



# **Prevenzione della recidiva HBV dopo trapianto di fegato**

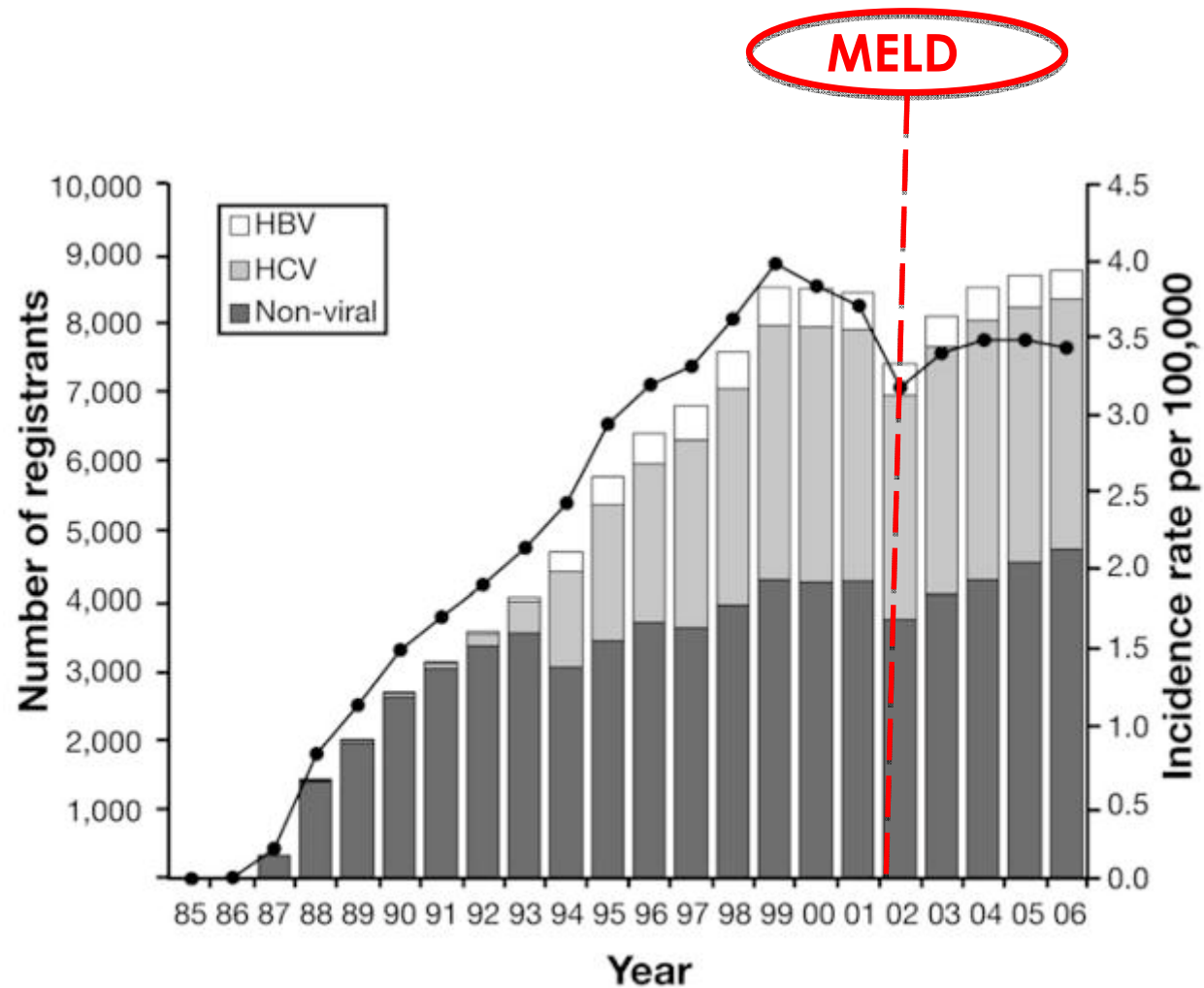
**Maria Cristina Morelli**

Gestione clinica delle epatiti croniche virali  
2 marzo 2013  
Nuovo ospedale di Cona

# TRAPIANTO DI FEGATO PER CIRROSI VIRALE

## WAITING LIST UNOS DATABASE (1985-2006)

- HBV 4.2%
- HCV 35.9%
- Non virale 60%



# TRAPIANTO DI FEGATO PER CIRROSI VIRALE

## WAITING LIST UNOS DATABASE

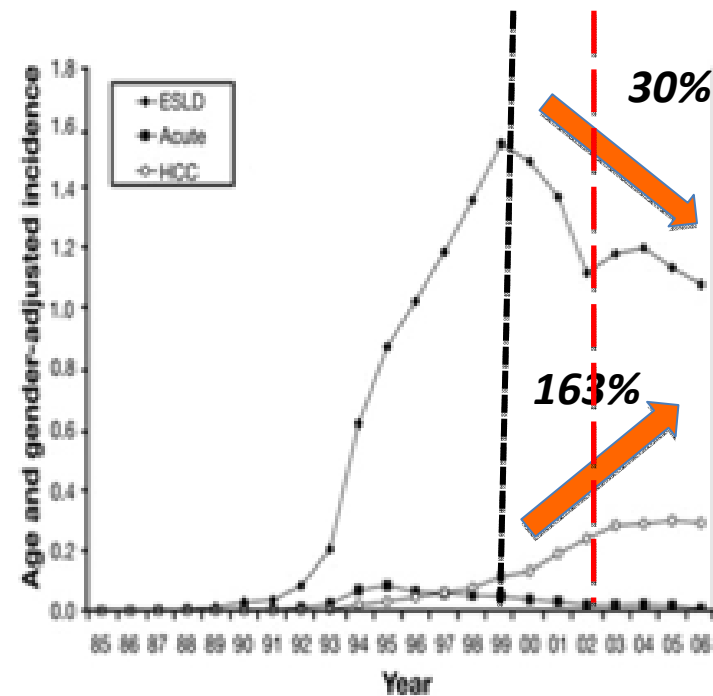
### HBV

LAM MELD



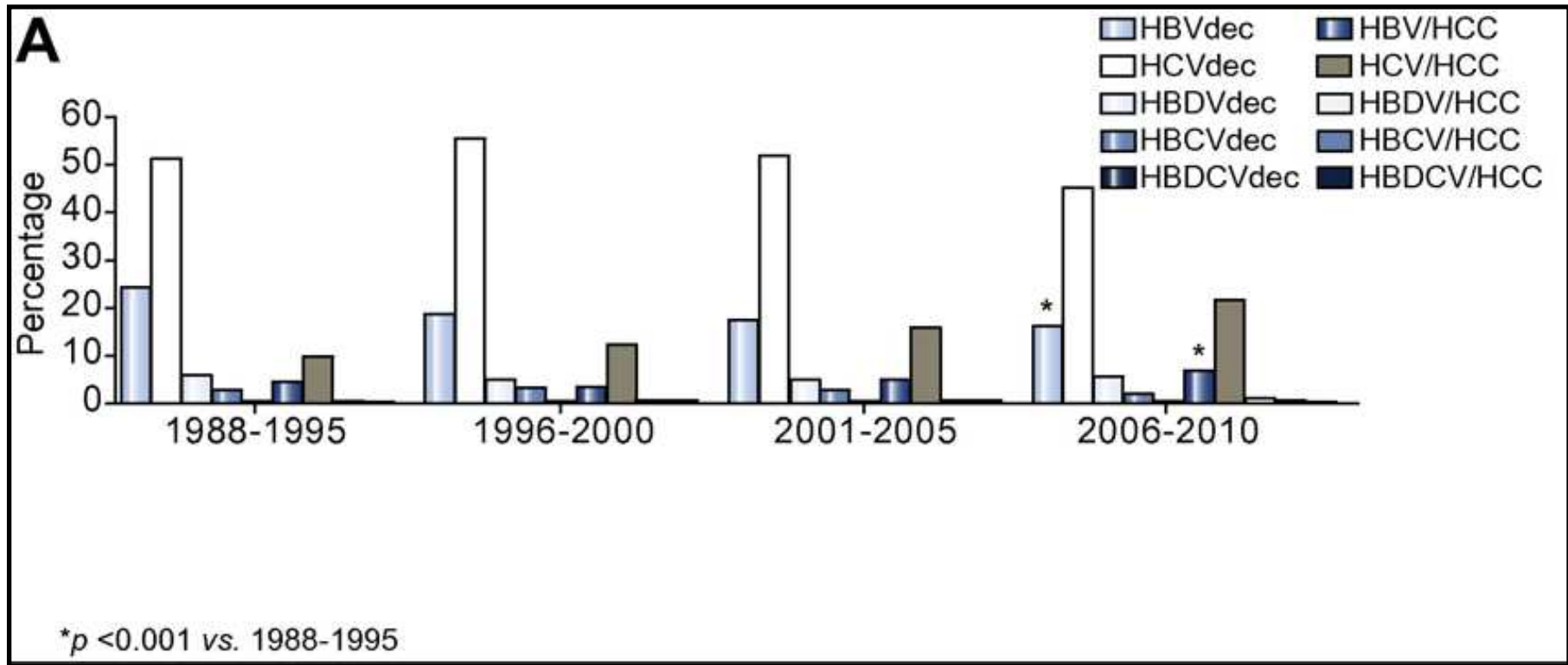
### HCV

MELD



# EVOLUZIONE TRAPIANTO DI FEGATO PER HBV

## ELTR DATABASE (1988-2010)



# LISTA UNICA REGIONE EMILIA-ROMAGNA

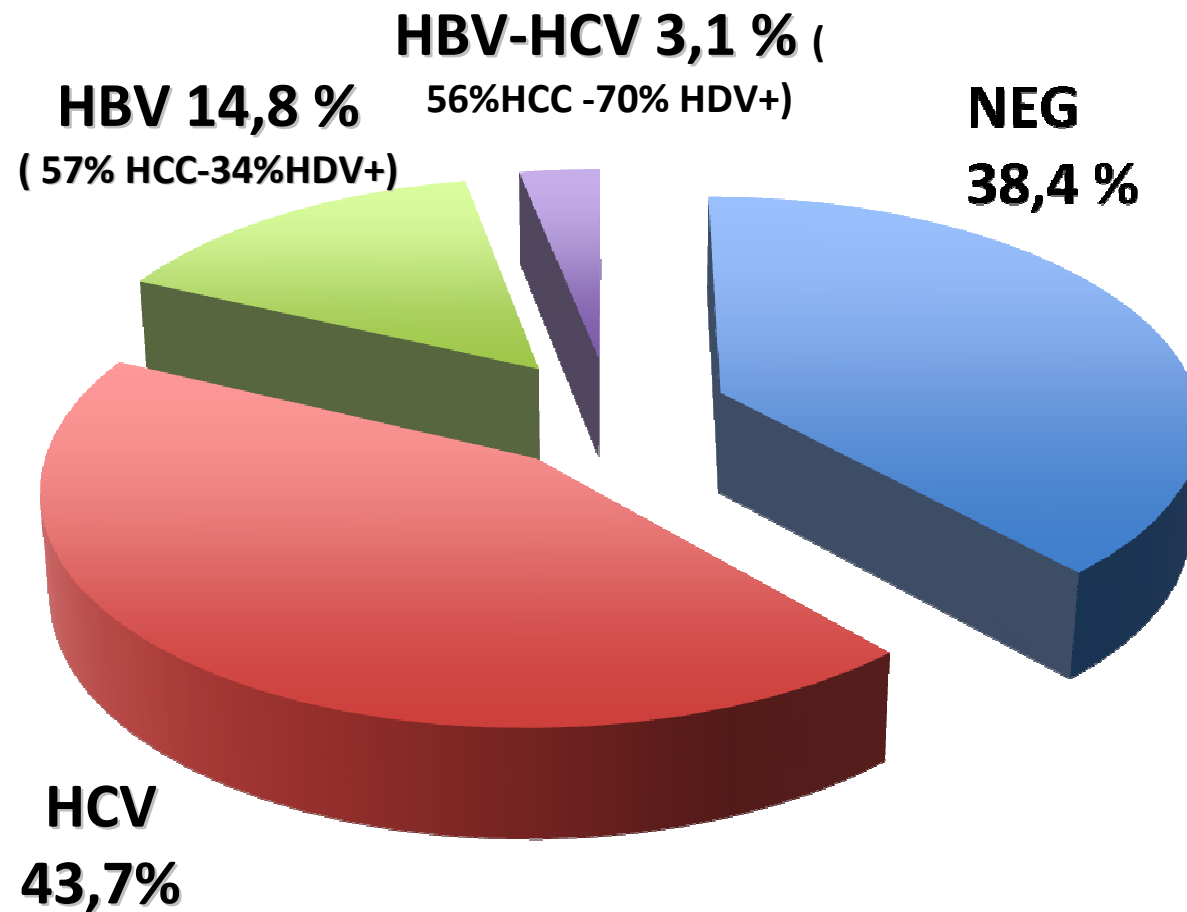
(aprile 2004-dicembre 2011)

● Età media ricevente	51±11
● F/M%	31/69
● HCC	39%
● HCV +	42%
● HBV +	12%
● MELD in cirrosi (mediana)	26
● MELD in HCC (mediana)	15

# TRAPIANTO DI FEGATO

## CENTRO TRAPIANTI BOLOGNA

### PATTERN VIROLOGICO (n.810 OLT 2002-2012)



# TRAPIANTO DI FEGATO

## CENTRO TRAPIANTI BOLOGNA (2002-2012)

### Trapianto per cirrosi HBV (n.146 )

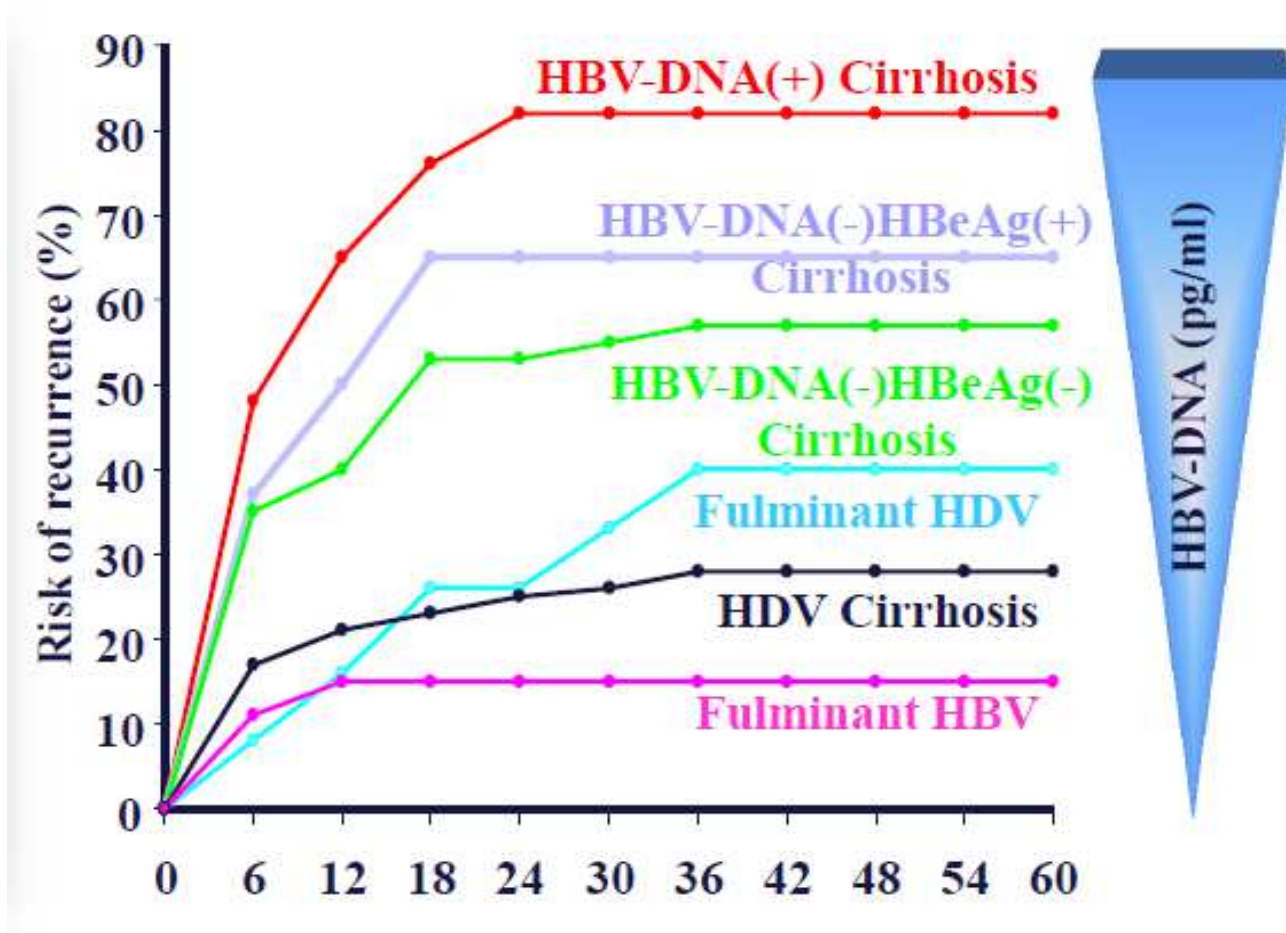
93% HBVDNA -

7 % HBVDNA + (media 1797 UI/mL )

#### TERAPIA ANTIVIRALE PRE-TRAPIANTO

	n.	%
No terapia	5	3 %
Lamivudina	84	57 %
Lamivudina+Adefovir	26	18 %
Lamivudina+Tenofovir	5	3 %
Adefovir	3	2 %
Entecavir	7	4 %
Tenofovir	8	5 %
Non conosciuta	7	4 %

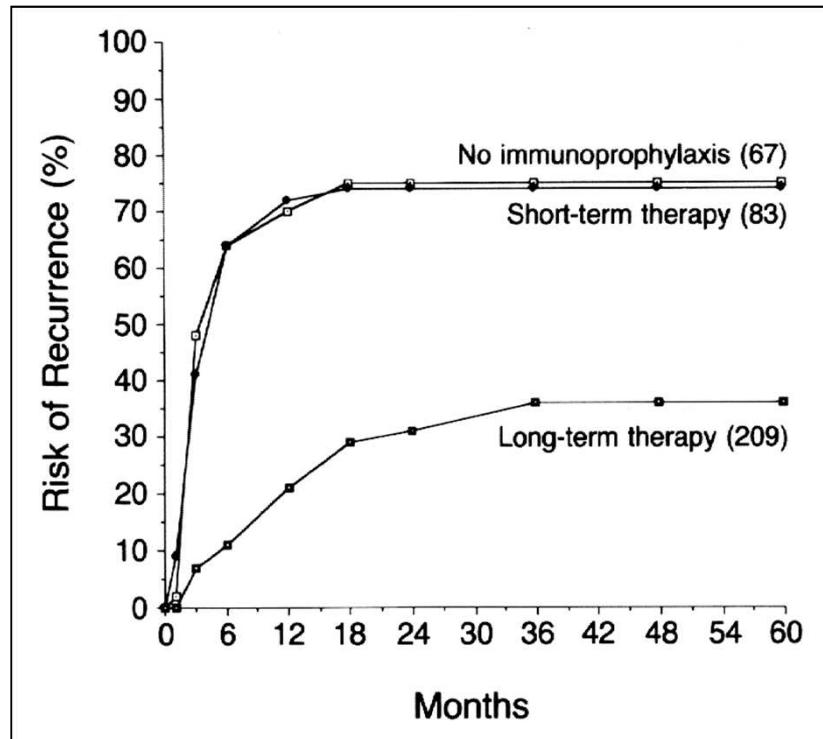
# RISCHIO RECIDIVA HBV POST-TRAPIANTO



# OLT AND HBV RECURRENCE

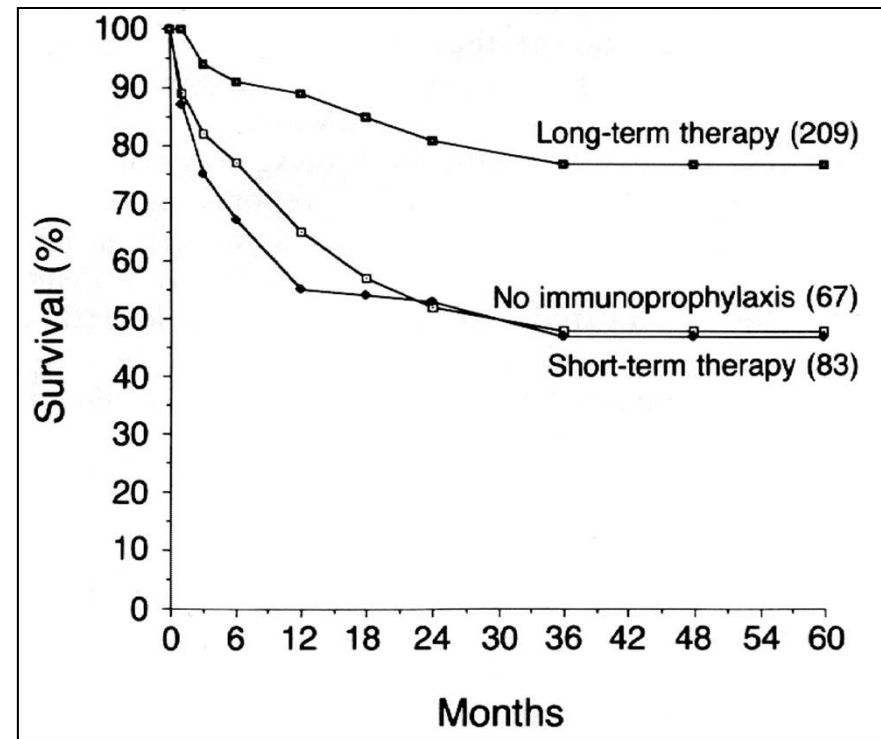
## HBV Recurrence

RISK of Post-OLT  
HBsAg POSITIVITY

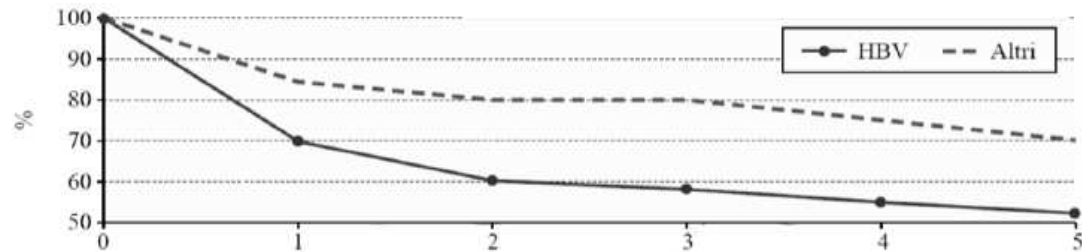


## Patient's survival

POST-OLT SURVIVAL  
IN HBsAg (+) PATIENTS

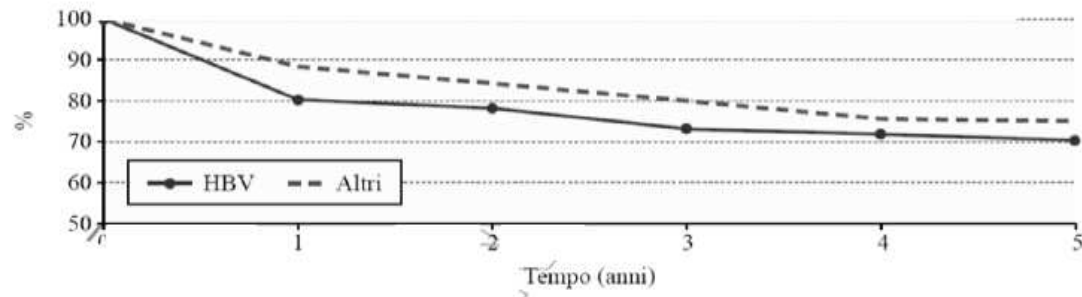


# EVOLUZIONE DEL TRAPIANTO DI FEGATO IN HBV



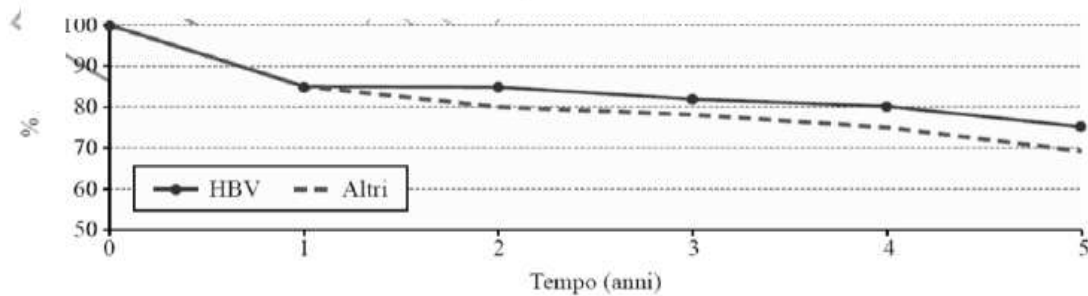
Era I  
(1987-1991)  
Numero pazienti  
HBV/totali  
675/6708  
P<0,01

**NO PROFILASSI**



Era II  
(1992-1996)  
Numero pazienti  
HBV/totali  
1005/3995  
P=0,19

**HBIG**

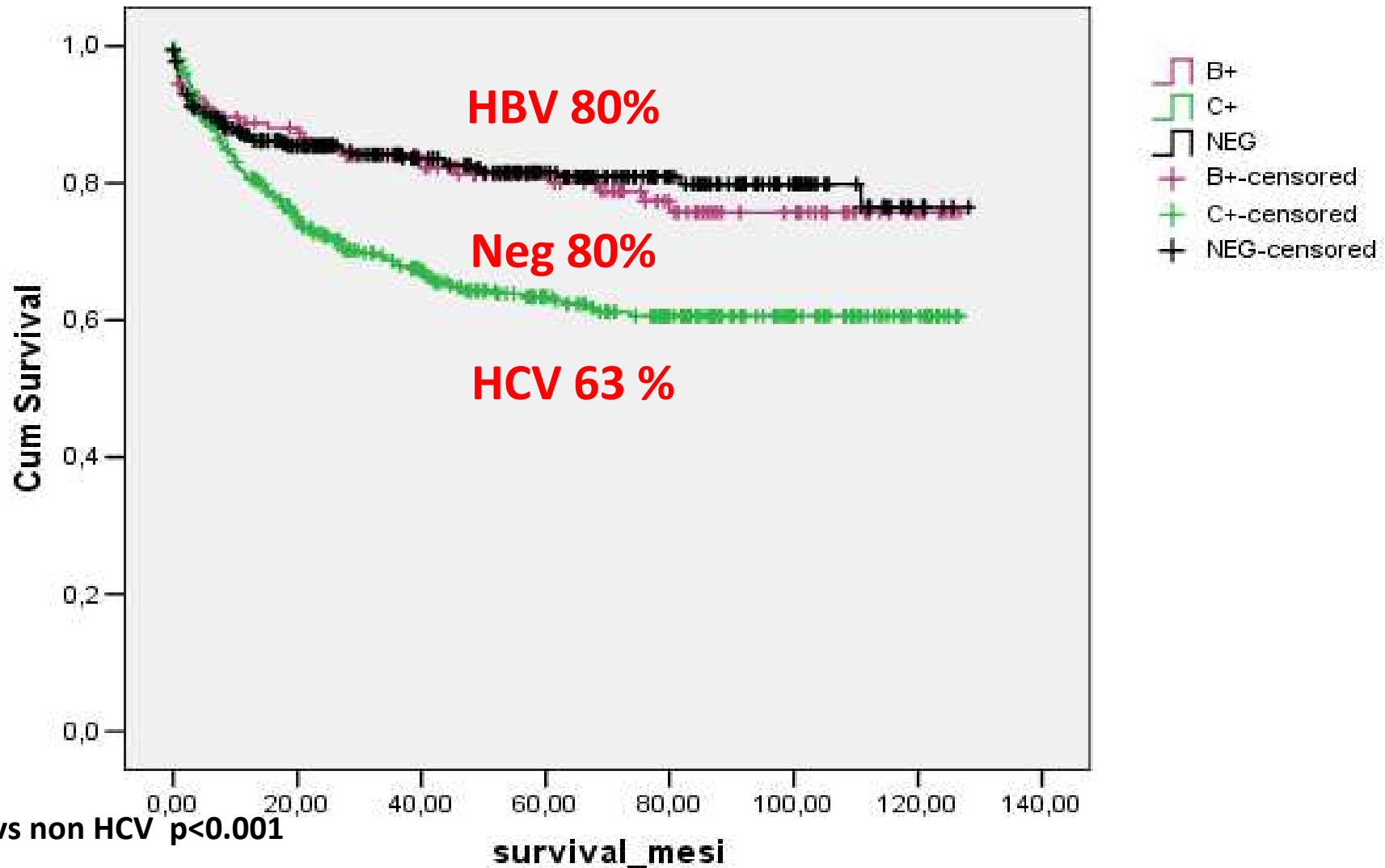


Era III  
(1996-2002)  
Numero pazienti  
HBV/totali  
11723/20730  
P=0,14

**HBIG+LAM**

# TRAPIANTO DI FEGATO CENTRO TRAPIANTI BOLOGNA

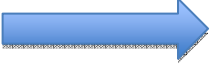

## 812 OLT (2002-2012)



# PROFILASSI RECIDIVA HBV IL PRESENTE

	Recidiva HBsAg
HBIG short term	>90 %
HBIG alte dosi	20-80 %
Lamivudina monoterapia	20-40%
HBIG alte dosi long term + Lamivudina	<5%

# PROFILASSI DELLA RECIDIVA HBV PROSPETTIVE FUTURE

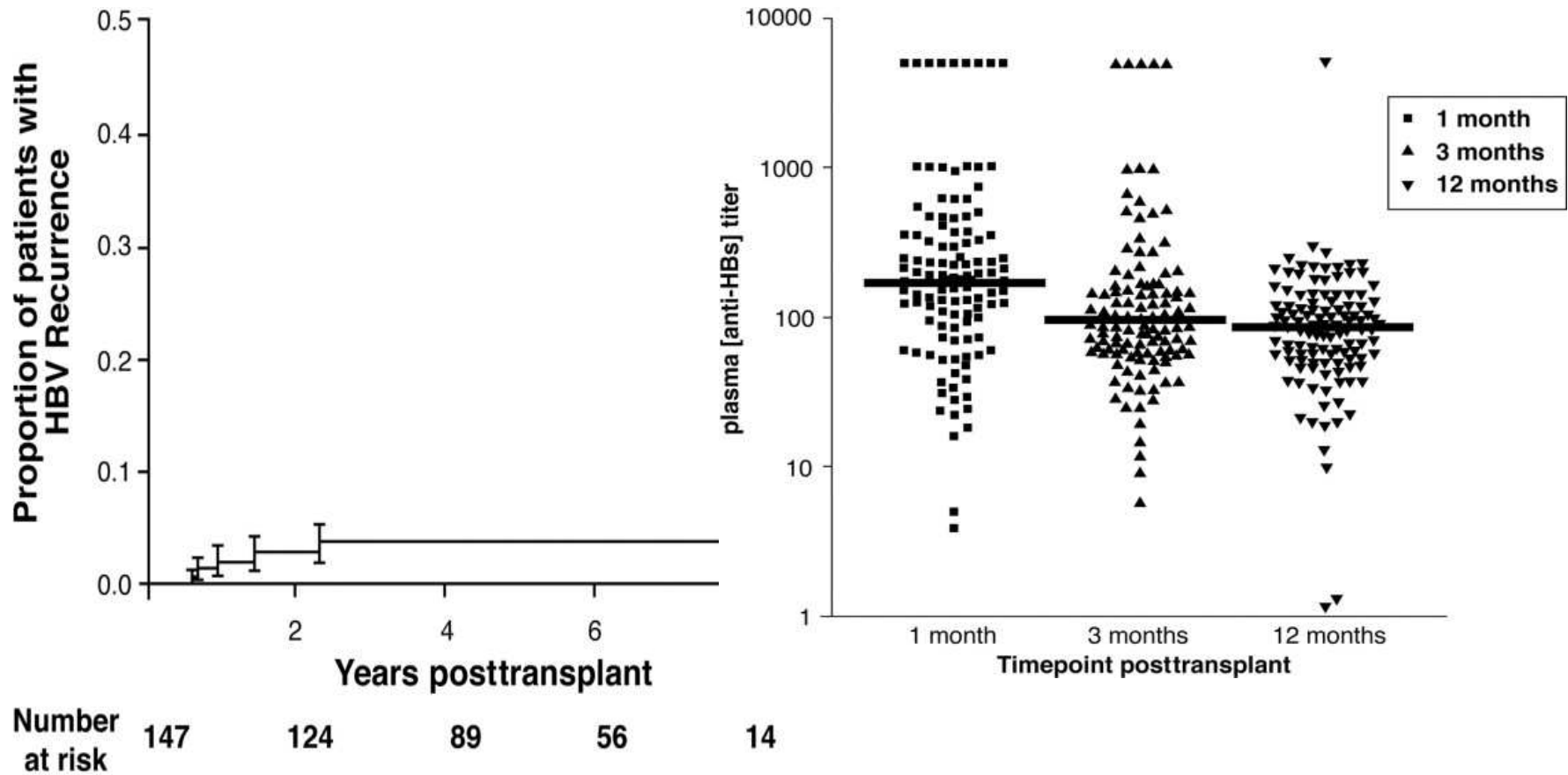
1. HBIG (basse dosi) + NUC
2. HBIG+NUC  NUC
3. NUC
4. HBIG+NUC  sospensione completa

# PROFILASSI HBIG BASSE DOSI +LAM

HBIG IM 800 UI/die per 7 gg

HBIG 800 UI/mese

147 pz ( 1998-2005)



# PROFILASSI HBIG BASSE DOSI + LAMIVUDINA vs ENTECAVIR

STUDIO CASO-CONTROLLO

HBIG IM 1600 UI/die

HBIG 800 UI/settimana ( Titolo antiHBS>500UI/L )

**372 pz (60% HBVDNA +)**

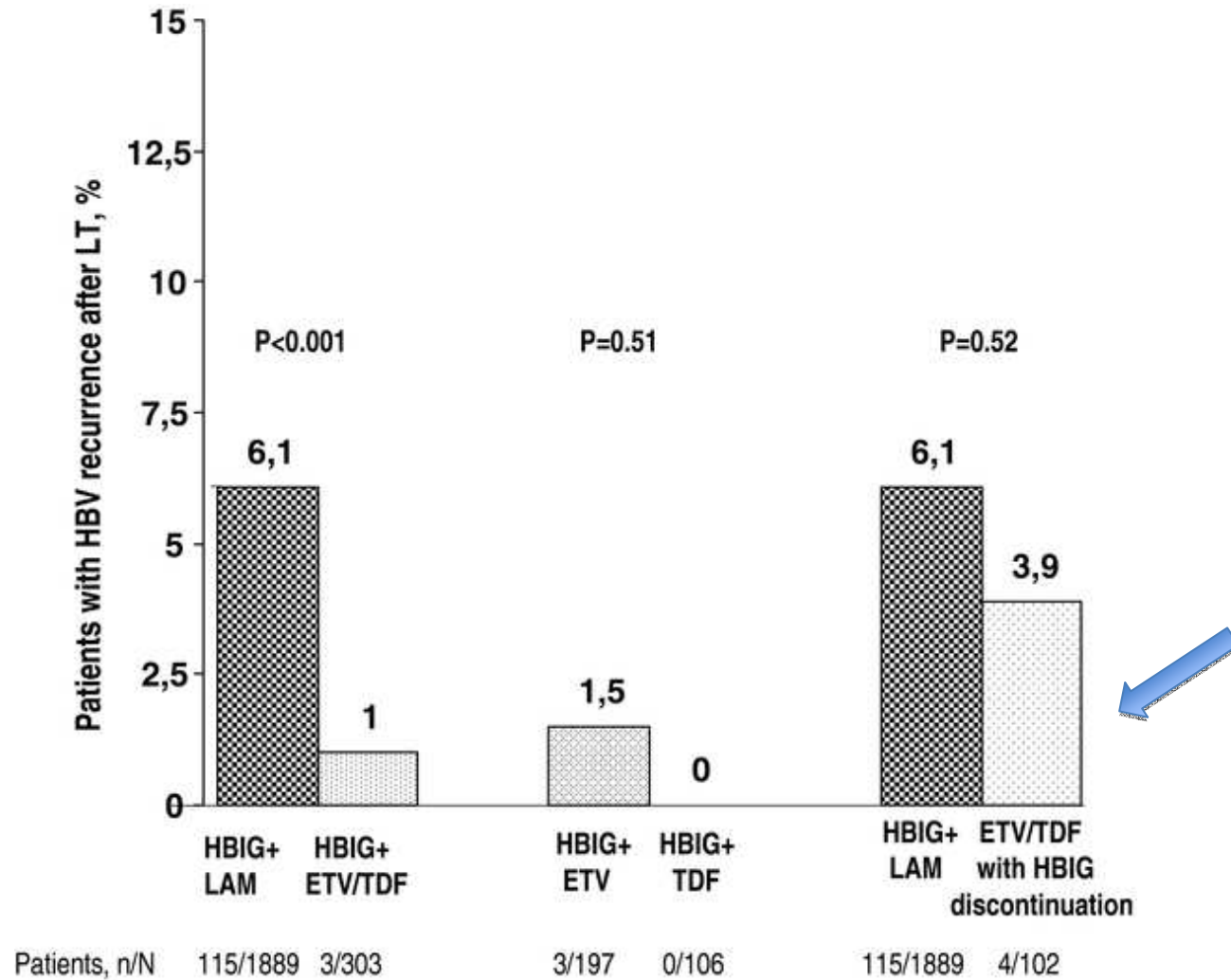
	ENTECAVIR	LAMIVUDINA	<i>P</i>
RECIDIVA HBV	0/30 (0%)	10/90 (11%)	0.04
HBsAb (1 mese)	667 UI/L	706 UI/L	ns
HBsAb (12 mesi)	297 UI/L	305UI/L	ns

Xi ZF J Dig Dis 2009

# SOSPENSIONE HBIG NUC LONG TERM

Autore	n.pz	Profilassi post-OLT	Durata	randomizzazione	Follow-up	Recurrence
Buti (2007)	29	HBIG+LAM	1 mese	HBIG+LAM vs LAM	83 mesi	11 vs 15%
Angus (2008)	34	IMHBIG +LAM	12	HBIG+LAM vs LAM+ADF	21 mesi	0 vs 6%
Taperman (2011)	37	HBIG+Tenofovir	6 mesi	HBIG+Tenofovir vs Tenofovir	24 mesi	0% vs 0%
Saab (2011)	61	IMHBIG +LAM	>12 mesi	LAM/ETV+ADF/Tenofovir	15 mesi	3.3%
Cholongitas (2012)	47	HBIG+LAM/ Entecavir	>12 mesi	LAM+ADF/Tenofovir Entecavir mono Tenofovir mono	24 mesi	3/47 6.3%)

# SOSPENSIONE HBIG → NUC ALTA BARRIERA GENETICA LONG TERM



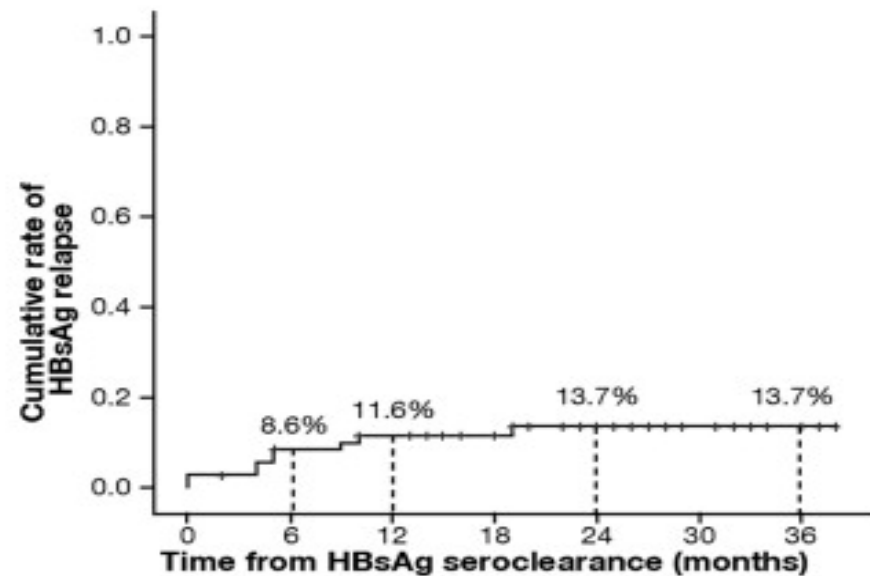
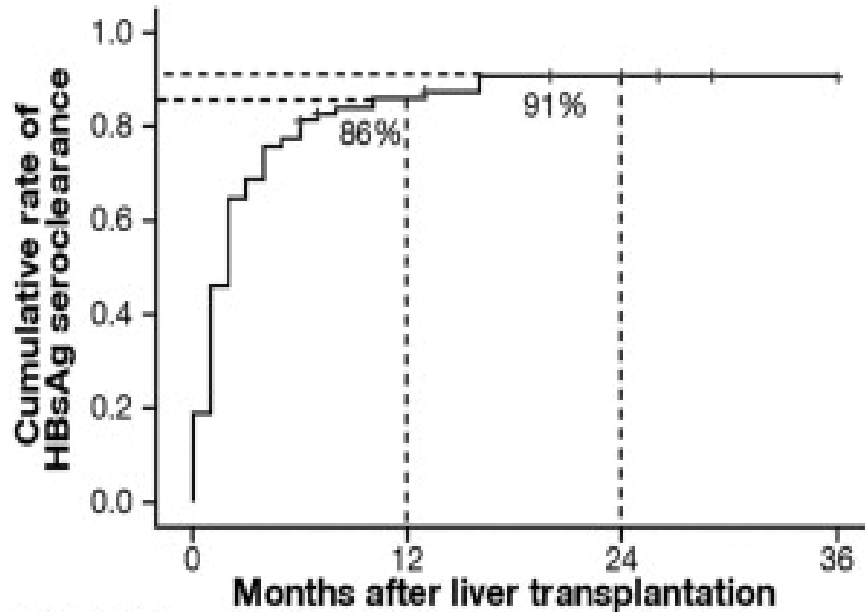
# NUC long-term

## ENTECAVIR IN MONOTERAPIA

n.80 Pazienti HBsAg+

n.59 (74%) HBVDNA+ a OLT

n.47 (59%) terapia antivirale pre-OLT



- 17/18 dei pazienti con recidiva o persistenza HBVDNA –
- No decessi correlati a recidiva HBV

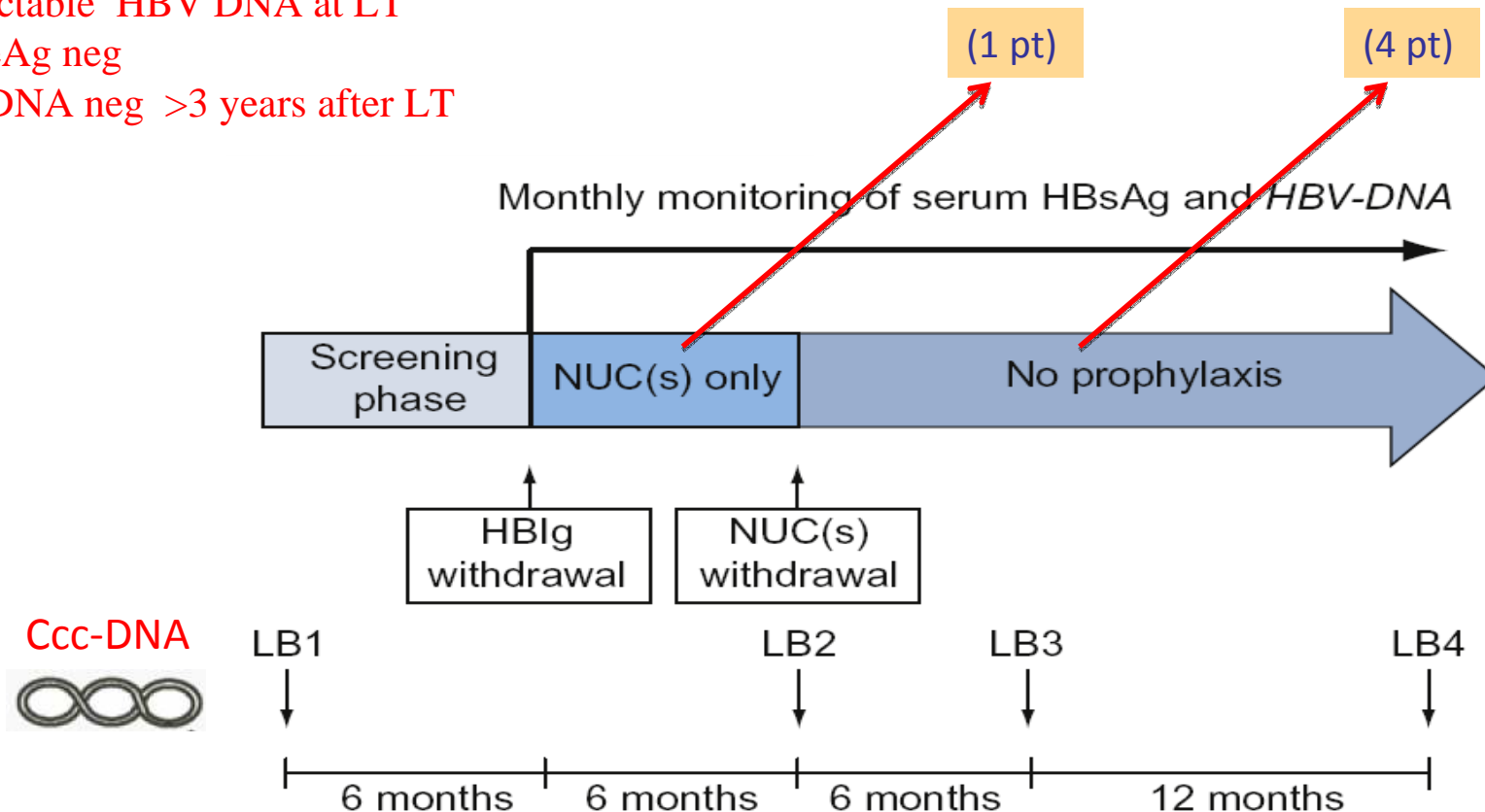
# Safety of complete and sustained prophylaxis withdrawal in patients liver-transplanted for HBV-related cirrhosis at low risk of HBV recurrence

Ilaria Lenci<sup>1,\*</sup>, Giuseppe Tisone<sup>2</sup>, Daniele Di Paolo<sup>1</sup>, Fabio Marcuccilli<sup>3</sup>, Laura Tariciotti<sup>2</sup>, Marco Ciotti<sup>3</sup>, Valentina Svicher<sup>3</sup>, Carlo Federico Perno<sup>3</sup>, Mario Angelico<sup>1</sup>

Journal of Hepatology 2011 vol. 55 | 587-593

## Low risk patients (n.30)

- 1) undetectable HBV DNA at LT
- 2) HBeAg neg
- 3) ccc-DNA neg >3 years after LT

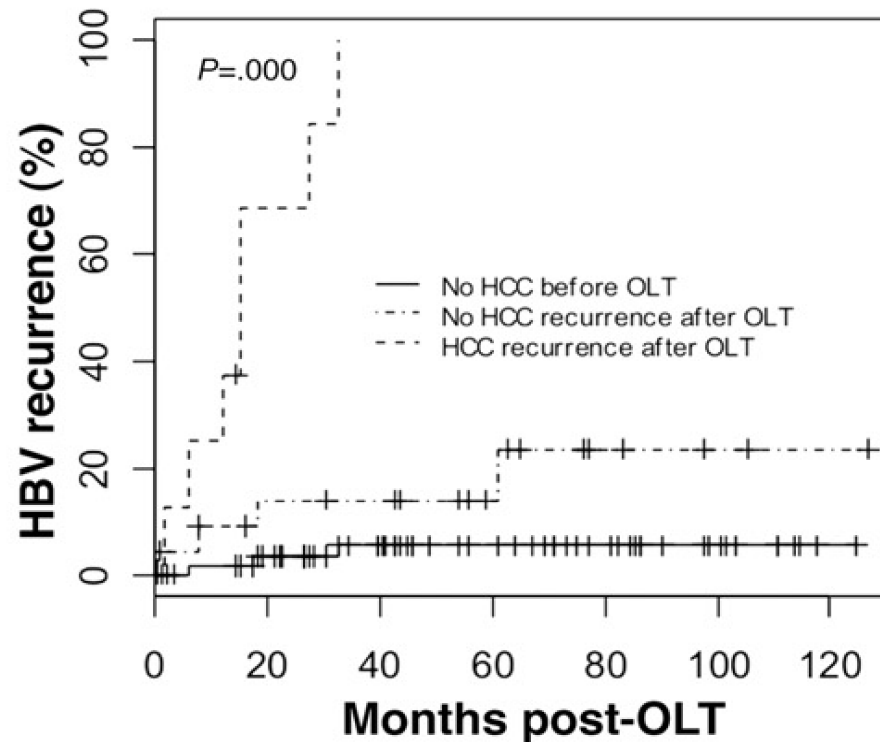


# **SIGNIFICATO CLINICO DELLA RECIDIVA HBV IN EPOCA ANALOGHI NUCLEOS(T)IDICI**

**Nessuna segnalazione di decesso o perdita  
dell'organo per recidiva HBV negli ultimi 10 anni**

# SIGNIFICATO CLINICO DELLA RECIDIVA HBV IN EPOCA ANALOGHI NUCLEOS(T)IDICI

**ALTO RISCHIO DI RECIDIVA HBV IN PAZIENTI CON RICORRENZA DI  
EPATOCARCINOMA**



# PROFILASSI HBV

## CONCLUSIONI

- Associazione HBIG+NUC efficace e sicura (ricidiva <10%)
  - Alti costi
  - Overtreatment
  - Compliance a lungo termine
- Ampia disponibilità di terapia antivirale di elevata efficacia e alta barriera genetica

# Conclusioni

## strategie di profilassi individualizzate ?

### BASSO RISCHIO

- HBVDNA –
- AntiHBe+
- HBV wild
- Alta compliance



### ALTO RISCHIO

- HBVDNA + HBeAg+
- HBV mutato
- Bassa compliance
- Coinfezione HIV

### MINIMIZZAZIONE HBIG

- HBIG+NUC → NUC long term
- NUC long-term ??

- HBIG basse dosi +NUC long term
- Scelta NUC su profilo di resistenza