

Hepatitis B: Control or Cure?

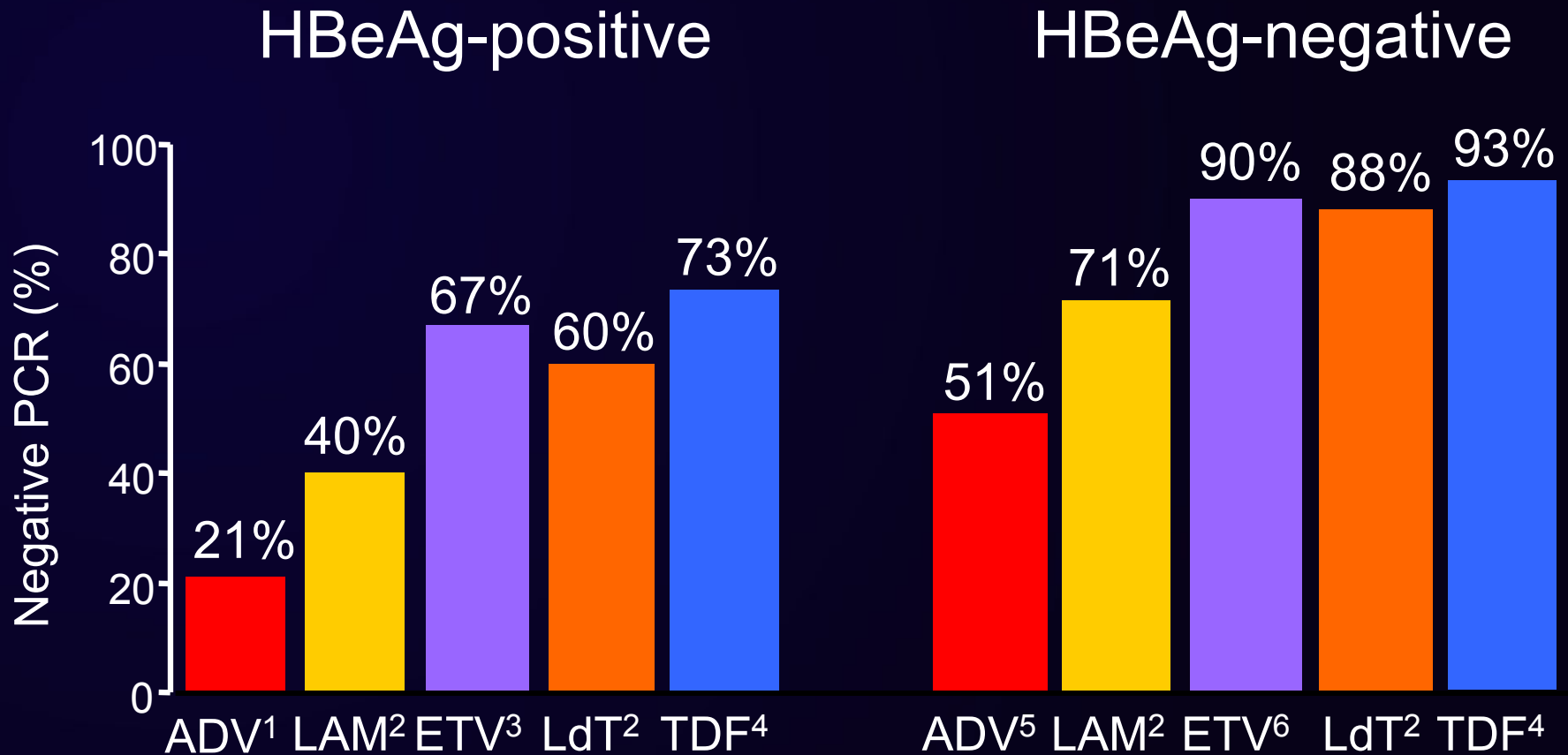
Patrick Marcellin

Where we are:
The achievements

ANALOGUES REGISTERED FOR THE TREATMENT OF CHRONIC HEPATITIS B

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

VIROLOGICAL RESPONSE AT 1 YEAR



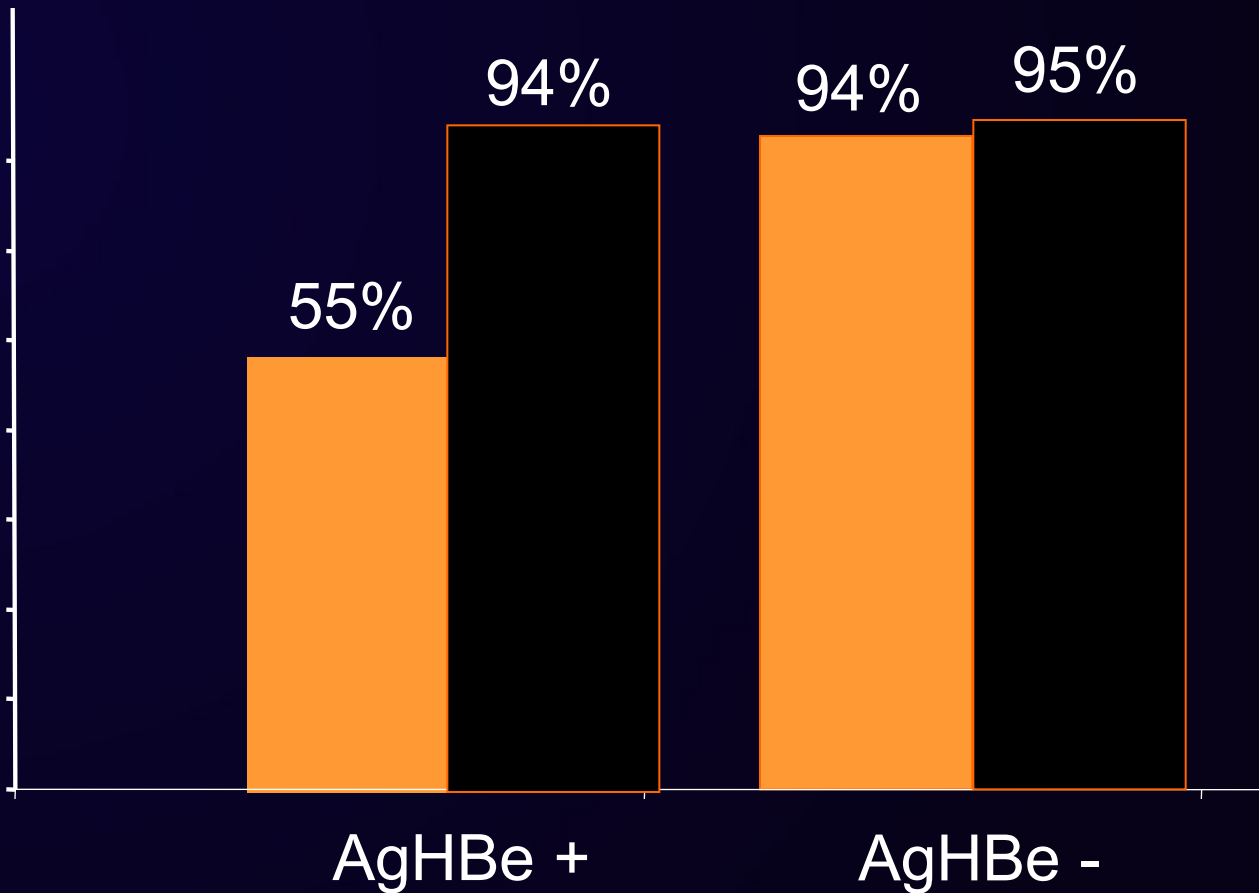
1. Marcellin et al. *N Engl J Med.* 2003
3. Chang et al. *N Engl J Med.* 2006
5. Hadziyannis et al. *N Engl J Med.* 2003

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

DURABILITY OF RESPONSE

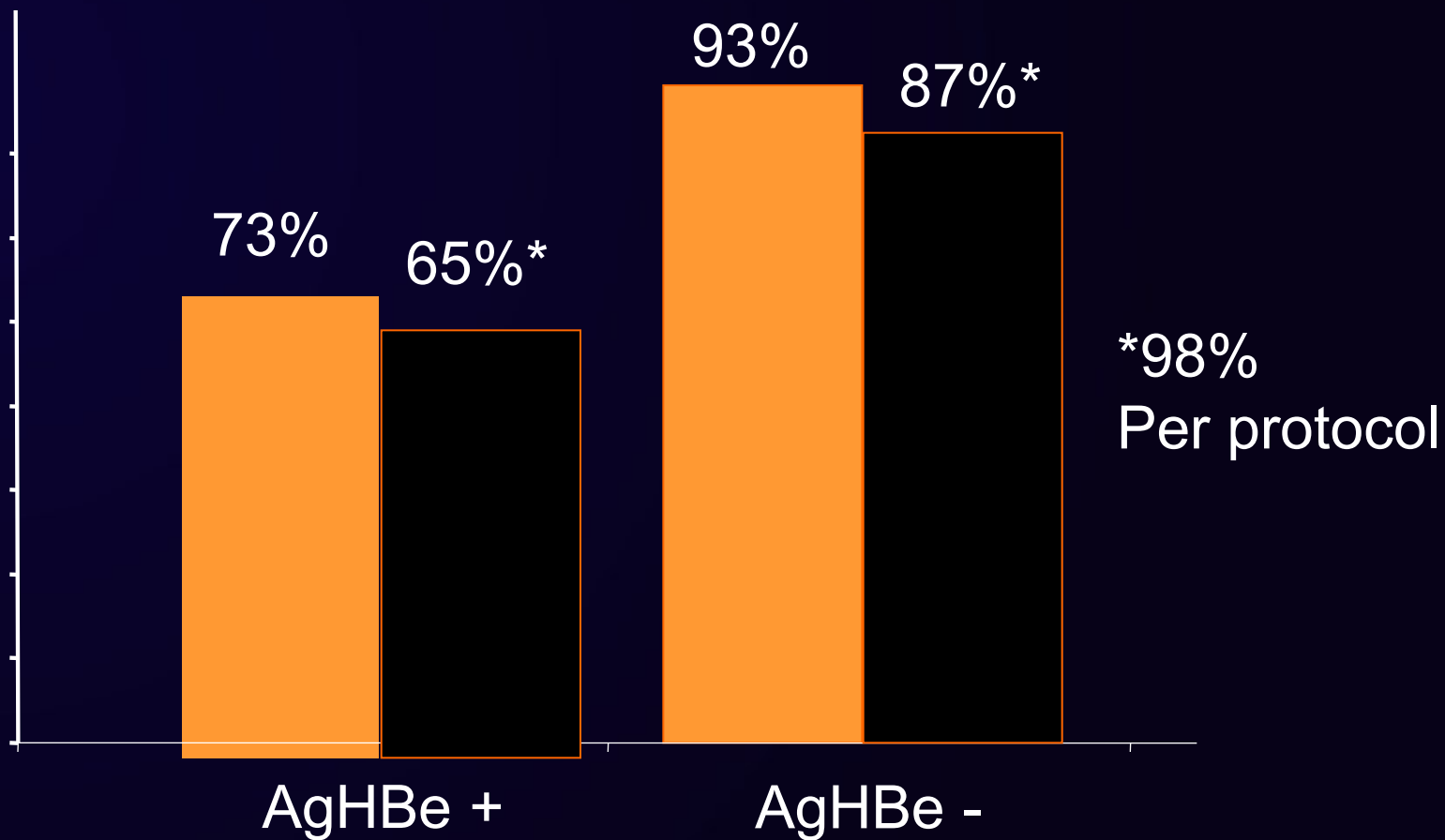
ENTECAVIR

UNDETECTABLE HBV DNA AT 1 AND 3-5 YEARS



TENOFOVIR

UNDETECTABLE HBV DNA AT 1 AND 5 YEARS

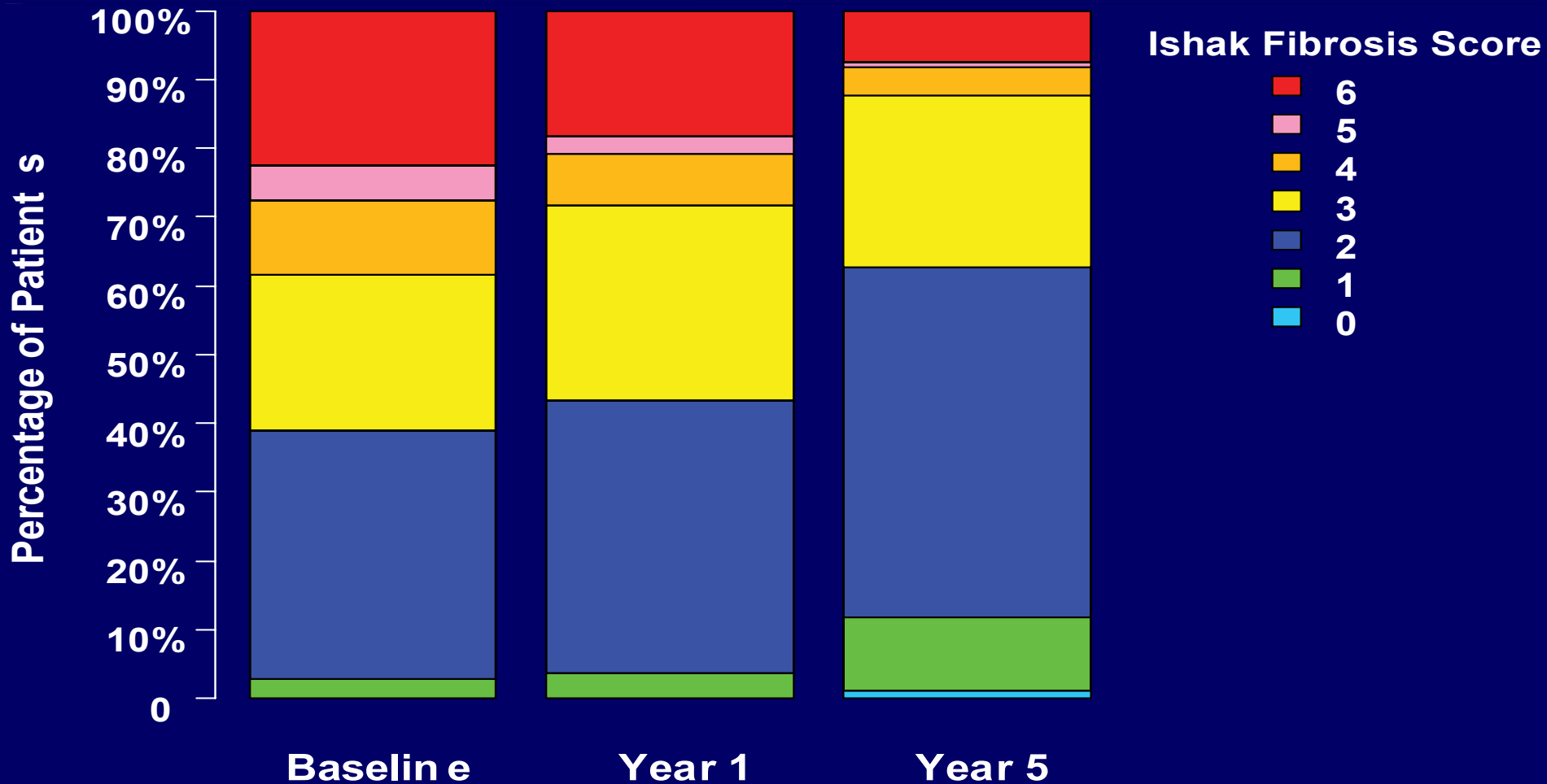


Marcellin et al. NEJM 2008

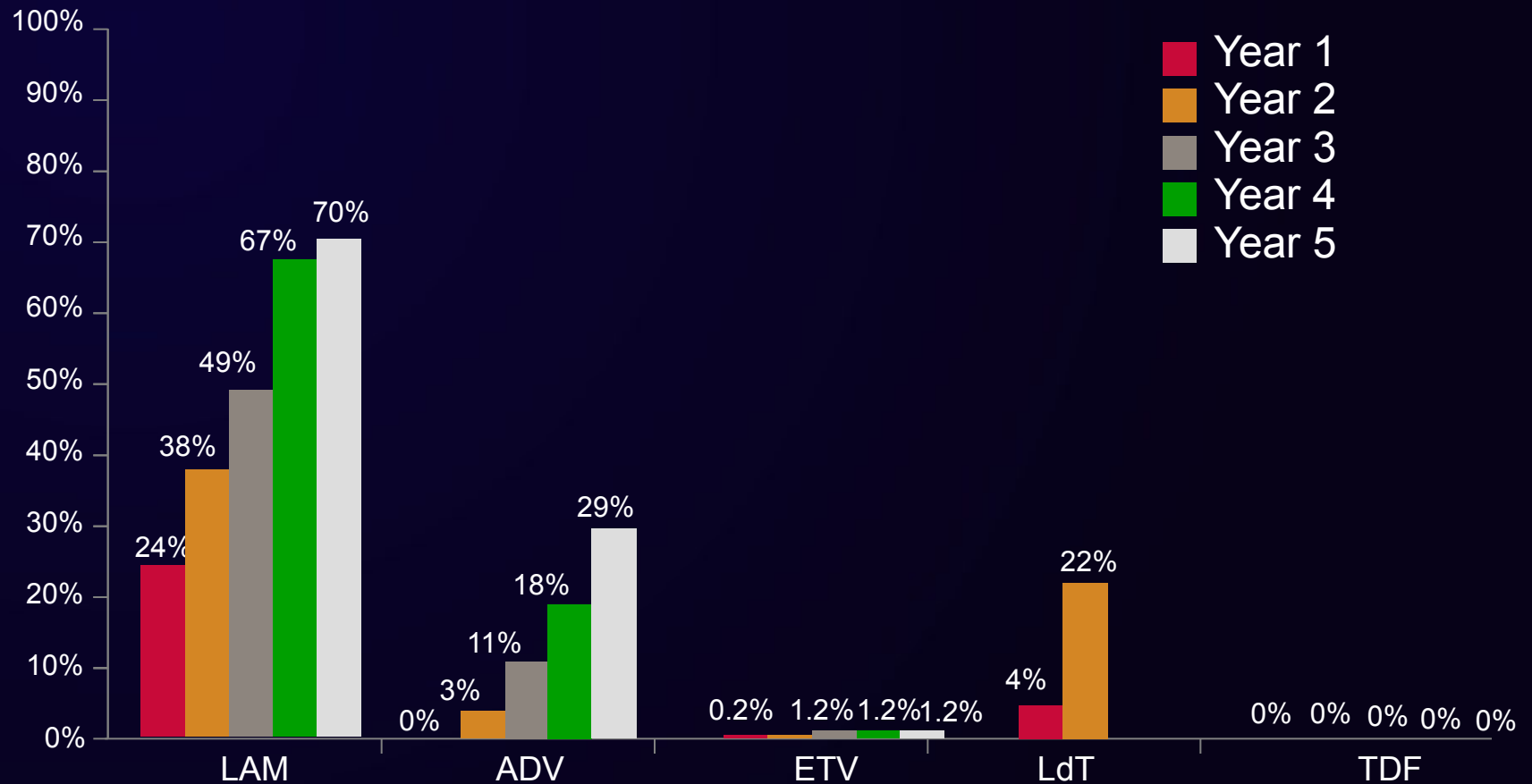
Marcellin et al. Lancet

LIVER HISTOLOGY AT 5 YEARS

n=348



Cumulative incidence of HBV resistance



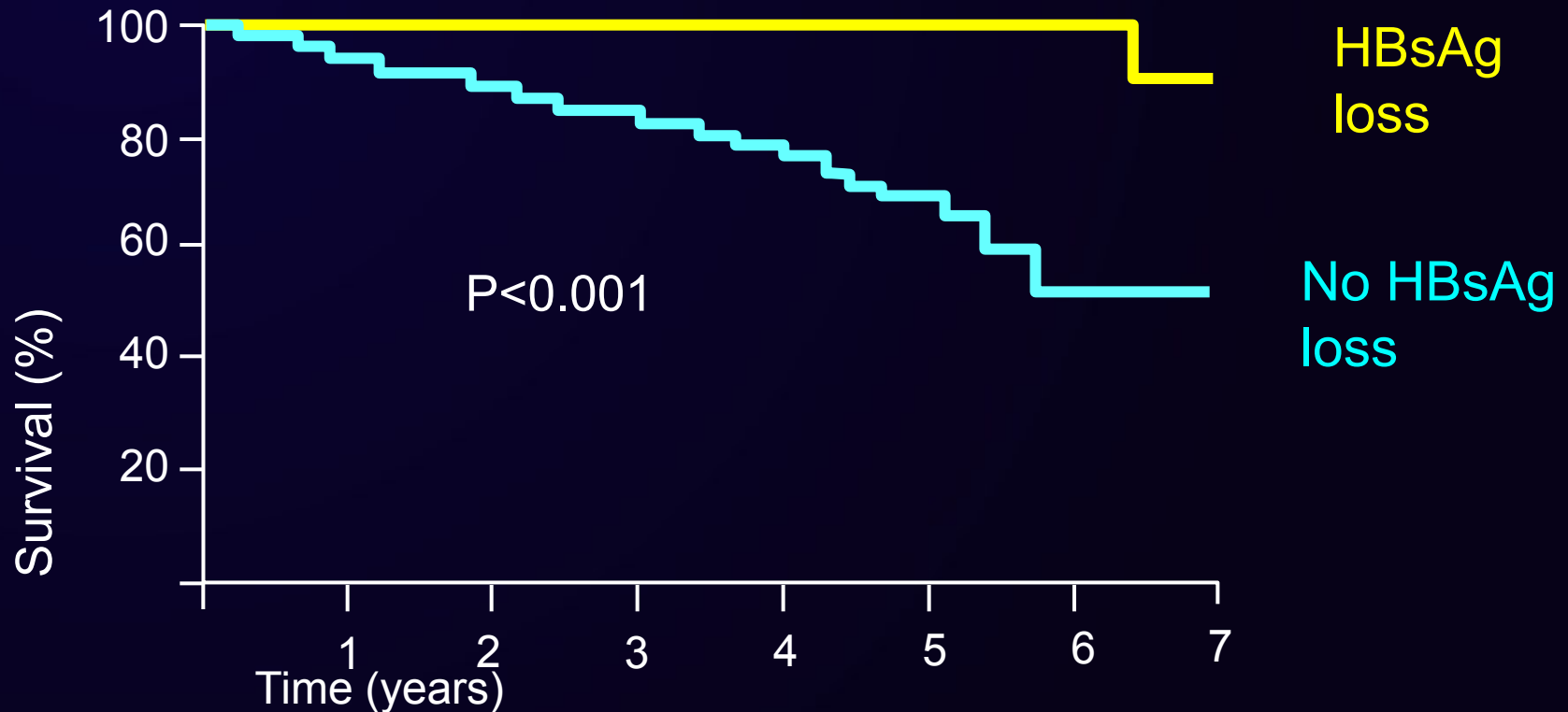
HBsAg AND THE RISK OF HCC

11,893 men in Taiwan

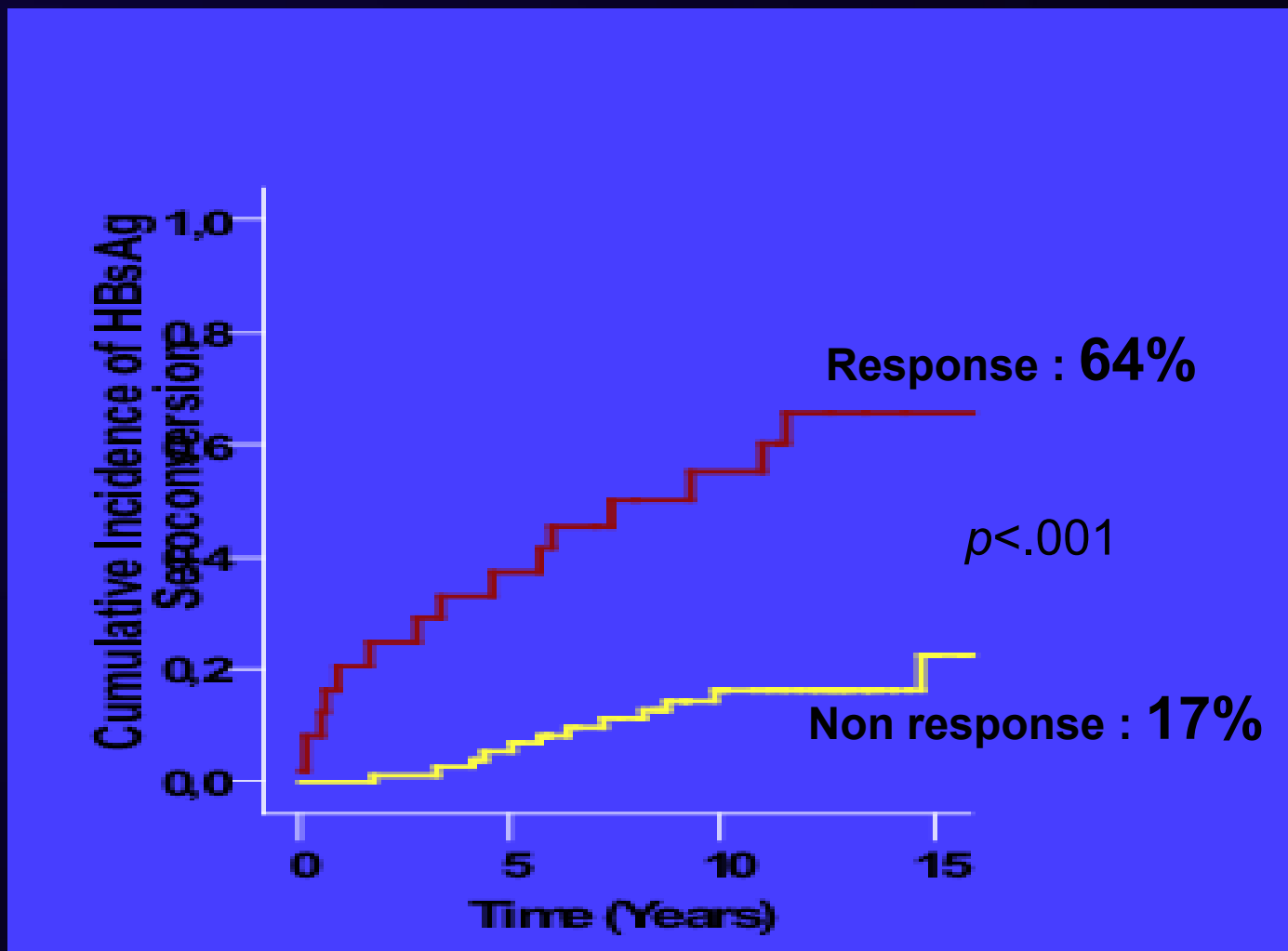
HBsAg	HBeAg	ALT	Relative Risk
--	--	normal	1
--	--	elevated	5
+	--	normal	10
+	--	elevated	30
+	+	normal	60
+	+	elevated	110

HBsAg Loss is Associated with Improved Survival

309 cirrhotics with a mean follow-up of 6 years



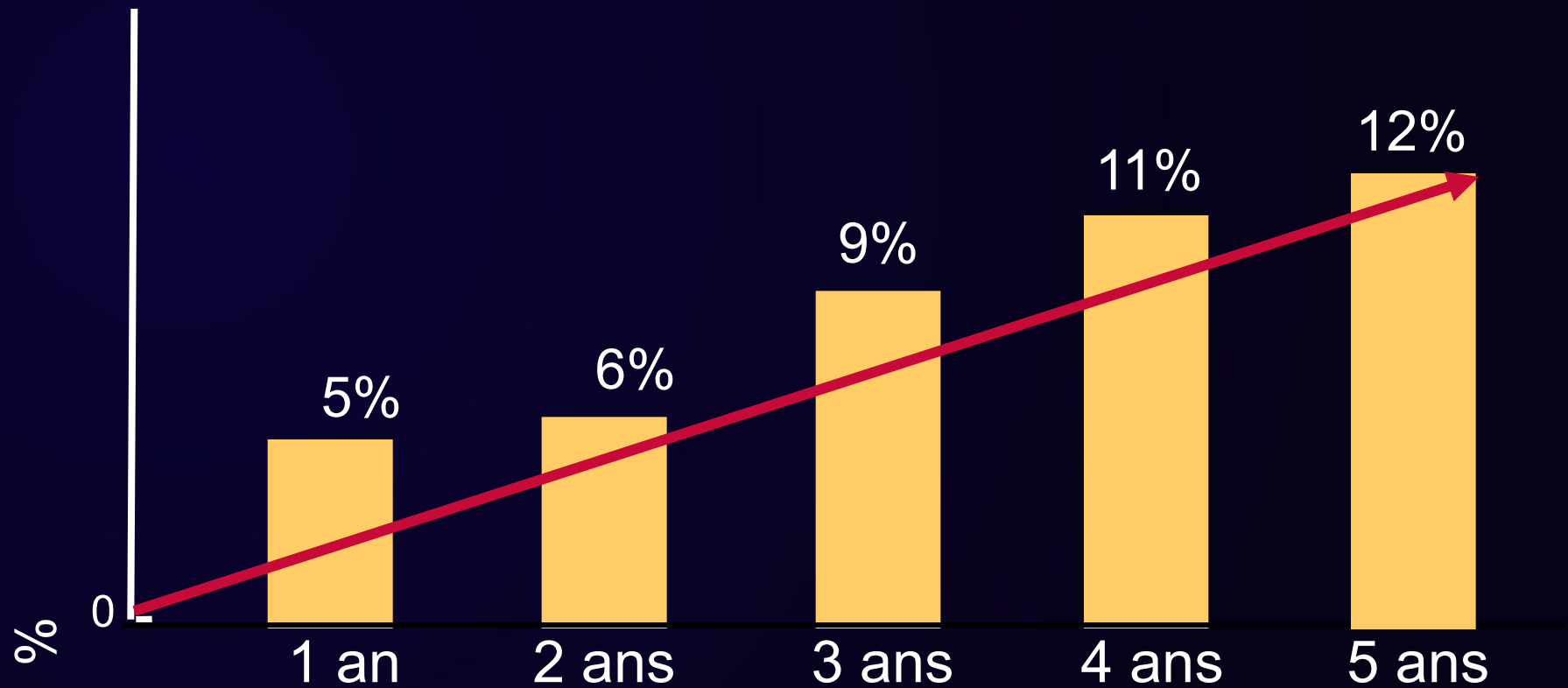
INCIDENCE OF HBsAg LOSS ACCORDING TO RESPONSE TO IFN (HBe seroconversion)



OUTCOME (10 years) AFTER IFN THERAPY

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

HBsAg LOSS after PEG IFN \pm LAM

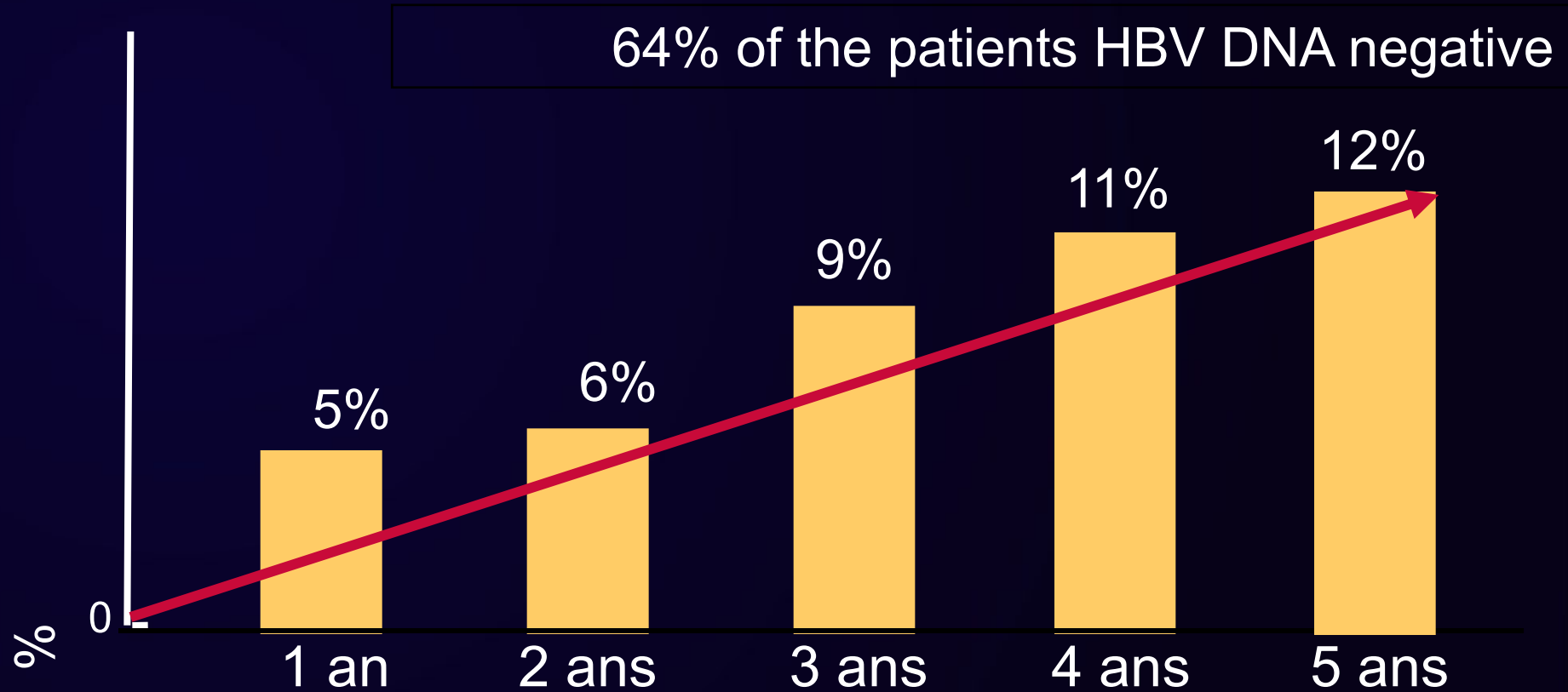


Marcellin et al. NEJM 2004

Marcellin et al. Gastroenterology 2009

Marcellin et al. Hepatology International 2012

HBsAg LOSS after PEG IFN \pm 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 is visible above the water surface, while the much larger, submerged part is below. The water is a deep blue, and the sky is a lighter blue with some clouds. The iceberg is white and jagged.

Insufficient screening
Insufficient access to treatment

Where we go

Where we go

Better use 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