

Hepatitis B: Who, When and How to Treat?

Patrick Marcellin

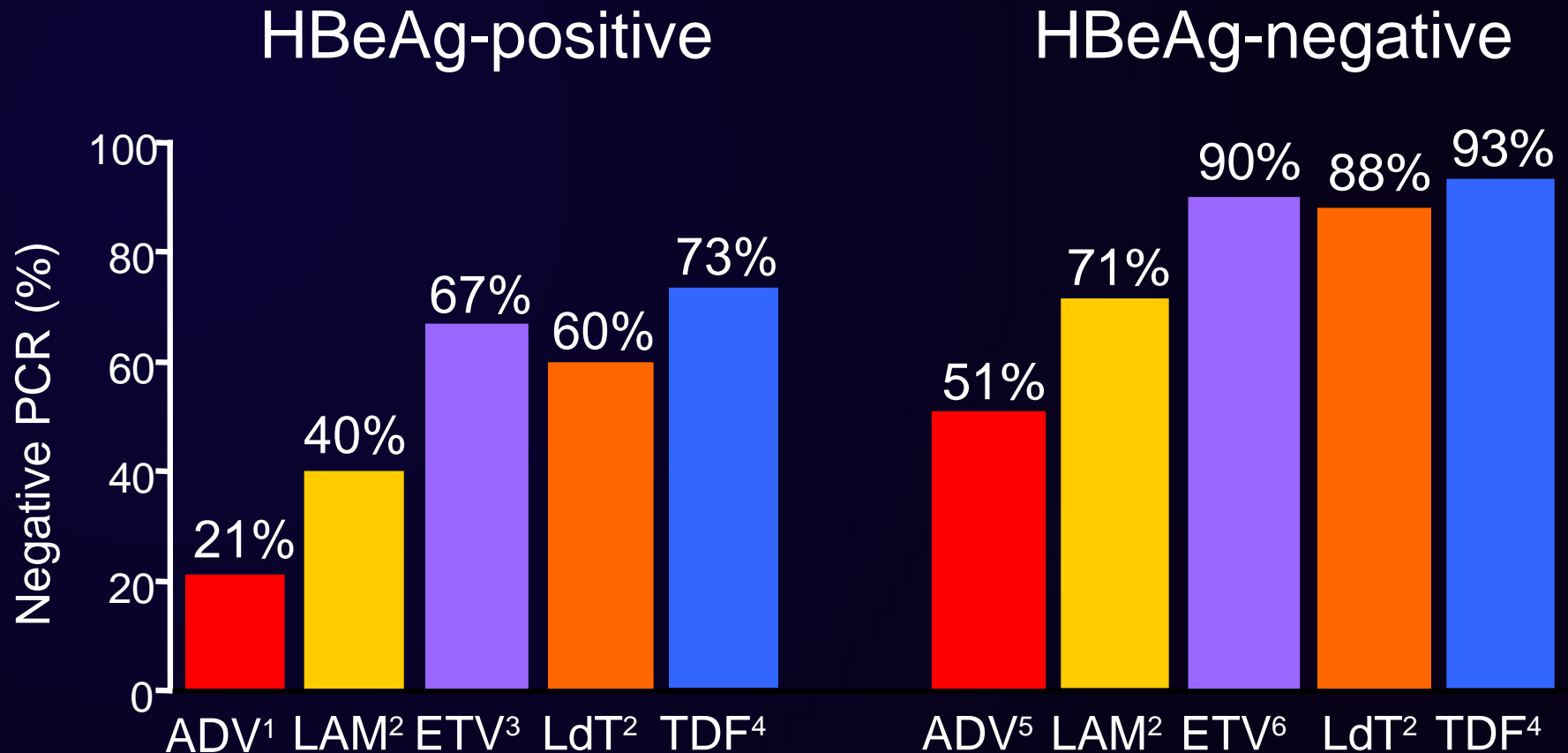
Where we are:
The achievements

ANALOGUES REGISTERED FOR THE TREATMENT OF CHRONIC HEPATITIS B

- Lamivudine -
- Adefovir -
- Telbivudine +

- Entecavir +++
- Tenofovir +++

VIROLOGICAL RESPONSE AT 1 YEAR

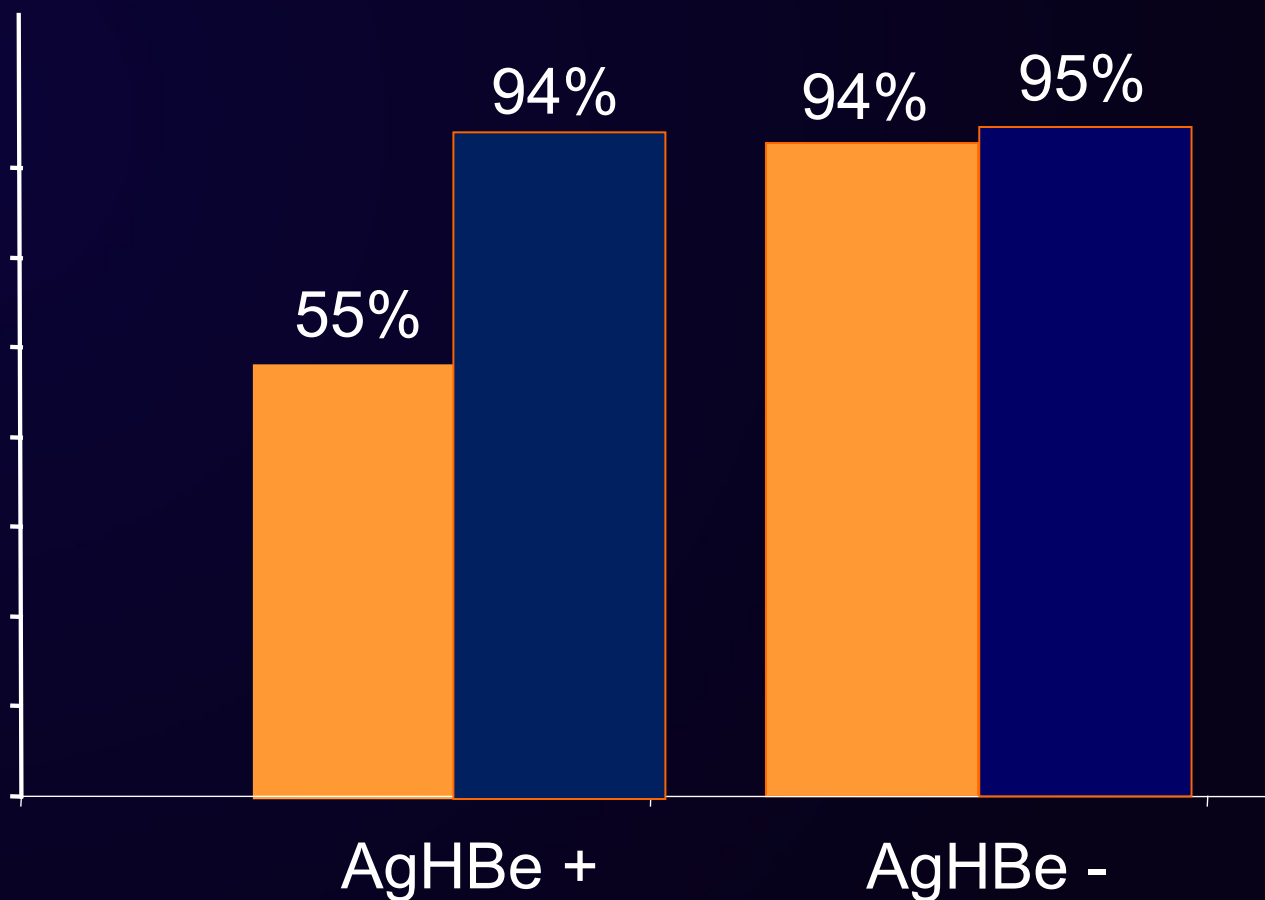


1. Marcellin et al. *N Engl J Med.* 2003
2. Lai et al. *N Engl J Med.* 2007
3. Chang et al. *N Engl J Med.* 2006
4. Marcellin et al. *N Engl J Med.* 2008
5. Hadziyannis et al. *N Engl J Med.* 2003

6. Lai et al. *N Engl J Med.* 2006

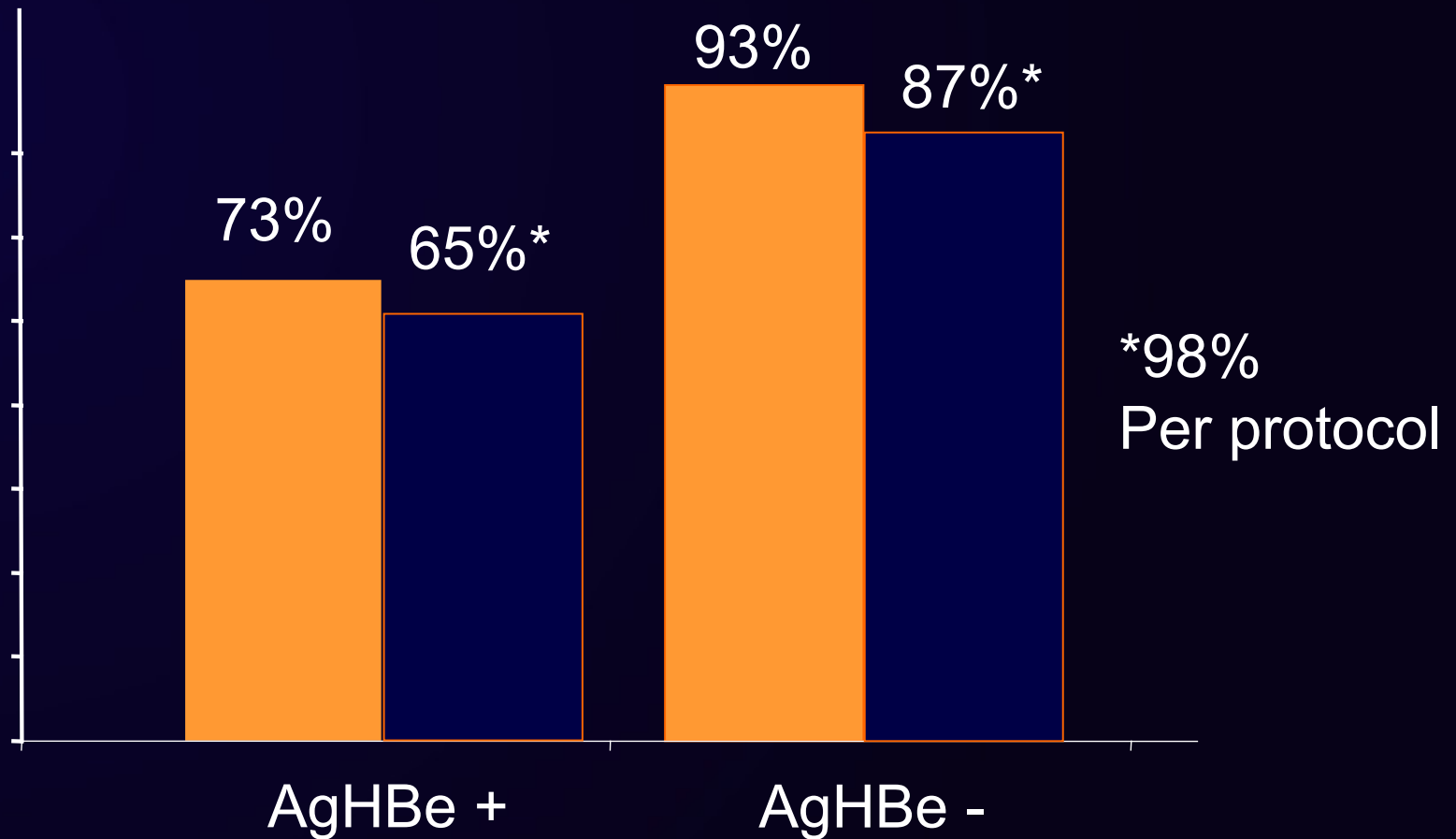
DURABILITY OF RESPONSE

ENTECAVIR UNDETECTABLE HBV DNA AT 1 AND 3-5 YEARS



TENOFOVIR

UNDETECTABLE HBV DNA AT 1 AND 5 YEARS

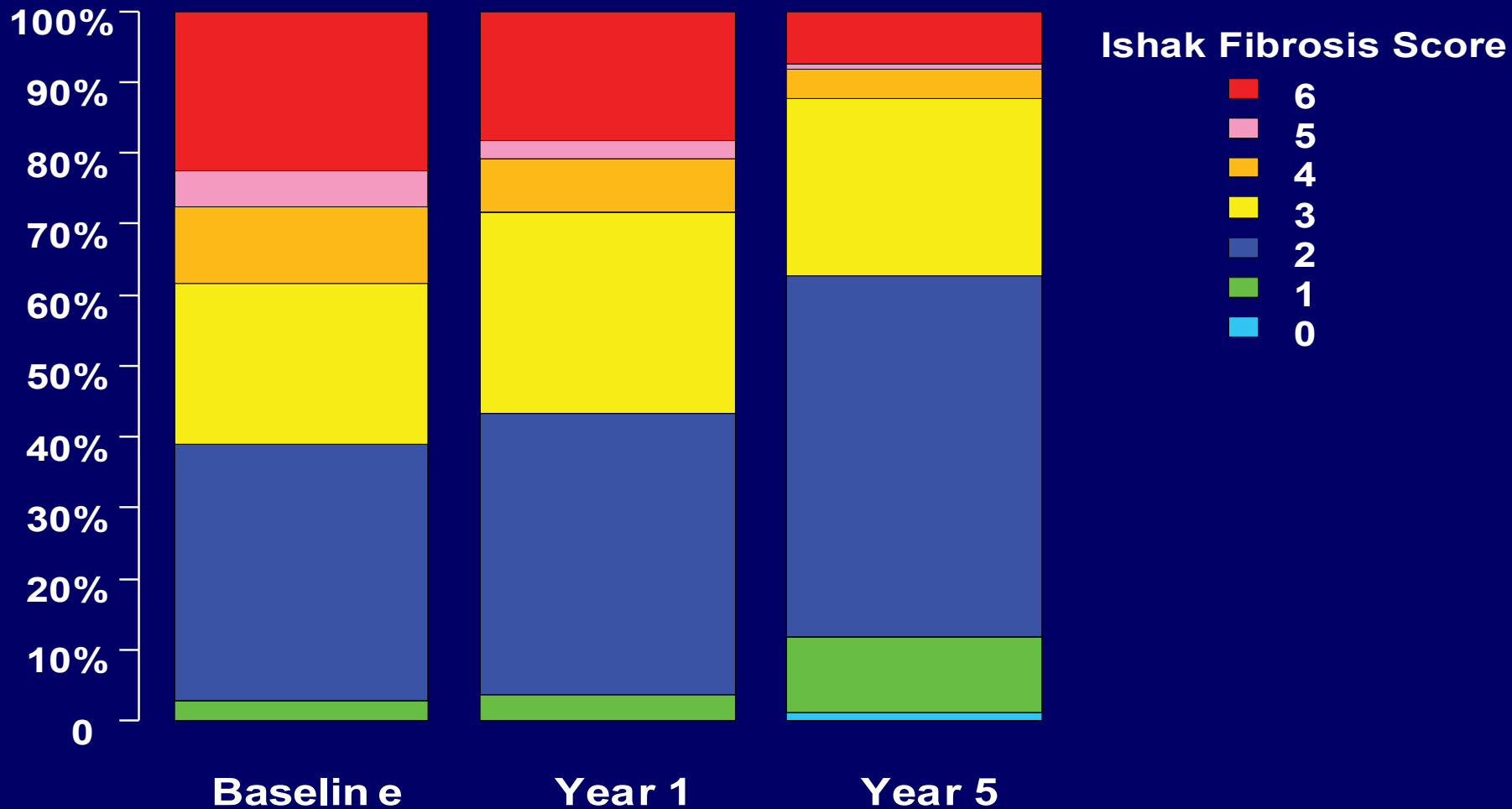


Marcellin et al. NEJM 2008

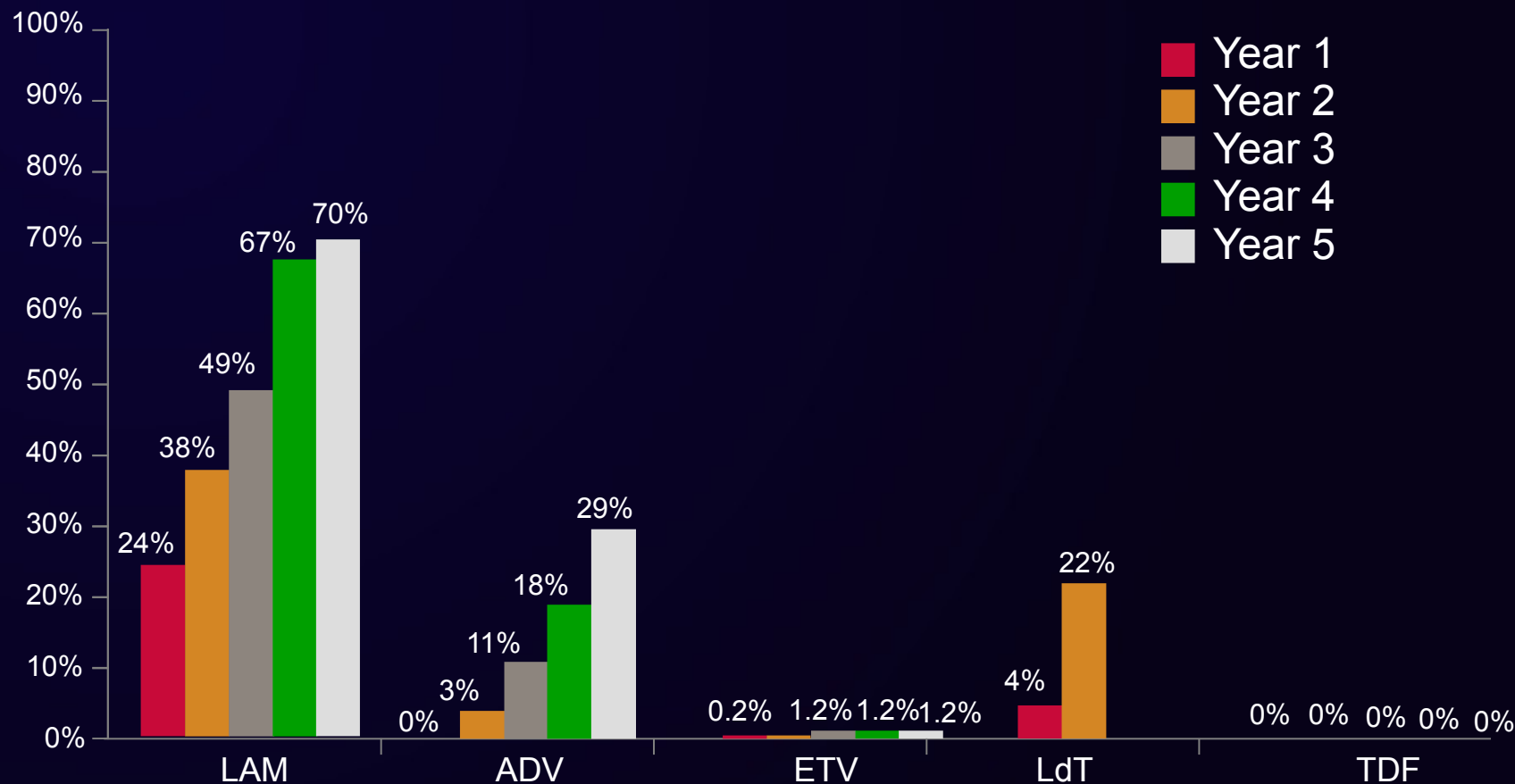
Marcellin et al. Lancet 2013

LIVER HISTOLOGY AT 5 YEARS

n=348



Cumulative incidence of HBV resistance



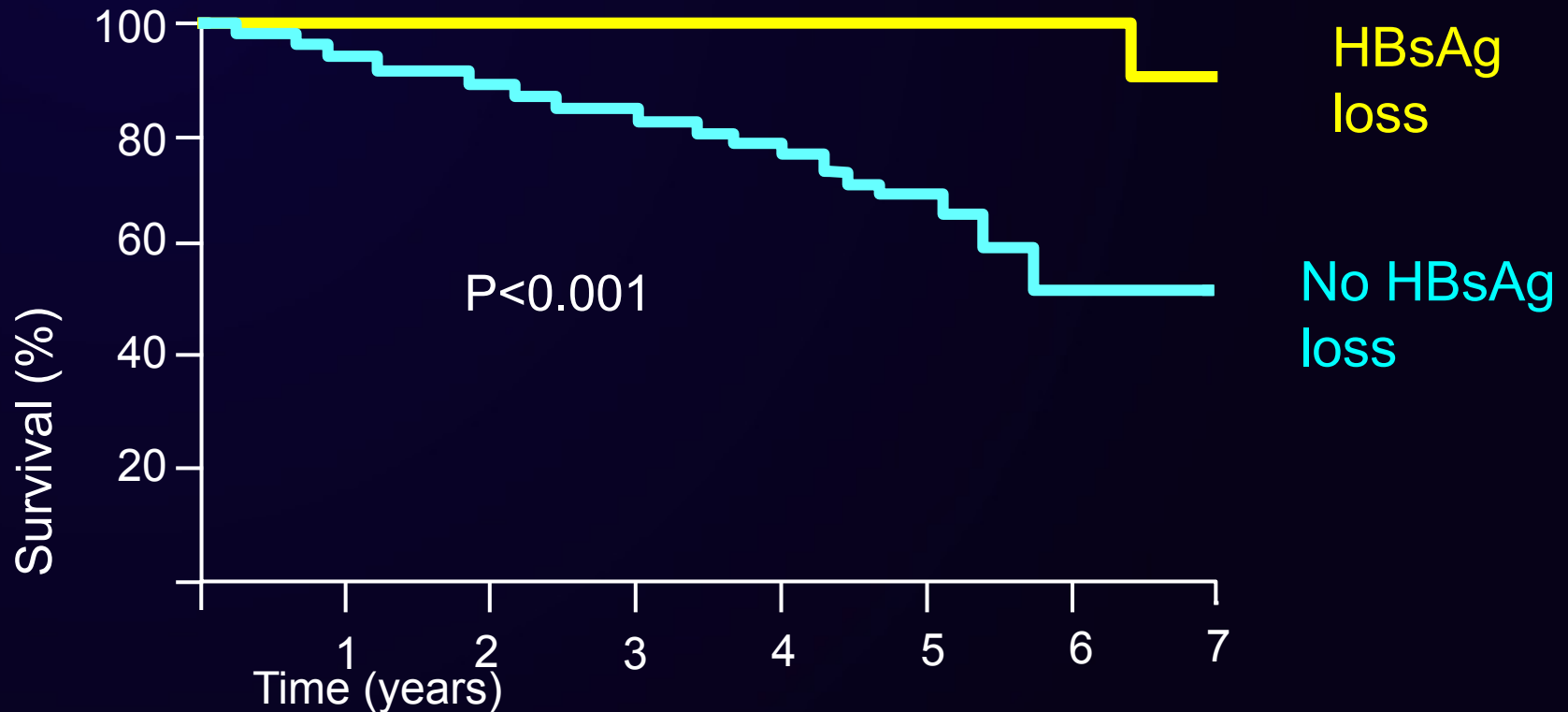
HBsAg AND THE RISK OF HCC

11,893 men in Taiwan

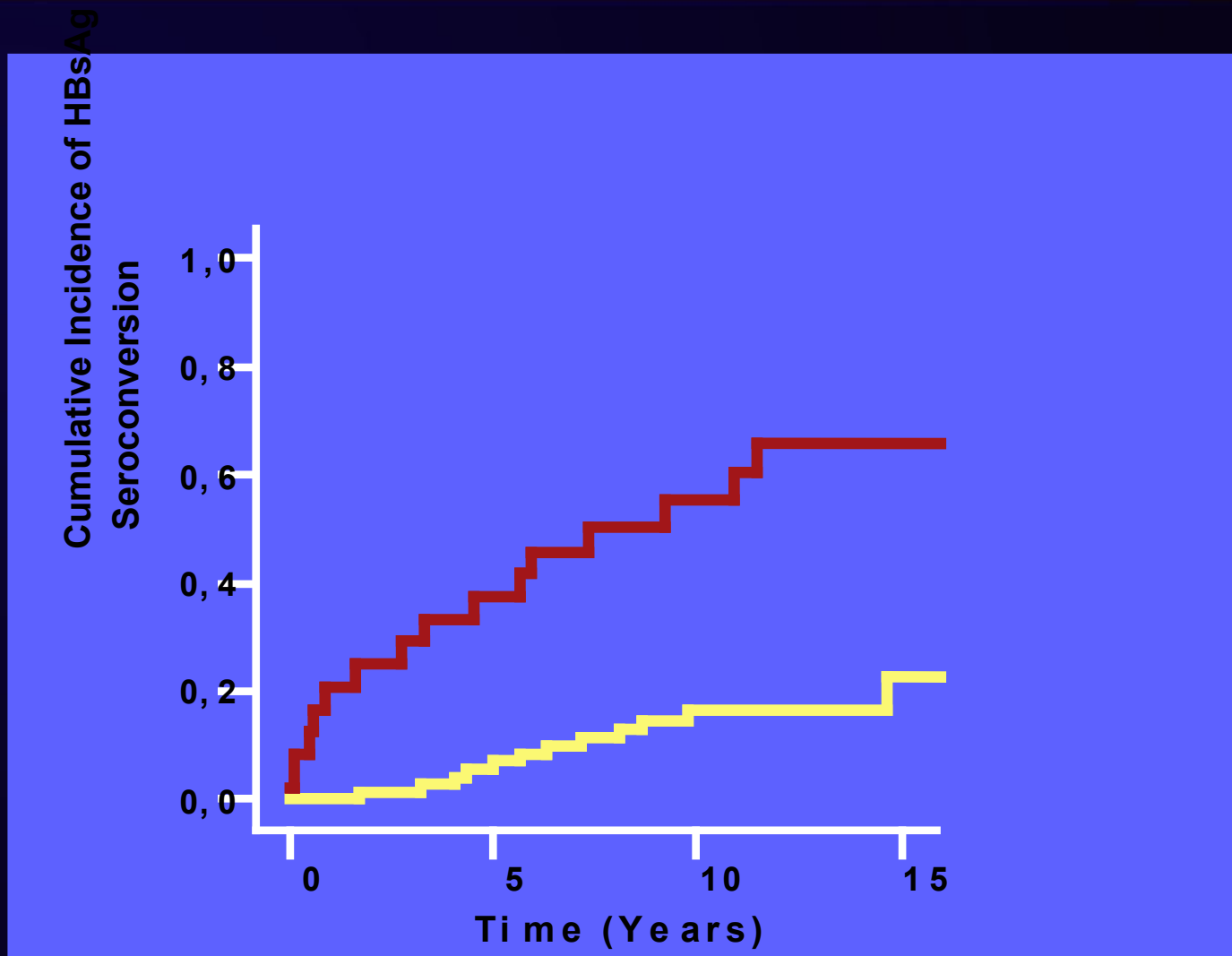
HBsAg	HBeAg	ALT	Relative Risk
--	--	normal	1
--	--	elevated	5
+	--	normal	10
+	--	elevated	30
+	+	normal	60
+	+	elevated	110

HBsAg Loss is Associated with Improved Survival

309 cirrhotics with a mean follow-up of 6 years



INCIDENCE OF HBsAg LOSS ACCORDING TO RESPONSE TO IFN (HBe seroconversion)



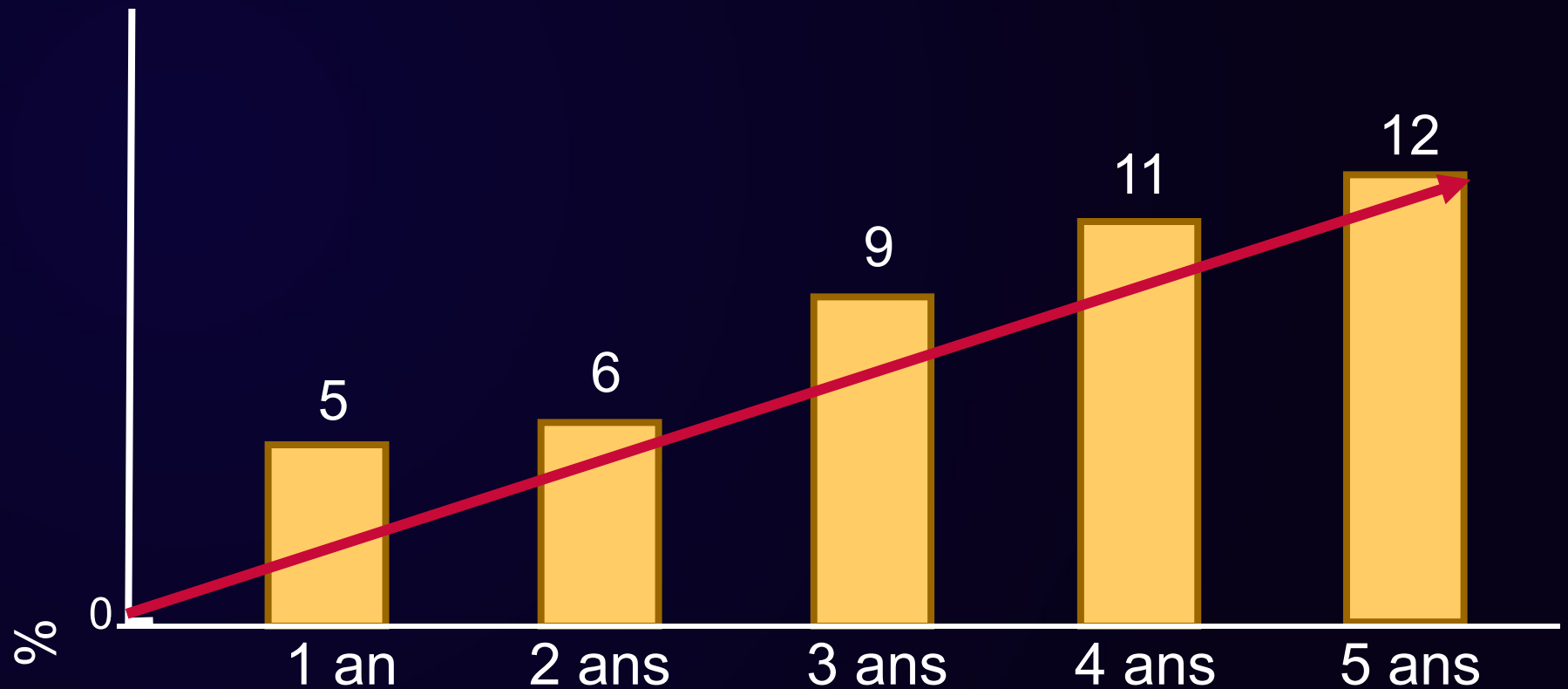
OUTCOME (10 years) AFTER IFN THERAPY

	HBsAg+	HBsAg-
■ HCC :	6	0
■ Ascitis :	5	0
■ Hemorrhage:	0	0
■ Transplantation:	0	0
■ Mortality (HCC):	4	0

PEG IFN

HBeAg negative CHB

HBsAg LOSS after PEG IFN \pm LAM

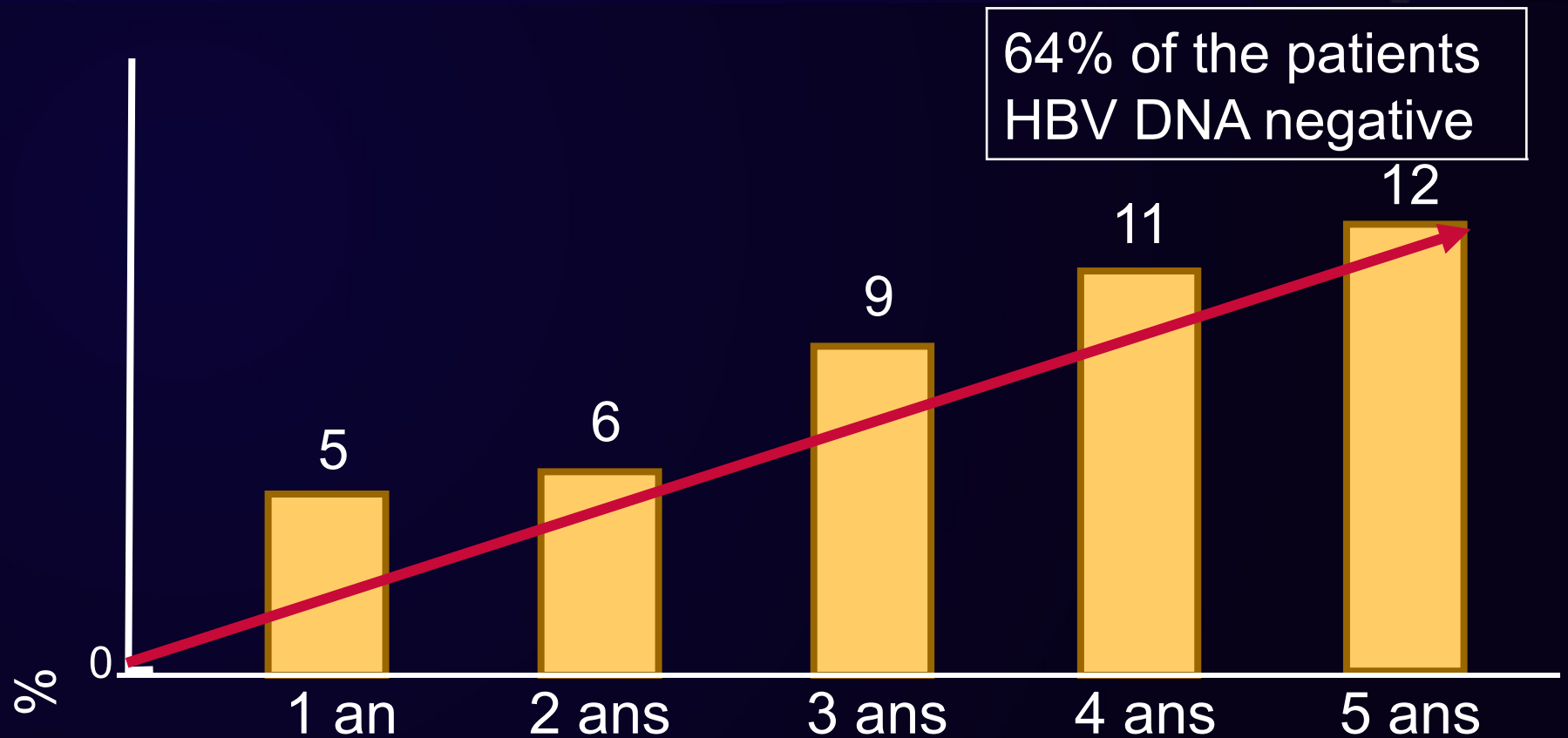


Marcellin et al. NEJM 2004

Marcellin et al. Gastroenterology 2009

Marcellin et al. Hepatology International 2012

HBsAg LOSS after PEG IFN ± LAM



Marcellin et al. NEJM 2004

Marcellin et al. Gastroenterology 2009

Marcellin et al. Hepatology International 2012

Where we are:
the limitations

Where we are: limitations

An iceberg floating in the ocean. The tip of the iceberg, which is visible above the water, is relatively small and jagged. The much larger, submerged part of the iceberg is visible below the water line, illustrating that the visible part is only a fraction of the whole. The water is a deep blue, and the sky is a lighter blue with some clouds.

Insufficient screening
Insufficient access to treatment

Where we go

Where we go

Use of quantification of HBsAg in combination with HBV DNA:

- Prognosis of the liver disease
- Tailoring therapy

Other viral markers (ccc DNA)

Where we go

Combination Therapy:

- PEG IFN + NUC

New Drugs

- Lambda IFN
- TLR7 agonists

Ultimate goal:

HBsAg loss