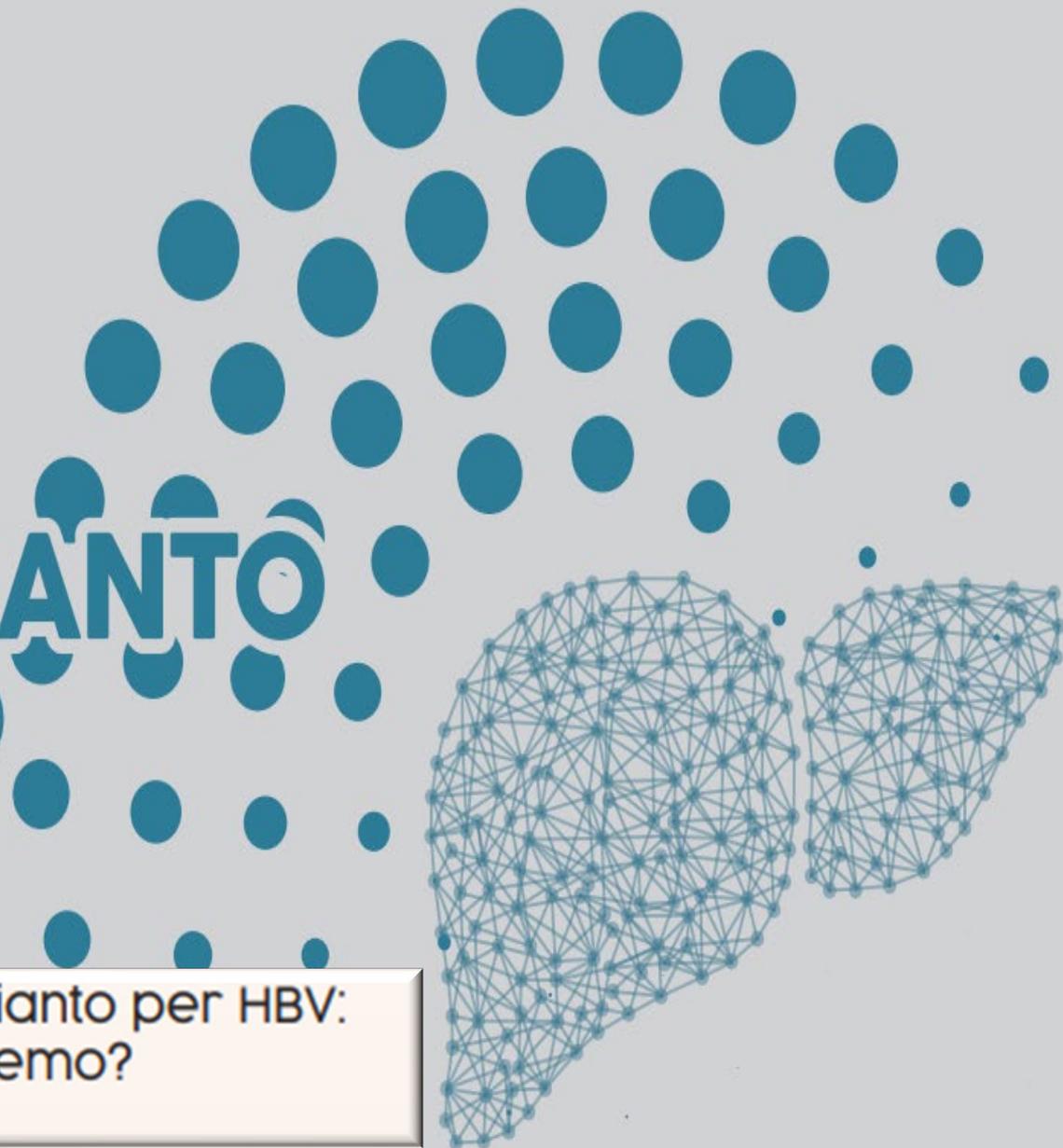




# LE SFIDE DEL TRAPIANTO DI FEGATO NEL 2023

Immunoprofilassi in trapianto per HBV:  
Dove siamo? Dove andremo?  
A. Marzano



# Immunoprofilassi in trapianto HBV

## Dove siamo? Dove andremo?



HBV and LT  
Epidemiology Impact in Italy

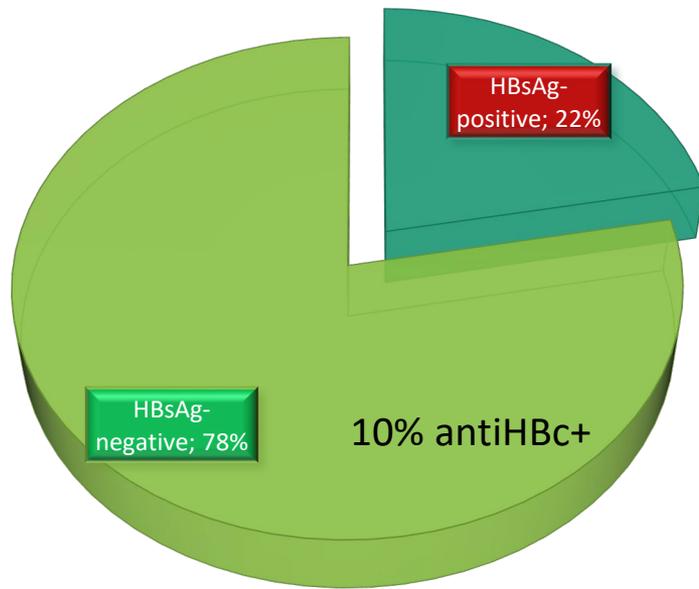
*«dove siamo»*

# HBV AND LIVER TRANSPLANTATION

## « an italian job »

### Italy

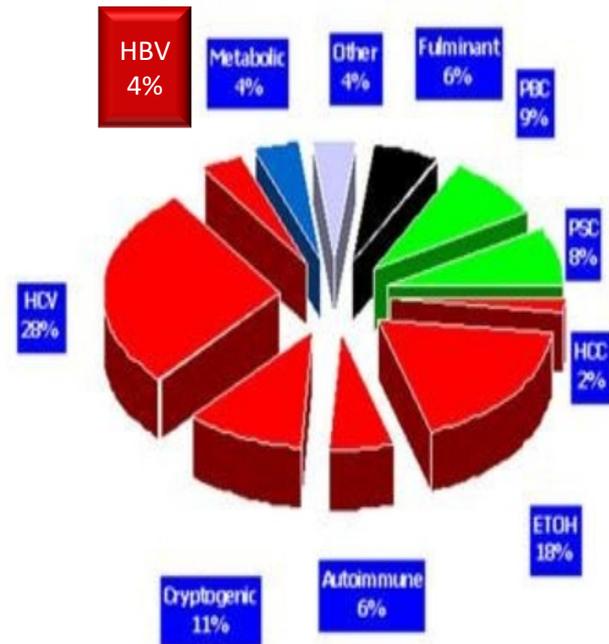
10,365 LT RECIPIENTS (1983-2011)



Marzano A et al; Min Gastroent 2018

### US

Figure 2: Frequency of Liver transplants by Diagnosis



LEGEND: HCV: Hepatitis C; HBV: Hepatitis B; PBC: Primary Biliary Cirrhosis; PSC: Primary Sclerosing Cholangitis; HCC: Hepatocellular Carcinoma; ETOH: Alcoholic Cirrhosis

Medscape 2019

# Liver Transplantation for Hepatitis D Virus in the United States: A UNOS Study on Outcomes in the MELD Era

Tatyana Kushner, MD, MSCE,<sup>1</sup> Ben L. Da, MD,<sup>2</sup> Aryana Chan, AGNP,<sup>1</sup> Douglas Dieterich, MD,<sup>1</sup> Keith Sigel, MD, PhD,<sup>3</sup> and Behnam Saber, MD<sup>1,4</sup>

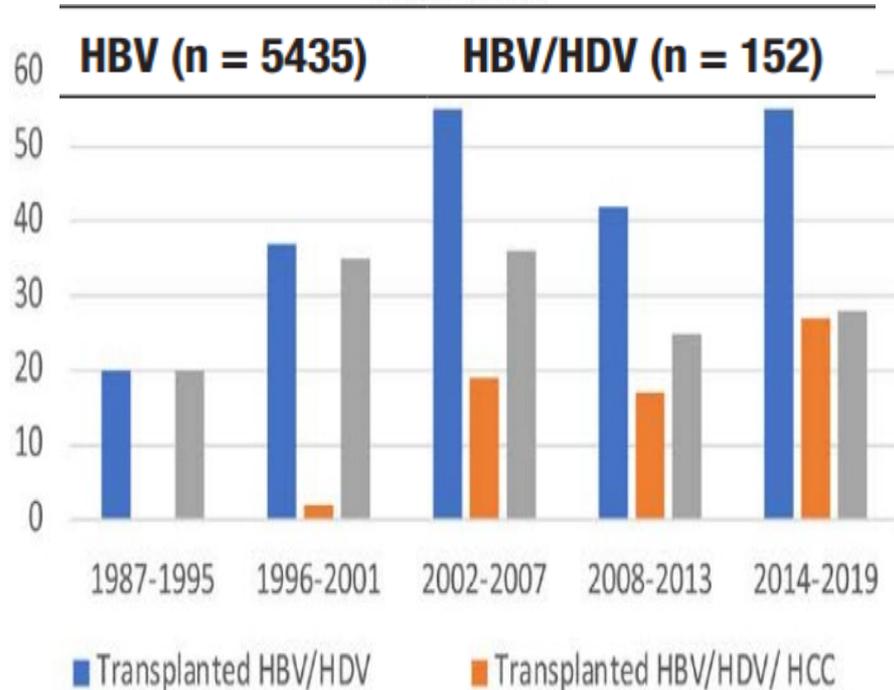


2002-2019 → 5435/152000

HDV 3% of HBV;  
HDV 0.1% total

HBV  
3.6%

Patients with HBV/HDV transplanted over time



# 2020 position statement and recommendations of the European Liver and Intestine Transplantation Association (ELITA): management of hepatitis B virus-related infection before and after liver transplantation

Christophe Duvoux<sup>1</sup> | Luca S. Belli<sup>2</sup> | James Fung<sup>3</sup> | Mario Angelico<sup>4</sup> | Maria Buti<sup>5</sup> | Audrey Coilly<sup>6</sup> | Paolo Cortesi<sup>2</sup> | François Durand<sup>7</sup> | Cyrille Féray<sup>6</sup> | Constantino Fondavila<sup>5</sup> | Pascal Lebray<sup>8</sup> | Silvia Martini<sup>9</sup> | Frederik Nevens<sup>10</sup> | Wojciech G. Polak<sup>11</sup> | Mario Rizzetto<sup>9</sup> | Riccardo Volpes<sup>12</sup> | Fabien Zoulim<sup>13</sup> | Didier Samuel<sup>6</sup> | Marina Berenguer<sup>14</sup>

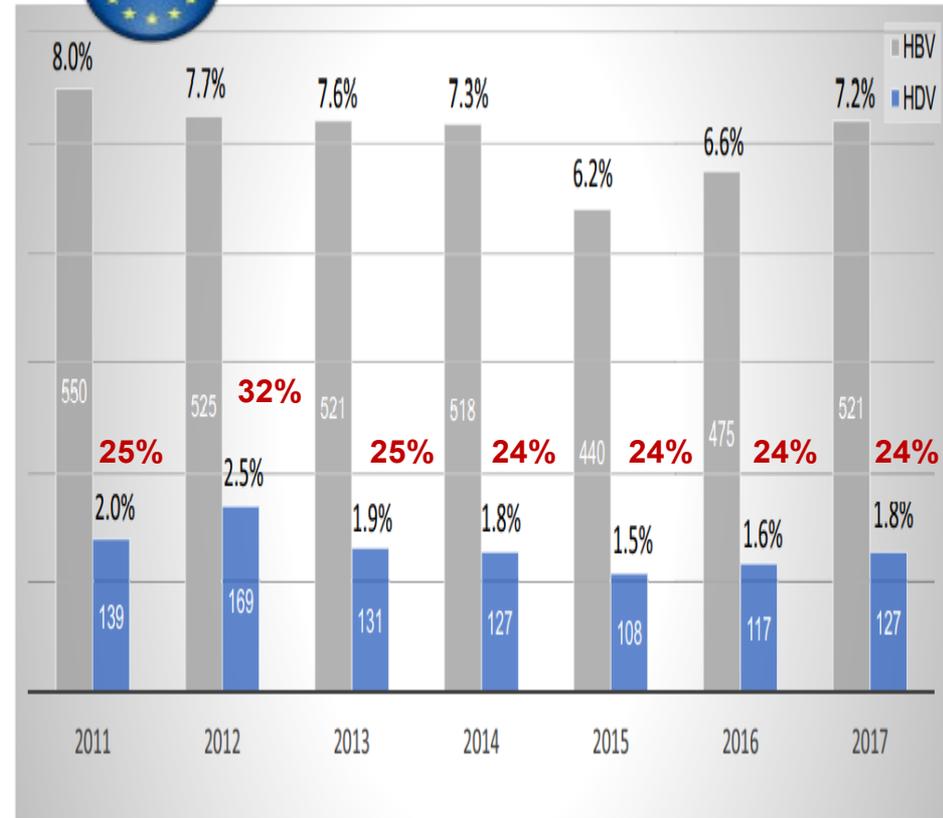
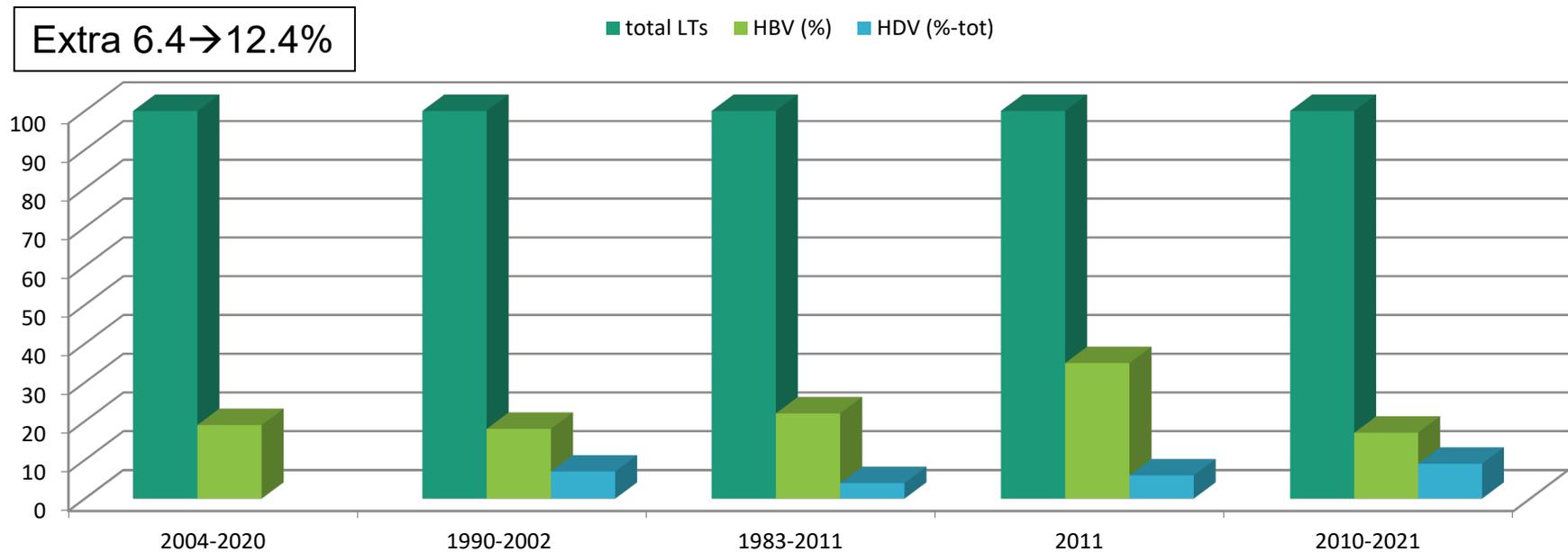


FIGURE 1 Prevalence of liver transplantation for HBV or HDV in Europe between 2011 and 2017 (ELTR data-www.eltr.org)



## Liver, Pancreas and Biliary Tract

## Temporal trends of waitlistings for liver transplantation in Italy: The ECALITA (Evolution of IndiCAtion in Liver transplantation in ITALy) registry study



	2004-2020	1990-2002 (TO)	1983-2011	2011	2010-2021 (TO)
LTx (n)	17,317	1,000	10,365	698	1710
HBV (%)	3332 (19.2)	177 (17.7)	2260 (22)	138 (19.7)	290 (17)
HDV /HBV (%)		68/177 (38.4)	433/2260 (19)	45/138 (35)	147/290 (51)

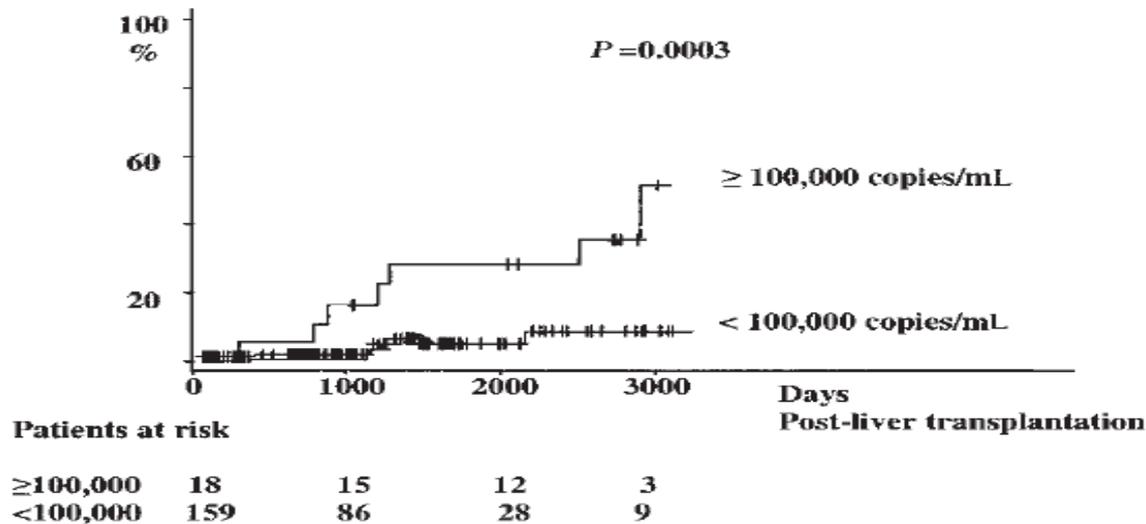
HBV and LT  
Prognostic indexes , results  
and real life in Italy

*«dove siamo stati»*

# Viral Load at the Time of Liver Transplantation and Risk of Hepatitis B Virus Recurrence

Alfredo Marzano,<sup>1</sup> Silvia Gaia,<sup>1</sup> Valeria Ghisetti,<sup>2</sup> Silvia Carezzi,<sup>1</sup>  
 Alberto Premoli,<sup>1</sup> Wilma Debernardi-Venon,<sup>1</sup> Carlo Alessandria,<sup>1</sup>  
 Alessandro Franchello,<sup>3</sup> Mauro Salizzoni,<sup>3</sup> and Mario Rizzetto<sup>1</sup>

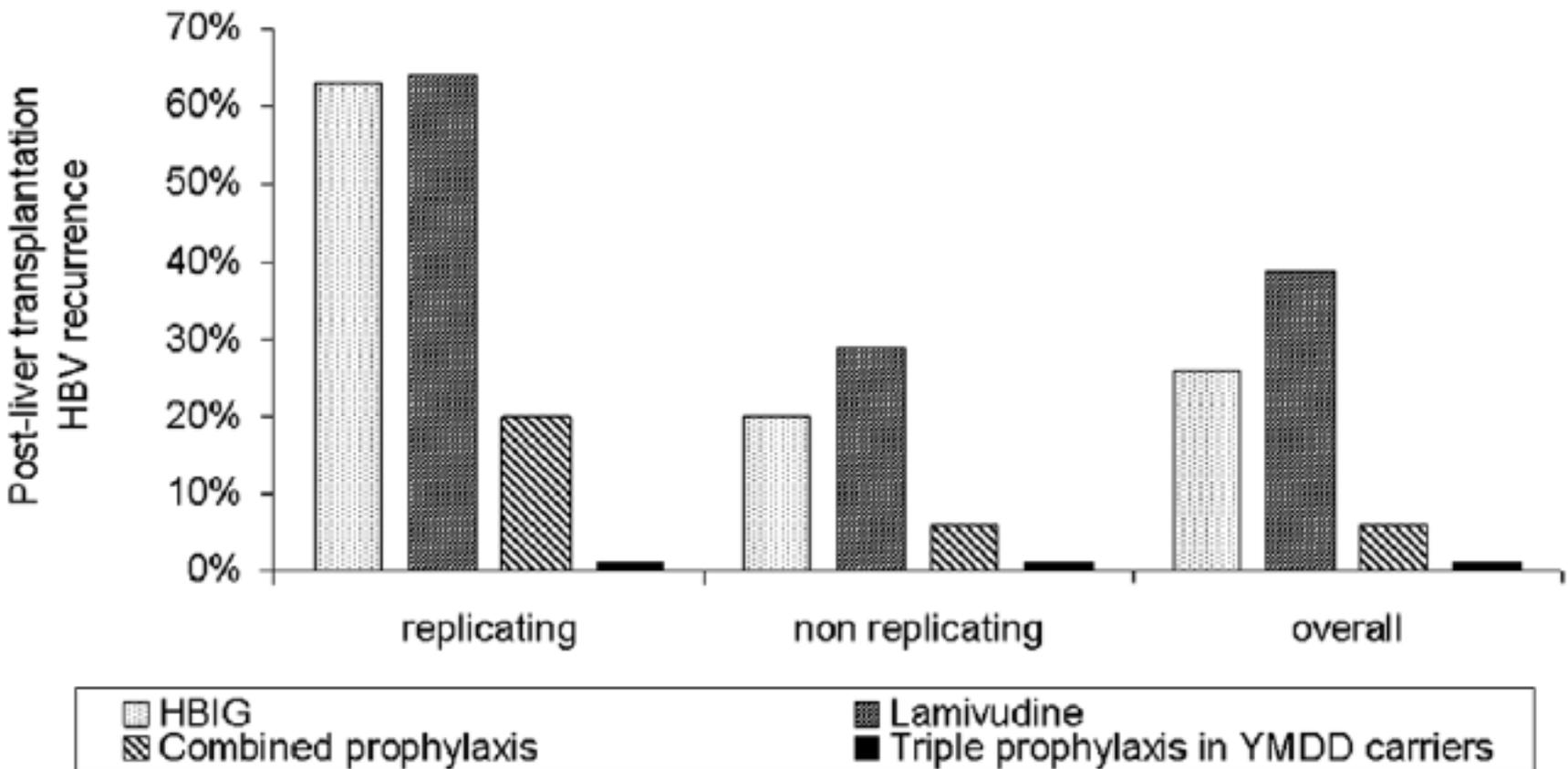
**Post-LT  
 hepatitis B  
 recurrence**



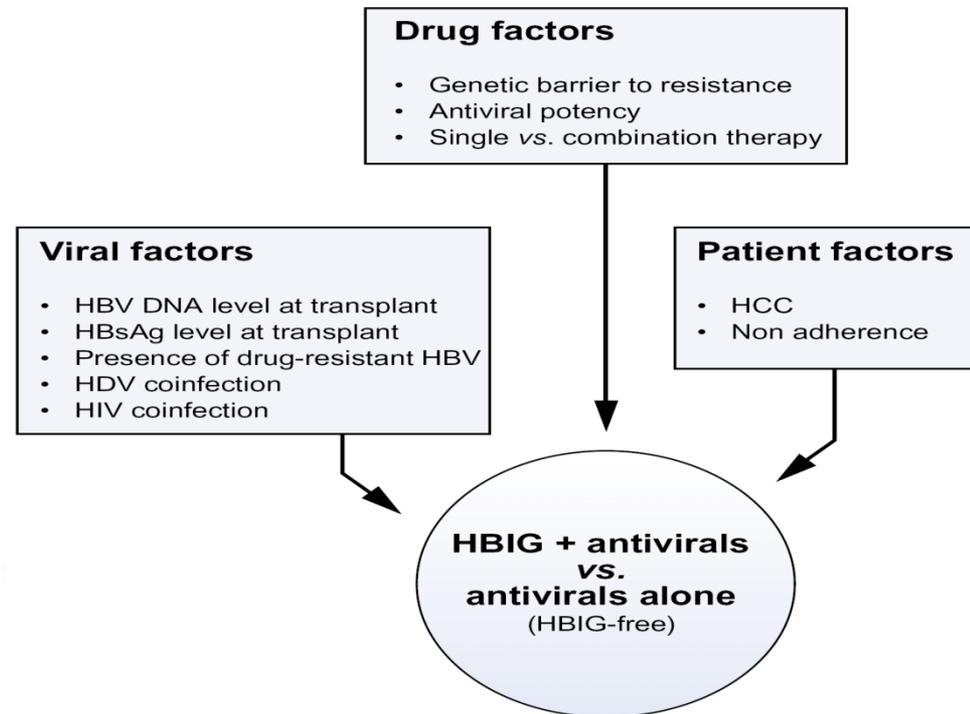
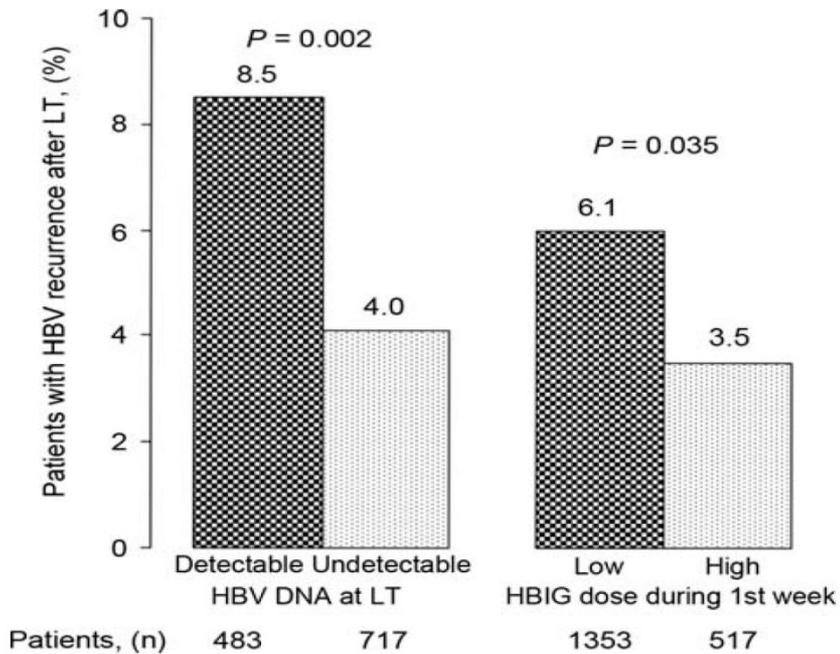
**Figure 3. Risk of hepatitis B recurrence after LT in patients with HBV DNA load (COBAS PCR) higher or lower than 100,000 copies/mL at the time of surgery.**

The prevention of viral recurrence in the long term

A. Marzano \*



# LOW RISK PATIENTS FOR HBIG-FREE PROPHYLAXIS?

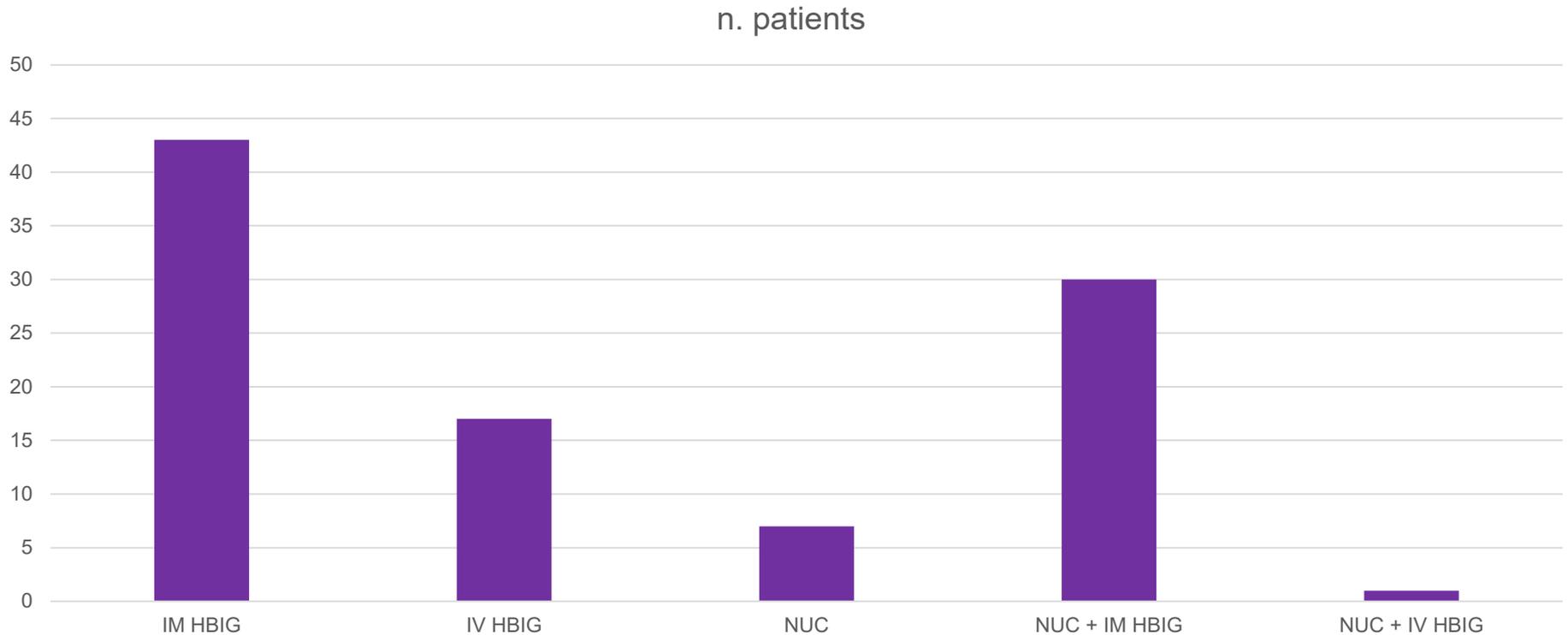


Colangitas E et al. Liver Transpl 2011

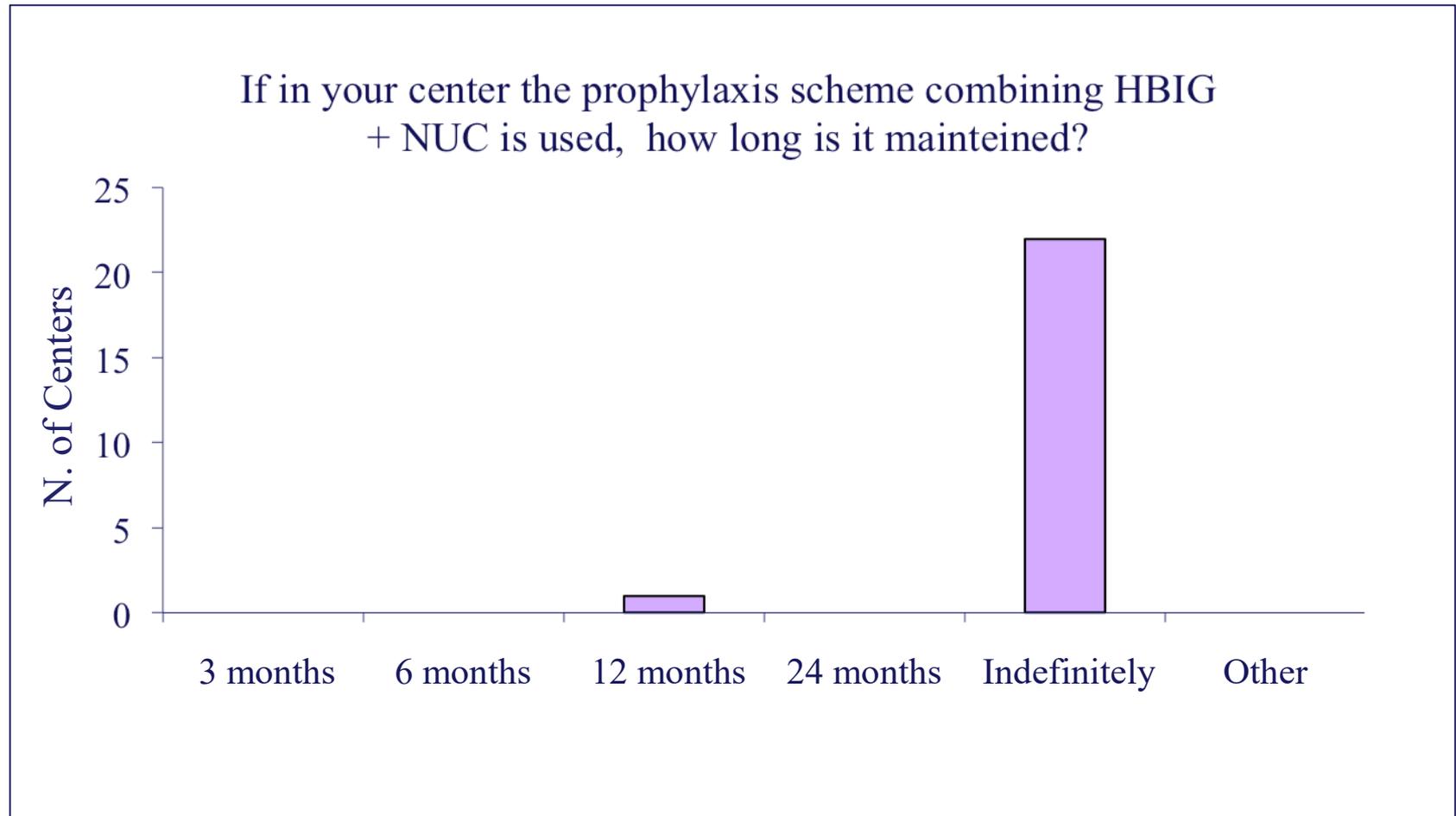
Alyson N, et al. J Hepatol 56:1189-1197, 2012

# HBV RECURRENCE AFTER LT

Italy (1983-2011)	Overall	2011
LTs in HBsAg-positive patients	2,260	128
Hepatitis B recurrence after LT	98 (4%)	0



# CLINICAL PRACTICE: PROPHYLACTIC STRATEGY AND DURATION ITALIAN SURVEY



HBV and LT

Combo vs HBIG-free vs HBIG discontinuation

*«dove siamo (andremo?)»*

# HBV recurrence after LT

## Definitions

Combo (HBIG+) vs NUC (s) prophylaxis (HBIG-)

Type prophylaxis	HBV recurrence	Post-LT hepatitis
Combo (HBIG+)	HBsAg+	yes
NUC(s) (HBIG-)	HBsAg+/HBV DNA-	no

# Efficacy and effectiveness of anti-HBV therapy with early withdrawal of HBIG prophylaxis to prevent HBV recurrence following liver transplantation

*Expert Opin. Biol. Ther. (2015) 15(5):665-677*

Winston Ku, Uerica Wang & Mindie H Nguyen

Rate of HBV relapse in post-LT patients treated with anti-HBV therapy only (No HBIG)

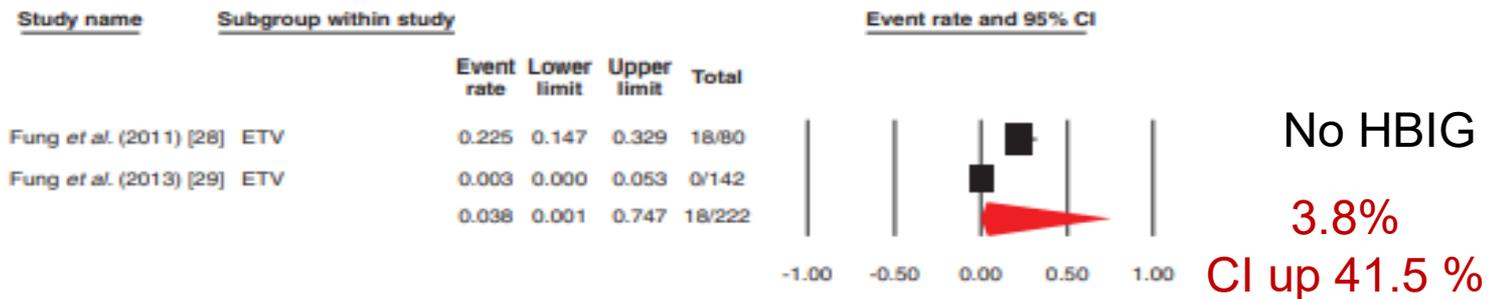


Figure 1. Post-LT patients treated with anti-HBV therapy only (No HBIG).

ETV: Entecavir; HBIG: Hepatitis B immune globulin; HBV: Hepatitis B virus.

Rate of HBV relapse in post-LT patients treated with anti-HBV therapy after 6 months of HBIG

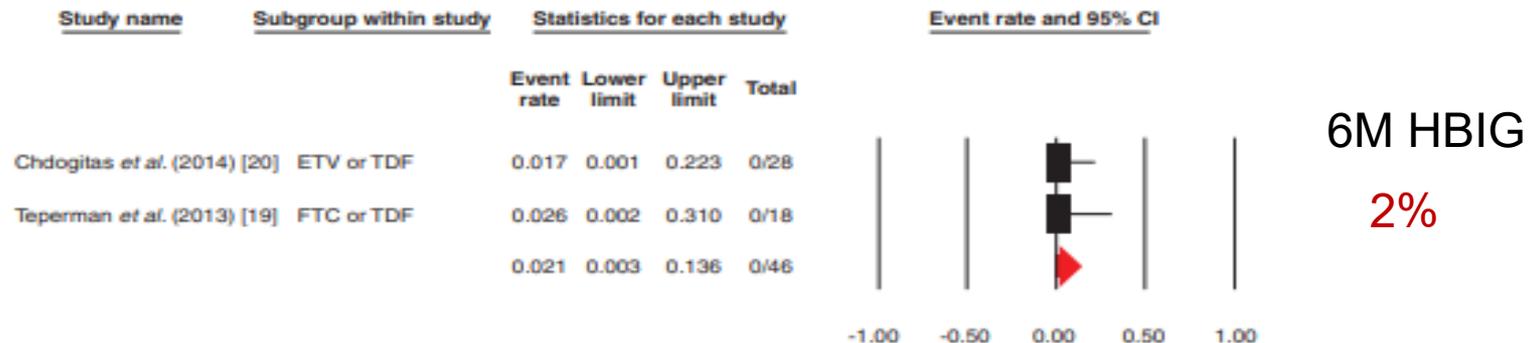


Figure 2. Post-LT patients treated with anti-HBV therapy only after 6 months of HBIG.

ETV: Entecavir; HBIG: Hepatitis B immune globulin; HBV: Hepatitis B virus; TDF: Tenofovir.

# Efficacy and effectiveness of anti-HBV therapy with early withdrawal of HBIG prophylaxis to prevent HBV recurrence following liver transplantation

*Expert Opin. Biol. Ther. (2015) 15(5):665-677*

Winston Ku, Uerica Wang & Mindie H Nguyen

Rate of HBV relapse in post-LT patients treated with anti-HBV therapy after 12 months of HBIG

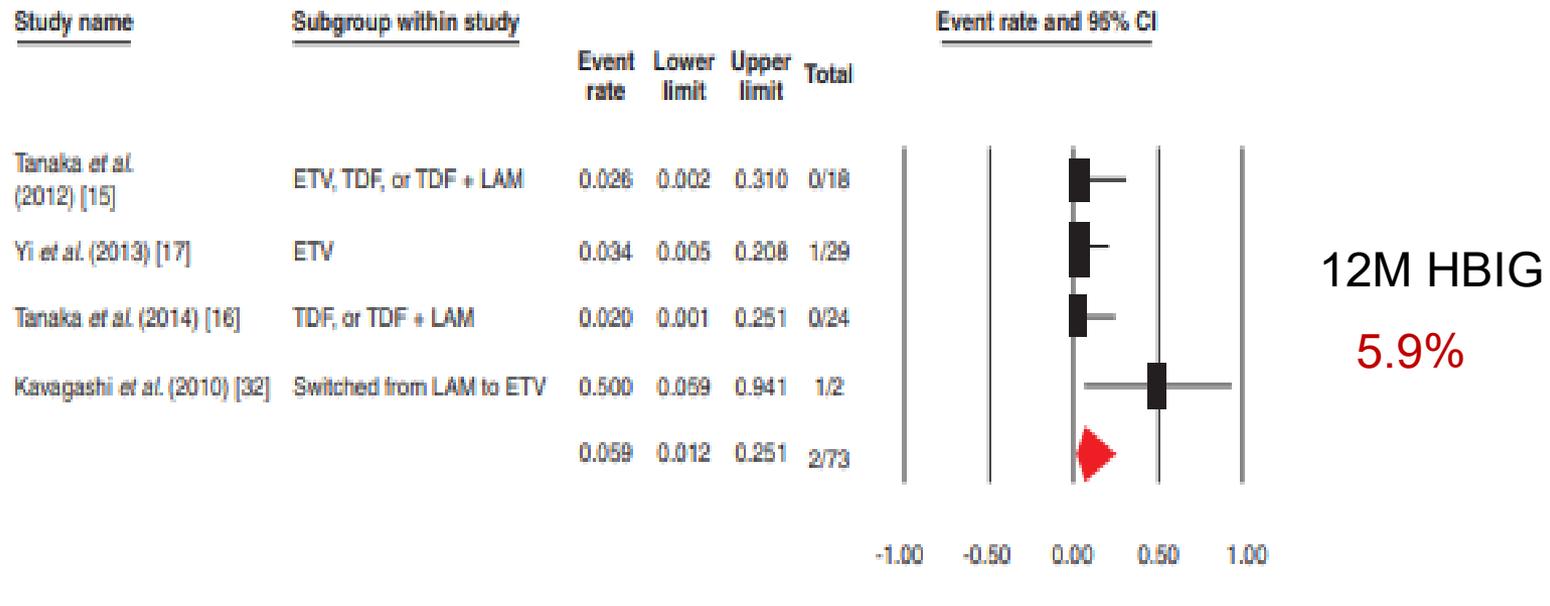


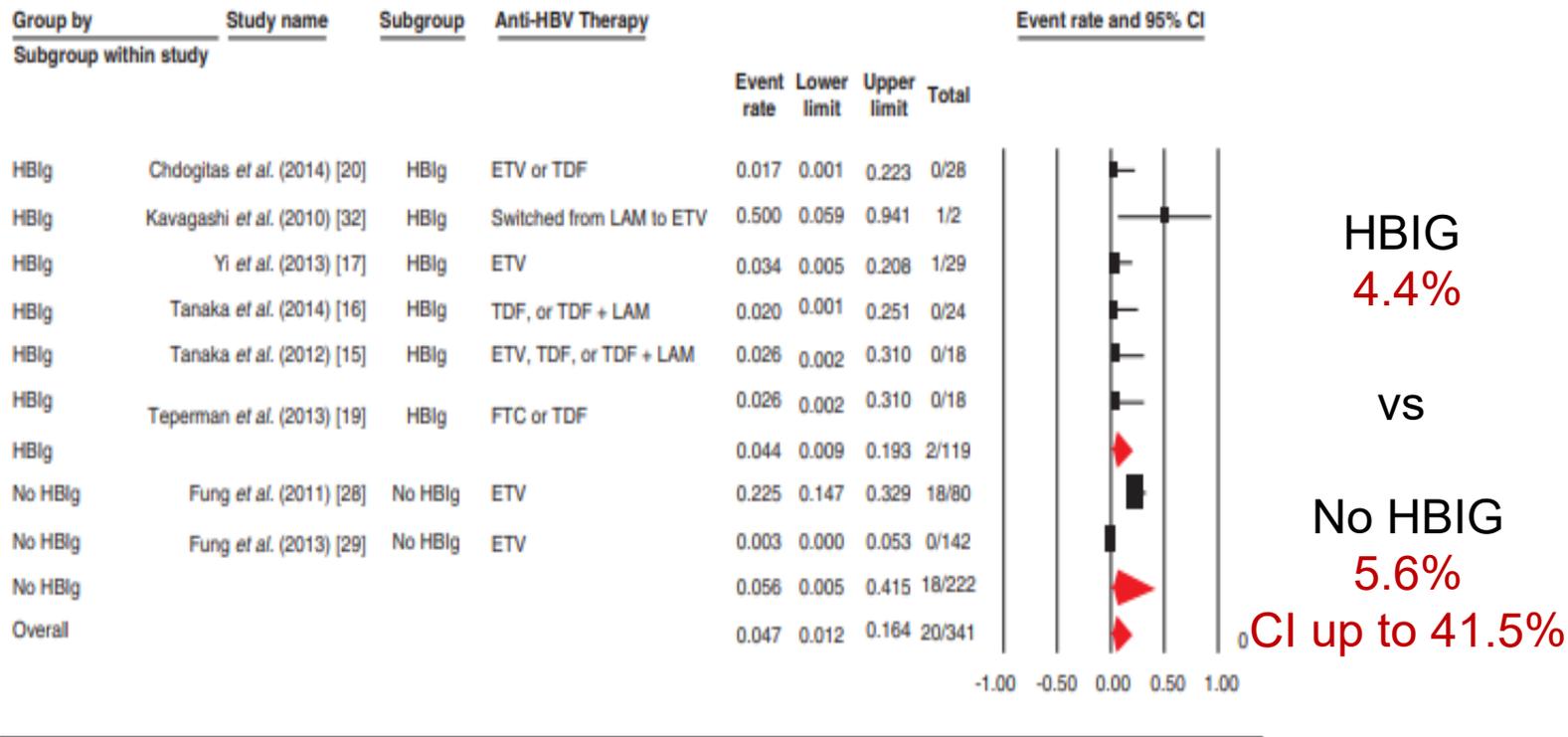
Figure 3. Post-LT patients treated with anti-HBV therapy after 12 months of HBIG.

ETV: Entecavir; HBIG: Hepatitis B immune globulin; HBV: Hepatitis B virus; LAM: Lamivudine; TDF: Tenofovir.

# Efficacy and effectiveness of anti-HBV therapy with early withdrawal of HBIG prophylaxis to prevent HBV recurrence following liver transplantation

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Winston Ku, Uerica Wang & Mindie H Nguyen



**Expert opinion: low risk patients → short term HBIG (12m) high risk long term HBIG**

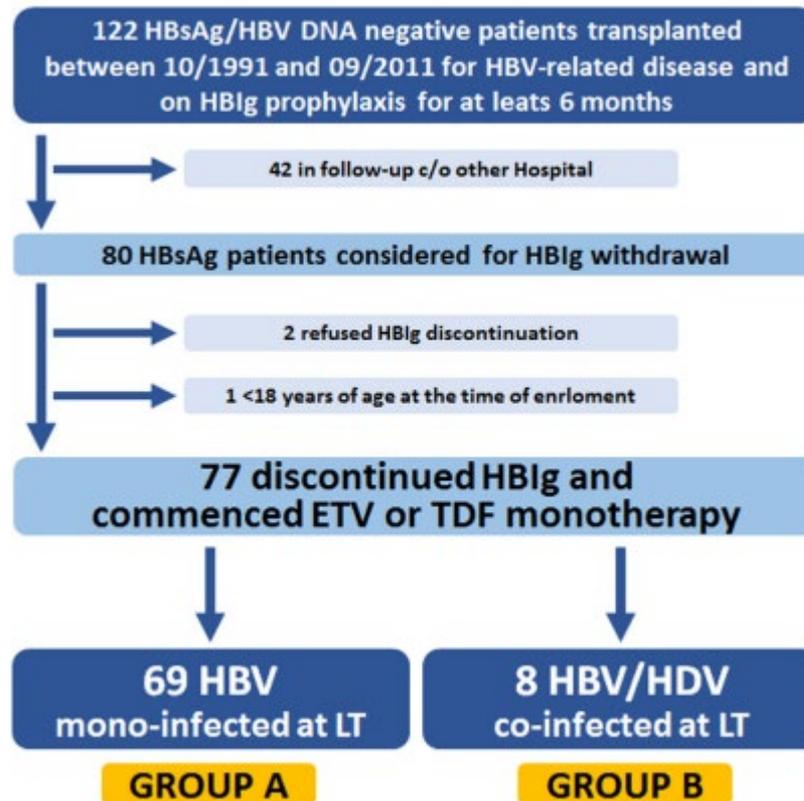


Liver, Pancreas and Biliary Tract

## Entecavir or tenofovir monotherapy prevents HBV recurrence in liver transplant recipients: A 5-year follow-up study after hepatitis B immunoglobulin withdrawal



Matteo A. Manini<sup>a,b,\*</sup>, Gavin Whitehouse<sup>a</sup>, Matthew Bruce<sup>a</sup>, Matteo Passerini<sup>b</sup>, Tiong Y. Lim<sup>a</sup>, Ivana Carey<sup>a</sup>, Aisling Considine<sup>a</sup>, Pietro Lampertico<sup>b</sup>, Abid Suddle<sup>a</sup>, Nigel Heaton<sup>a</sup>, Michael Heneghan<sup>a</sup>, Kosh Agarwal<sup>a</sup>



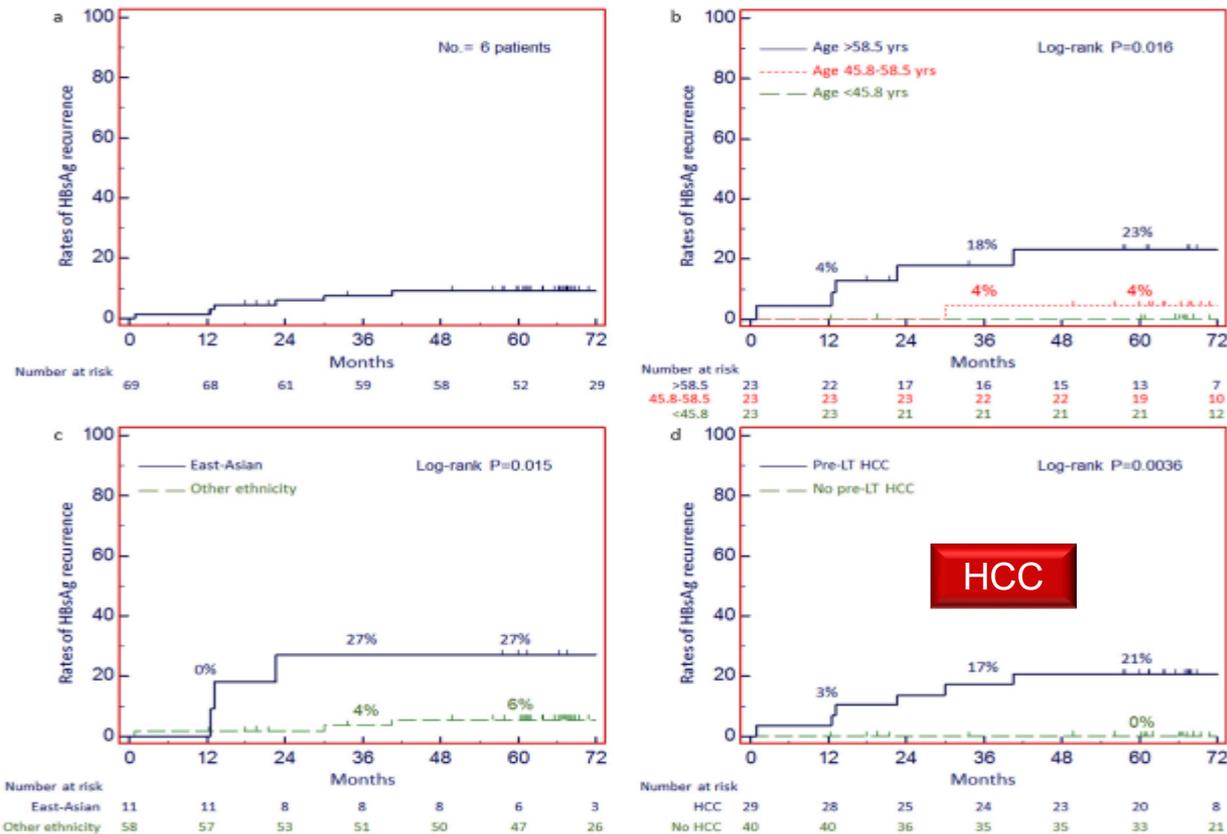


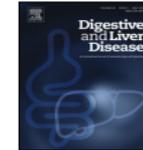
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Liver, Pancreas and Biliary Tract

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Nigel Heaton<sup>a</sup>, Michael Heneghan<sup>a</sup>, Kosh Agarwal<sup>a</sup>

### HBsAs+/no HBV DNA or hepatitis

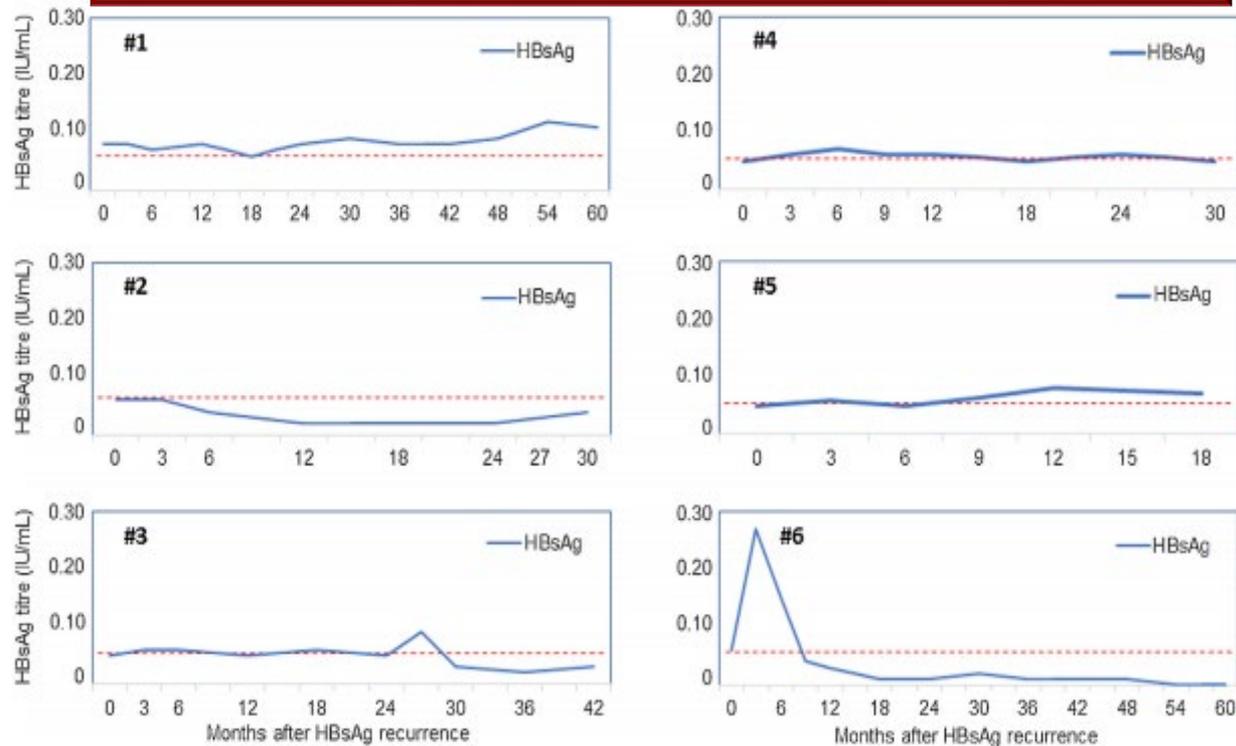
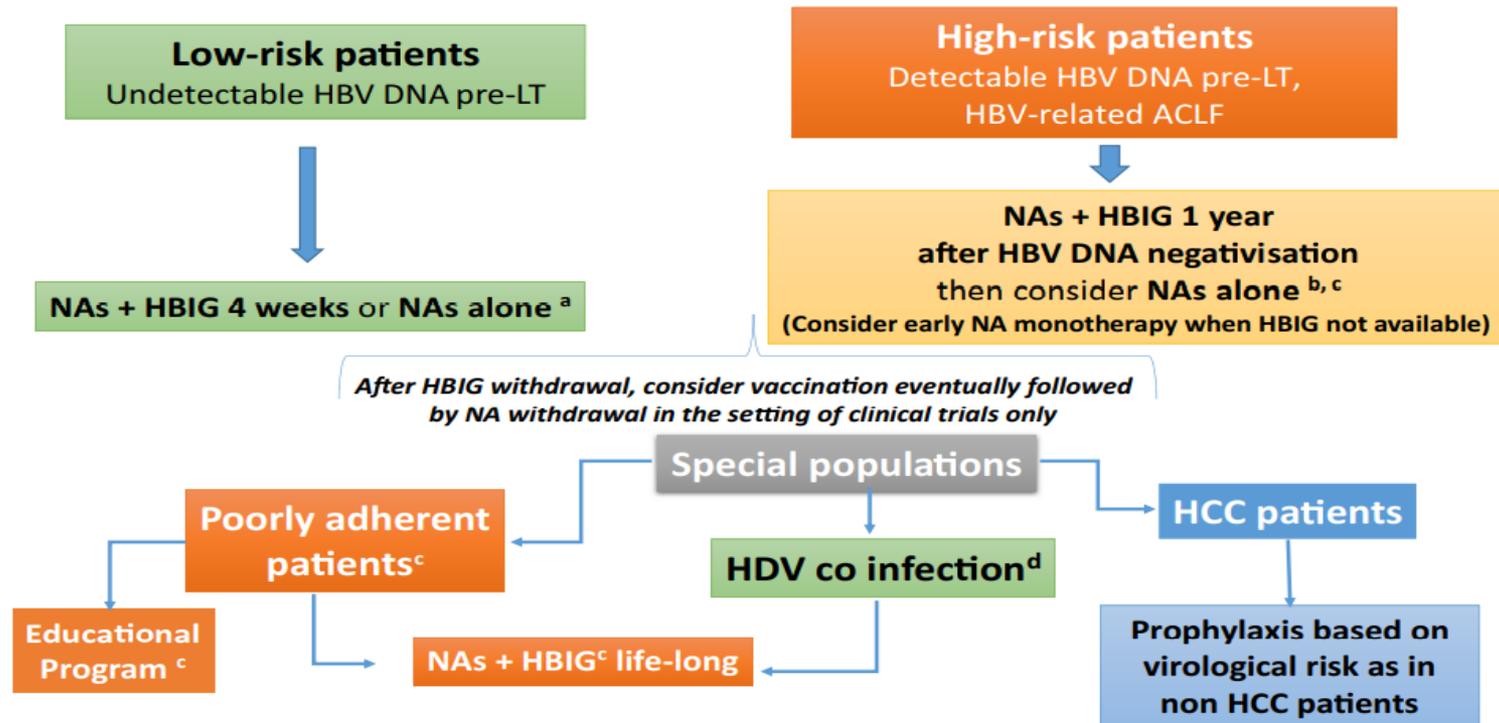


Fig. 3. HBsAg kinetics in 6 patients who relapsed HBsAg during third-generation NAs monotherapy.

# 2020 position statement and recommendations of the European Liver and Intestine Transplantation Association (ELITA): management of hepatitis B virus-related infection before and after liver transplantation

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**FIGURE 2** 2020 ELITA algorithm for de novo prophylaxis of HBV recurrence after liver transplantation for HBV-related liver disease. A, In Western countries, early NAs monoprophyllaxis should preferentially be undertaken in the setting of prospective cohorts or clinical trials addressing the prevalence of ccc DNA and DNA integration. B, Registries are encouraged after late HBIG withdrawal to generate more data about this strategy. C, Consider specific educational programmes in poorly adherent patients and in patients receiving NAs alone or subcutaneous HBIG in the long term. D, In HDV population, HBIG withdrawal can be considered in the setting of clinical trials. Abbreviations: HBIG : hepatitis B immunoglobulins; HBV: Hepatitis B virus; HDV: Hepatitis D virus; NA: nucleoside analogues

**a. Estimation of lifetime costs for patients receiving a transplant: the case of liver transplantation related to Hepatitis B in Italy**

**Commento:** Modello non realta' clinica

**Dephy-Panel**