Impact of antiviral therapy on the outcome of chronic hepatitis B

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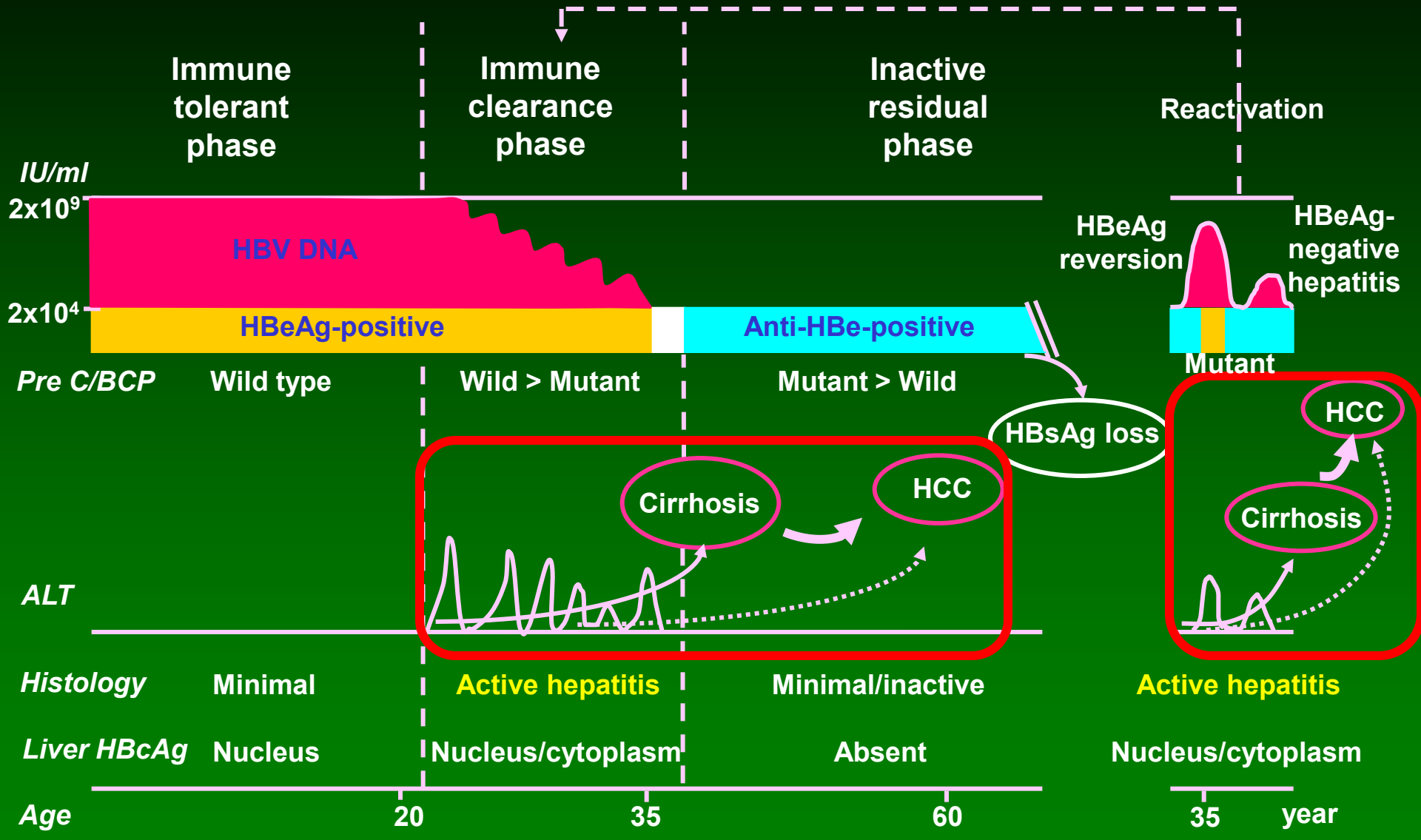
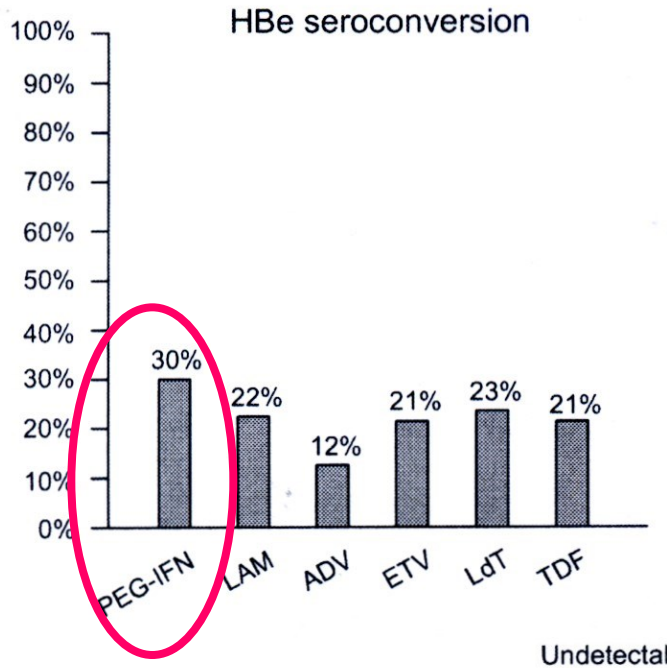
Extended immune clearance phase leads to higher risk of cirrhosis and HCC

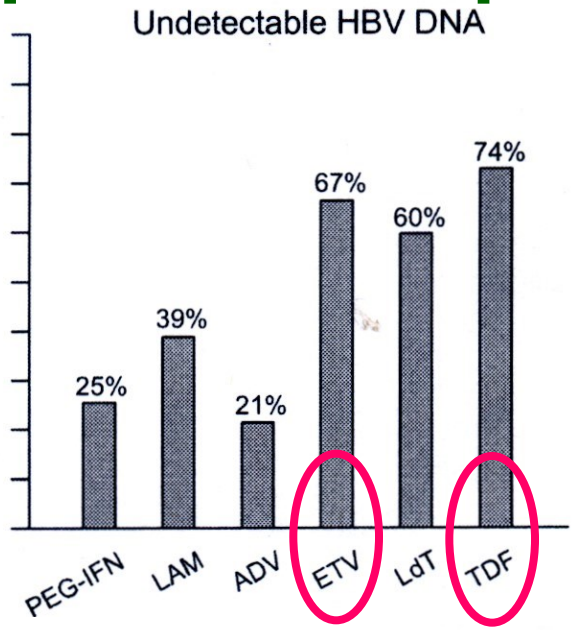


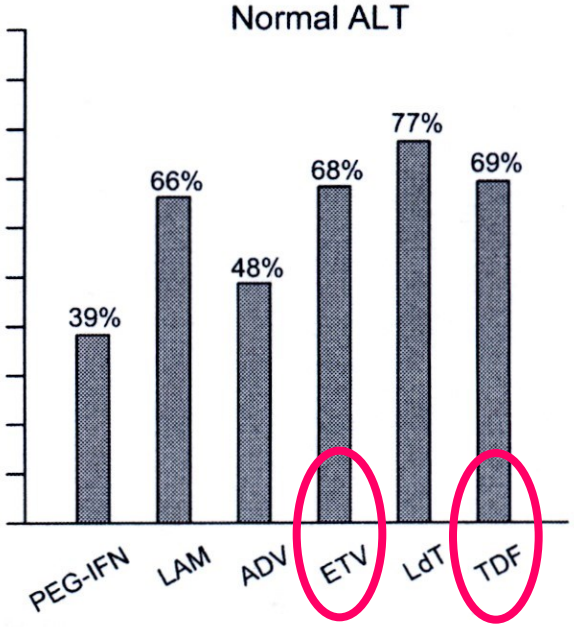
HBV is the deriver!

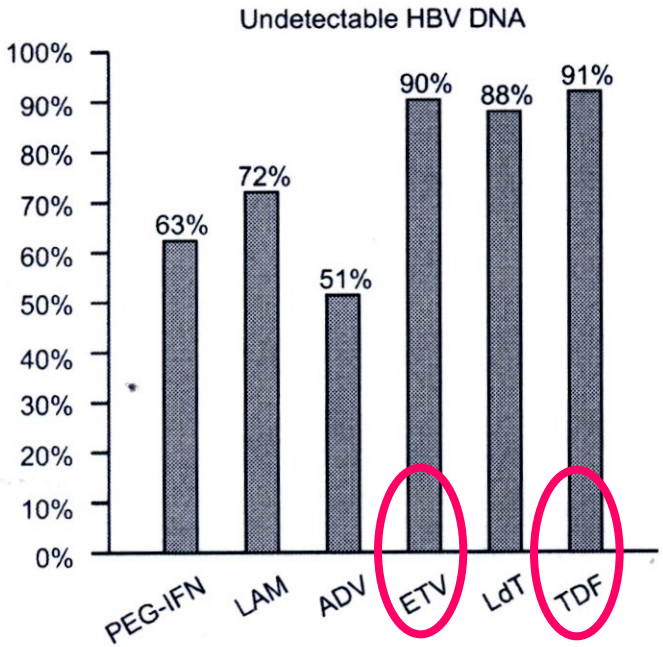
Liaw & Chu Lancet 2009;373:582-592

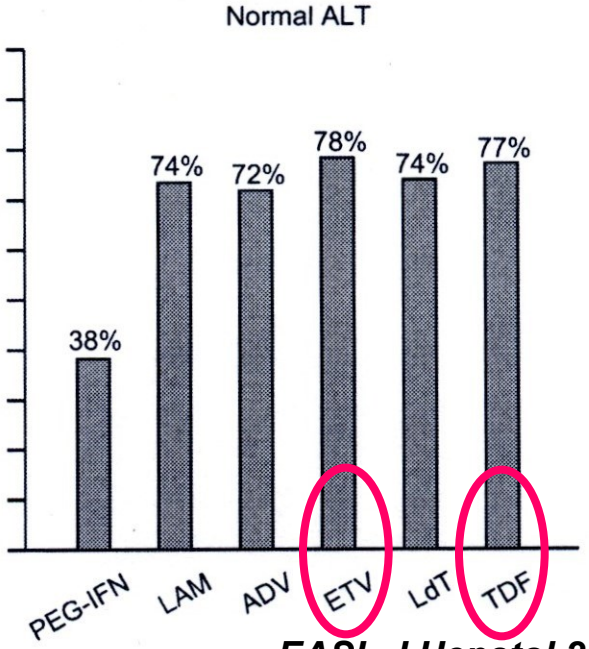
Short-term impact in compensated CHB





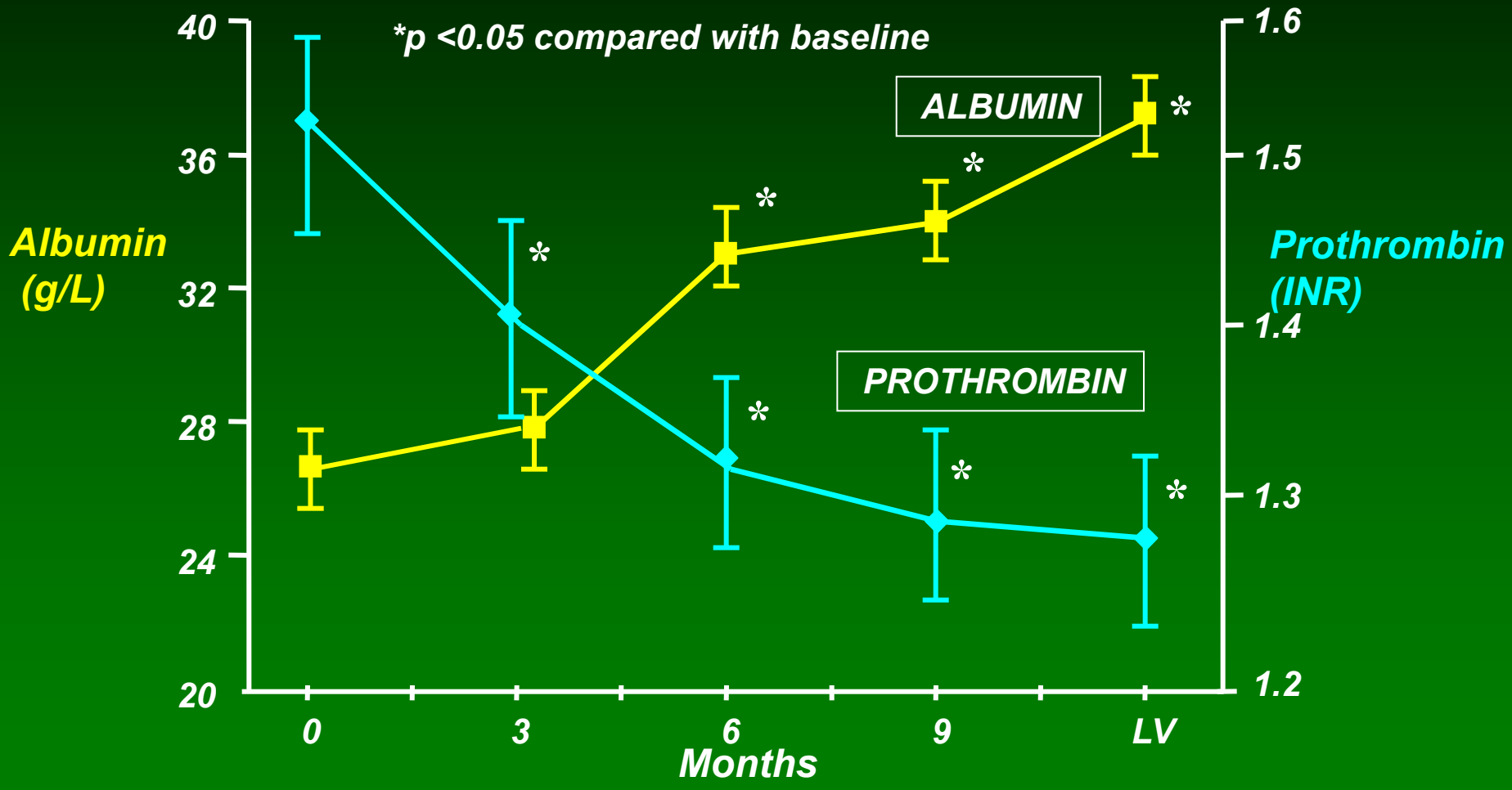






EASL J Hepatol 2009;50:227-242

Lamivudine improves clinical, biochemical, virological markers and reduces need for OLT, prolongs survival in decompensated cirrhosis



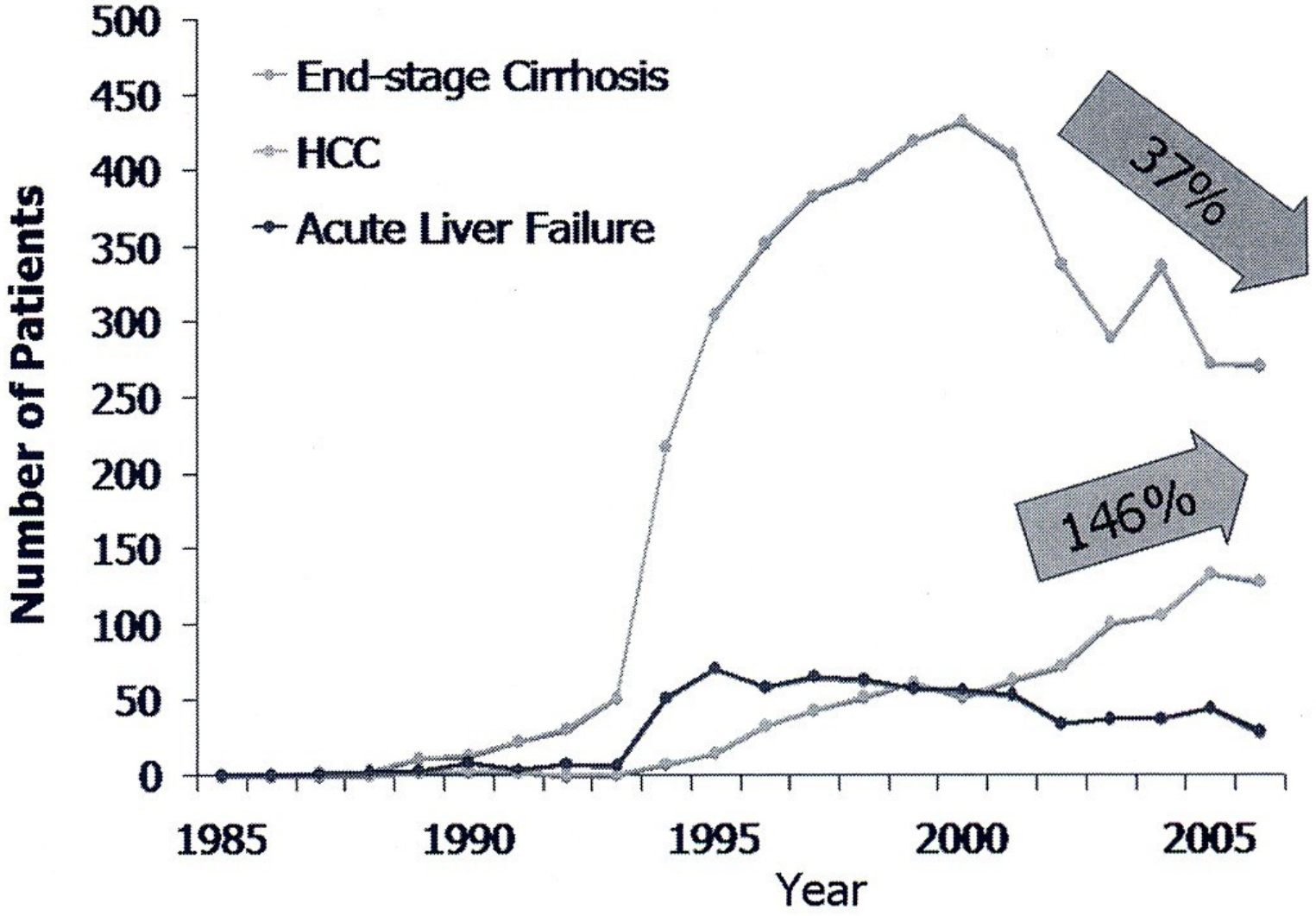
Villeneuve et al, Hepatology 2000; Hann 2000; Kapoor 2000; Yao 2000; Fontana 2000; Perrillo 2001

Nuc therapy in hepatic decompensation

Study	Shim JH 2010	Liaw YF 2011	Liaw YF 2011	Chan HLY 2012	Hyun JJ 2012	Hsu YC 2012
Drug(s) used	ETV	ETV/ADV	TDF/TDF+ FTC/ETV	LdT/LAM	ETV/LAM	ETV/LAM
No. patients	70	100/91	45/45/22	114/114	45/41	53/73
CTP score	8.4	8.8/8.4[g]	7/7/7[b]	8.1/8.5c	9.6/9.1	NR
MELD score	11.5	17.1/15.3	11/13/10.5	14.7/15.5	16.7/16.1	18.6/20.4
1-year survival, (%)	87	77/67	96/96/91	94/88	91/92	64/55
↓ CTP score ≥ 2, (%)	49	35/27	26/48/42	32/39	NR	NR
MELD score ↓	-2.2	-2.6/-1.7	-2/-2/-2	-1.0/-2.0	NR	NR

The earlier the better !

Decline in the Need for LT for ESLD Secondary to HBV in the US



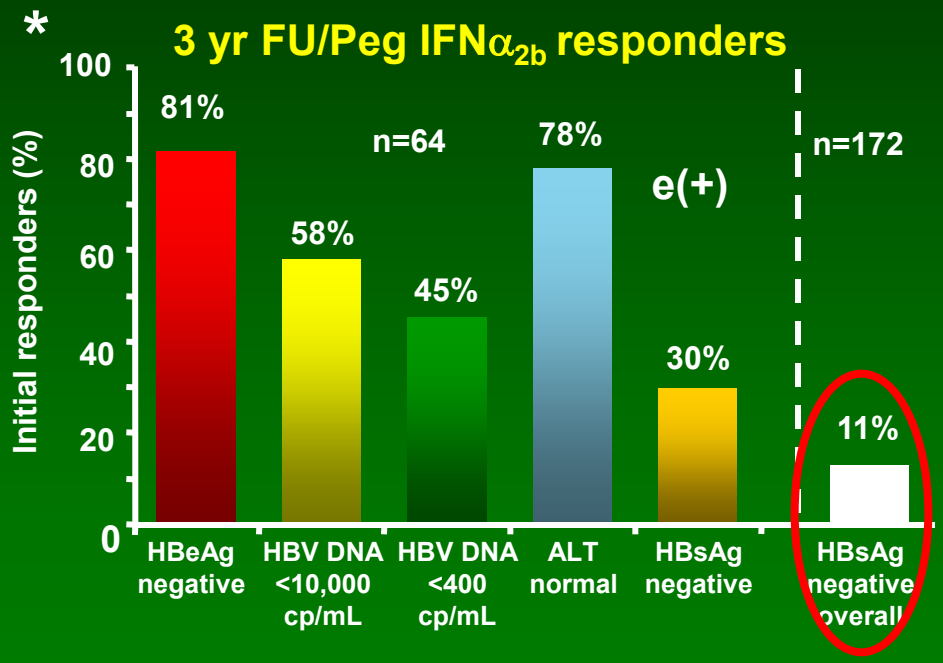
1st Nuc approval in 1998

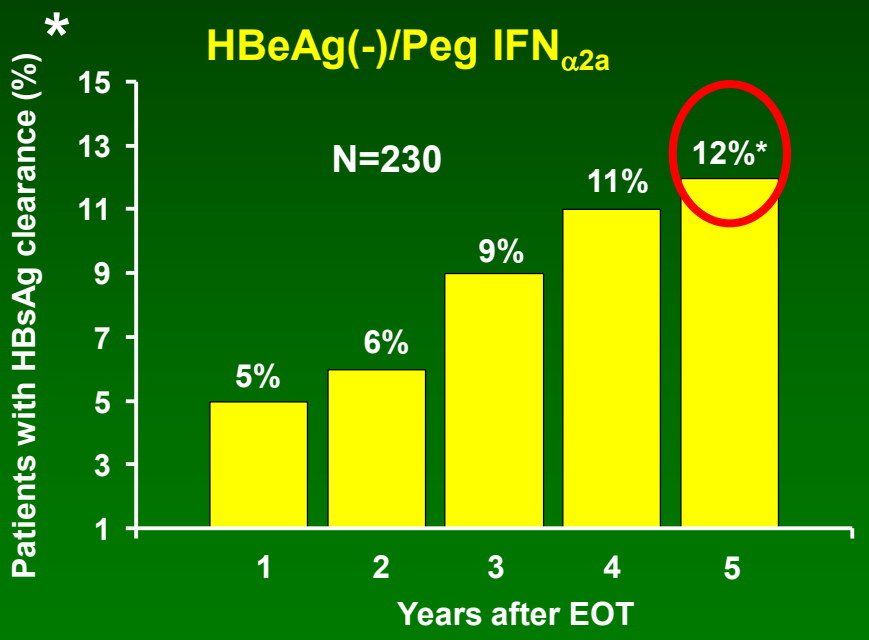
Kim WR. Hepatology. 2009;49:S28-S34

Impact of 1-yr Peg IFN on 3-5 yr serological outcomes

* HBeAg seroconversion: 37% at EOT; 60% at 5 yr

Wong VWS et al Hepatology 2010





* *23% if qHBsAg ↓ ≥ 10% at wk 12, 28% if HBV DNA ≤ 2000 IU/mL 1yr after EOT*

Buster et al. Gastroenterology 2008

Marcellin et al. APASL 2009; Hepatol Int 2012 (in press)

Long-term impact of IFN-based therapy

* HBeAg response and HBsAg loss increase over time

Lampertico Hepatology 2003; van Zonneveld Hepatology 2004

* Cirrhosis reduced 35% *Yang YF et al JVH 2009**

* HCC reduced 41% (49% in cirrhotics) *Yang YF et al JVH 2009**

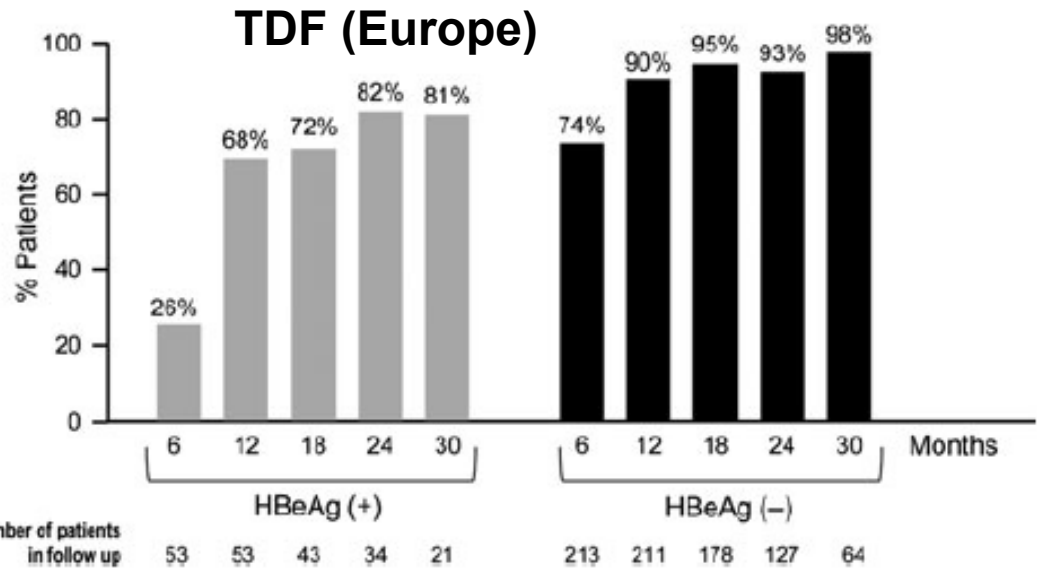
• only 1/230 or 1/55 $F_{3,4}$ HBeAg (-) patients developed HCC 3-yr after Peg $IFN_{\alpha 2a}$ therapy *Marcellin et al Gastroenterology 2009*

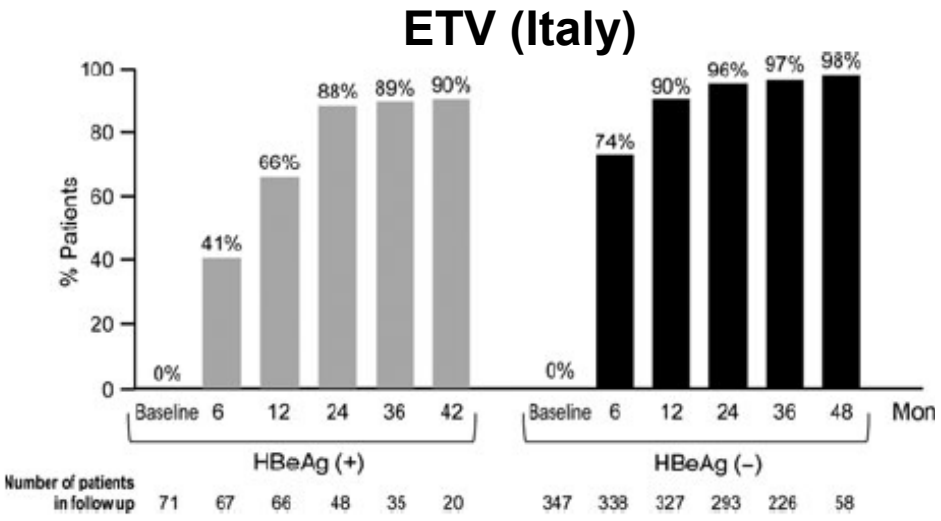
* Liver death reduced 37% (80% in initial responders)

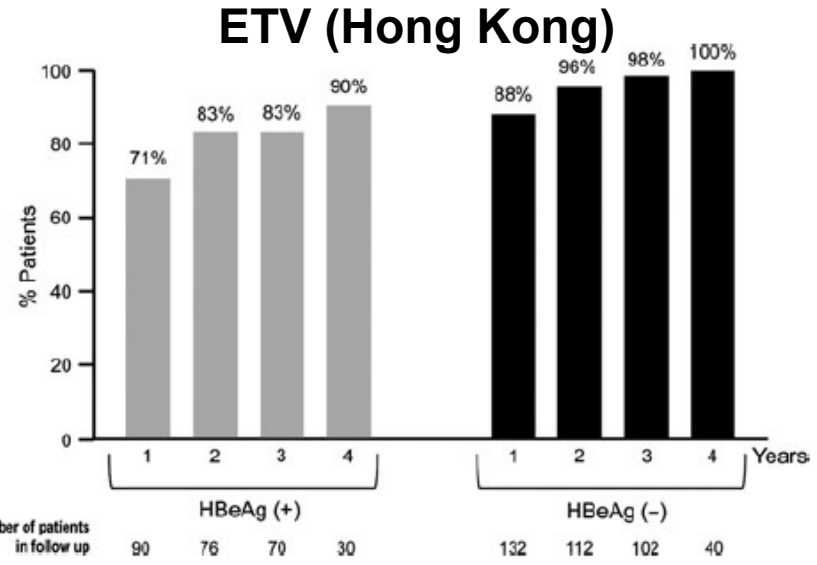
*Wong GLH Aliment Pharmacol Ther 2010**

** Meta-analysis*

Maintained HBV suppression by ETV/TDF







adapted from Plo & Lampertico JVH 2012;19:377-86

Fibrosis regression during Nuc therapy

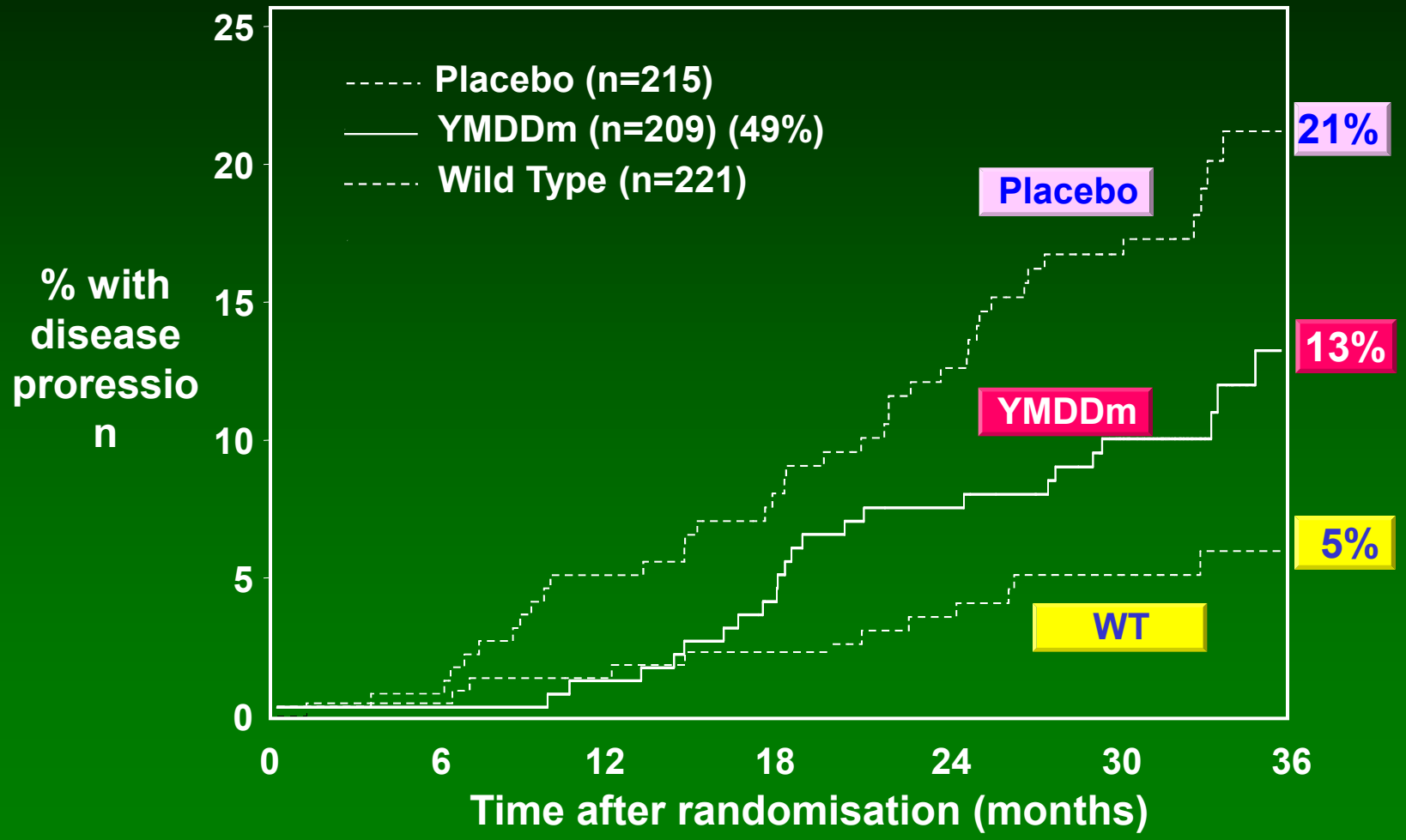
Nucleos(t)ide	n	HBeAg	Duration	Fibrosis Regression
Lamivudine	63	+	3 yrs	33%
Entecavir	21	+/-	3 yrs	57%
Adefovir	15/24	+/-	5 yrs	60%/71%
Entecavir[a]	57	+/-	6 yrs	88%
Tenofovir[b]	348 (96[b])	+/-	5 yrs	51% (74%[b])

adapted from Liaw YF Liver Int 2013

a. ETV improved Ishak fibrosis (-1.53) ≥ 2 in 58% and in all 4 cirrhotics *Chang et al Hepatology 2010*

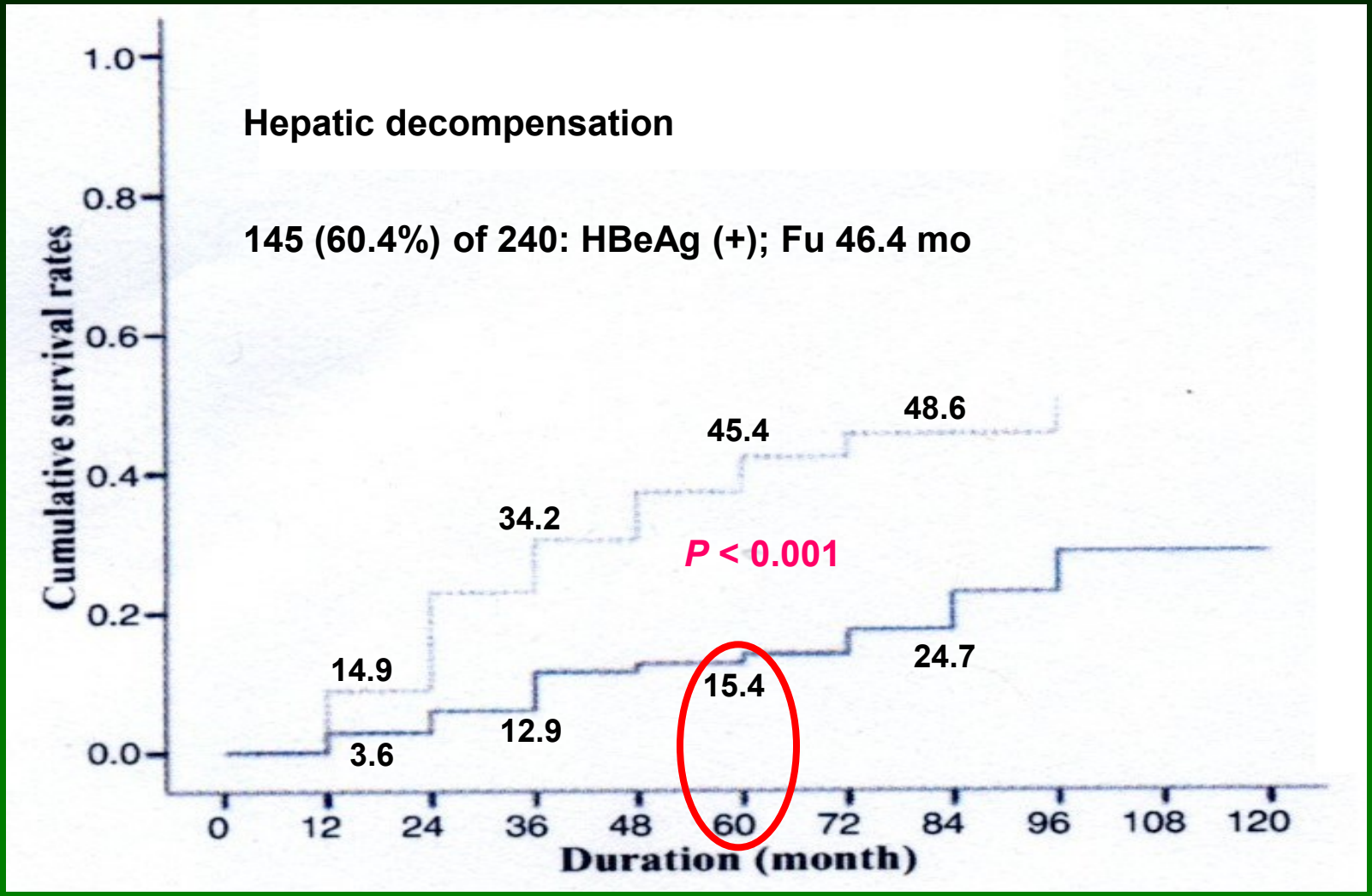
b. Cirrhosis at baseline, ≥ 2/3 ↓ in 73/58% *Marcellin et al Lancet 2013*

3-yr LAM therapy reduced disease progression but effect negated with LAMr



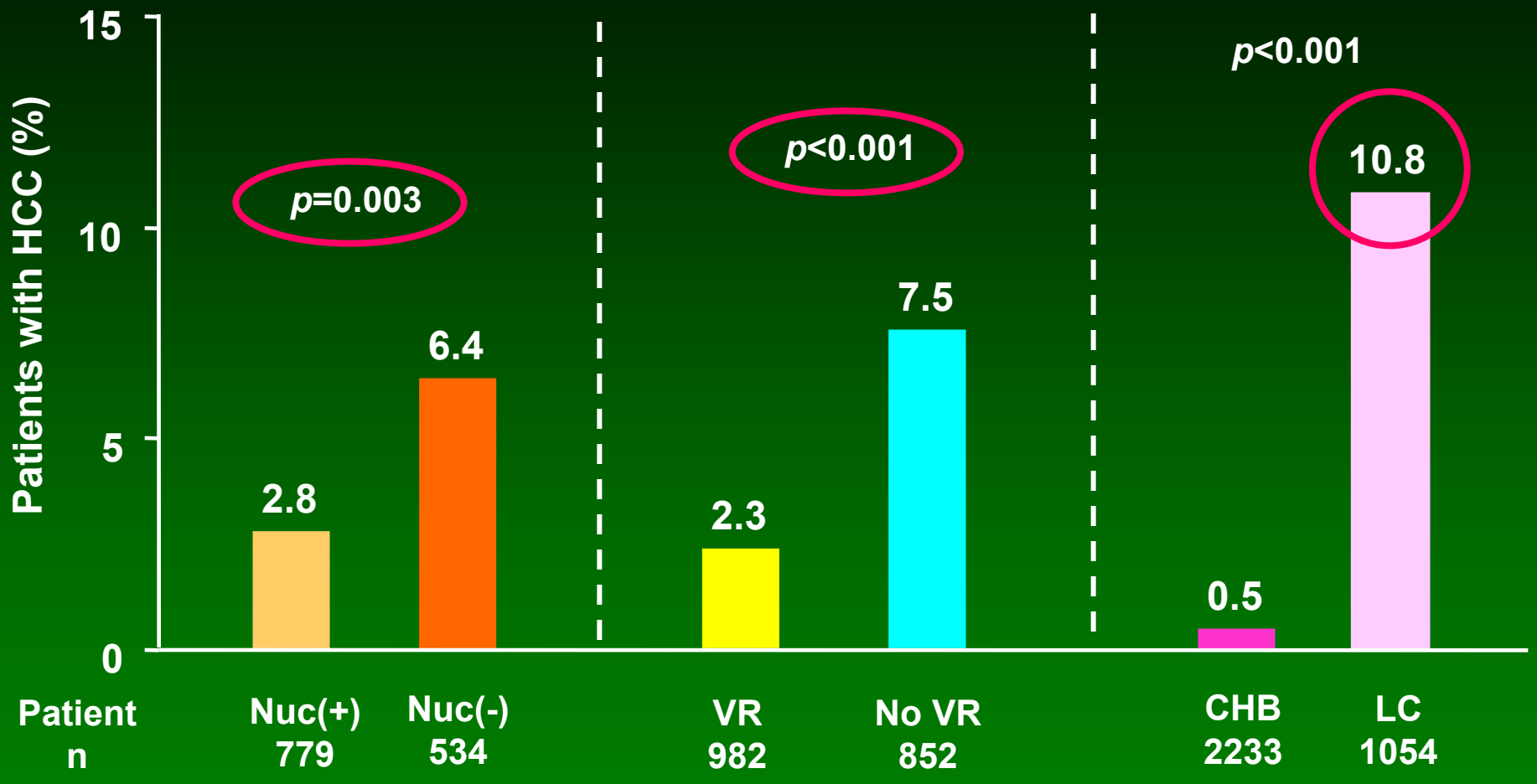
Liaw YF NEJM 2004; Sem Liver Dis 2005

Nuc therapy starting with LAM reduced complications in HBV-cirrhosis



Kim et al JGH 2012;27:1589-95

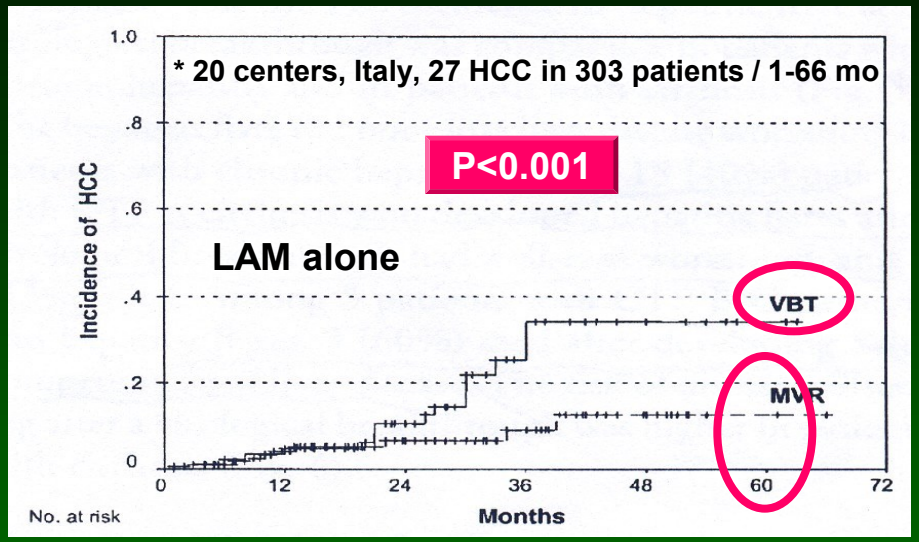
LAM therapy reduced HCC in CHB



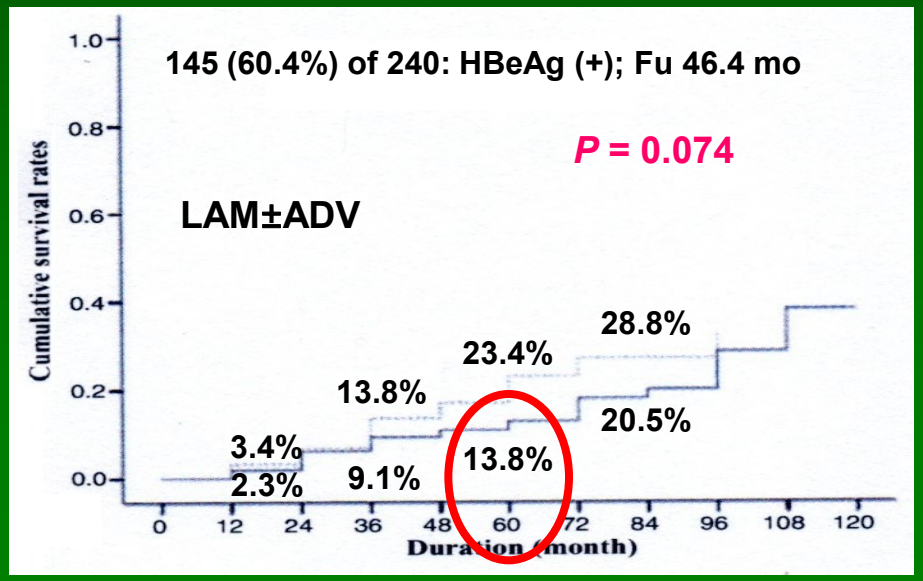
A systematic review: 3381 patients /21 studies

Papatheodoridis GV J Hepatol 2010;53:348

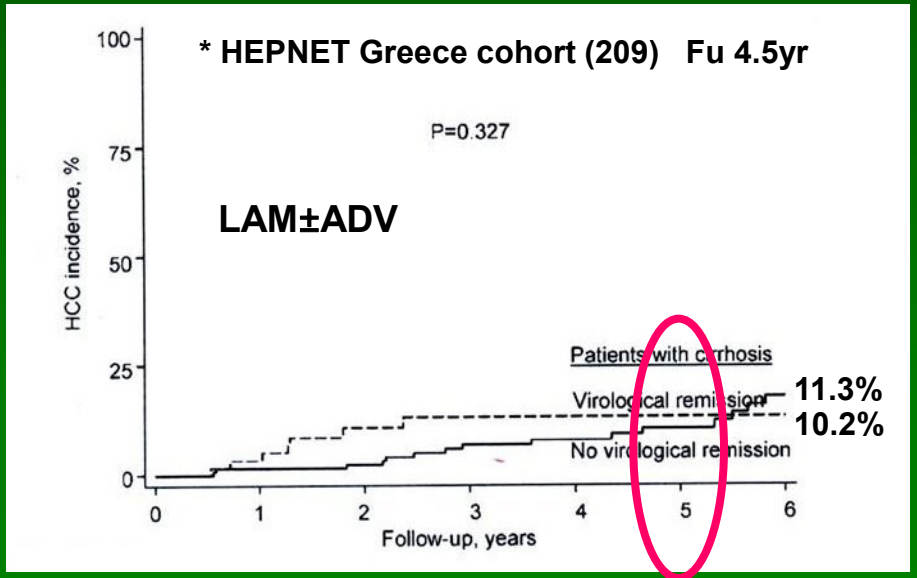
Maintained HBV suppression reduced HCC in HBeAg (-) cirrhosis



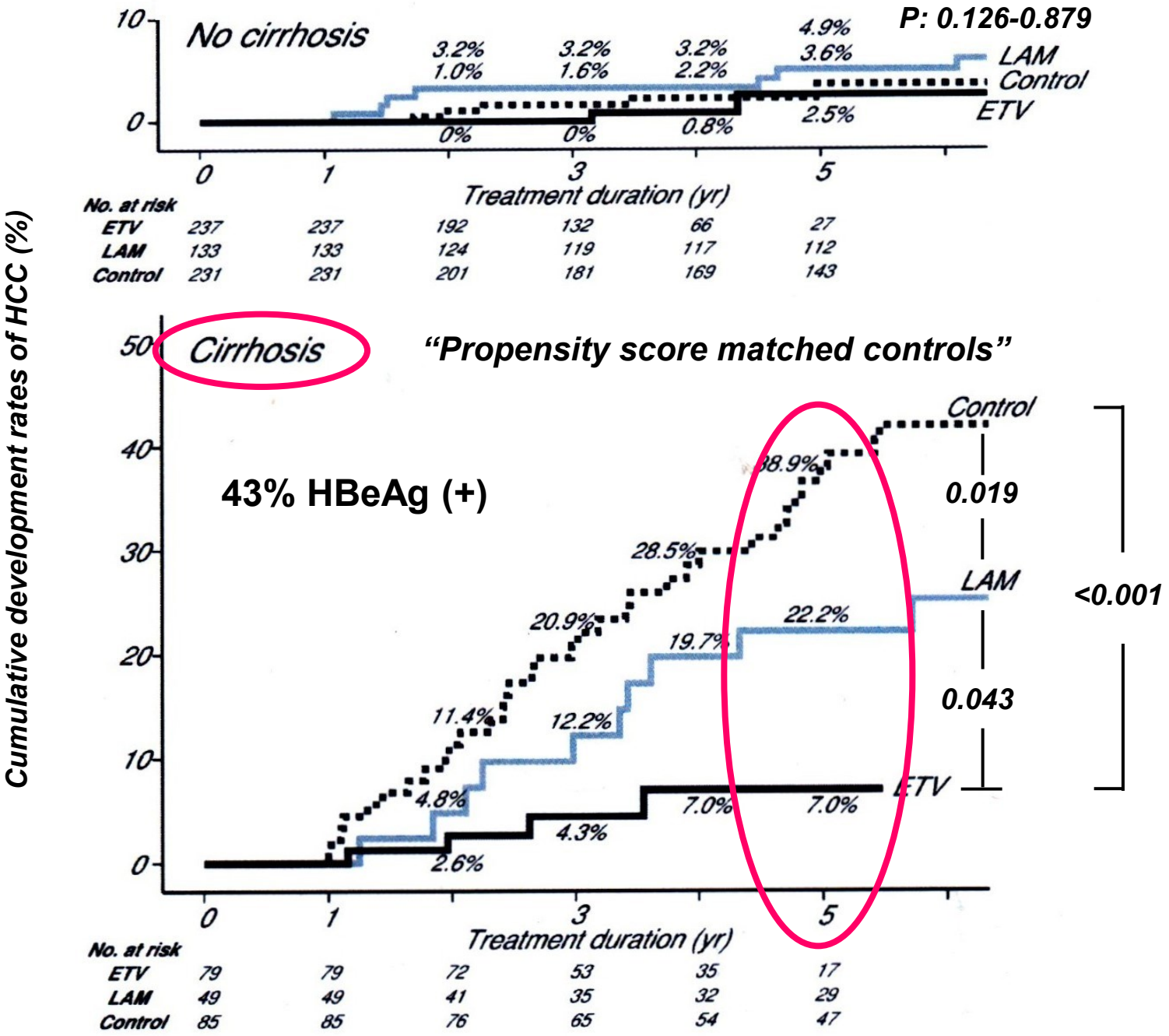
after Di Marco V et al Hepatology 2004



Kim et al JGH 2012;27:1589-95

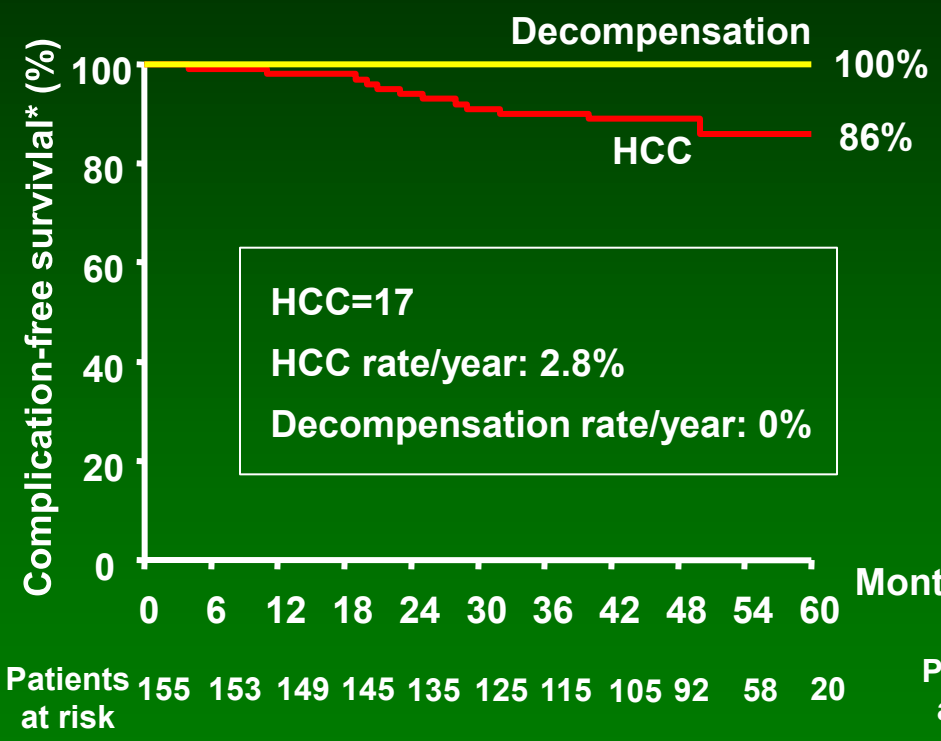


Papatheodoridis et al Gut 2011;60:1109-16

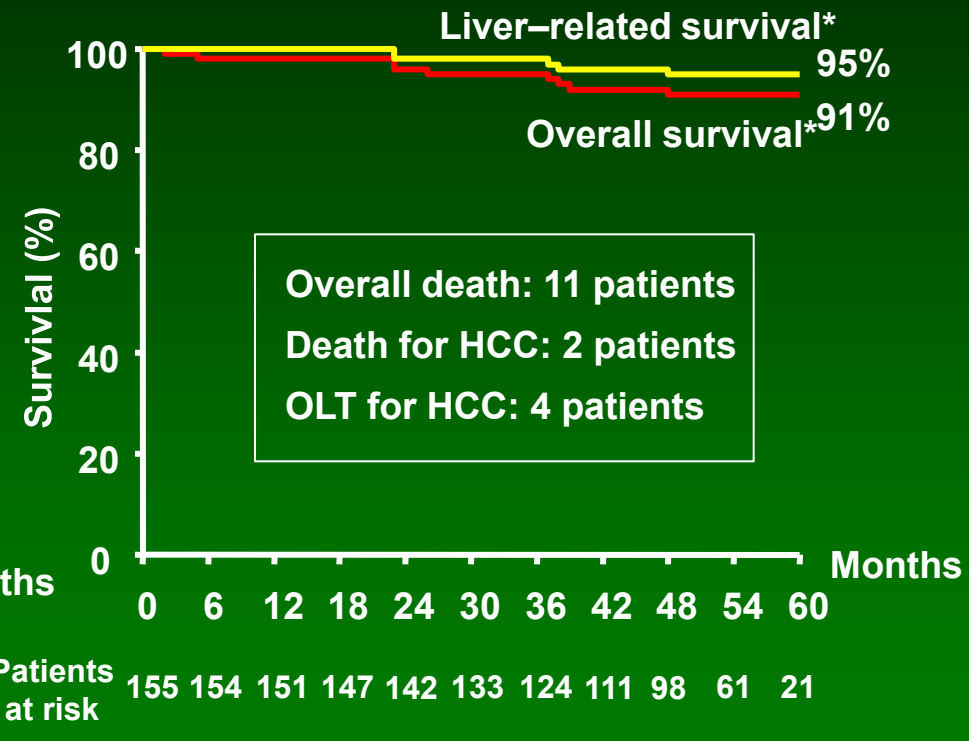


Hosaka T et al Hepatology 2013 in press

Survival of ETV treated patients with compensated cirrhosis



* Kaplan-Meier estimates

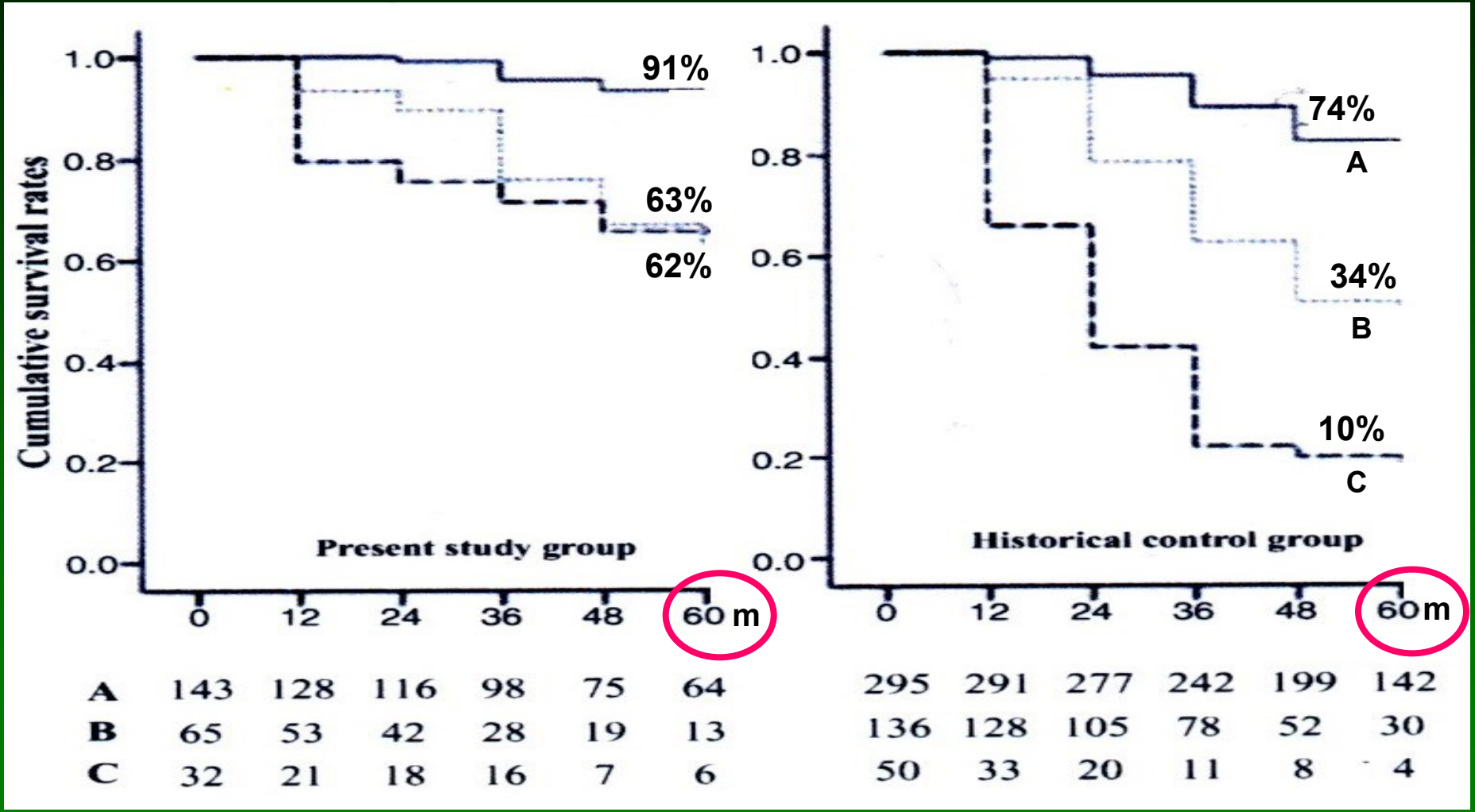


* Kaplan-Meier estimates; OLT=death

83% HBeAg (-); Fu 53 mo

Courtesy of Lampertico P 2012 AASLD poster 366

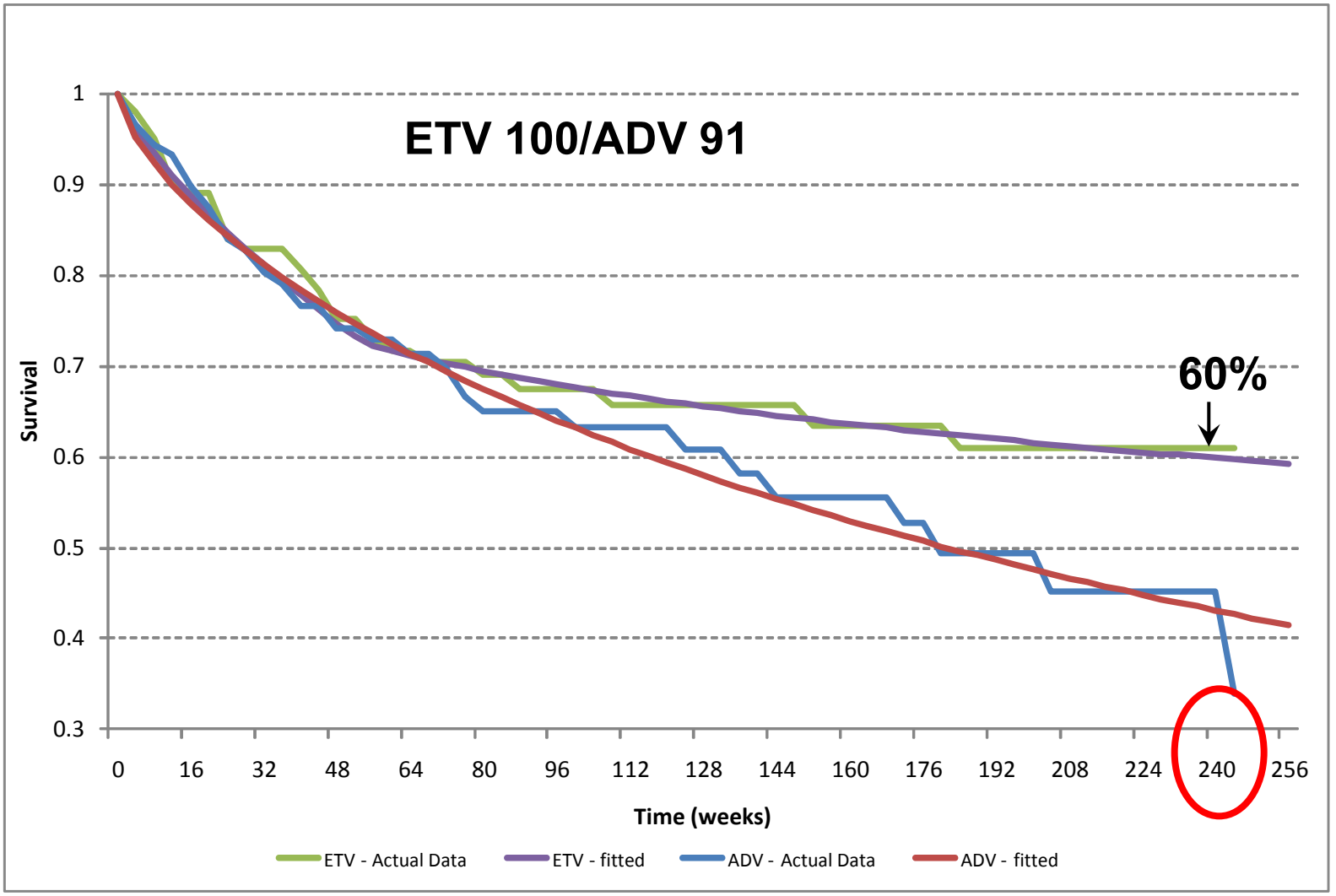
Nuc therapy starting with LAM reduced mortality even in child B and C cirrhotic patients



40% HBeAg (-); Fu 46.4 mo

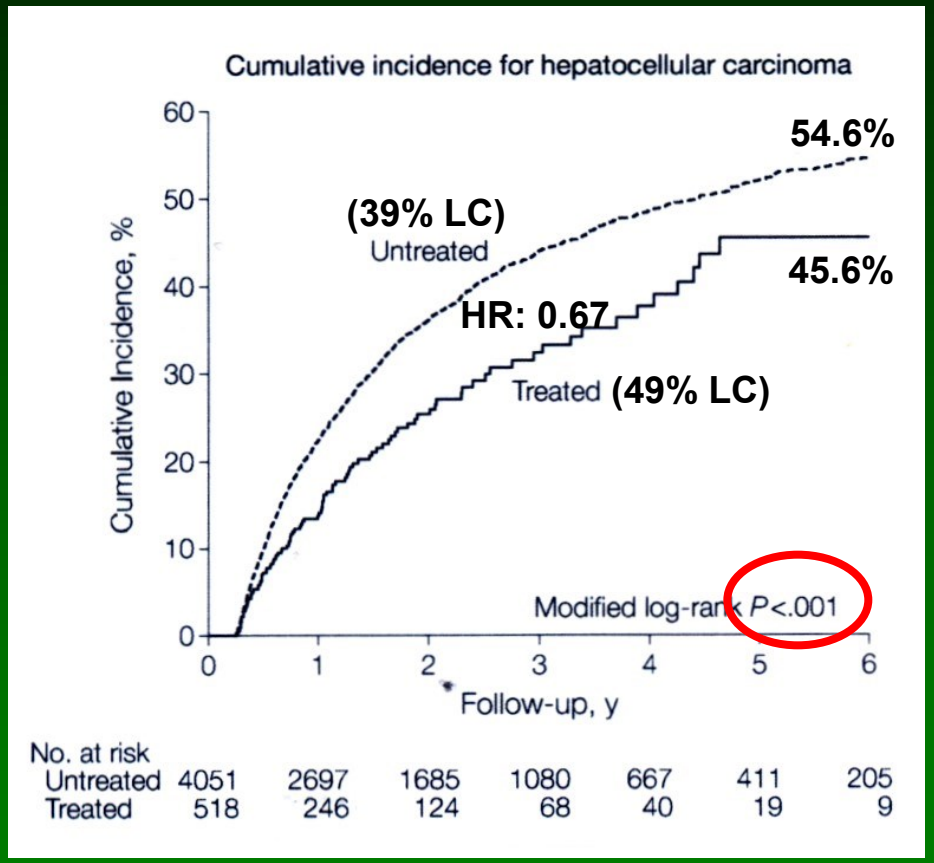
adapted from Kim et al JGH 2012;27:1589-95

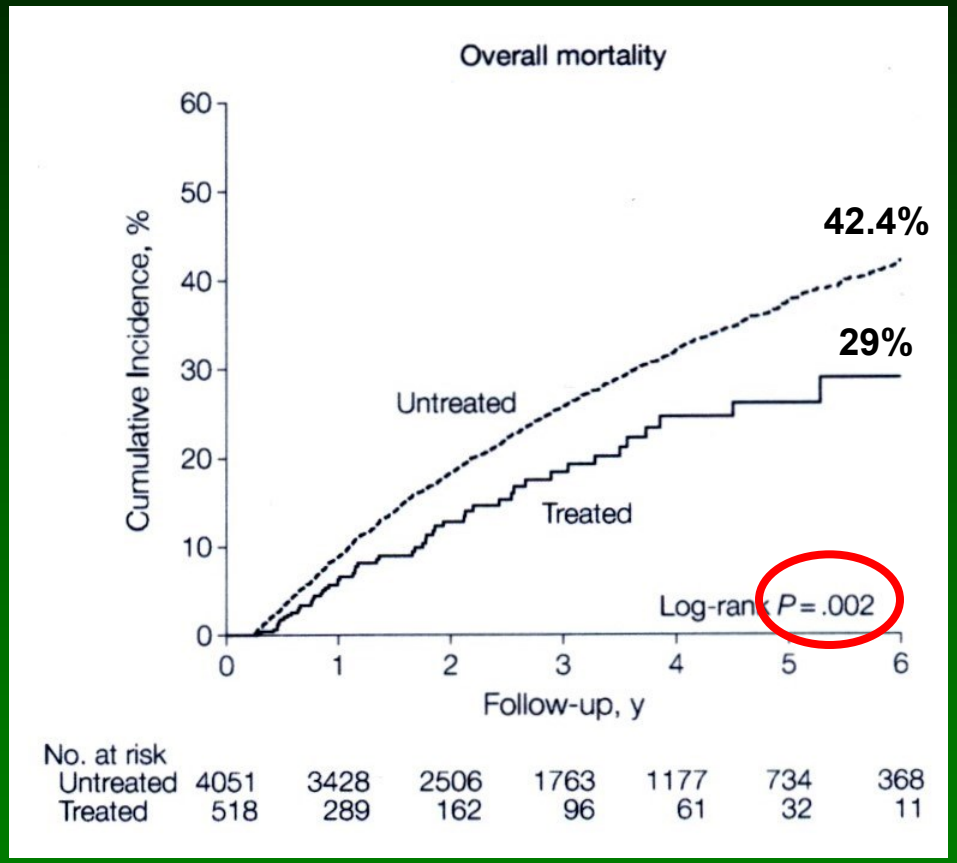
HCC-free survival in ETV/ADV treated patients with hepatic decompensation



Courtesy of Tsai N et al Clinicoecon Outcomes Res2012;4:227)

Nuc therapy reduced post-resection HCC recurrence and mortality

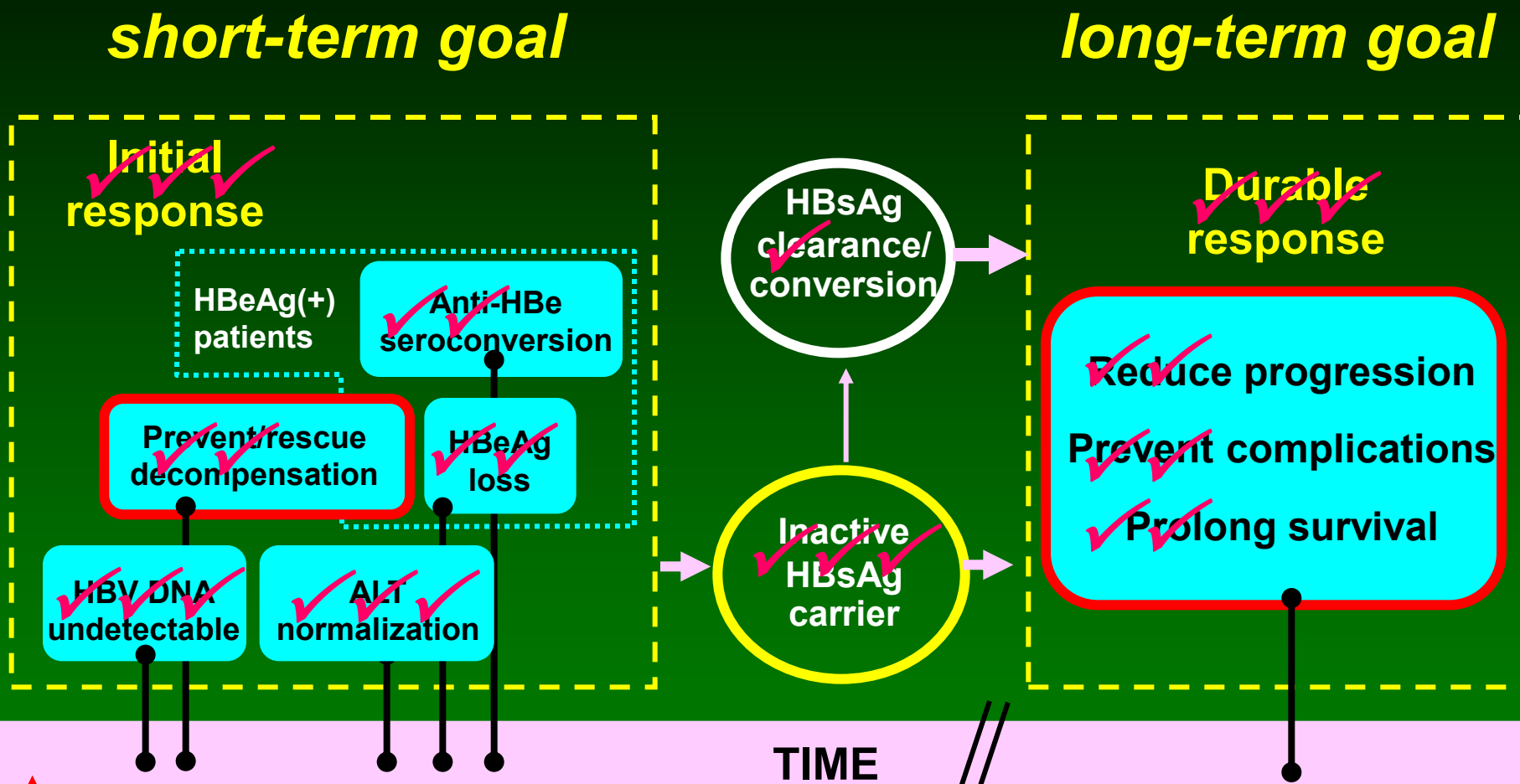




A nation wide cohort study based on Taiwan National Health Insurance Research Database (99% coverage) 2003-2010

adapted from Wu CY et al JAMA 2012:308;1906-1913

Goals of therapy for chronic HBV infection



adapted from Liaw YF et al Hepatol Int 2012;6:531-561

✓ *Goals achievable but not satisfactory!!*