

Long term benefits of NUCs

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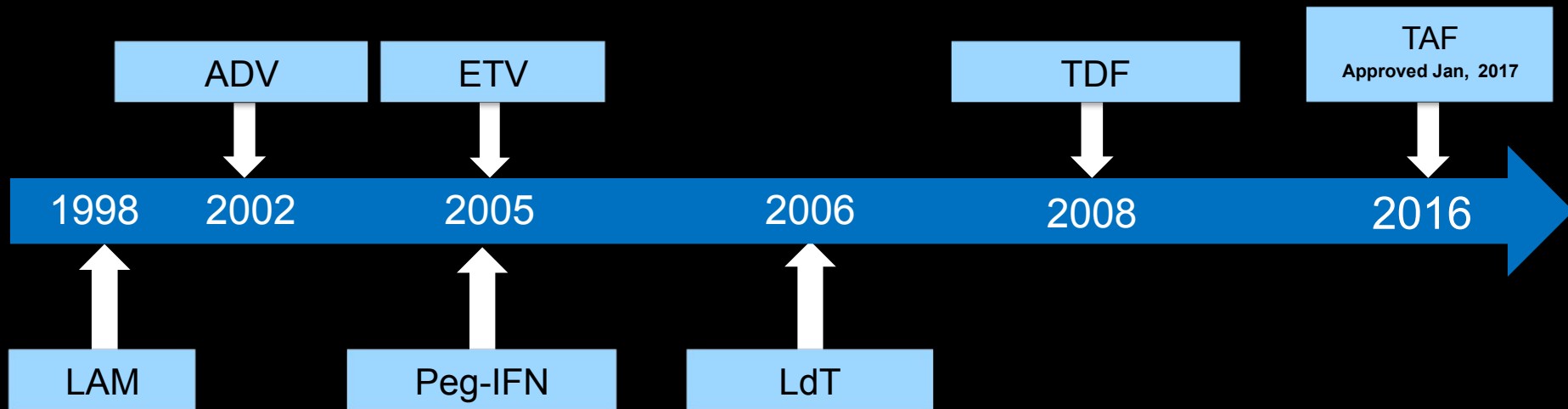
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Evolution of Current CHB Therapies



Summary of Preferred CHB Therapies

Guidelines	HBeAg+ or HBeAg- Without Cirrhosis	Compensated Cirrhosis	Decompensated Cirrhosis
AASLD 2015	TDF, ETV, or Peg-IFN	TDF or ETV	TDF or ETV
EASL 2012	TDF, ETV, or Peg-IFN	TDF or ETV; Peg-IFN may be used in well-compensated cirrhosis	TDF or ETV
APASL 2015	TDF, ETV, or Peg-IFN	TDF or ETV; PegIFN for well-compensated disease	TDF or ETV
US Algorithm 2015	TDF, ETV or Peg-IFN	TDF or ETV; Peg-IFN may be used in well-compensated cirrhosis	TDF or ETV
AATA 2011	TDF or ETV	TDF or ETV	TDF or ETV

Terrault NB et al. *Hepatology* 2015; Published online November 13, 2015: doi:10.1002/hep.28156.

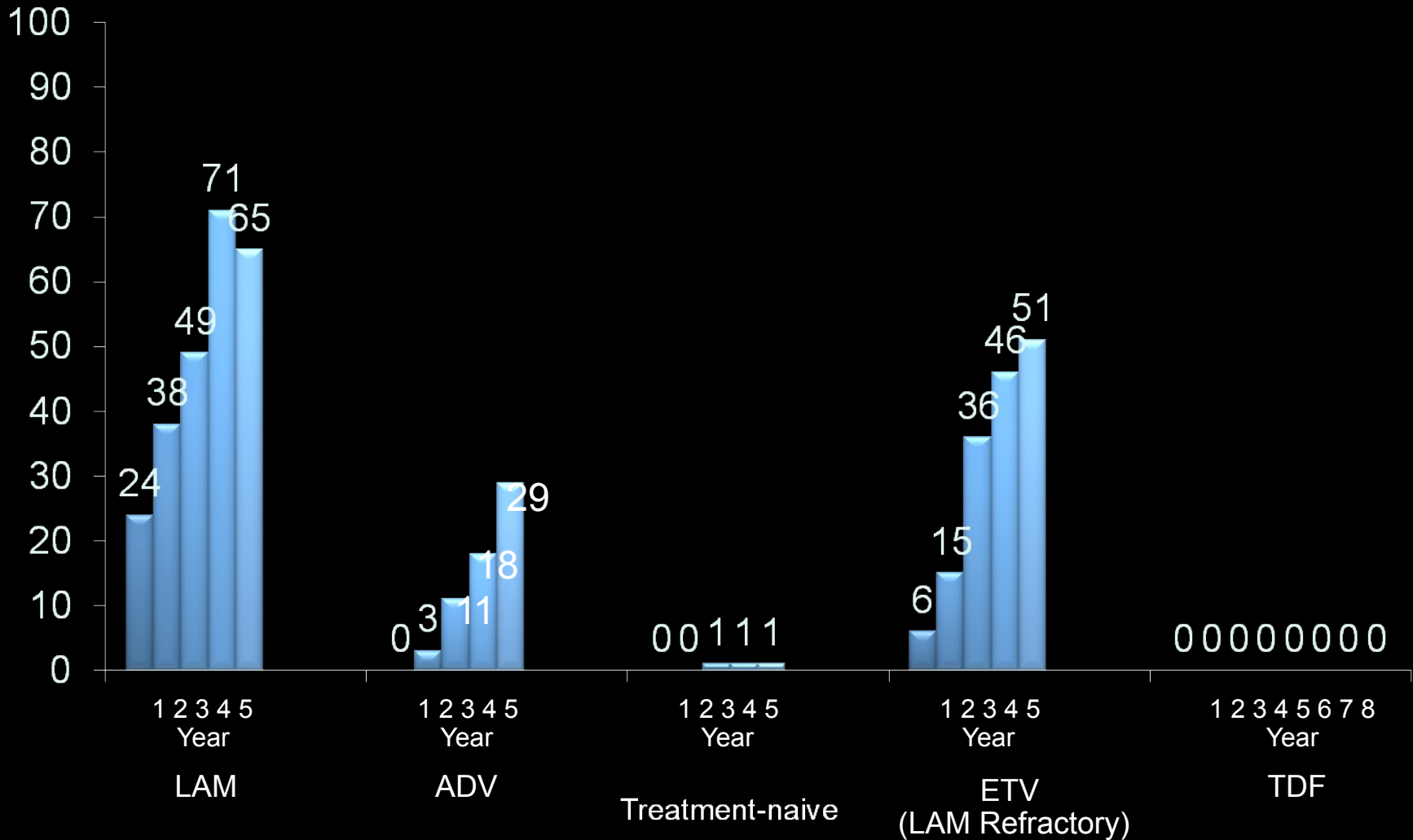
European Association for the Study of the Liver. *Journal Hepatol* 2012;57:167-185

Sarin SK, et al. *Hepatology* 2015; Published online November 13, 2015: doi 10.1007/s12072-015-9675-4

Martin P, et al. *Clin Gastroenterol Hepatol* 2015; Published online July 15, 2015: <http://dx.doi.org/10.1016/j.cgh.2015.07.007>

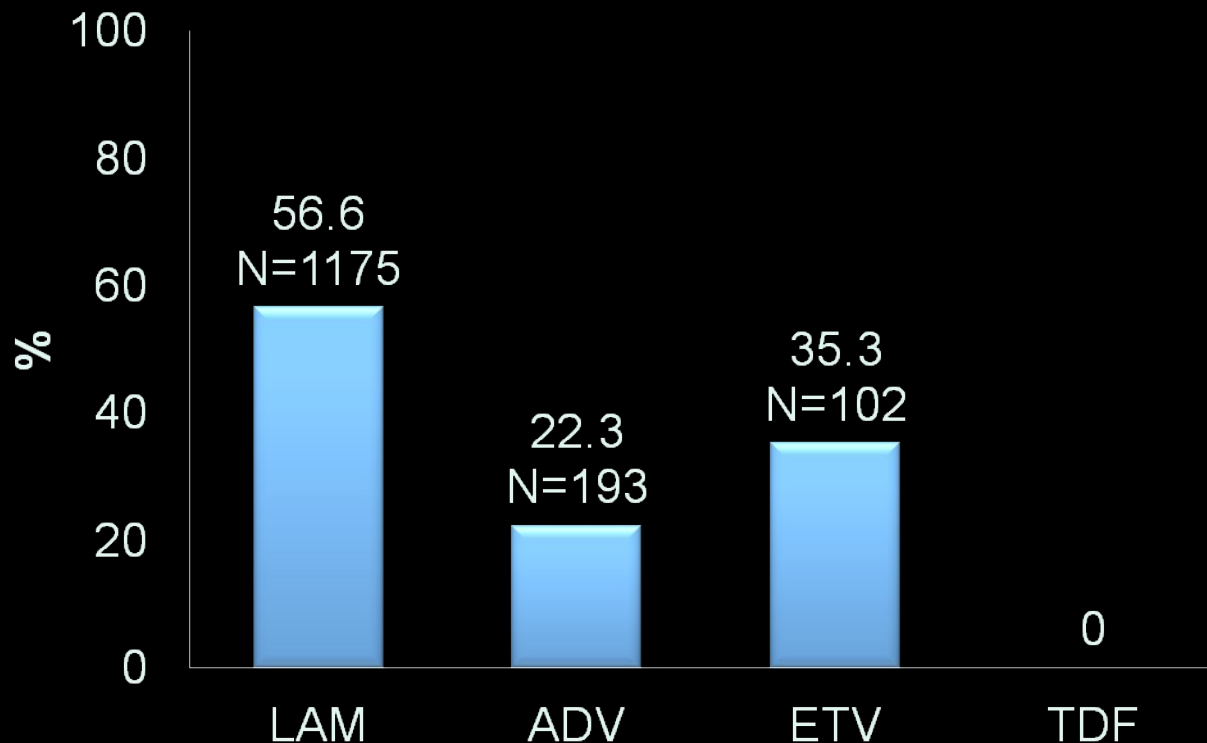
Tong MJ, et al. *Dig Dis Sci* 2011;56:3143-3162

Resistance Rates Among Nucleos(t)ides



Prevalence of HBV Drug Resistance HBV in Treatment Experienced Patients

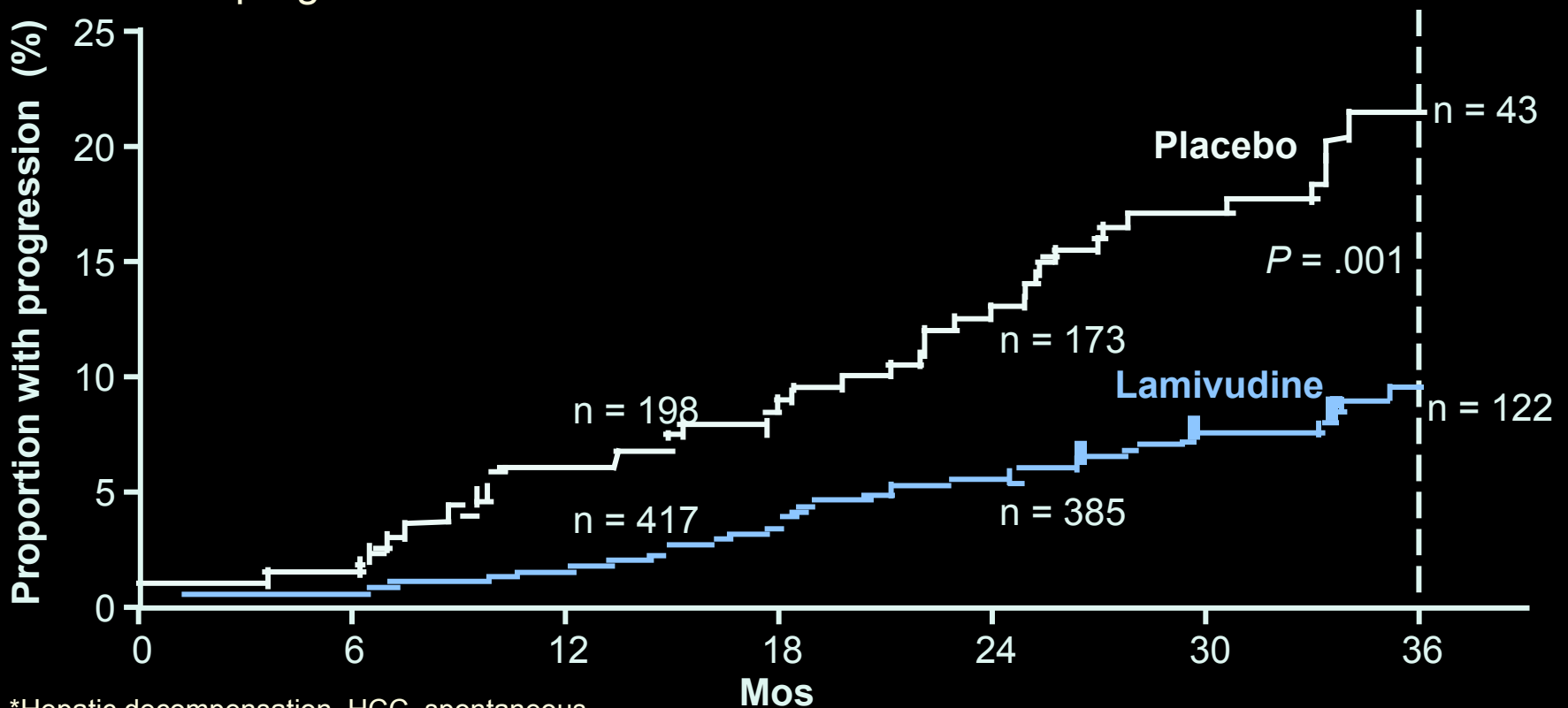
Survey of genotypic resistance testing results in 1,568 NUC-experienced patients from European tertiary referral centers



Drug resistant strains detected in 52.7% (827/1568) of patients

LAM reduces risk of liver disease progression

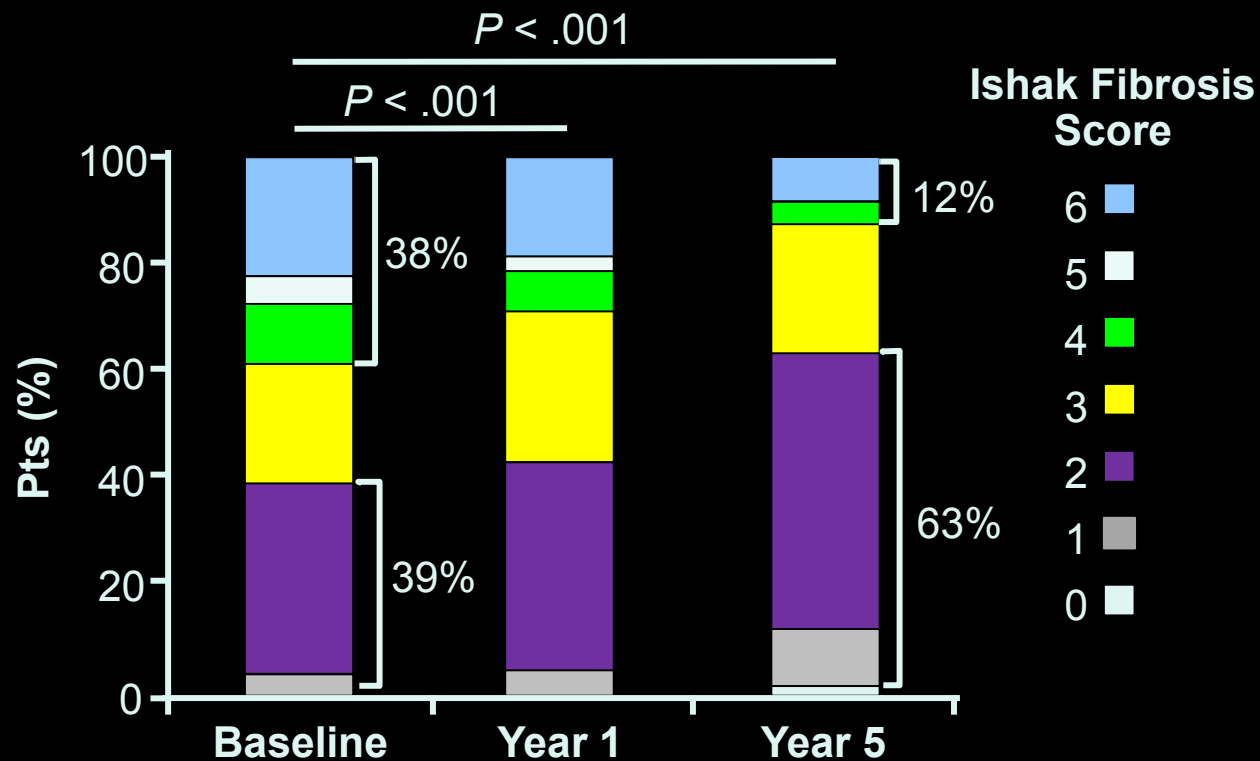
- Placebo-controlled, double-blind, parallel group study of pts with chronic HBV infection and cirrhosis (F4) (N = 651) followed until HBeAg seroconversion or disease progression*



*Hepatic decompensation, HCC, spontaneous bacterial peritonitis, bleeding gastroesophageal varices, or death related to liver disease.

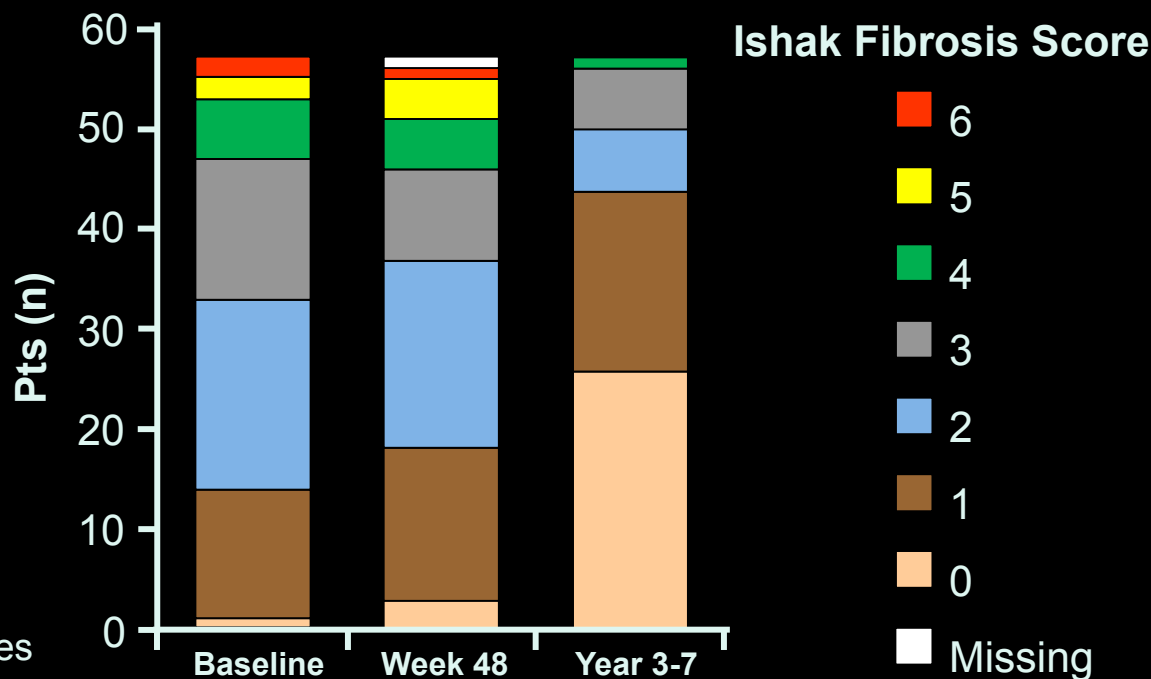
Tenofovir: fibrosis, cirrhosis regression

- Overall regression of fibrosis in 51% of pts through 5 yrs
- Reversal of cirrhosis in 74% of pts through 5 yrs



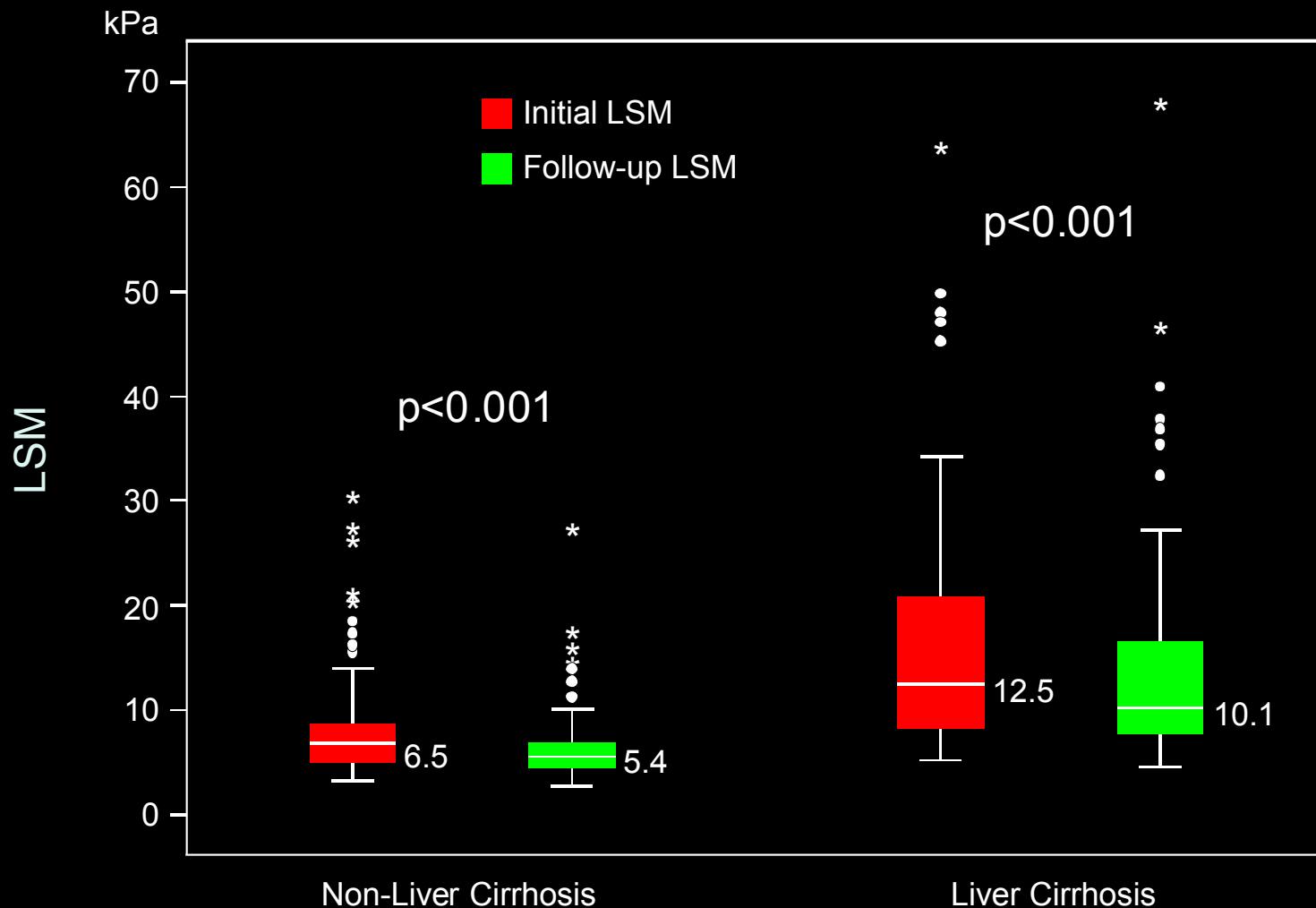
Entecavir : Regression of Fibrosis, Cirrhosis

- Regression of fibrosis (≥ 1 -point decrease in Ishak score) in 88% of pts
- Reversal of cirrhosis in 4/10 pts with cirrhosis at baseline (median decrease in Ishak score: 3 points)



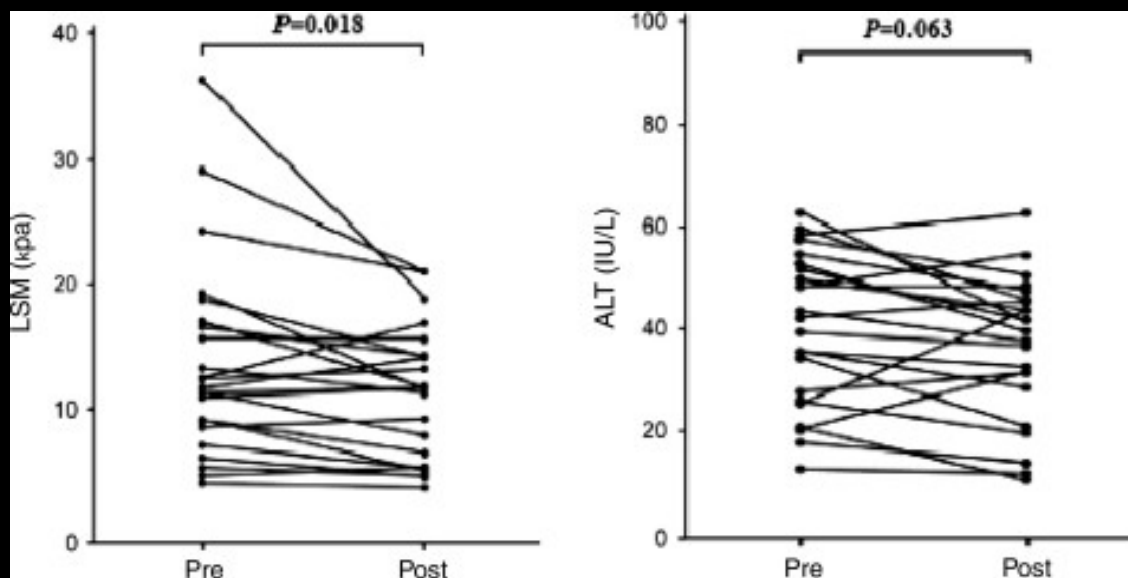
n = 57
matched biopsies

Liver Stiffness Measurement (LSM) changes ETV Treatment for 1 year, Taiwan.

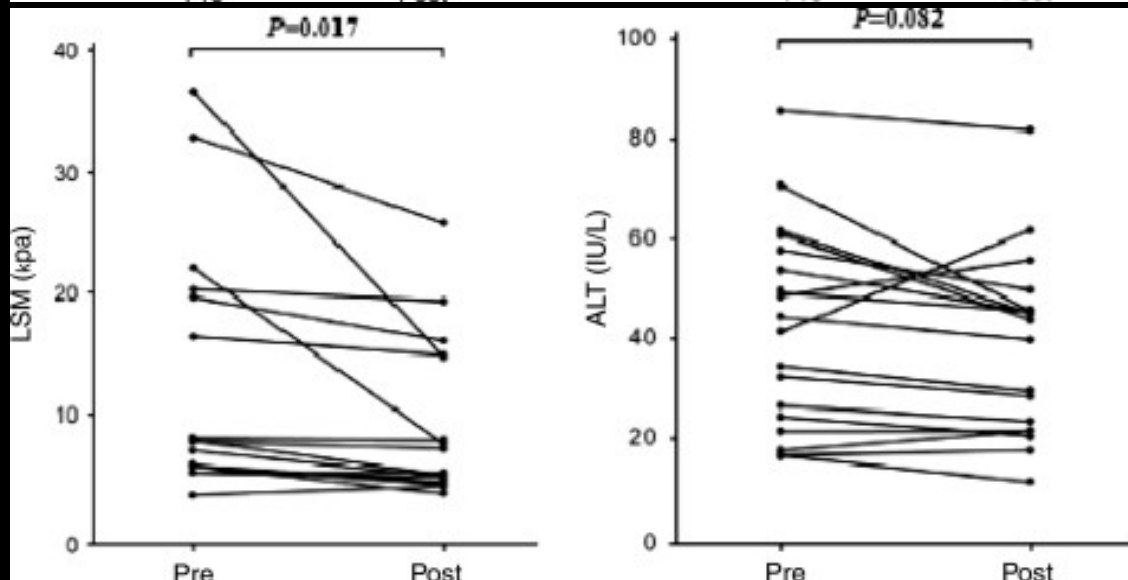


LSM (Fibroscan®) changes, multiple NUCs

1st year

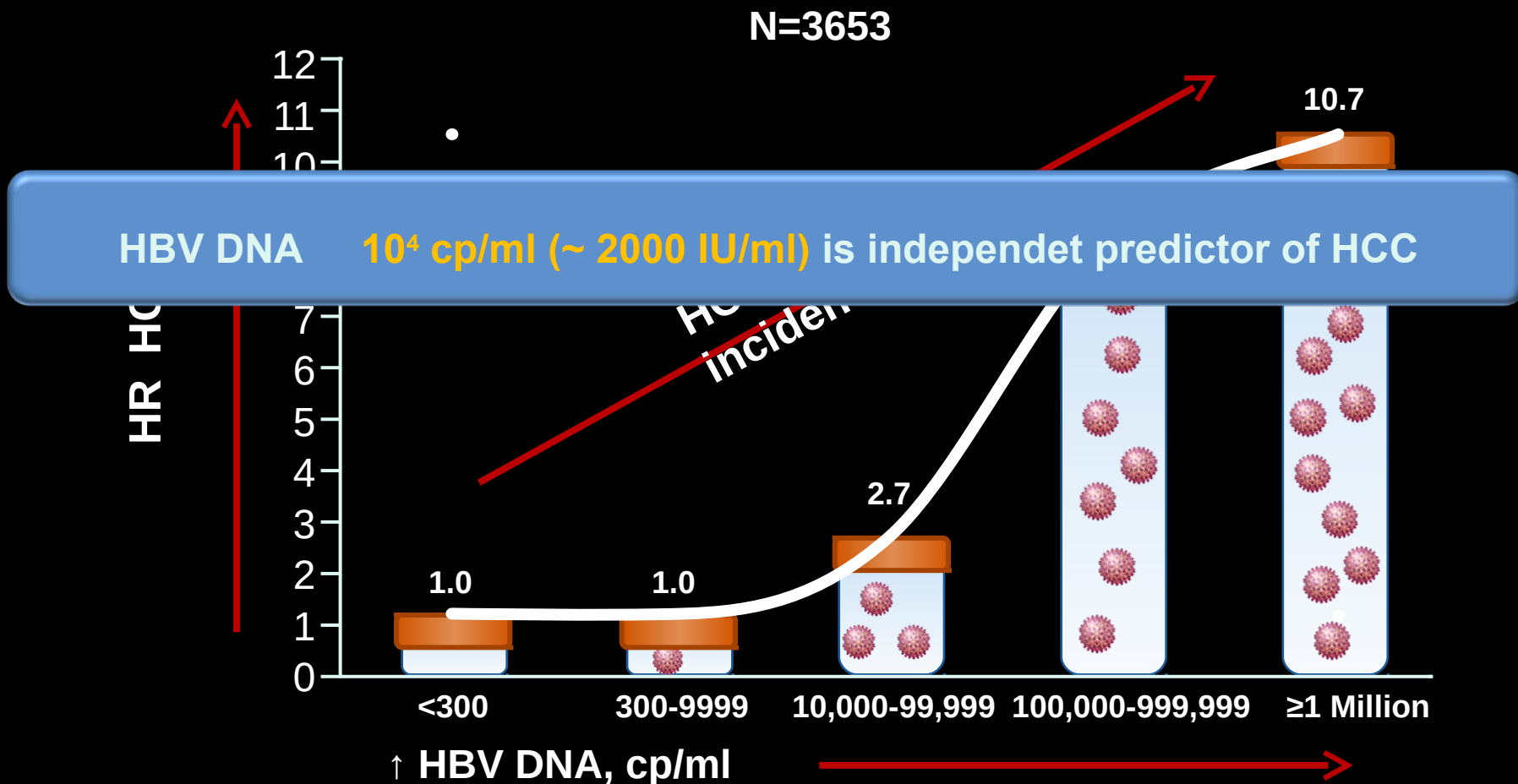


2nd year



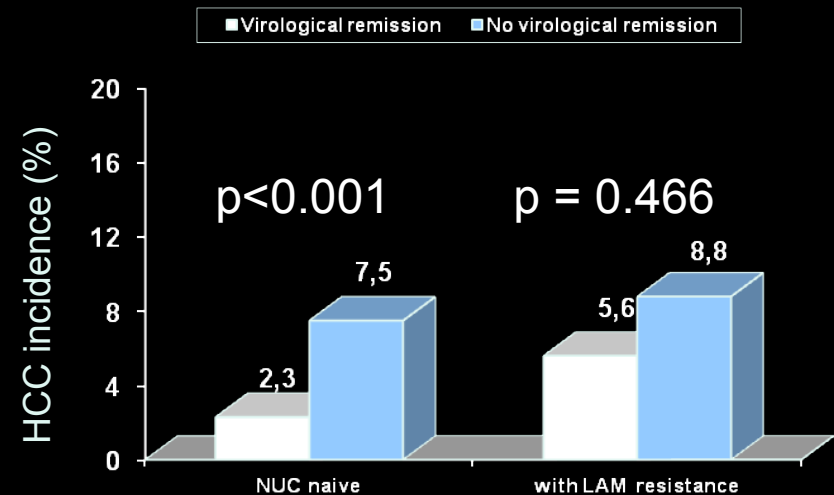
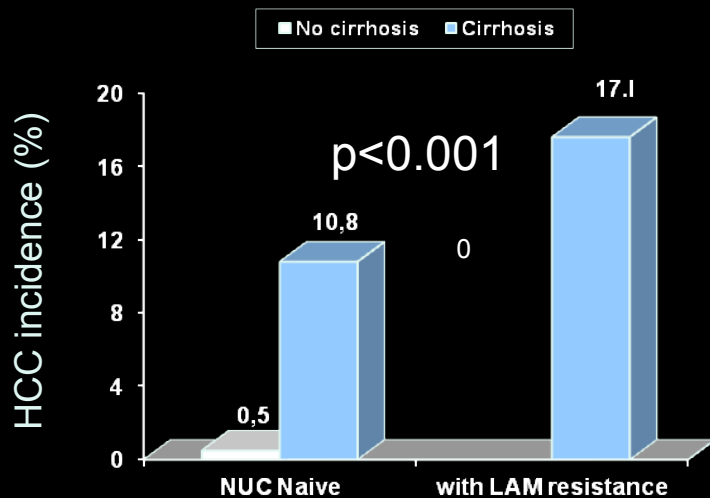
South Korea
LAM
ADF
ETV

REVEAL: HCC increases with HBV DNA

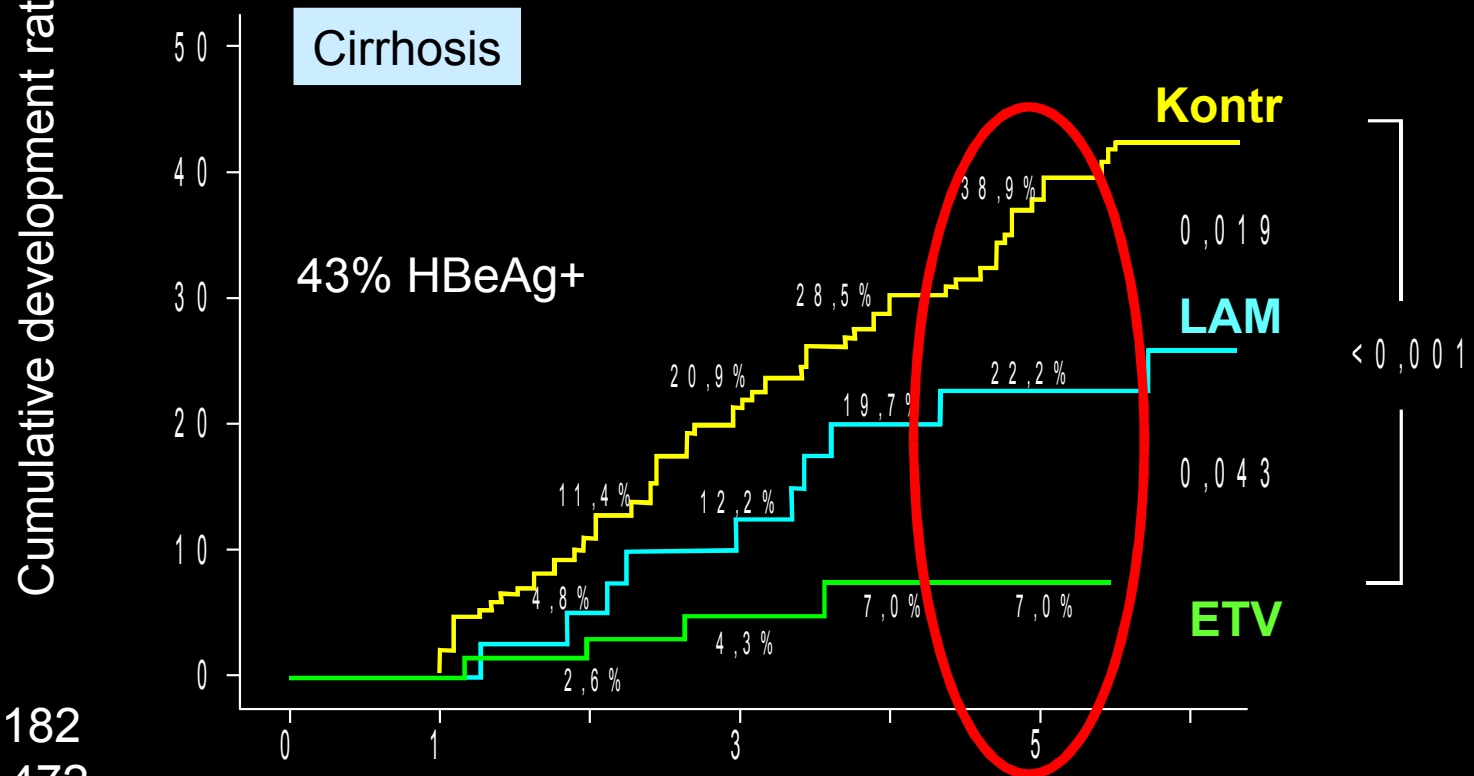
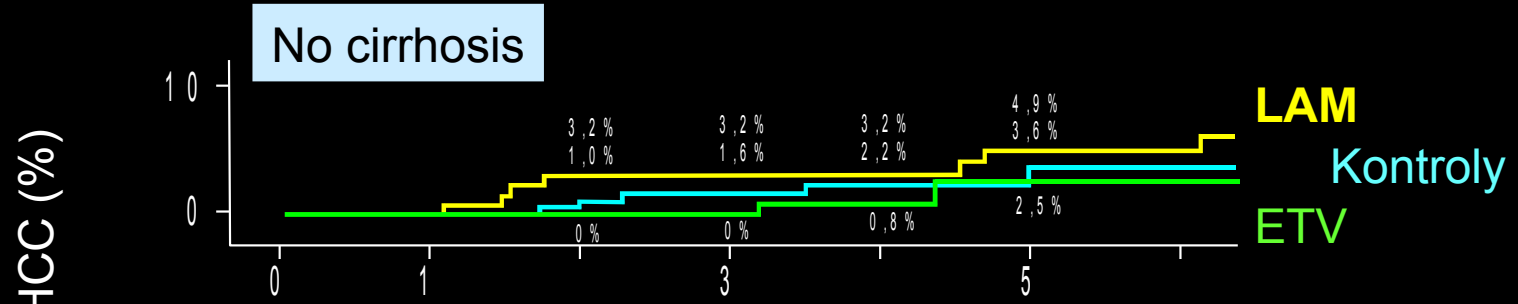


HCC incidence and NUC

- 21 studies, treated pts n=3881, untreated pts n=534
- HCC / treated 2,8 %
- HCC / untreated 6,4 %
- Mean FU 46 months



LAM vs. ETV vs. Untreated control group



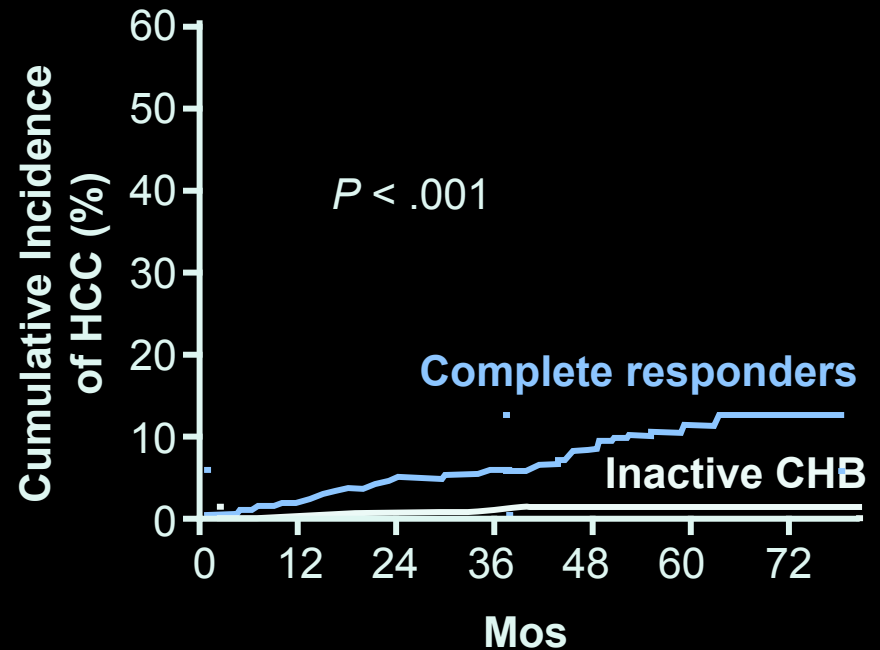
LAM n=182

ETV n= 472

Historical control n=1143

NUCs vs. Inactive Disease

- Retrospective cohort study of treatment-naive pts with HBV starting oral nucleos(t)ide analogues (n = 1378) vs HBeAg-negative pts with inactive CHB (n = 1014)

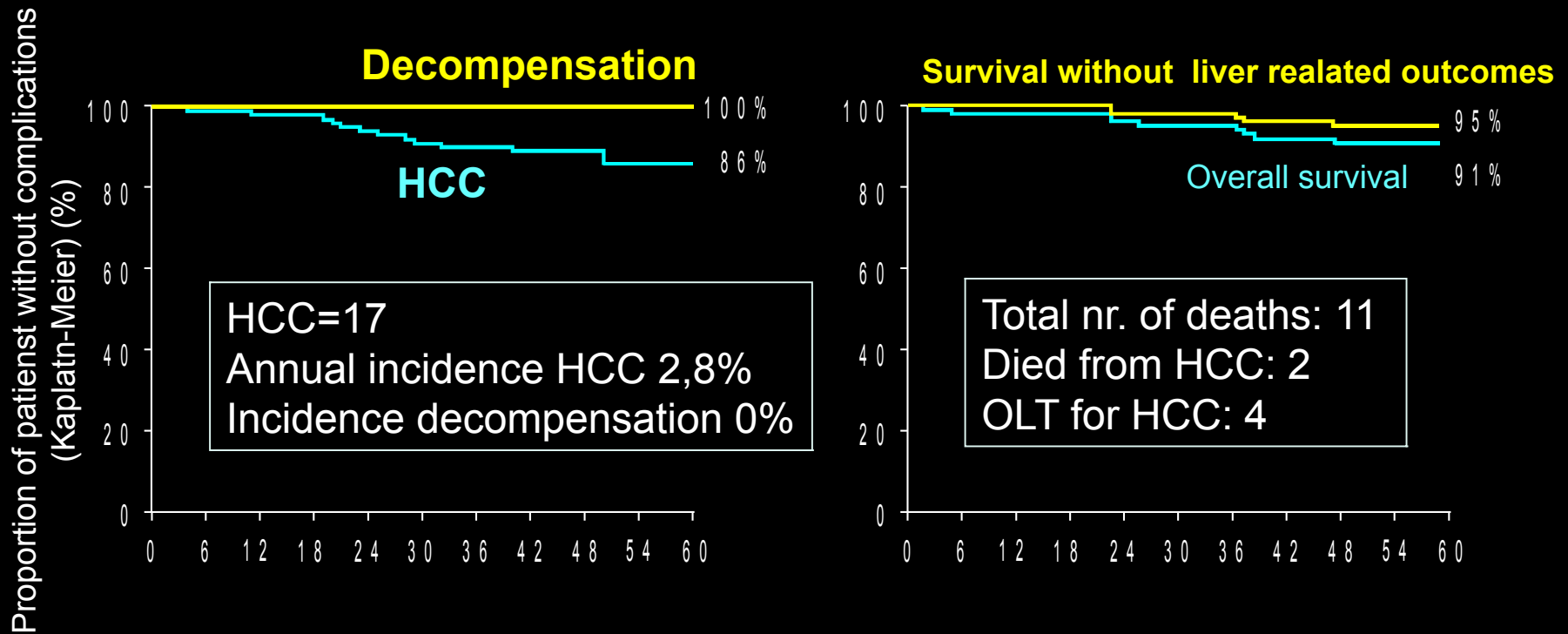


- Spontaneous control better than treatment

Pts at Risk, n

NUC CR	1132	848	564	497	380	128	19
Inactive CHB	1014	918	724	594	469	304	80

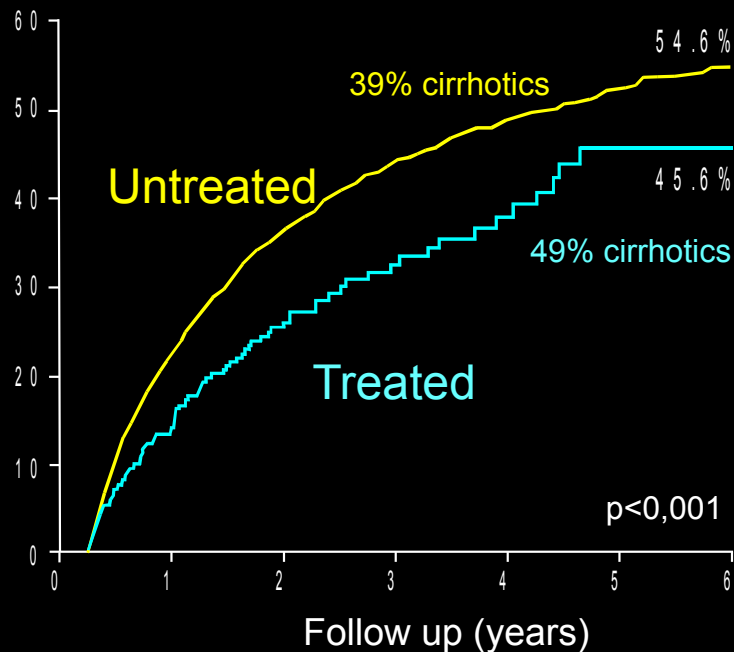
Overall survival of ETV treated patients with compensated cirrhosis at baseline



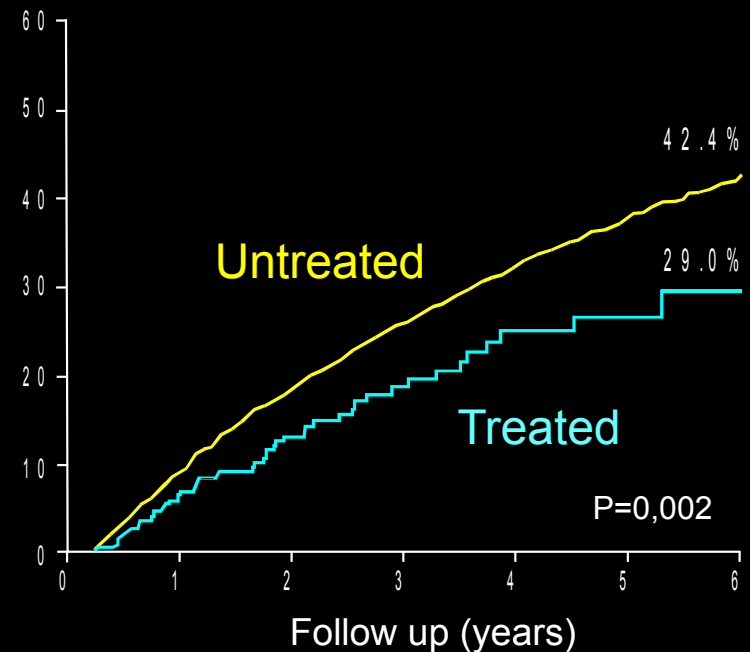
83% HBeAg (-); FU 53 months

NUCs lower HCC recurrence after surgical resection

Cumulative recurrence after HCC resection



Overall mortality



Conclusions

- Ideal goal of HBV treatment is HBsAg seroconversion – „closest to cure“
- sustained HBV DNA $<$ LOD leads to improvement in long term survival of HBsAg positive patients