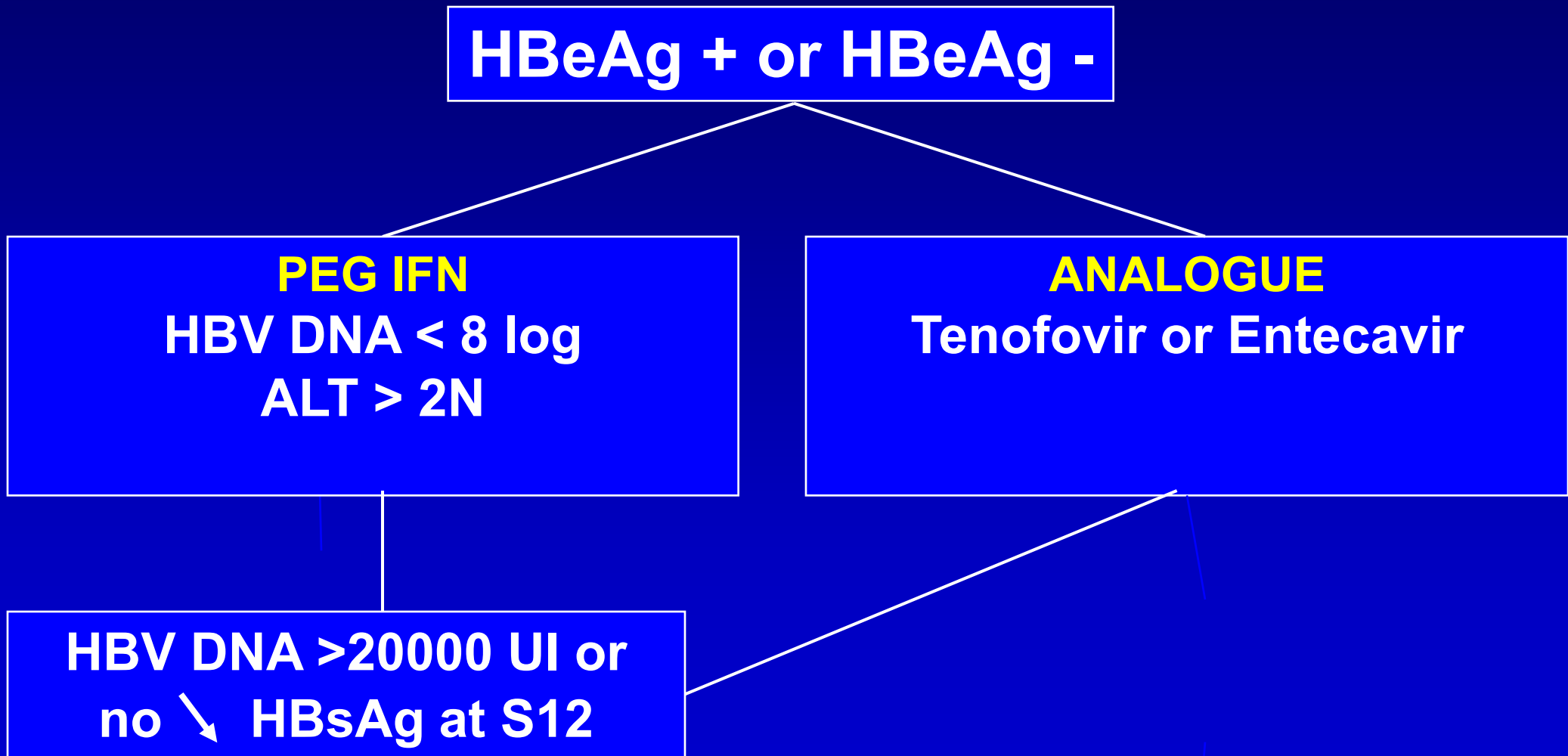
ALT > 2N

**HBV DNA > 20 000 UI or
no ↘ HBsAg at S12**

EASL Clinical Practice Guidelines: Management of chronic hepatitis B.

J Hepatol 2012

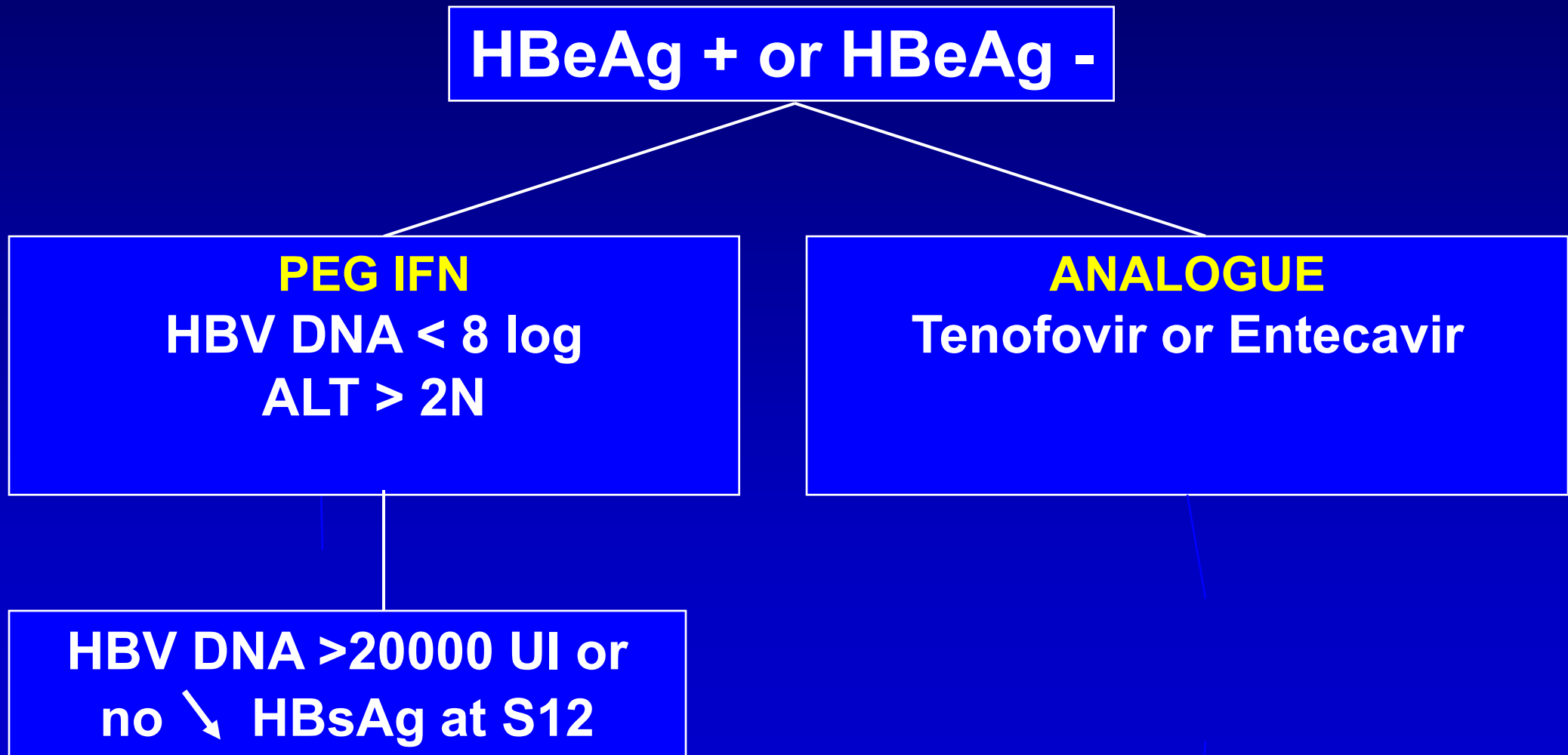
HOW TO TREAT EASL Guidelines



EASL Clinical Practice Guidelines: Management of chronic hepatitis B.

J Hepatol 2012

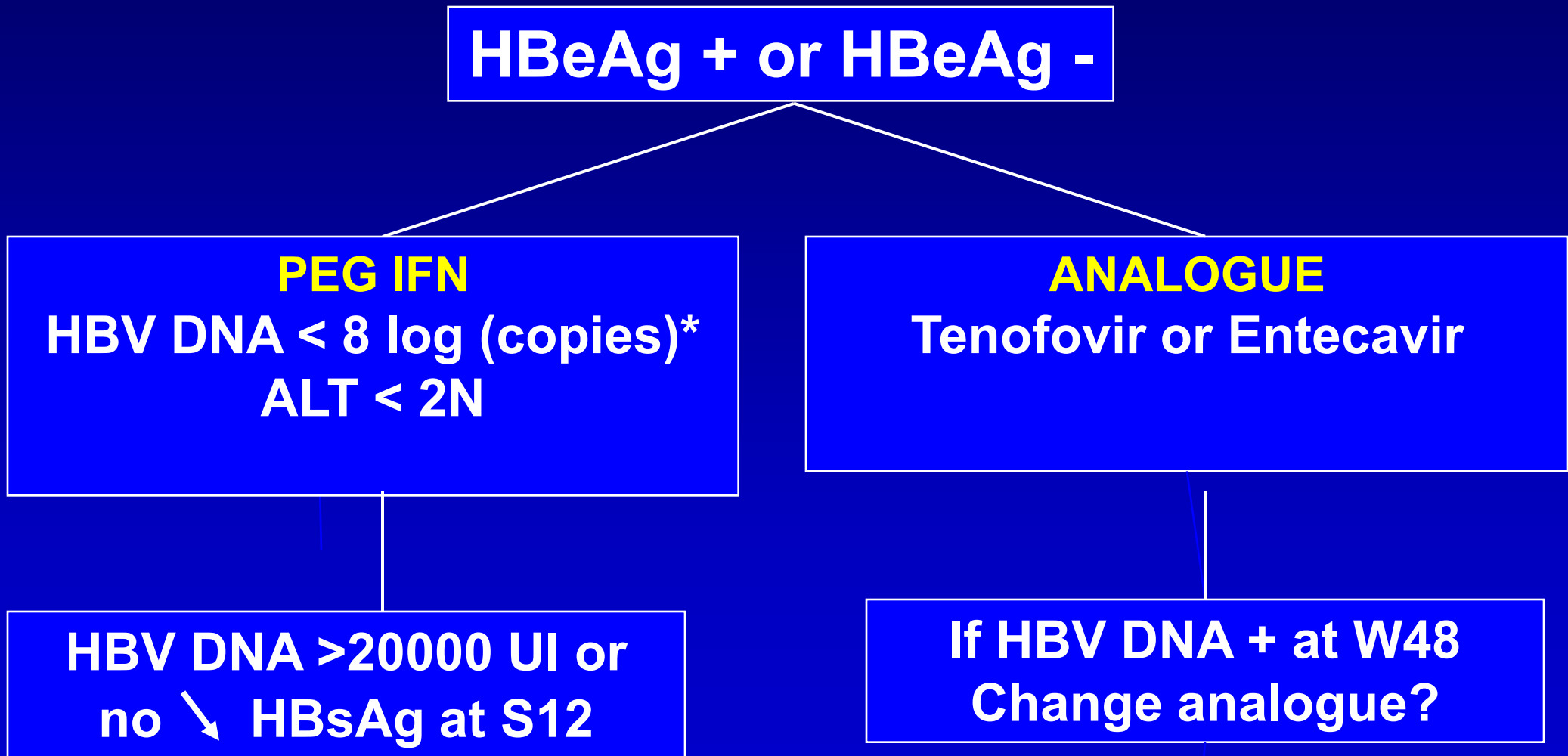
HOW TO TREAT EASL Guidelines



EASL Clinical Practice Guidelines: Management of chronic hepatitis B.

J Hepatol 2012

HOW TO TREAT EASL Guidelines



EASL Clinical Practice Guidelines: Management of chronic hepatitis B.

J Hepatol 2012

WHAT WE LEARNED

- Long term follow-up
 - The importance of qHBsAg
 - The potential efficacy of combo
-

WHAT WE LEARNED

- **Long term follow-up**
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RESULTS WITH ANALOGUES

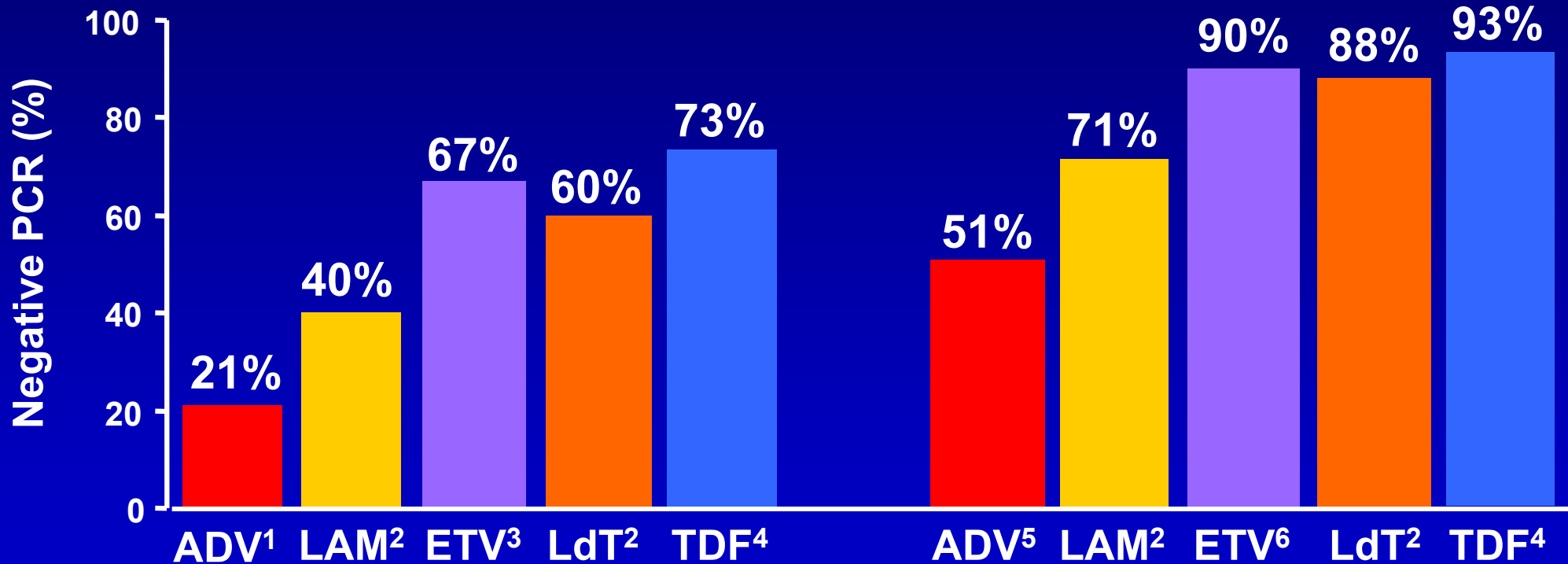
ANALOGUES REGISTERED FOR THE TREATMENT OF CHRONIC HEPATITIS B

- Lamivudine	-
- Adefovir	-
- Telbivudine	+
- Entecavir	+++
- Tenofovir	+++

VIROLOGICAL RESPONSE AT 1 YEAR

HBeAg-positive

HBeAg-negative



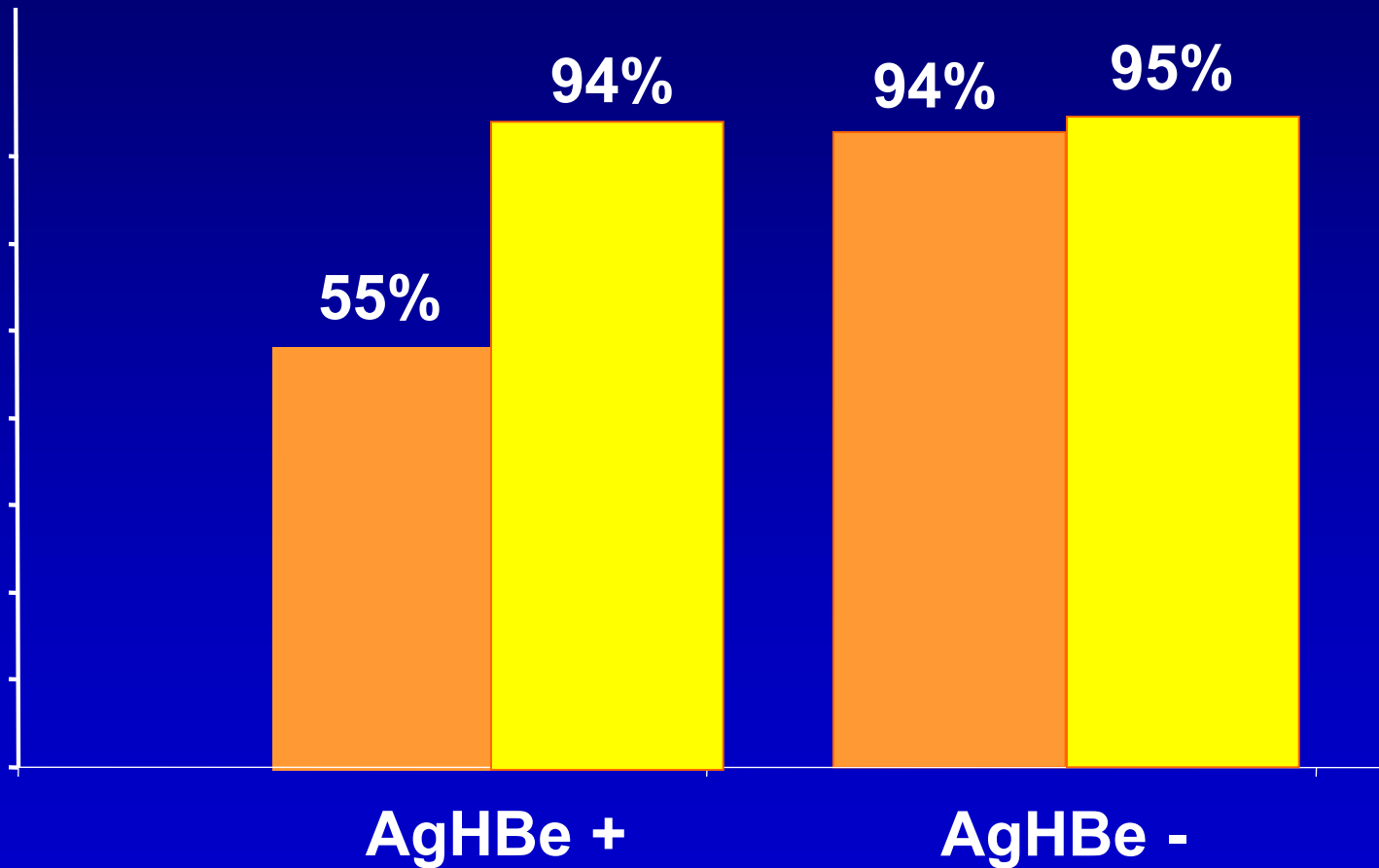
1. Marcellin et al. *N Engl J Med.* 2003
3. Chang et al. *N Engl J Med.* 2006
5. Hadziyannis et al. *N Engl J Med.* 2003

2. Lai et al. *N Engl J Med.* 2007
4. Marcellin et al. *N Engl J Med.* 2008
6. Lai et al. *N Engl J Med.* 2006

ENTECAVIR

ENTECAVIR

UNDETECTABLE HBV DNA AT 1 AND 3-5 YEARS

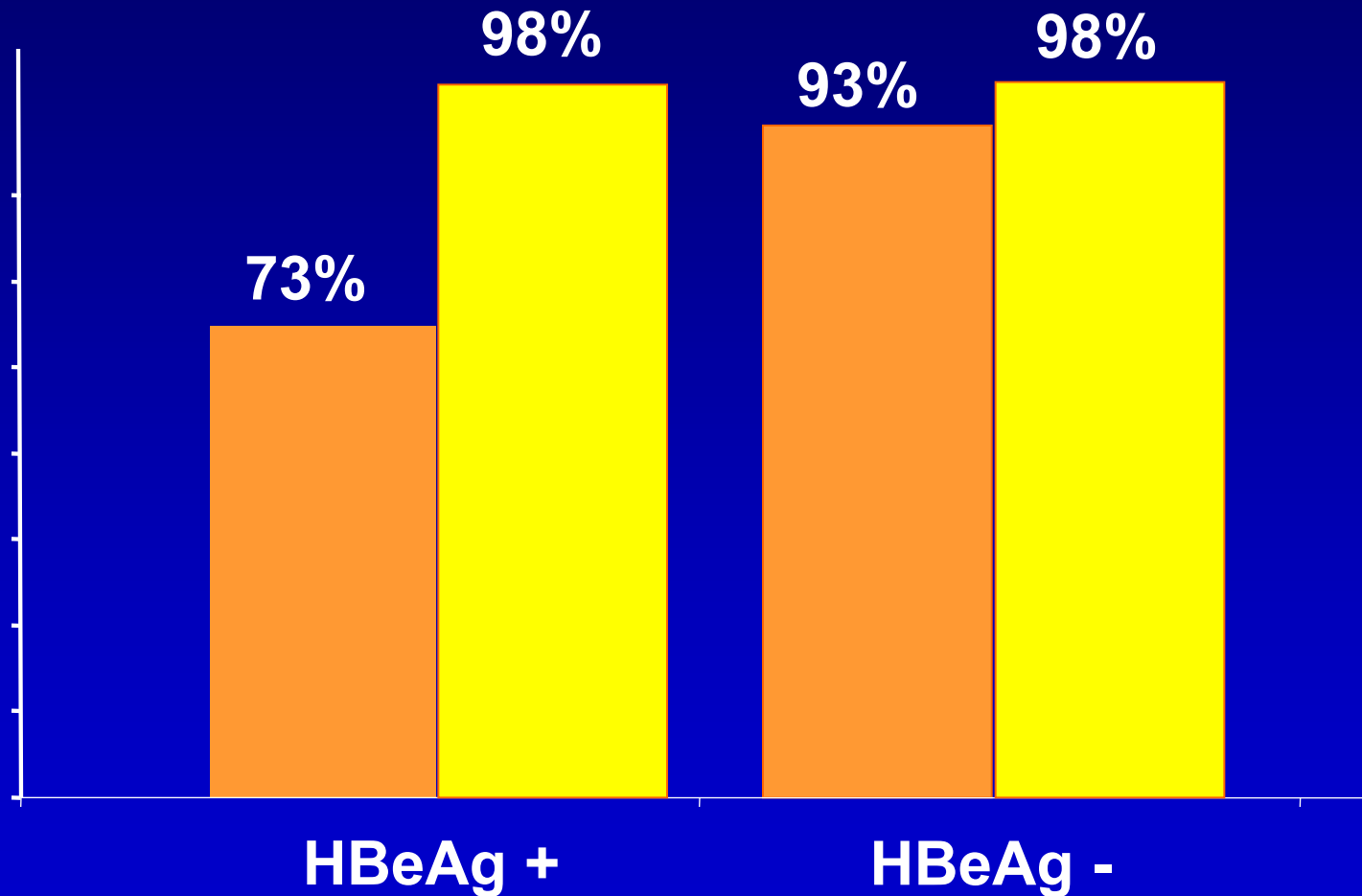


Chan et al. Hepatology 2010

TENOFOVIR

TENOFOVIR

UNDETECTABLE HBV DNA AT 1 AND 8 YEARS



Marcellin et al. NEJM 2008

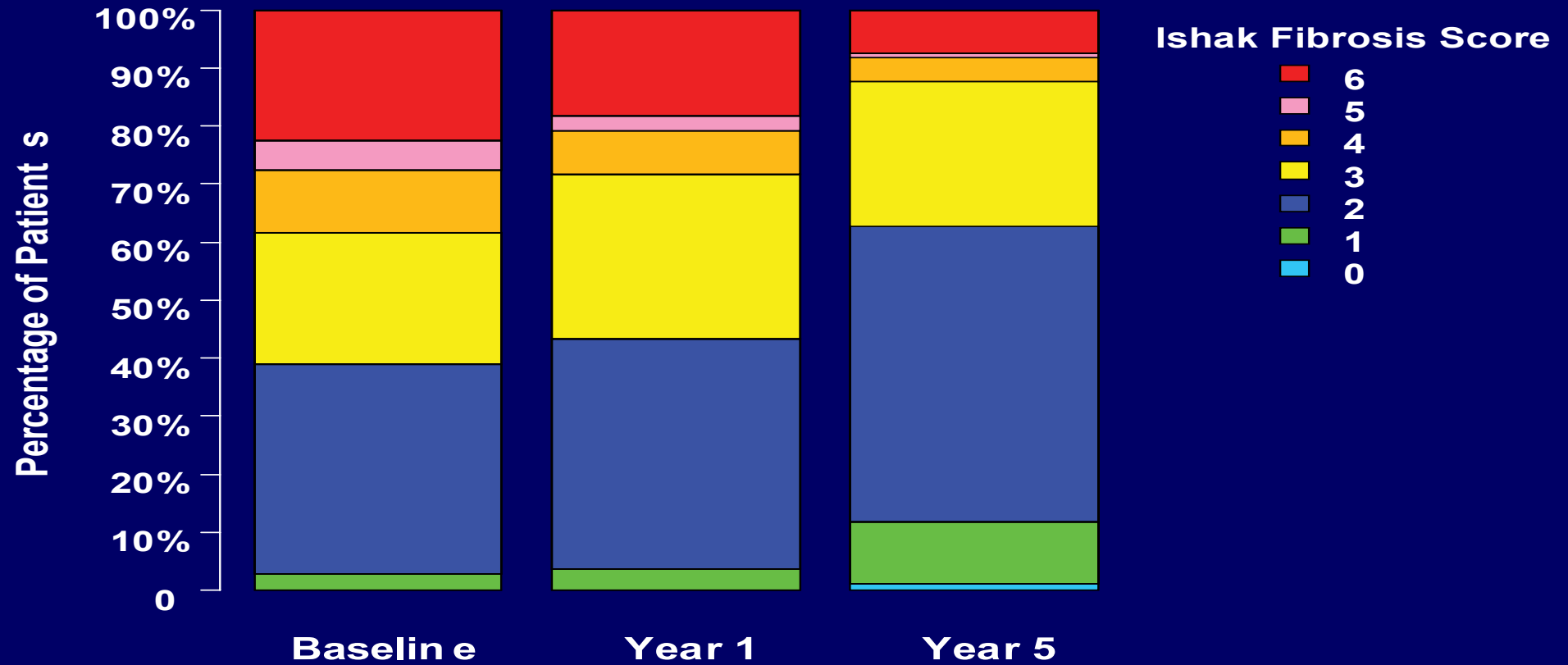
Marcellin et al. Lancet 2013

Marcellin et al. AASLD 2014

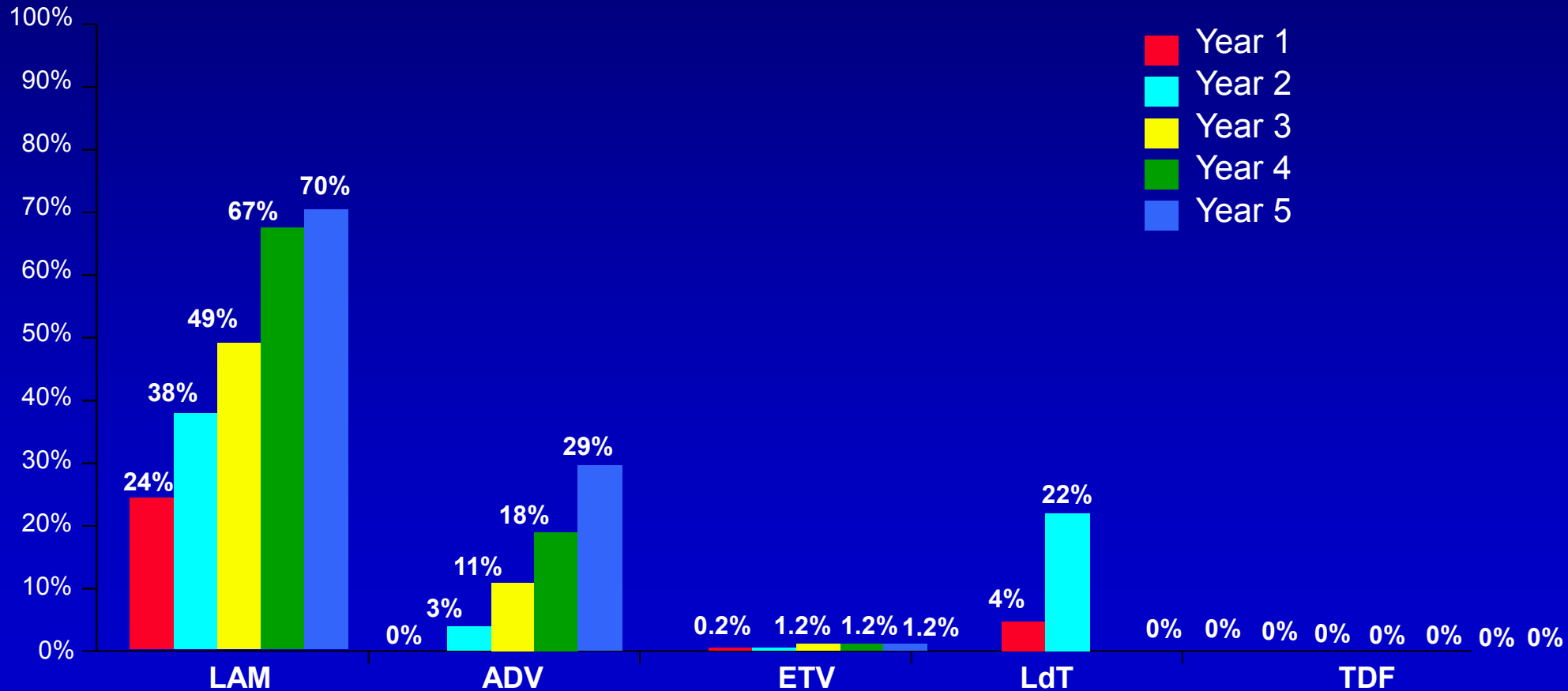
LIVER HISTOLOGY AT BASELINE, 1 and 5 YEARS

Regression of fibrosis in n=348

Reversal of cirrhosis in 75% n=96



Cumulative incidence of HBV resistance



WHAT WE LEARNED

- Long term follow-up
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 - The potential efficacy of combo
-

RESULTS WITH INTERFERON

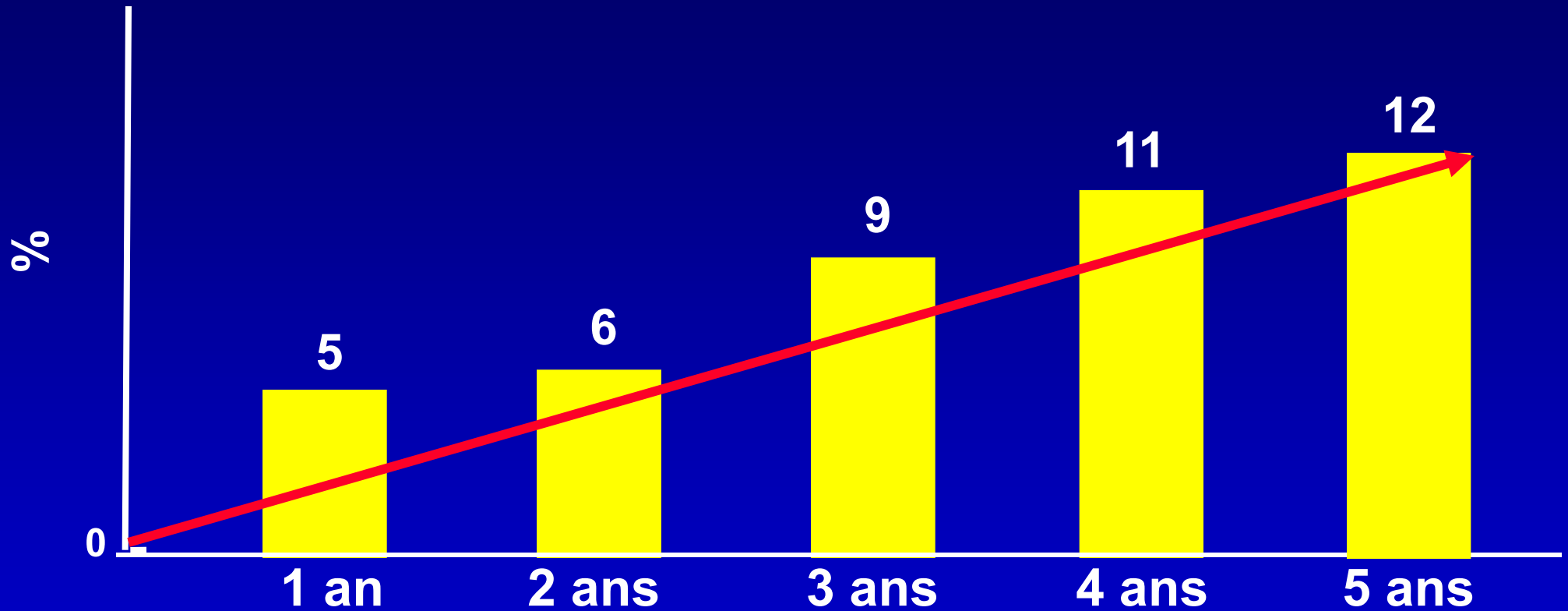
COMPLICATIONS AND MORTALITY (10 years) AFTER IFN THERAPY

	HBsAg+	HBsAg-
◆ Complications	35%	0
◆ Mortality (HCC):	20%	0

PEG IFN

HBeAg negative CHB

HBsAg LOSS after PEG IFN ± LAM



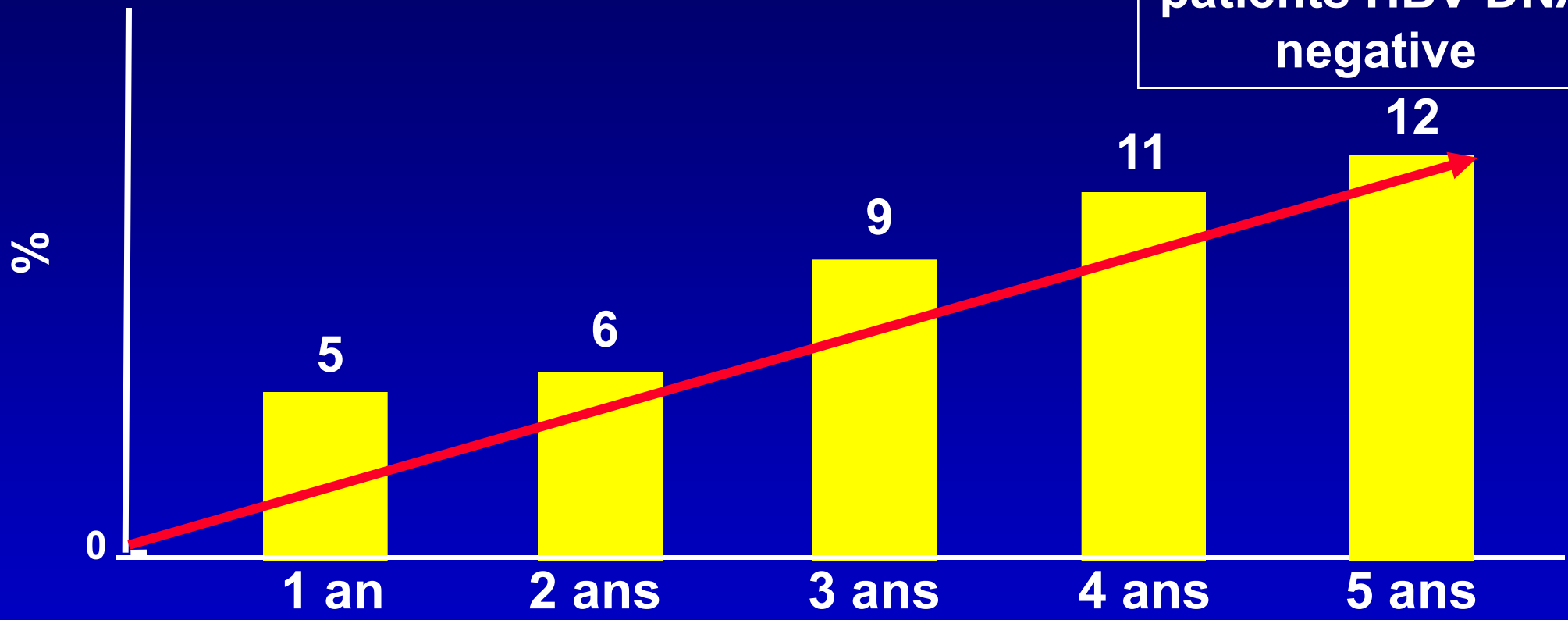
Marcellin et al. NEJM 2004

Heathcote, Marcellin et al. Gastroenterology 2009

Marcellin et al. Hepatology International 2012

HBsAg LOSS

64% of the patients HBV DNA negative



Marcellin et al. NEJM 2004
Heathcote, Marcellin et al. Gastroenterology 2009
Marcellin et al. Hepatology International 2012

THE ROLE OF HBsAg QUANTIFICATION

A

Treatment

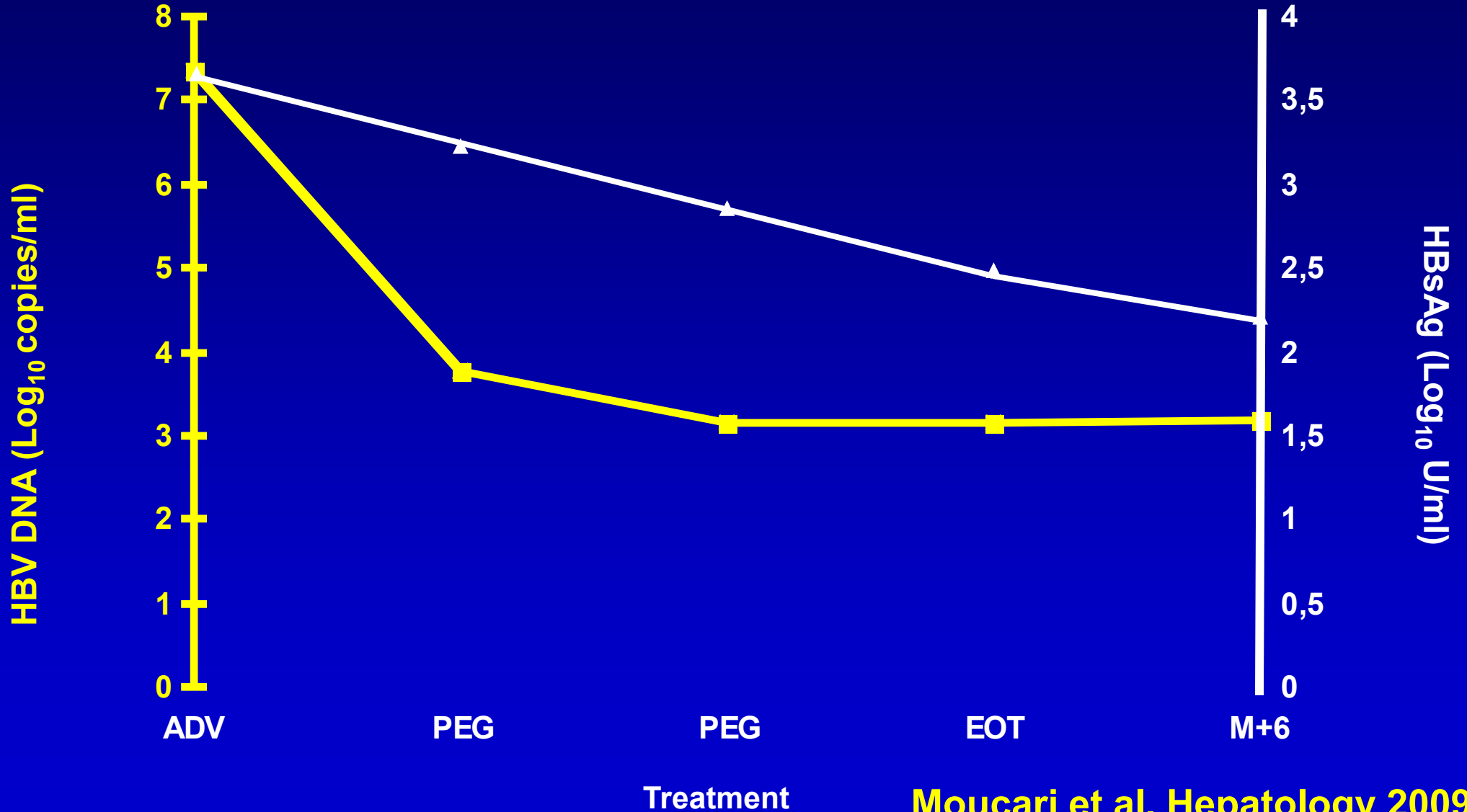
LAM

**PEG-IFN α -2a
+ LAM**

PEG-IFN α -2a

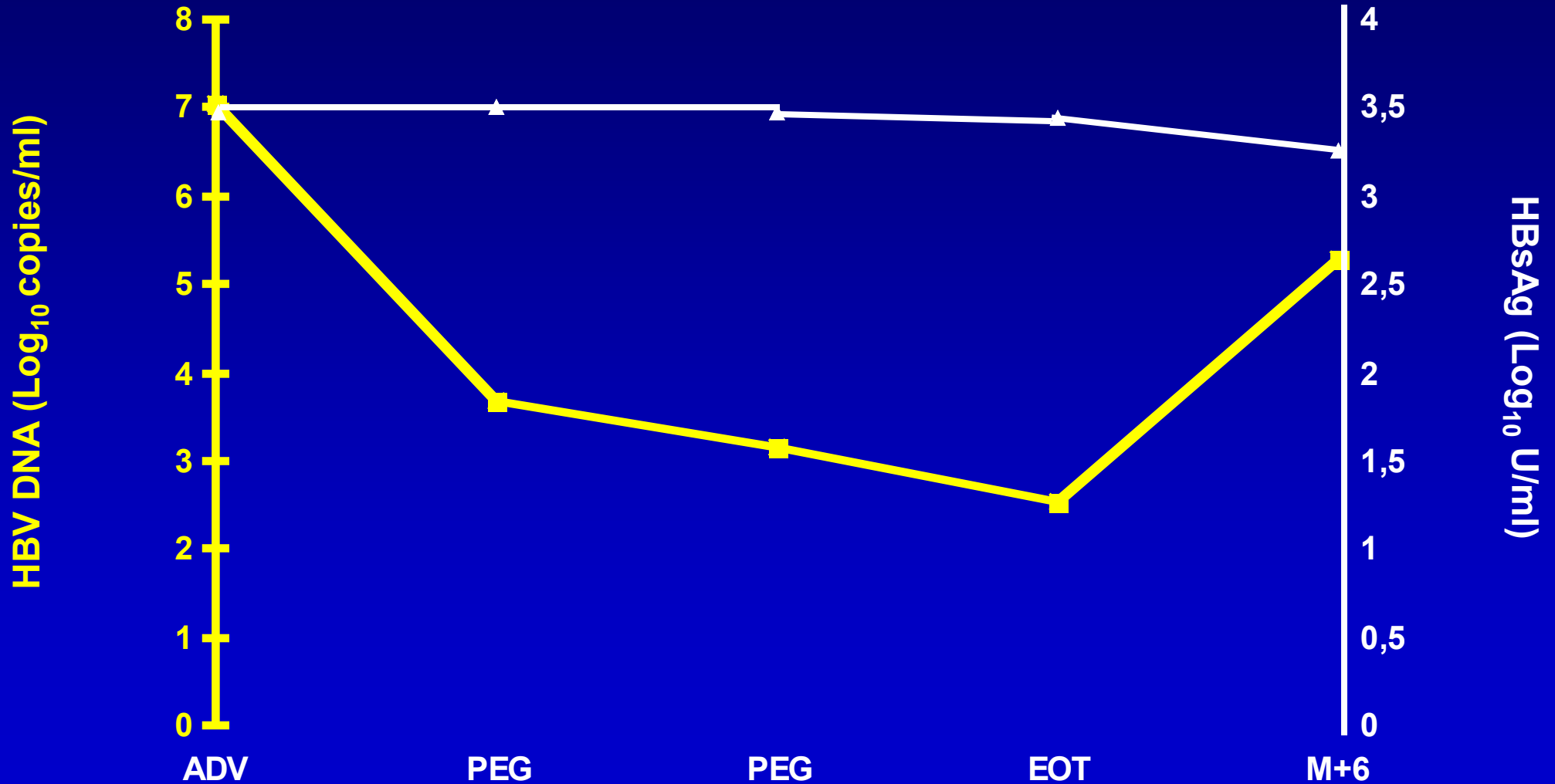
HBsAg Kinetics: PEG IFN

Patients with SVR



HBsAg Kinetics: PEG IFN

Patients without SVR

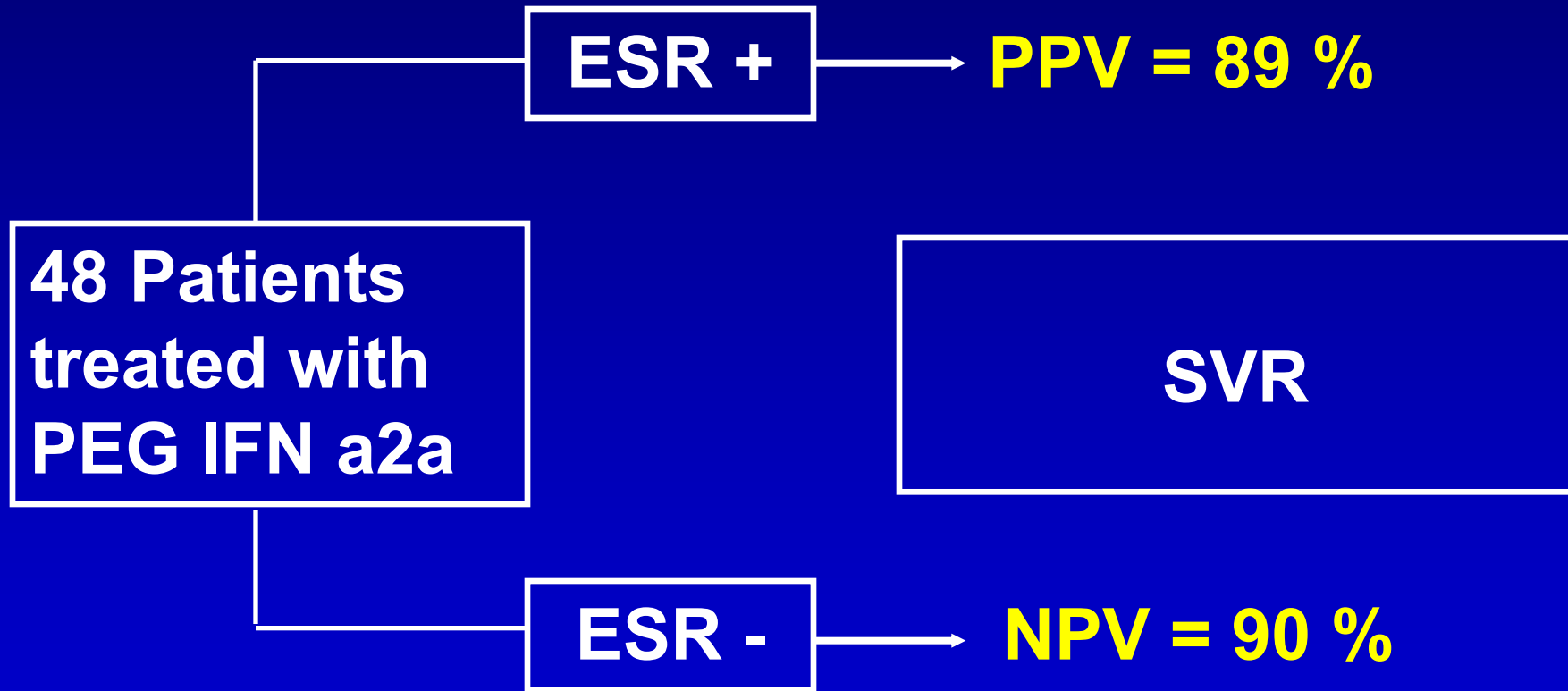


Treatment

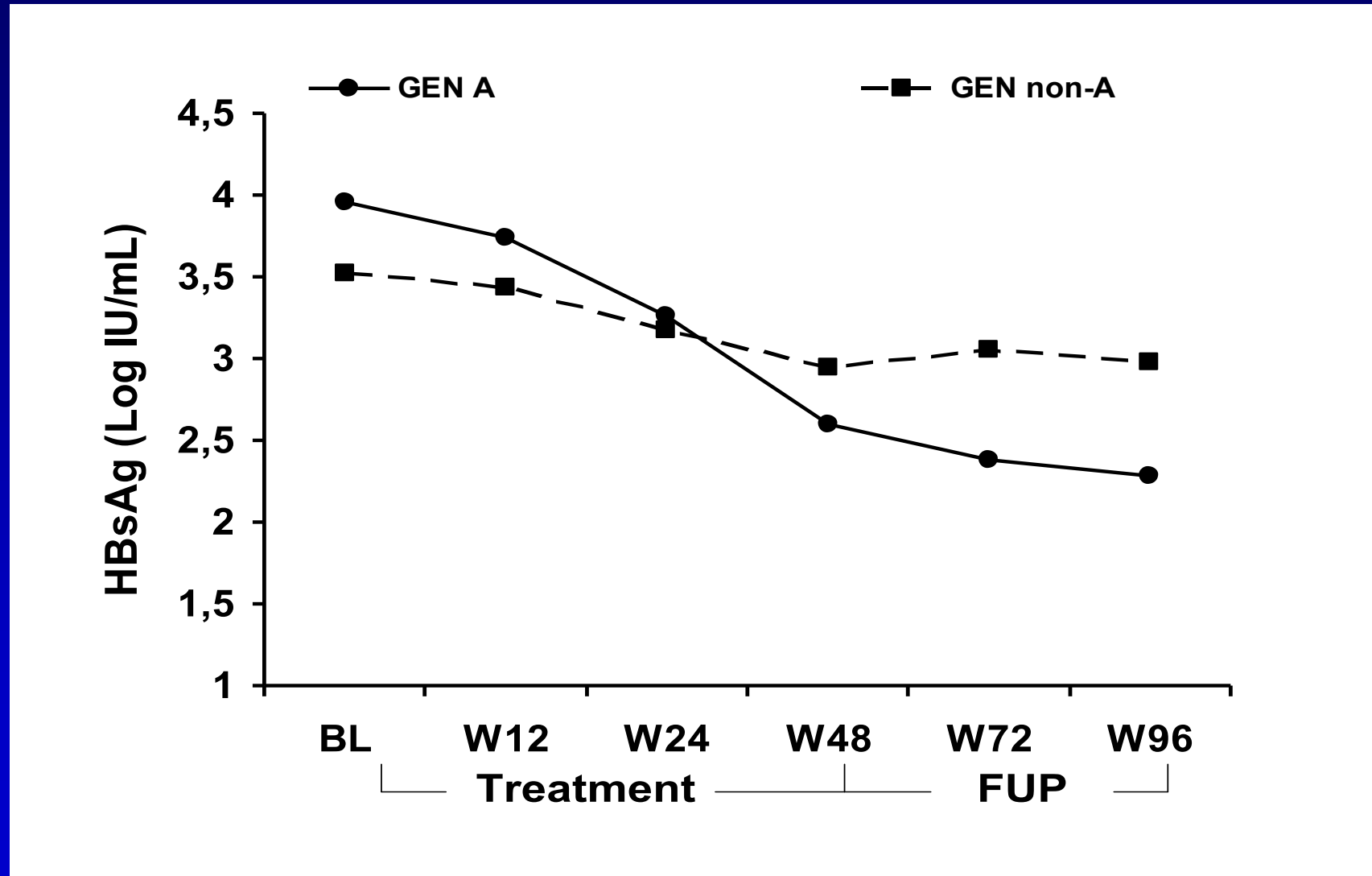
Moucari et al. Hepatology 2009

Quantification of HBsAg: “Stopping Rule”

Early Serological Response = 0.5 log at W12



HBsAg under PEG IFN According to Genotype



WHAT WE LEARNED

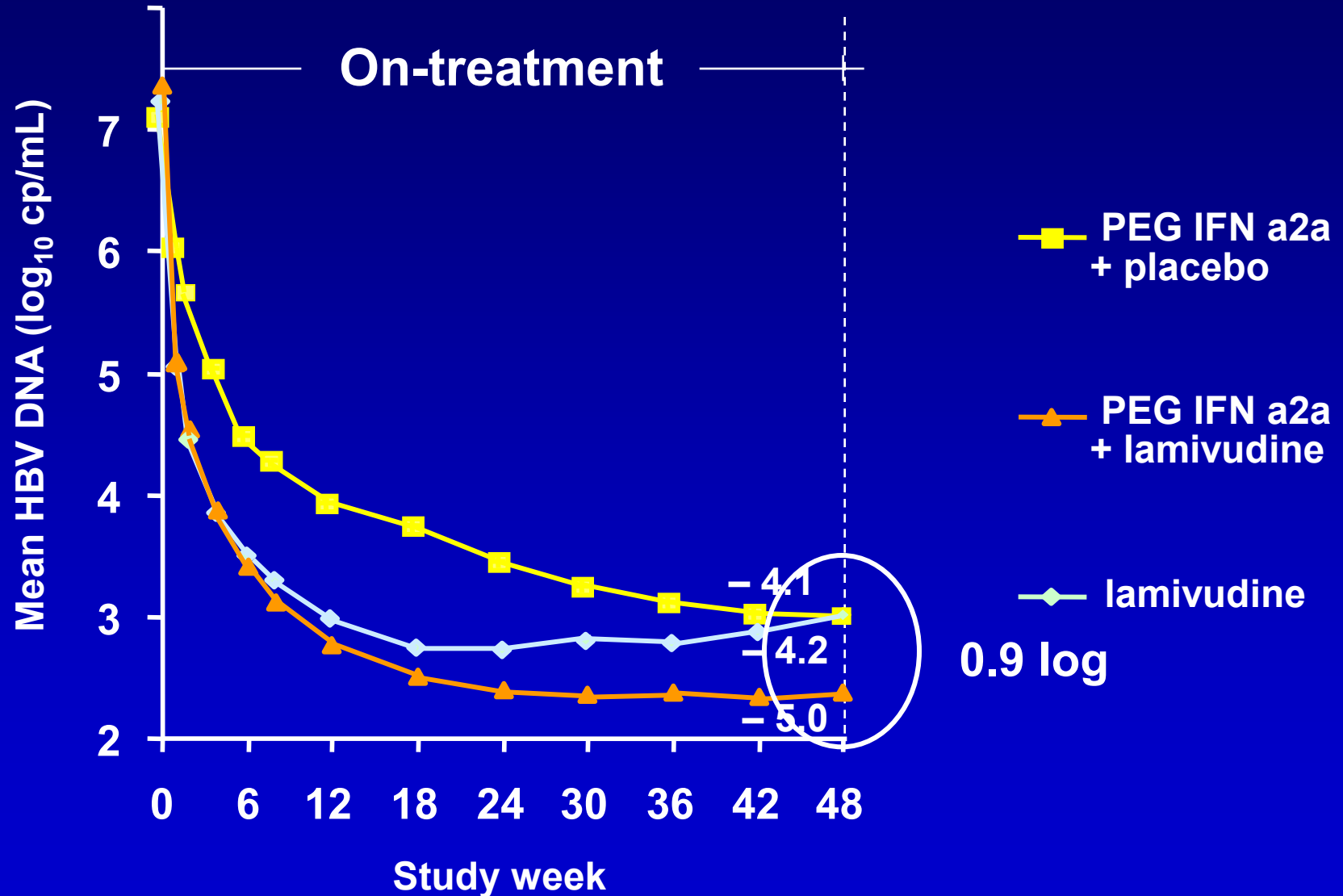
- Long term follow-up
 - The importance of qHBsAg
 - **The potential efficacy of combo**
-

THE FUTURE OF THERAPY

FOR HBV

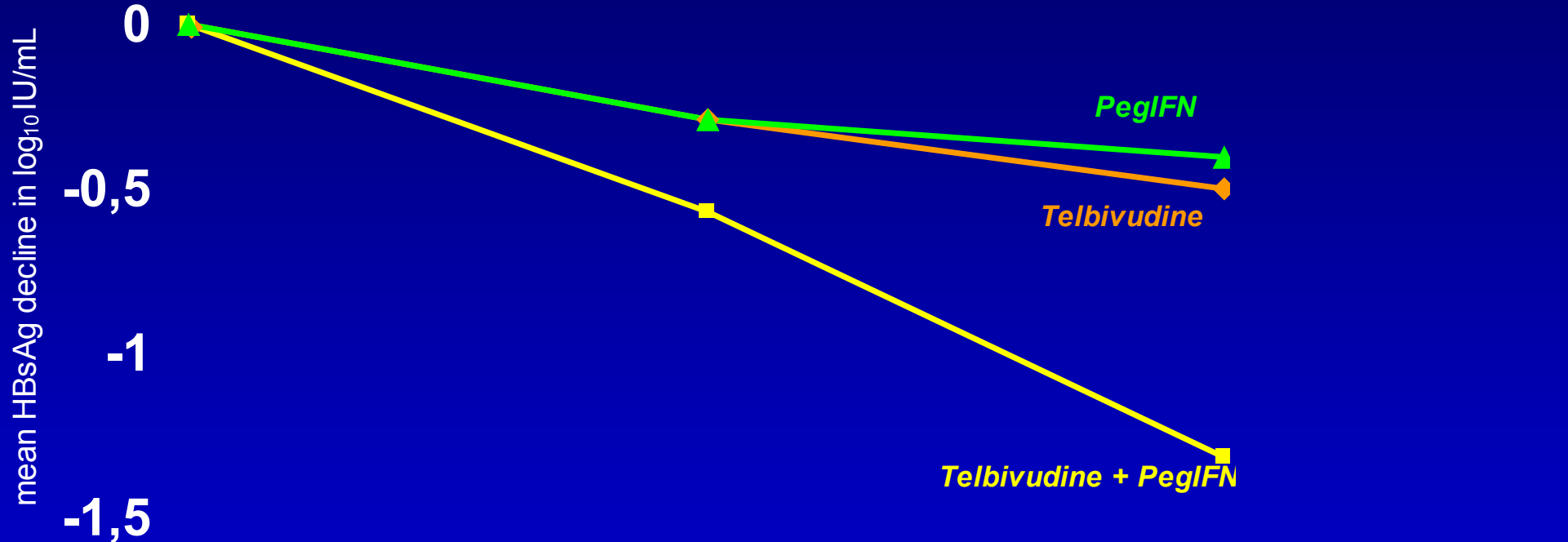
PEG IFN + NUC

PEG IFN + LAM SERUM HBV DNA



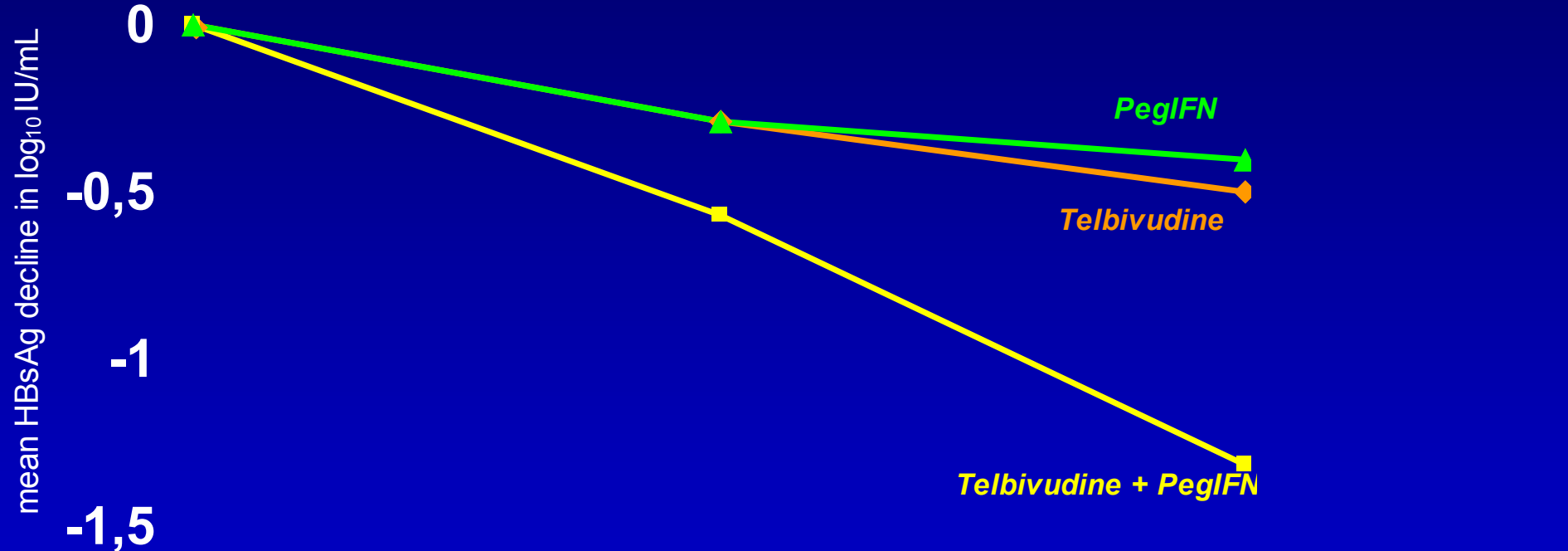
PEG IFN + Telbivudine

HBsAg decline baseline to week 24



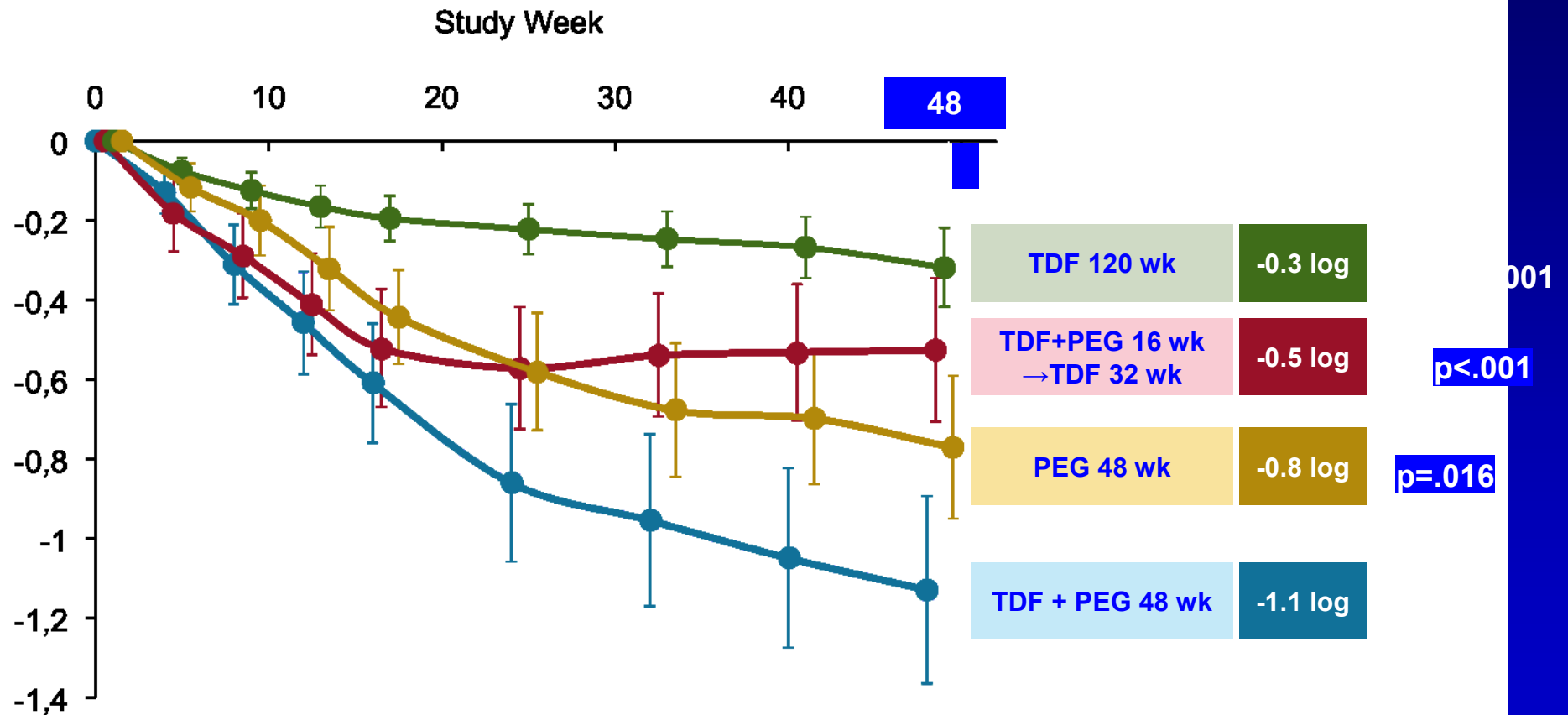
	Baseline	Week 12	Week 24
PEG	42	42	42
LDT	46	46	46
LDT+PEG	16	16	16

NEUROTOXICITY!!!

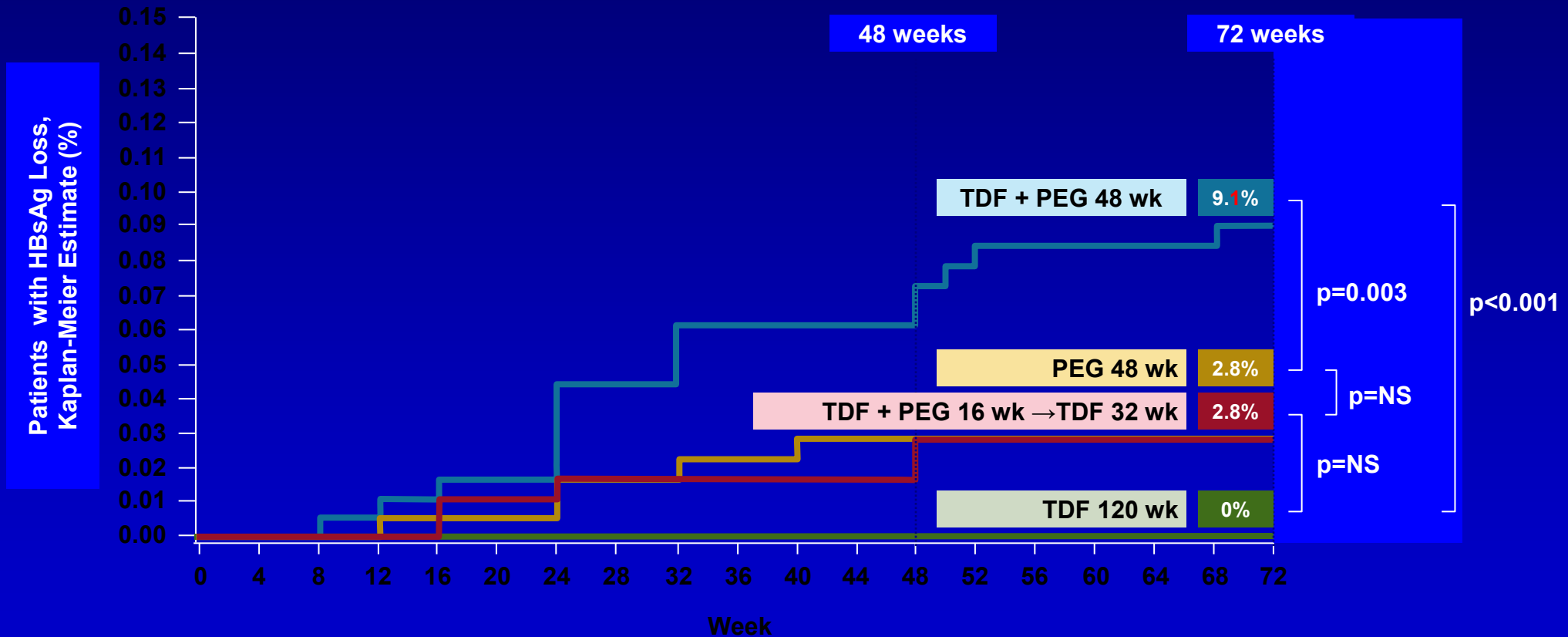


	Baseline	Week 12	Week 24
PEG	42	42	42
LDT	46	46	46
LDT+PEG	16	16	16

Efficacy: On-Treatment Changes in HBsAg Levels at Week 48



Results: HBsAg Loss Over Time (Week 72)



WHAT WE NEED TO LEARN

- Longer follow-up
 - Precise the role of HBsAg quantification
 - How and in who to use combination TX
-

WHAT WE NEED TO LEARN

**The right treatment for
the right patient**
