

XXXI Congreso Nacional de la Sociedad Española de Medicina Interna

II Congreso Ibérico de Medicina Interna

OVIEDO

17-20 Noviembre 2010

Auditorio-Palacio de Congresos
"Príncipe Felipe"

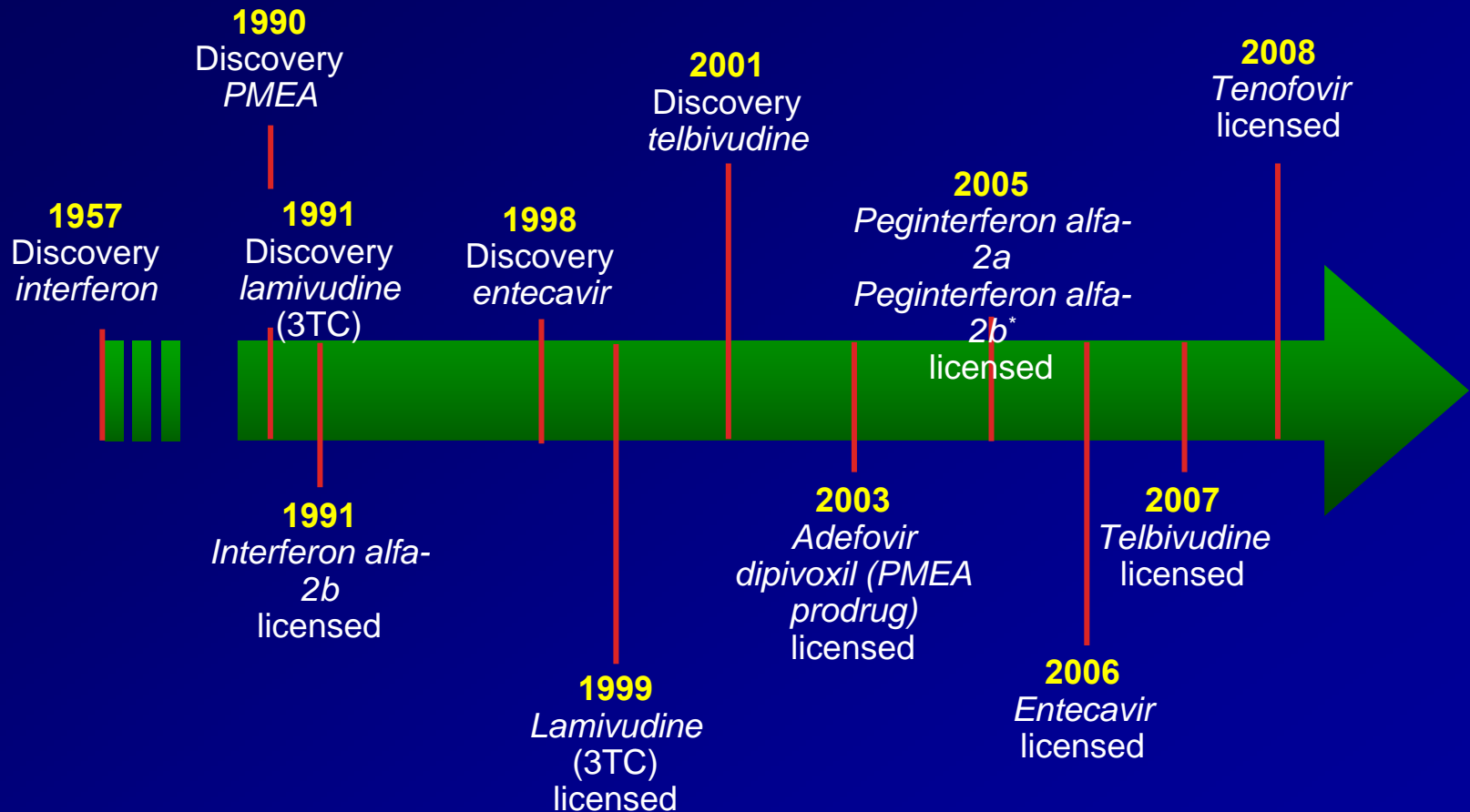
VII Congreso de la Sociedad
Asturiana de Medicina Interna

Tratamiento Hepatitis B

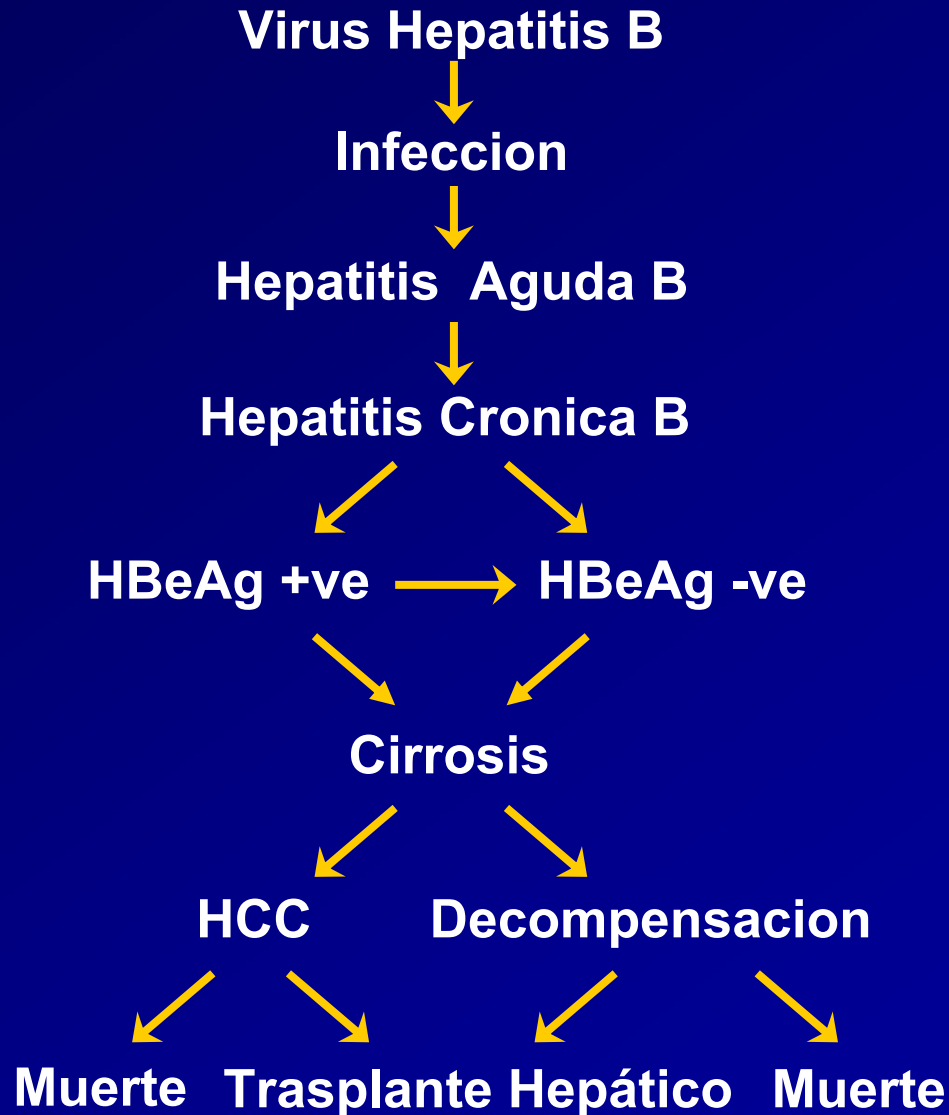
Maria Buti

Hospital General Universitario Valle de Hebrón Barcelona

Advances in HBV Treatment



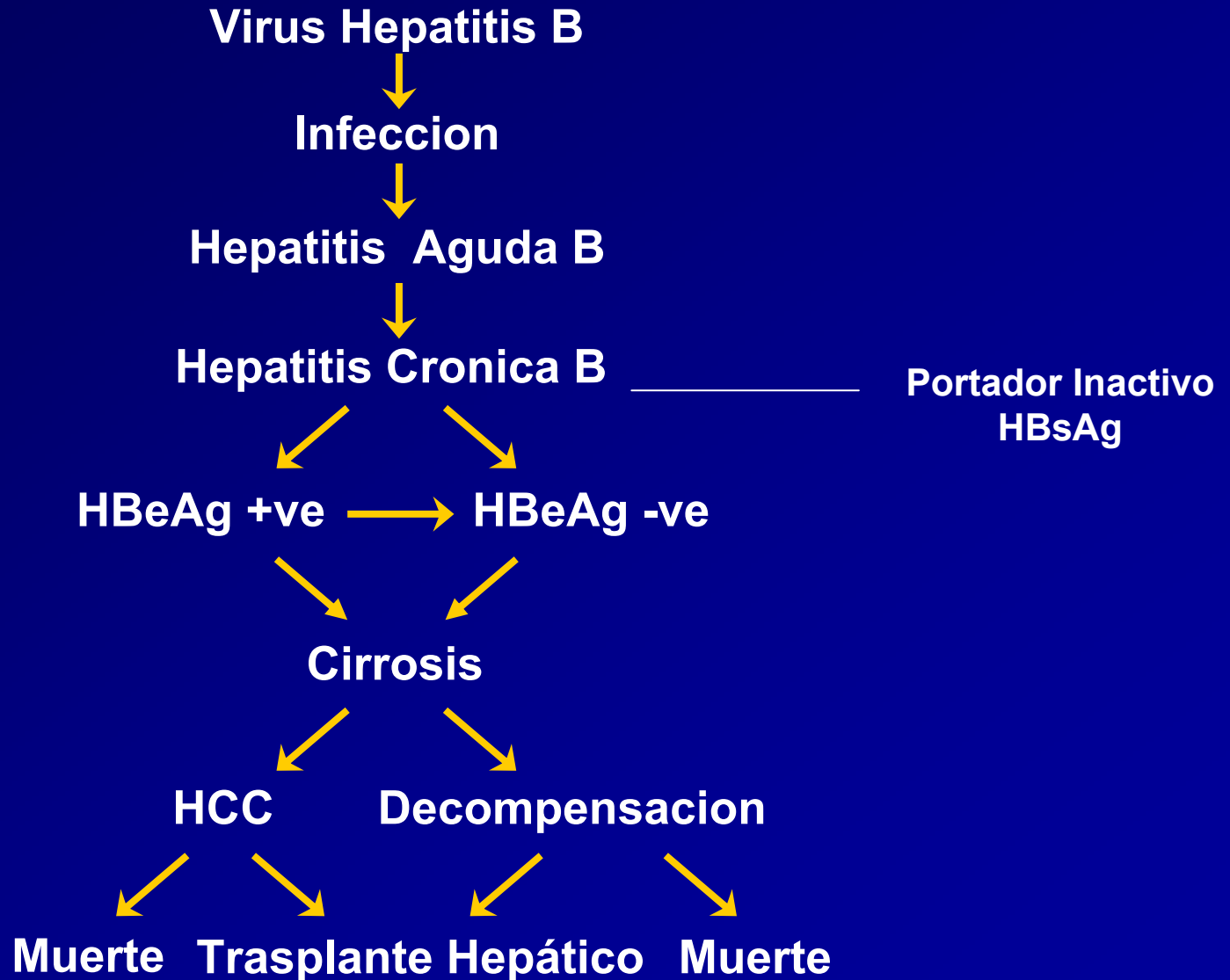
Hepatitis B: Progresion de la Enfermedad



¿A quien debemos tratar?

- **Tratamiento Obligatorio**
- **Tratamiento recomendable**
- **No tratamiento**

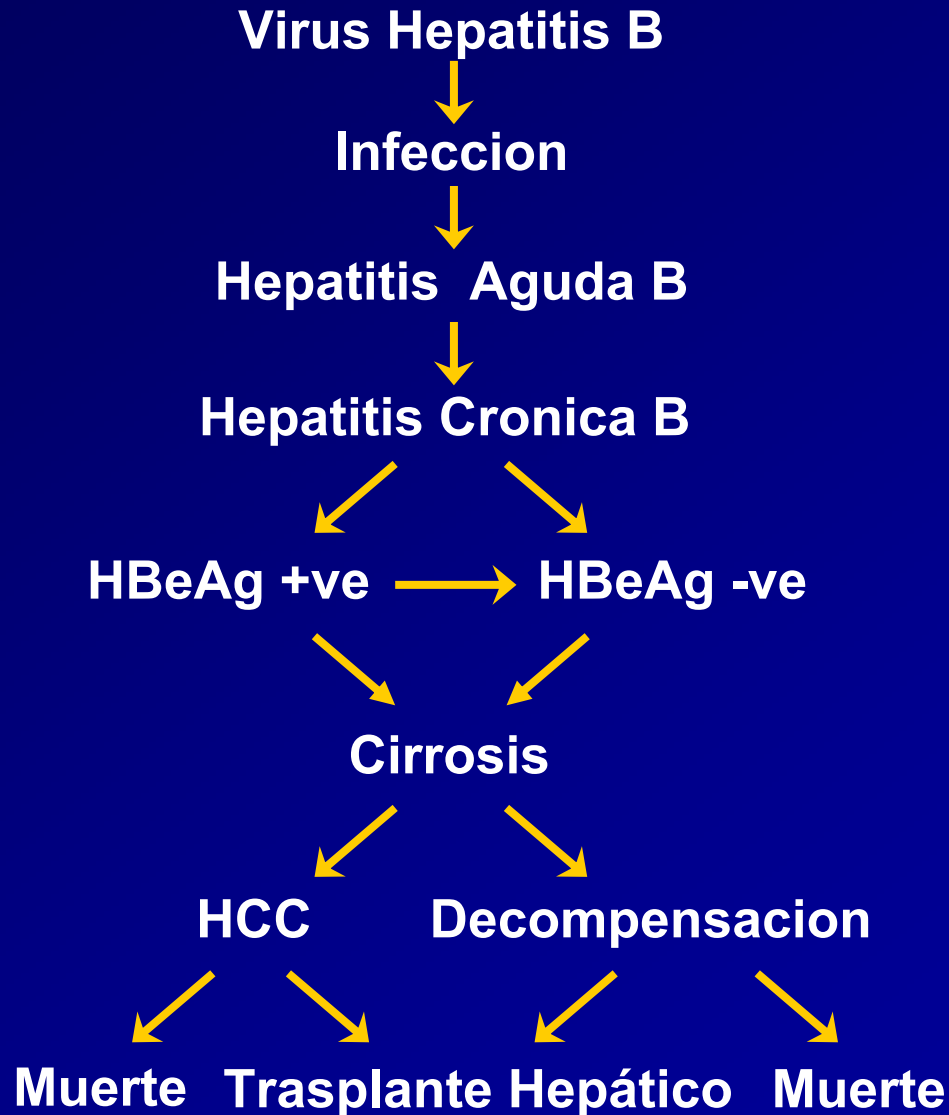
Hepatitis B: Progresion de la Enfermedad



Tratamiento No Recomendable

- Hepatitis Aguda B excepto en la Hepatitis Fulminante
- Fase de Inmunotolerancia
 - ALT normales y altos valores DNA-VHB
- Portadores Inactivos
 - ALT normales y DNA-VHB < 2.000 UI/mL

Hepatitis B: Progresion de la Enfermedad

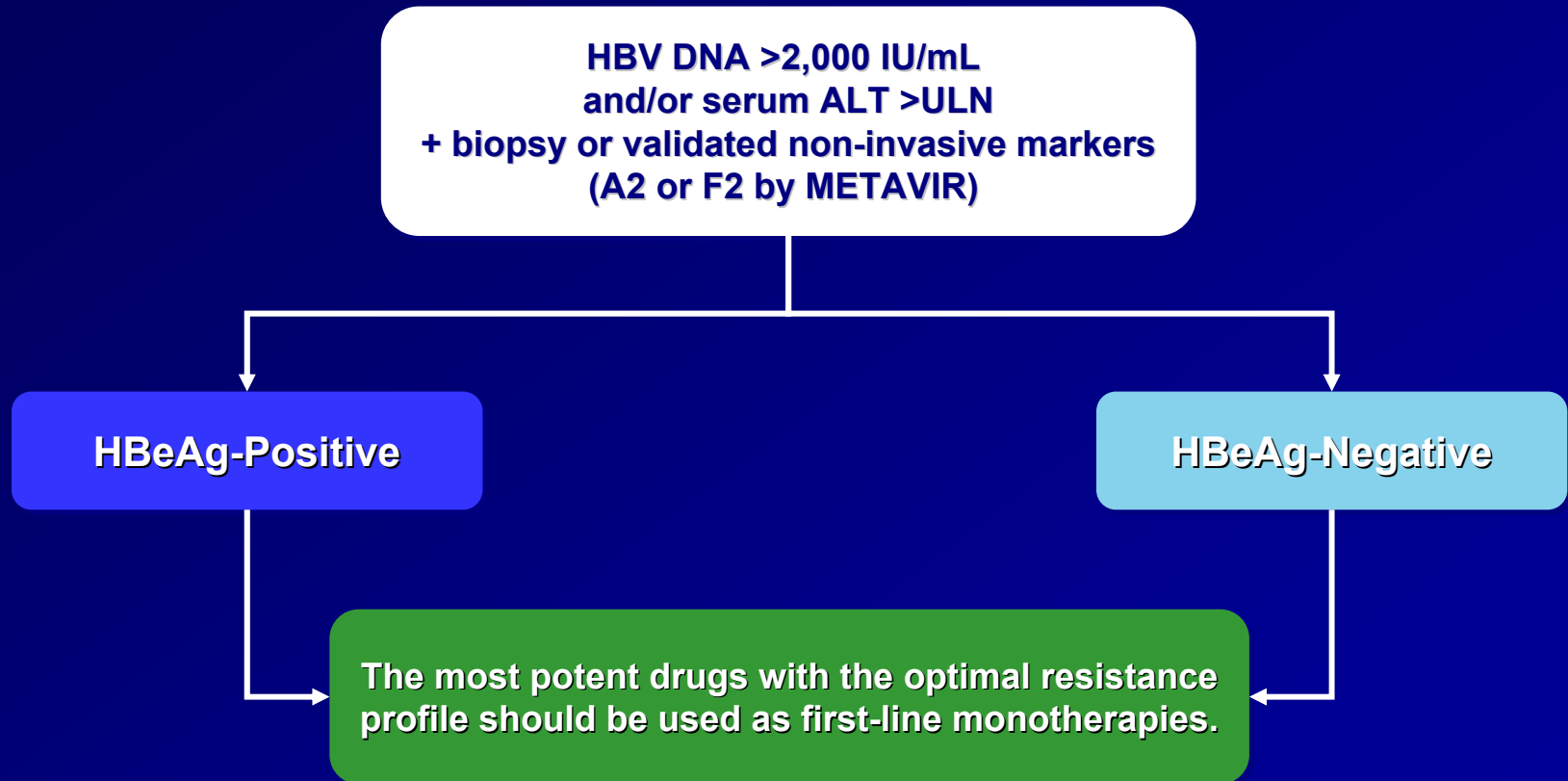


Tratamiento Recomendable

■ Hepatitis Crónica B

- HBeAg positivo
- HBeAg negativo

EASL Guidelines: Indication For 1st Line Treatment Algorithm

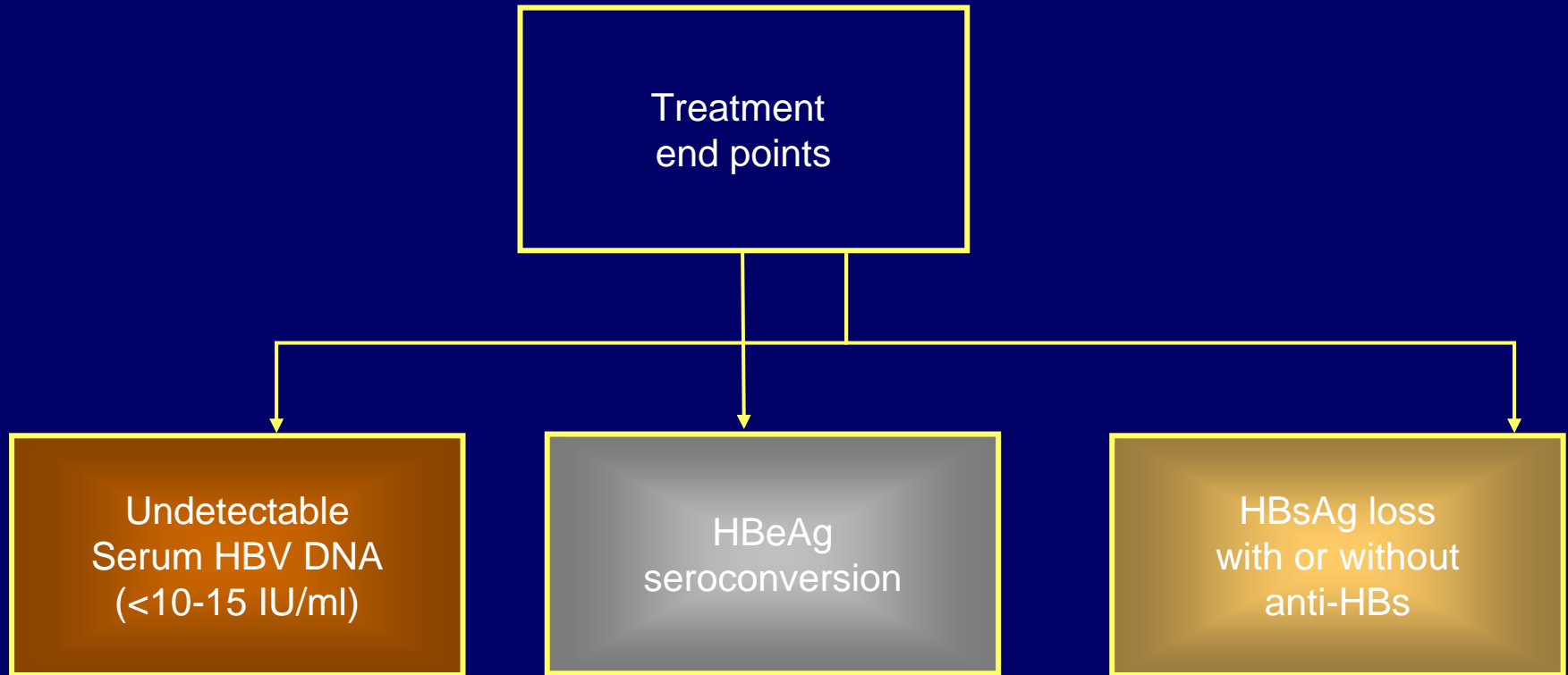


- Indications for treatment must also take into account age, health status, and availability of anti-viral agents in individual countries.

Antivirals approved for hepatitis B

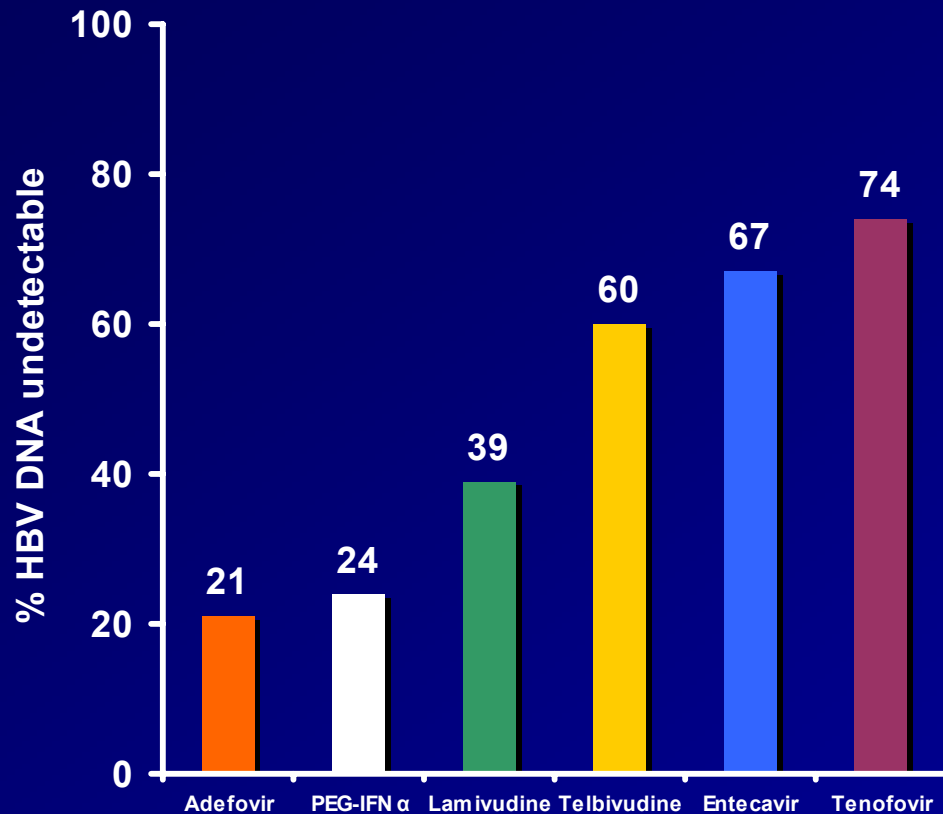
Drug Type	Approved
Nucleoside analogs	<ul style="list-style-type: none">• Lamivudine*• Entecavir• Telbivudine
Nucleotide analogs	<ul style="list-style-type: none">• Adefovir dipivoxil• Tenofovir
Cytokines	<ul style="list-style-type: none">• Interferon alfa• Pegylated Interferon alfa-2a

Current Treatment End Points in CHB

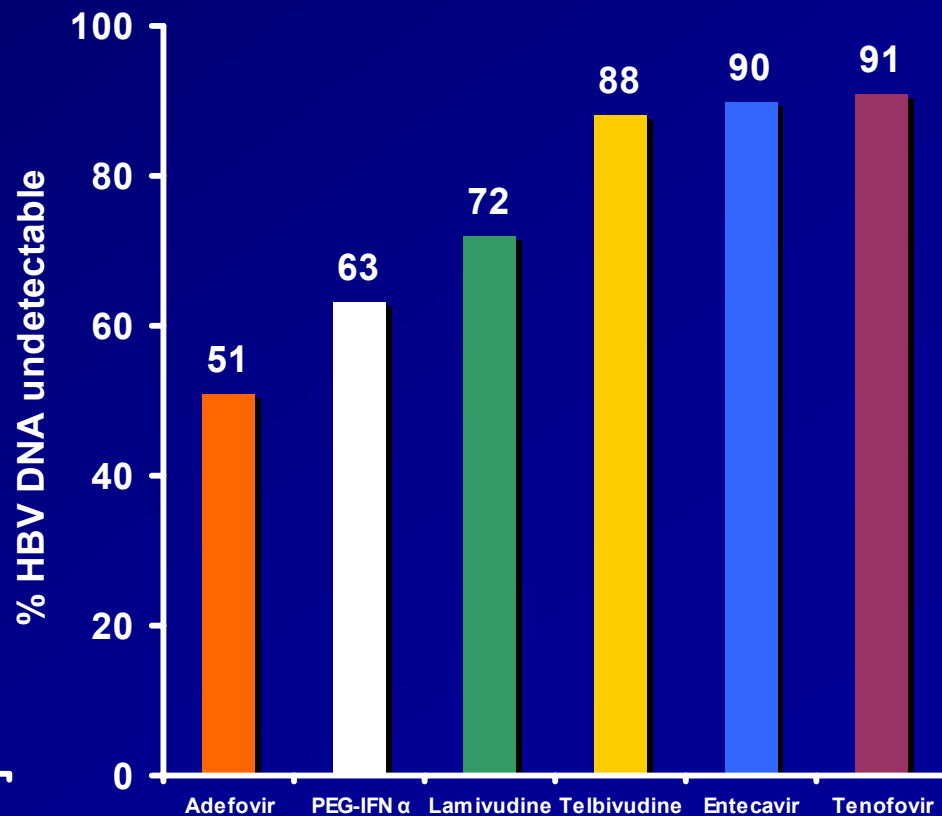


Undetectable HBV DNA In HBeAg-Positive and HBeAg-Negative Patients At 1 Year

HBeAg-Positive

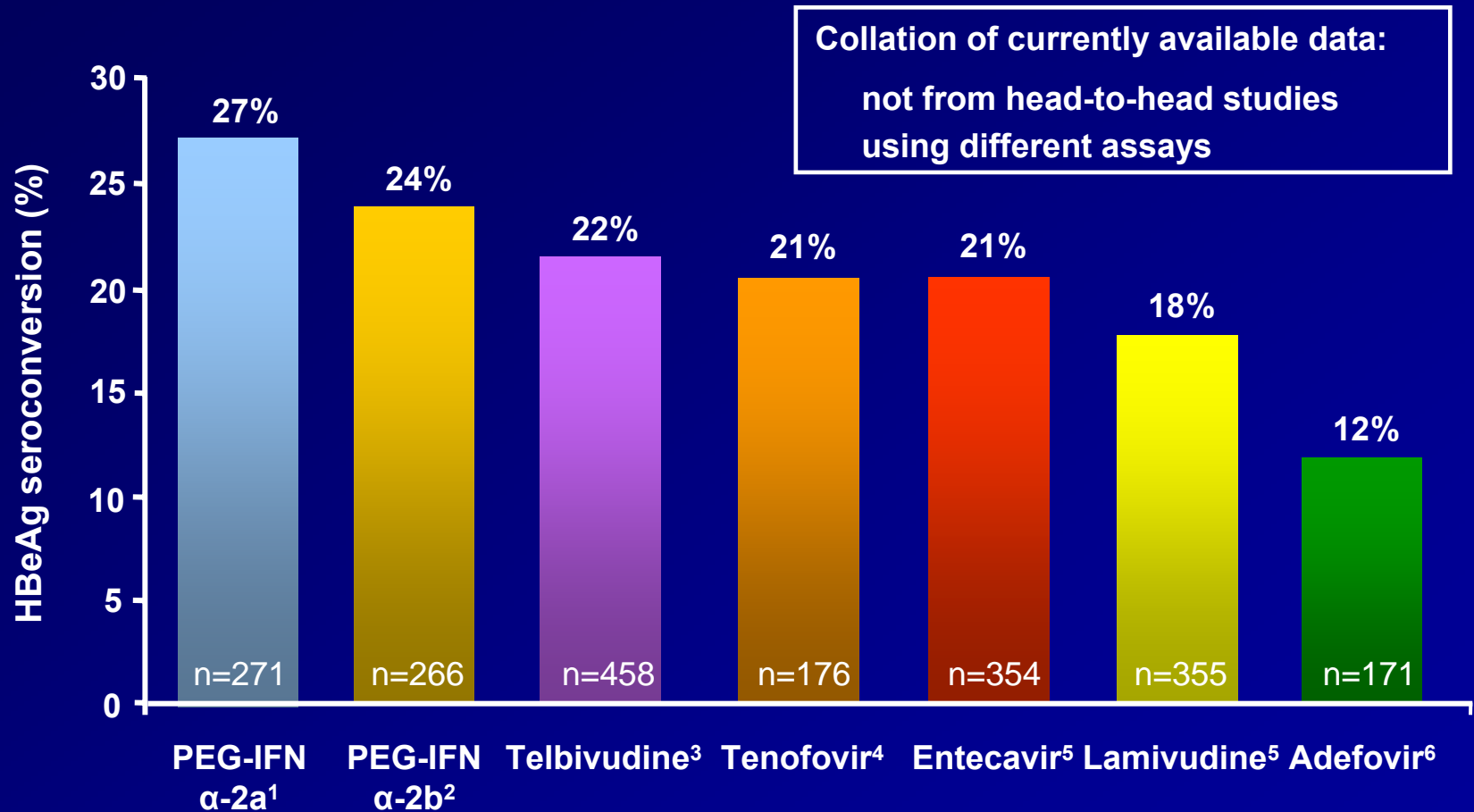


HBeAg-Negative



These trials used different HBV DNA assays and they were not head-to-head comparisons for all the drugs.

Overview HBeAg Seroconversion Rates



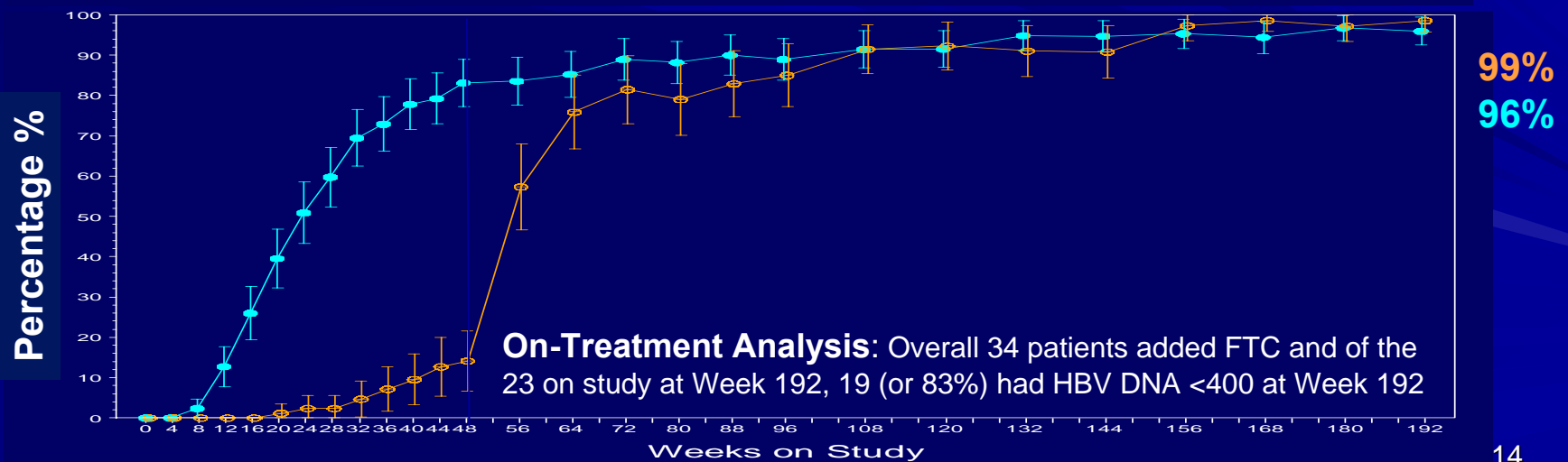
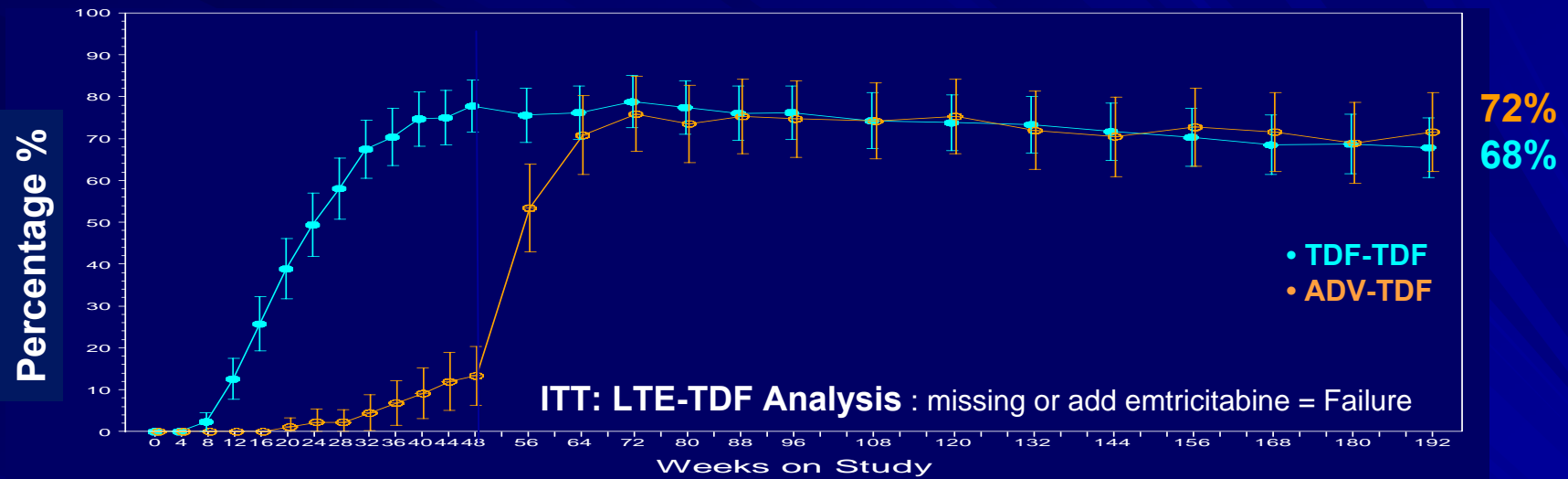
¹Lau, NEJM 2005; ²Janssen, Lancet 2005; ³Lai, AASLD 2005; ⁴Heathcote, AASLD 2007; ⁵Chang, NEJM 2006;

⁶Marcellin, NEJM 2003

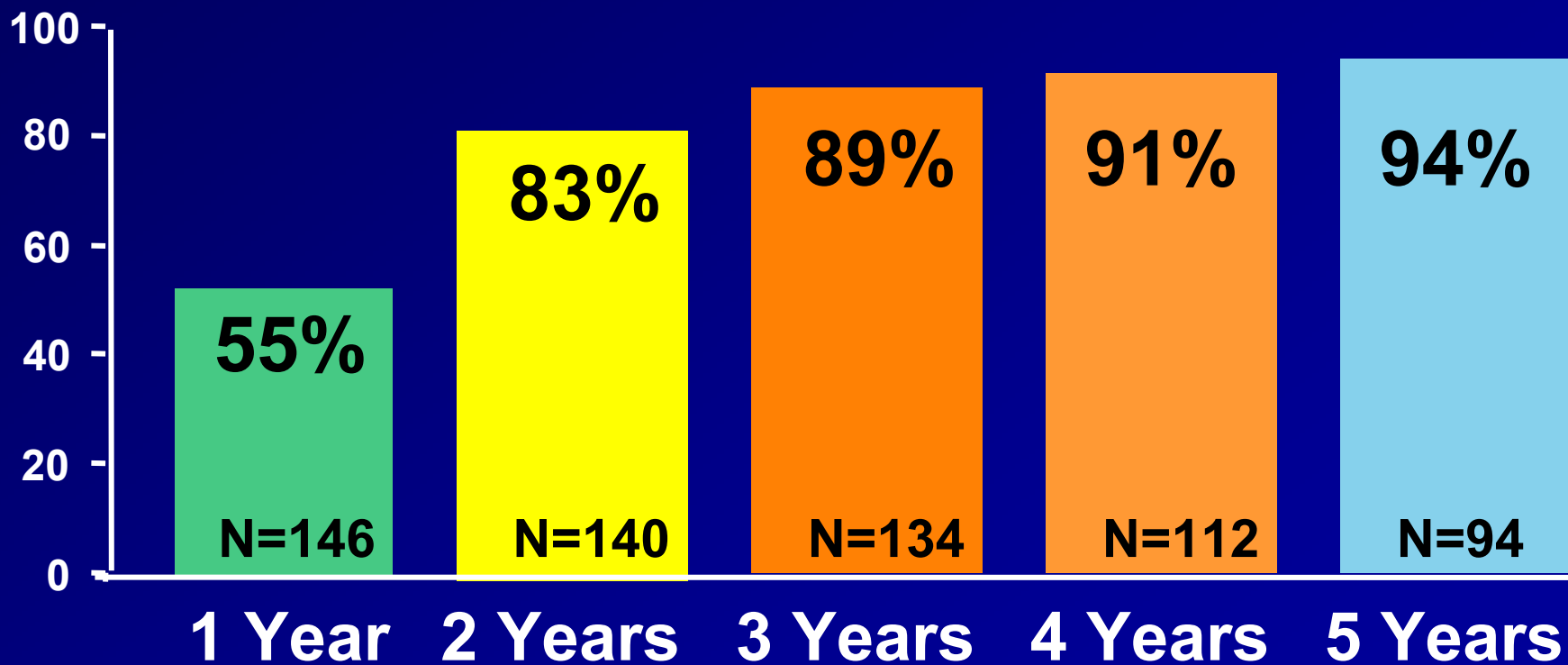
Study 103 - HBeAg-Positive Patients

Virological Response:

HBV DNA <400 copies/mL at Week 192

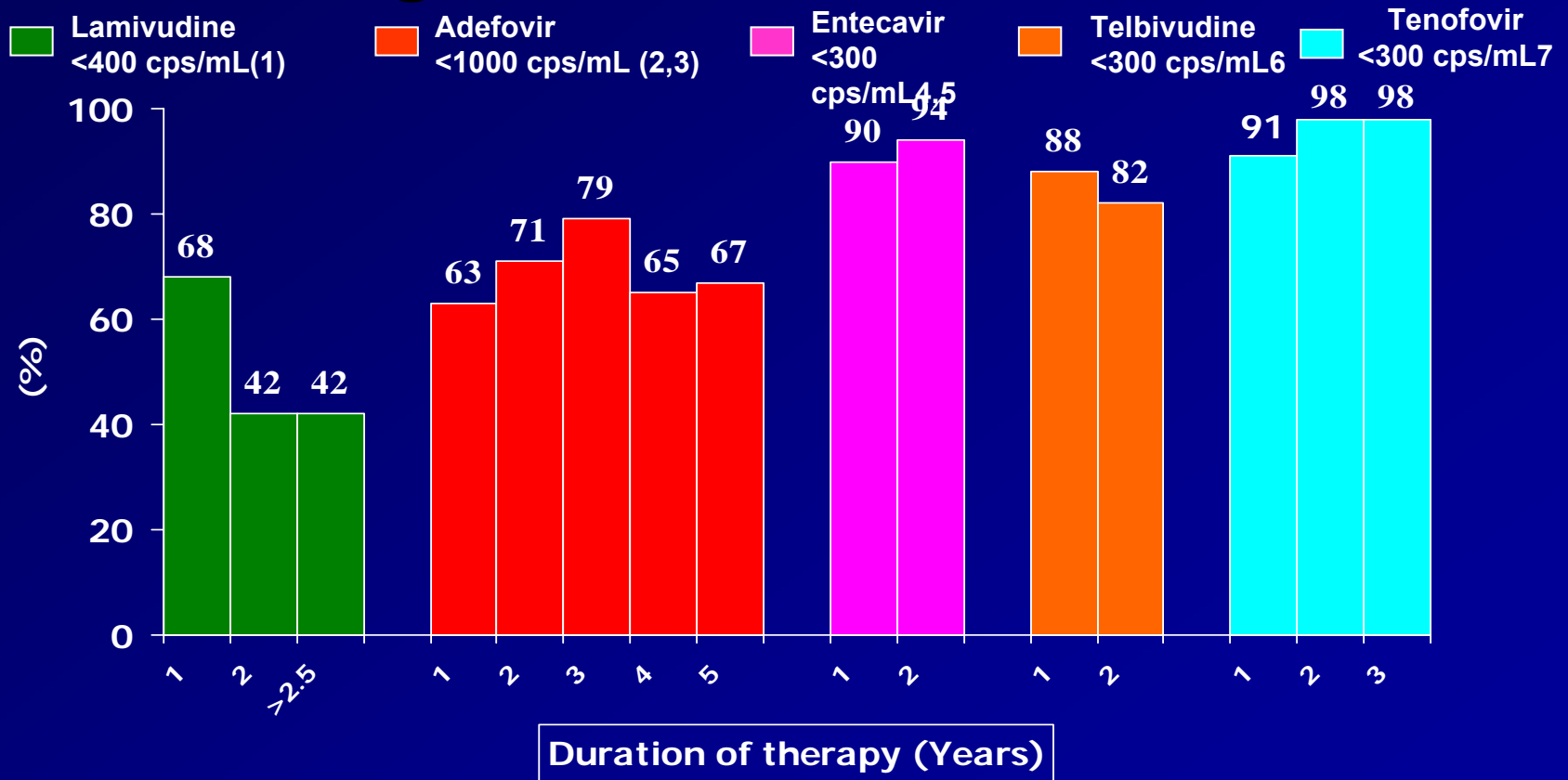


ENTECAVIR IN HBeAg + Efficacy at 5 years



Comparison of antivirals in HBeAg(-) Patients

Percentage of Undetectable HBV DNA *



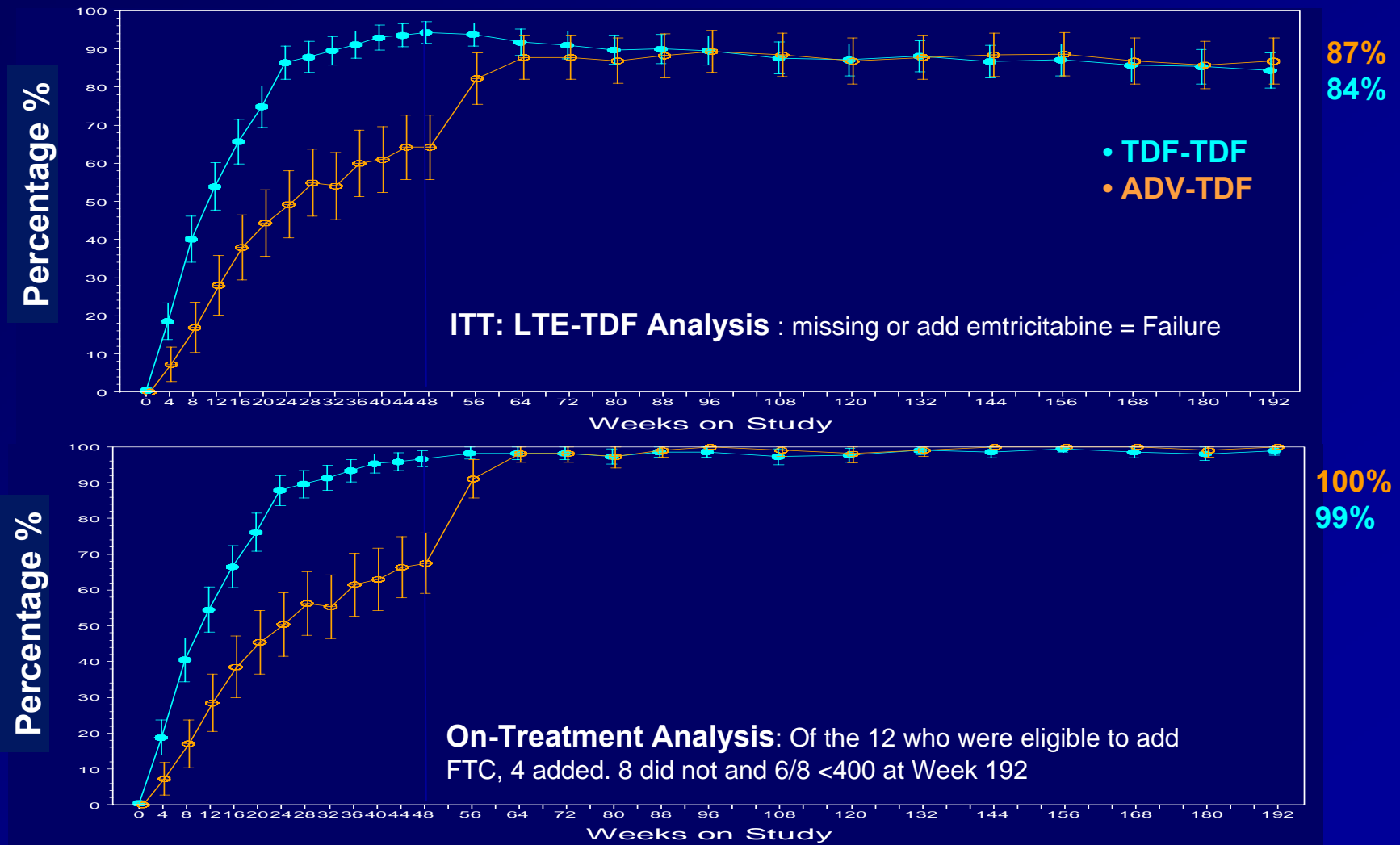
*Collation of currently available data – not from head-to-head studies

1. Hadziyannis S, et al. *Hepatology* 2000;32:847–851. 2. Hadziyannis S, et al. *NEJM* 2005; 352: 2673–2681. 3. Hadziyannis S, et al. *Hepatology* 2005; 42 (suppl 1):754A (Abstract LB14). 4. Lai C-L et al. *NEJM* 2006;354: 1011–1020; 5. Shouval D, et al. *EASL* 2006, Vienna, Austria, Oral abstract 45 6. Lai CL, AASLD 2006

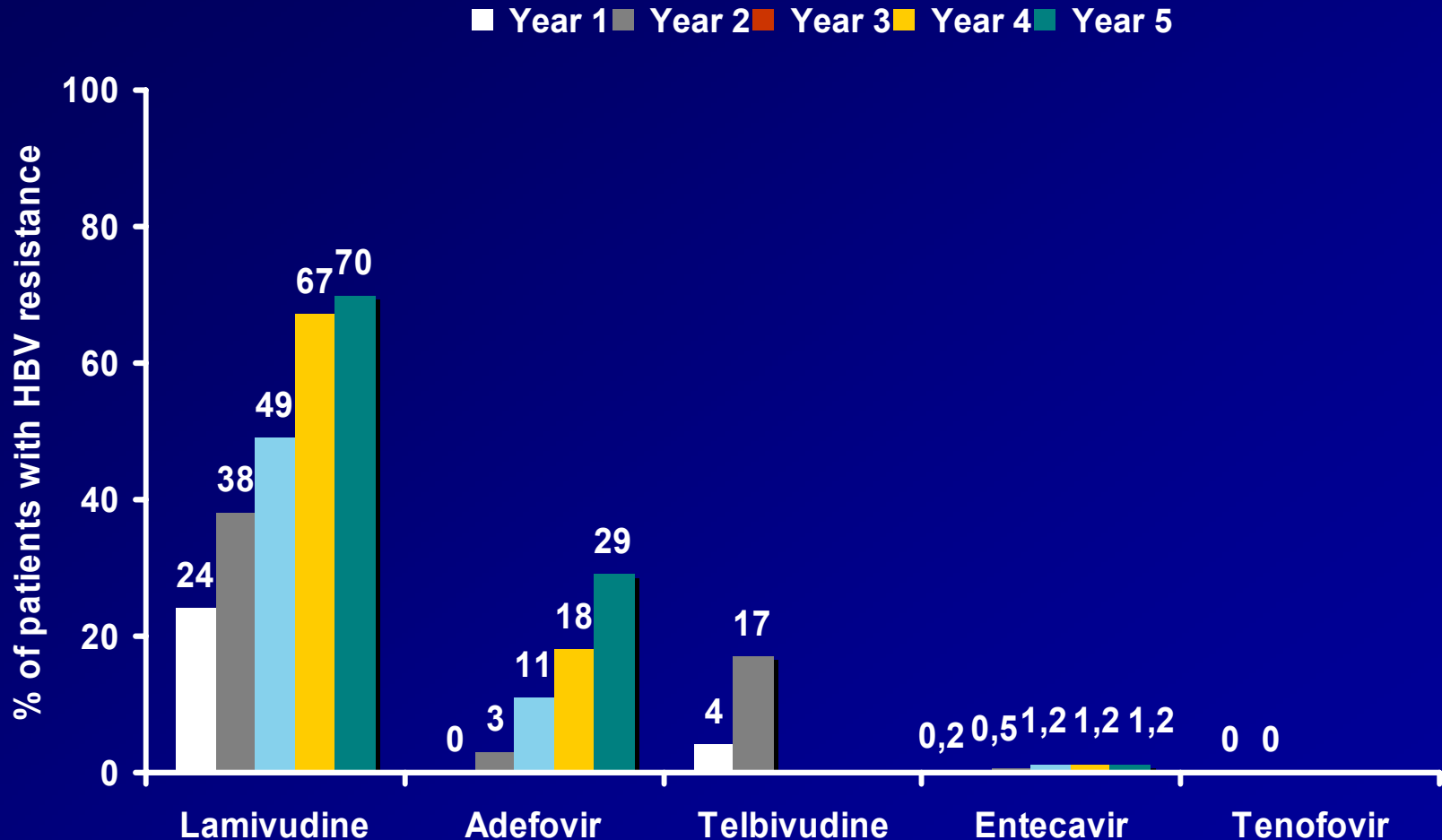
Study 102 - HBeAg-Negative

Patients

Virological Response: HBV DNA <400 copies/mL at Week 192

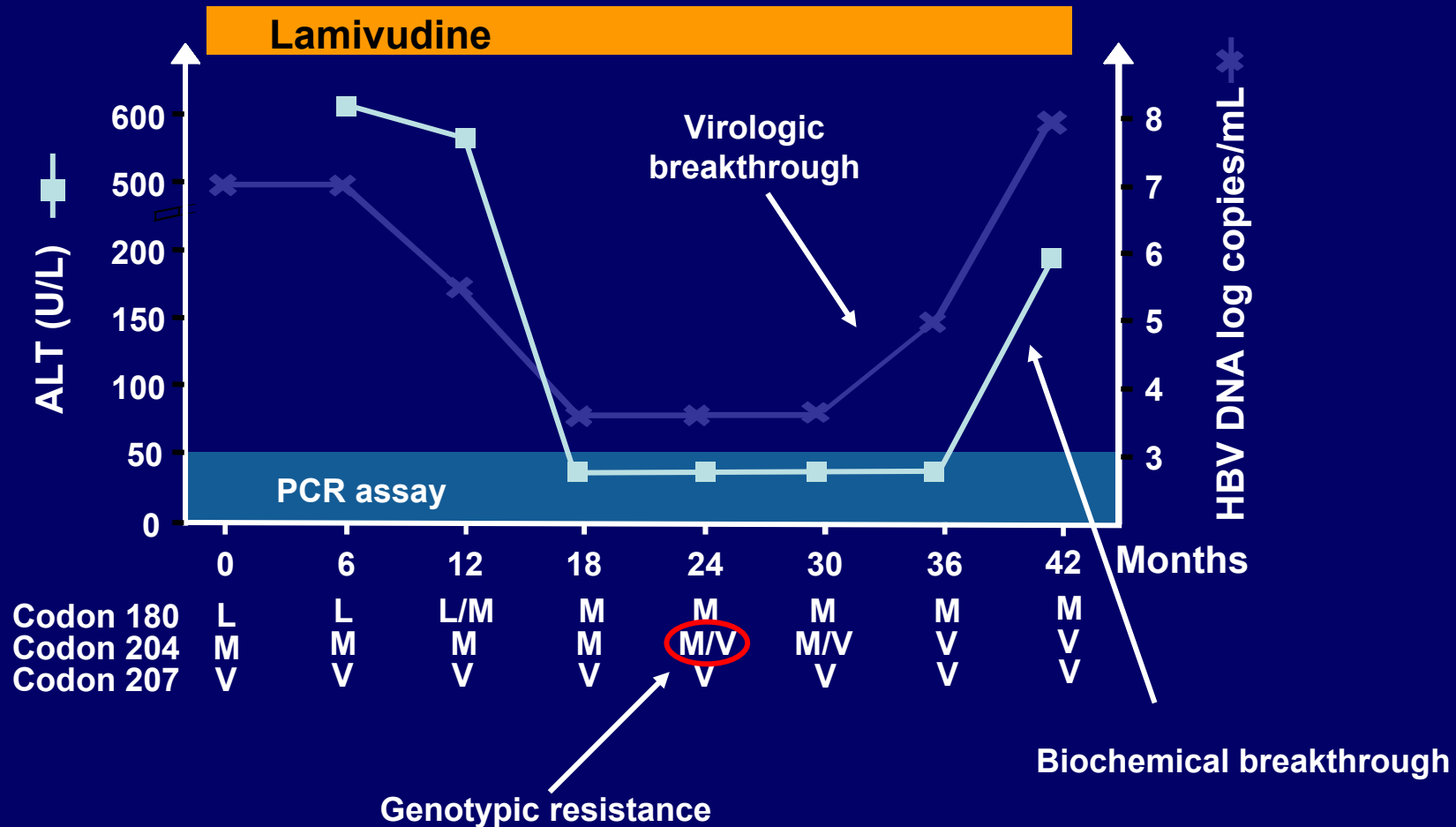


Cumulative Incidence Of HBV Resistance In Published Pivotal Trials In NUC-Naïve Patients



These trials used different populations, exclusion criteria, follow-up end points, and they were not head-to-head comparisons for all the drugs.

Dynamics of Lamivudine Resistance



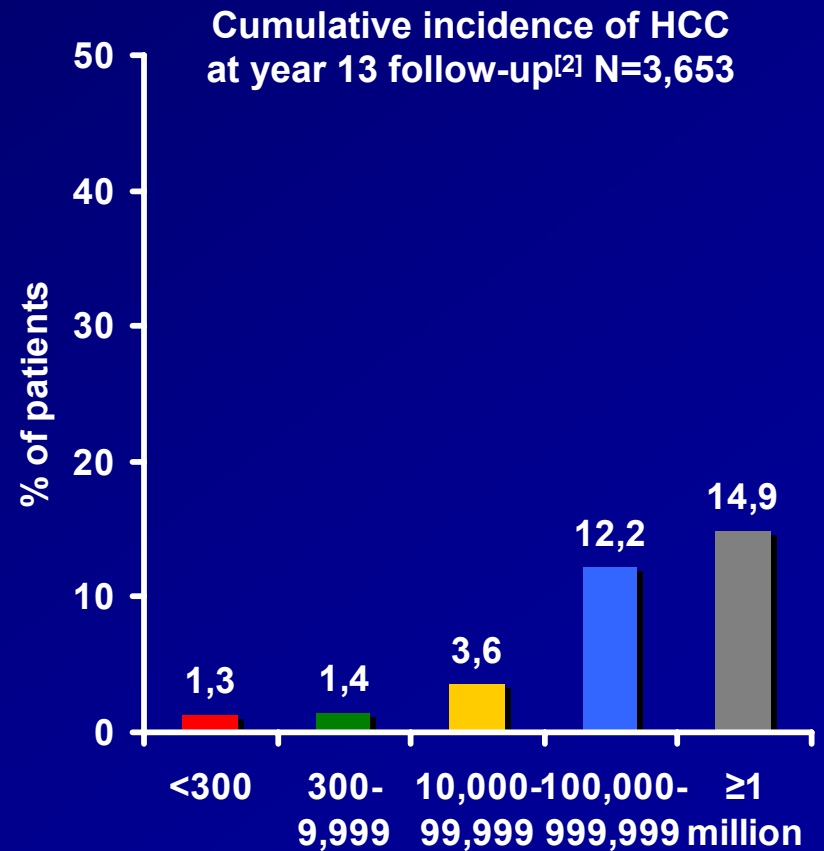
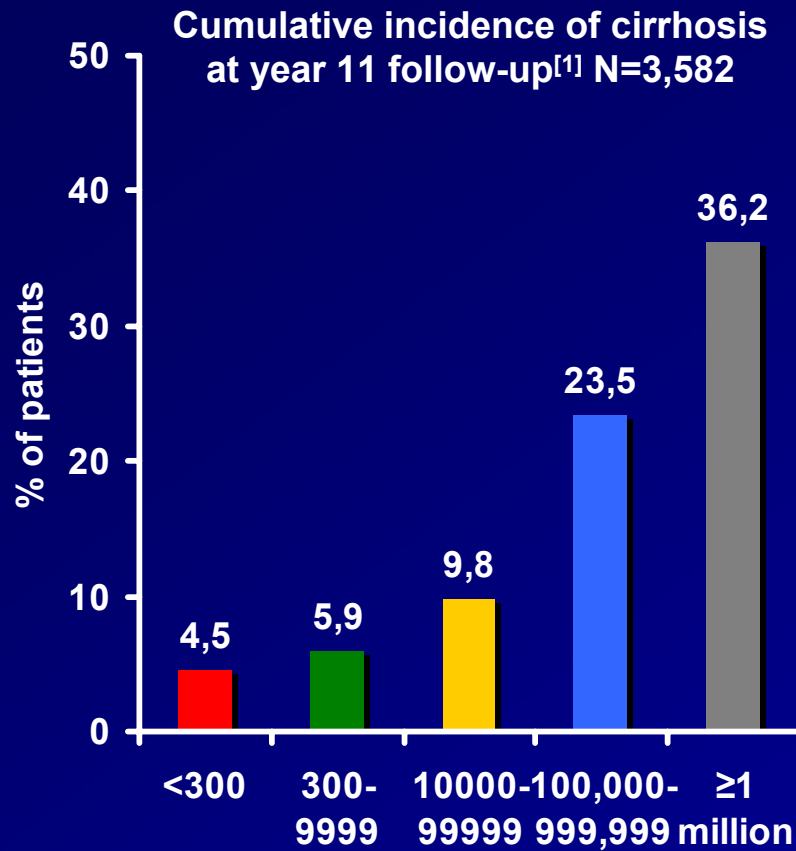
Guidelines for the Management of Antiviral-Resistant HBV

Resistance	Recommendations
LAM	Add ADV or TDF Switch to TDF/FTC* Switch to ETV (preexisting LAM-R predisposes to ETV-R)
ADV	Add LAM Switch to TDF/FTC* Switch to or add ETV
ETV	Switch to or add ADV or TDF
Telbivudine	Add ADV or TDF Switch to TDF/FTC* Switch to ETV (preexisting LdT-R predisposes to ETV-R)

Tratamiento Obligatorio

- **Cirrosis Hepática y Complicaciones**
- **Sujetos HBsAg positivo que deben recibir inmunosupresion**
- **Hepatitis Fulminante**

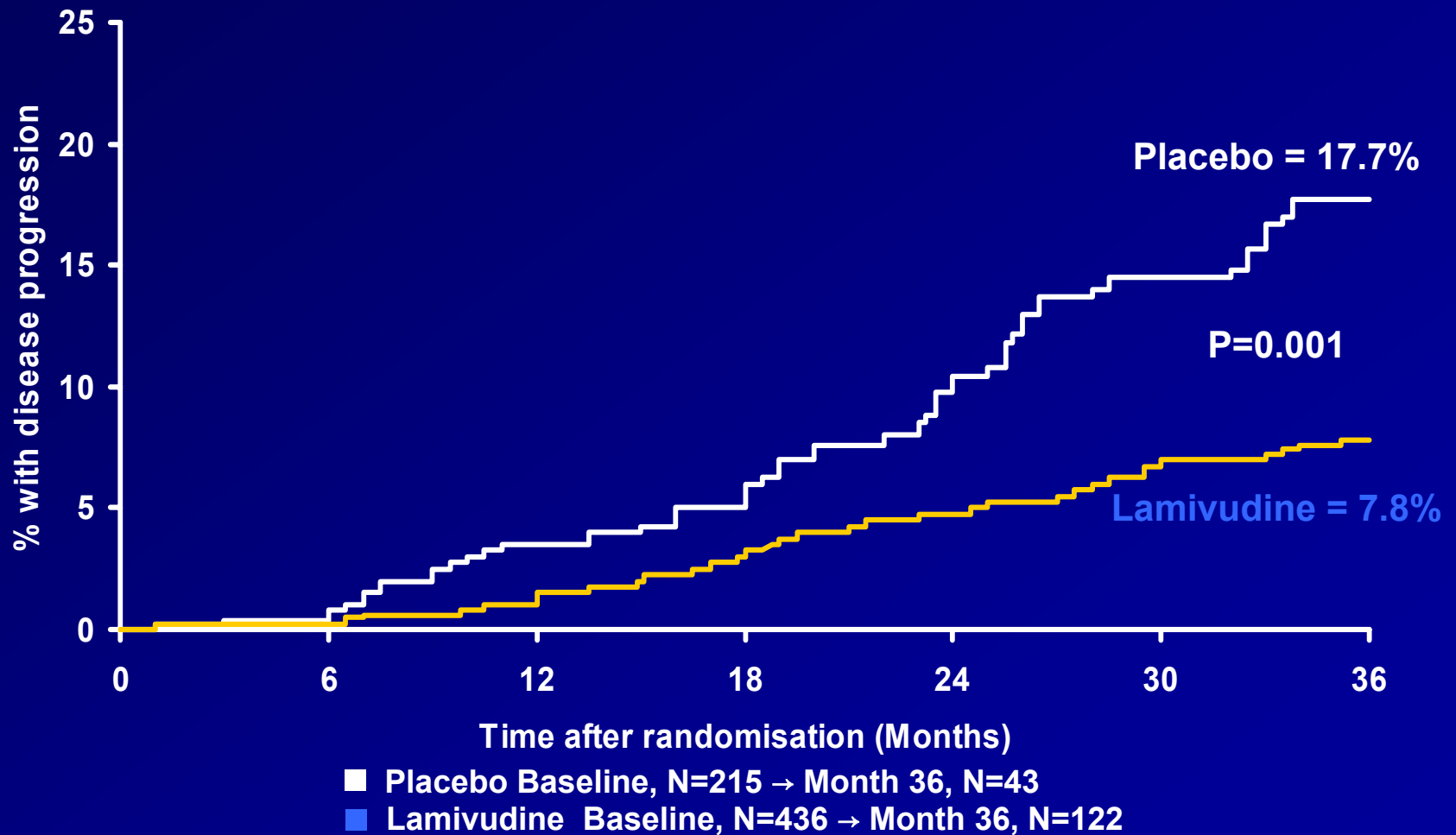
High Baseline HBV DNA Associated With Increased Risk Of Cirrhosis And HCC



Baseline HBV DNA (copies/mL)

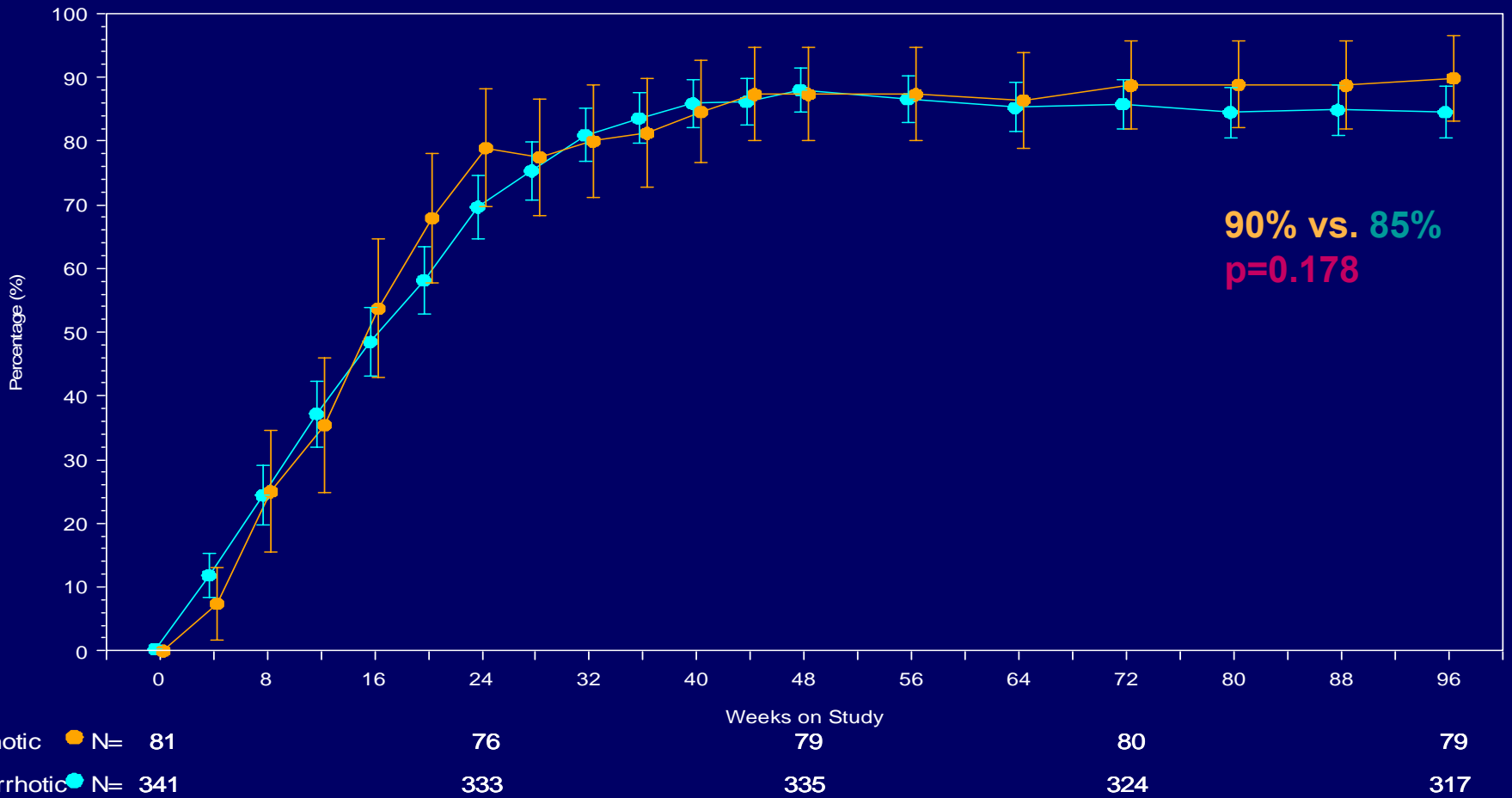
1. Iloeje UH, et al. *Gastroenterology* 2006;130:678-86.
2. Adapted from: Chen C, et al. *JAMA* 2006;295:65-73.

Decrease In Disease Progression With Effective Antiviral therapy

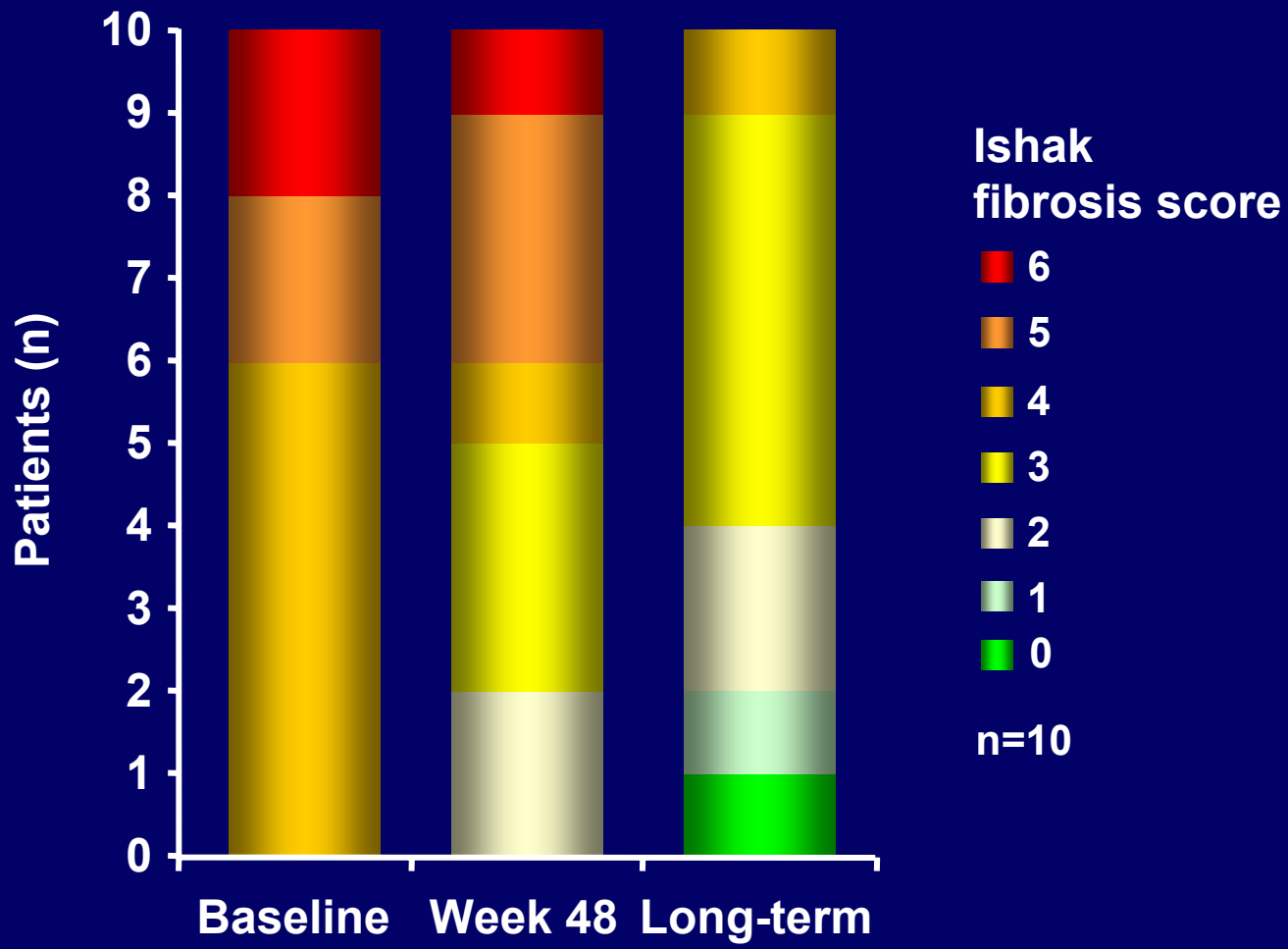


Tenofovir Patients with Cirrhosis

Proportion of HBV DNA <400 c/mL

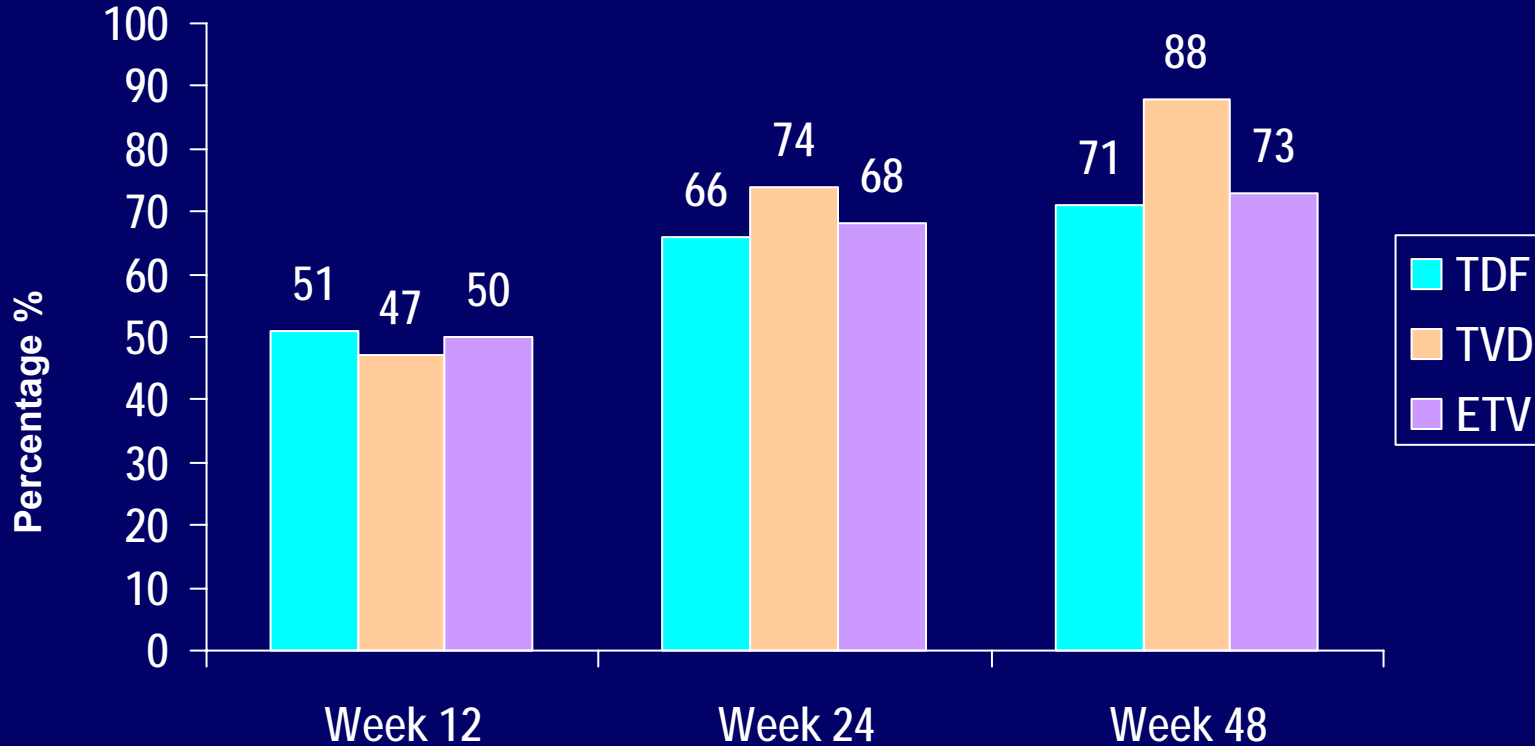


Long term Histological efficacy of ETV in patients with advanced fibrosis or cirrhosis at baseline



Tenofovir vs. Entecavir vs. Truvada in Decompensated Chronic Hepatitis B Liver Disease.

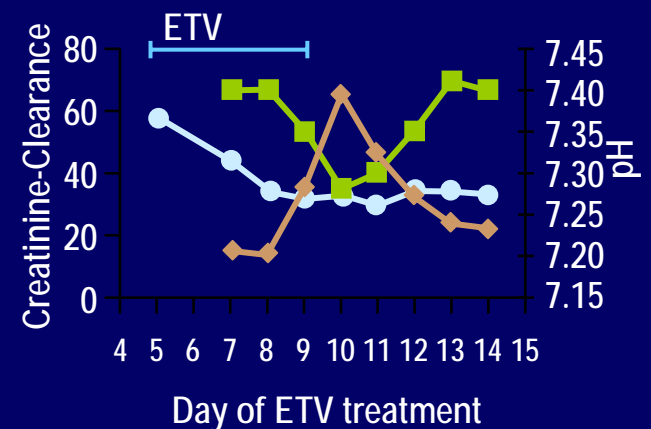
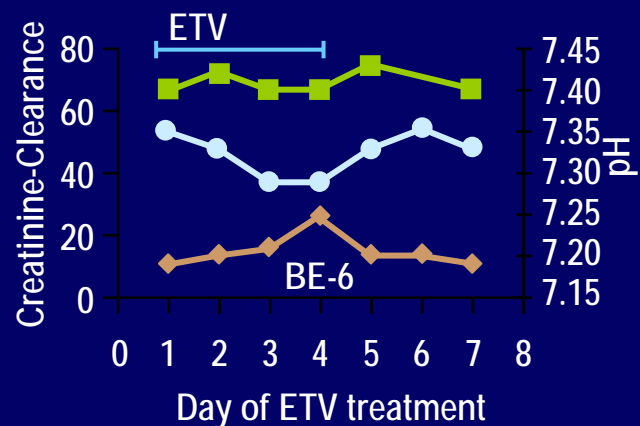
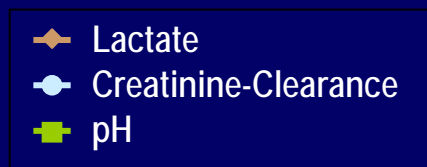
HBV DNA < 400 Copies/mL (69 IU/mL): ITT



	TDF (N=45)	TVD (N=45)	ETV (N=22)
Median CPT score (Q1, Q3) Baseline	7 (6-8)	7 (6-9)	7 (6-8)
Mean Change week 48	-1	-1	-1

Severe Lactic Acidosis during Treatment of CHB with ETV in Patients with Impaired Liver Function

- 13 treatment-naïve patients received entecavir at a dose of 0.5 mg daily. Three patients with lamivudine-refractory hepatitis B were treated with 1 mg entecavir daily.
- Mean Age 50.25) years (24-80) including 13 Caucasians (81.3%) and three Asians (62% male).
- All patients had liver cirrhosis with MELD scores between 6 and 38.



Sujetos HBsAg positivo que deben recibir inmunosupresion

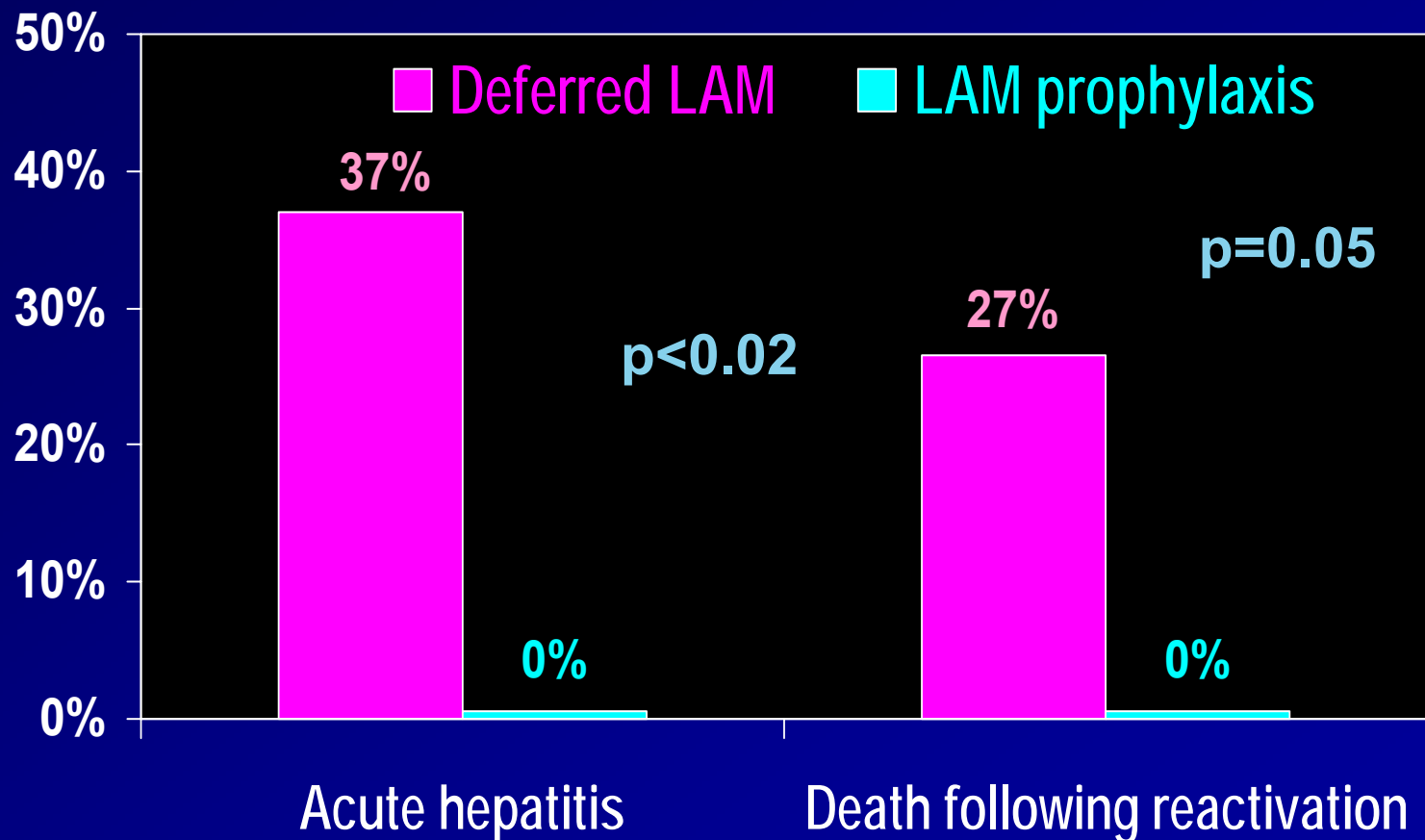
- Reactivaciones graves de la infección por VHB
- Hepatitis Aguda
- Elevada Mortalidad
- Riesgo de reactivacion depende
 - Presencia de DNA-VHB
 - Tratamiento inmunosupresor
 - Ac Monoclonales > Citostaticos y Corticoides
- Iniciar Profilaxis con un antiviral oral desde antes de la IS hasta 6-12 meses despues de terminar

HBV Reactivation during chemotherapy

Prophylaxis vs. deferred treatment

Prophylaxis (n=16): Start LAM when start chemo

Deferred treatment (n=19): Start LAM only when \uparrow ALT > 5xULN



Tratamiento de Hepatitis B

Resumen

- **No todos los pacientes deben tratarse**
- **Antivirales Potentes**
- **Alta Barrera Genética evitar resistencias**
- **Monoterapia como primer tratamiento**
- **Tratamiento debe individualizarse**