Massimo Puoti

University Milano Bicocca
School of Medicine and Surgery
SC Malattie Infettive
ASST Grande Ospedale Metropolitano Niguarda

HBV: gestione clinica corrente e prospettive di eradicazione

SCHOOL OF MEDICINE AND SURGERY

HBV gestione clinica corrente e prospettive di eradicazione

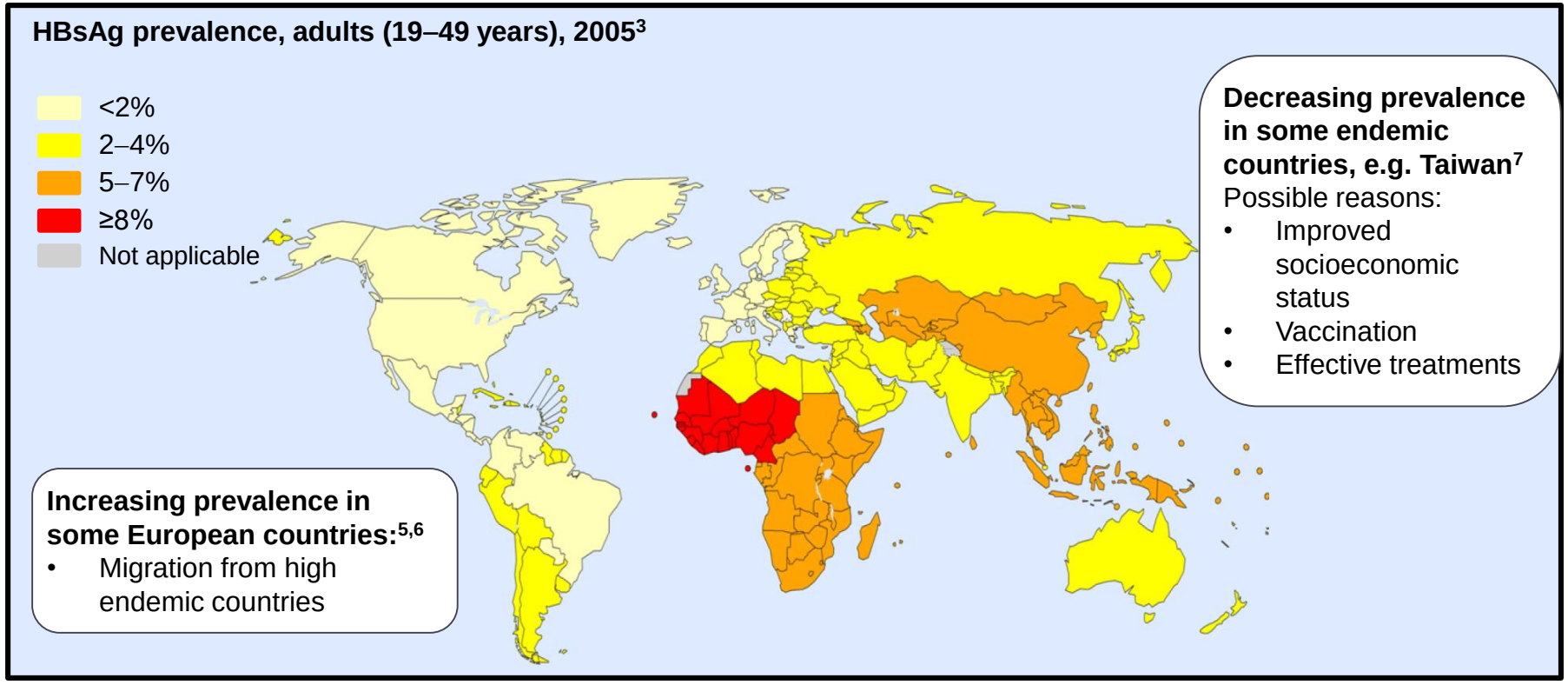
- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

HBV gestione clinica corrente e prospettive di eradicazione

- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

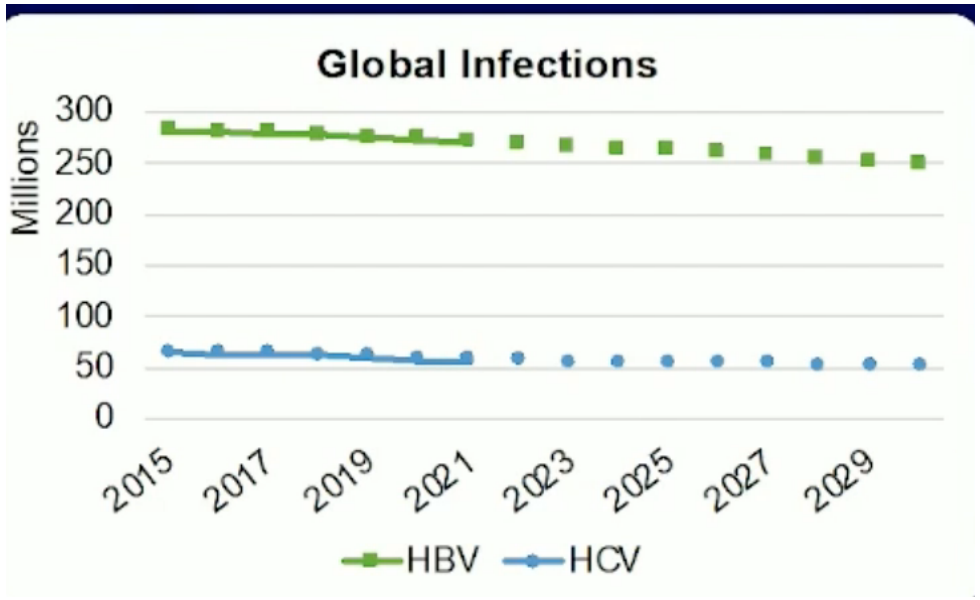
Epidemiology and public health burden[1]

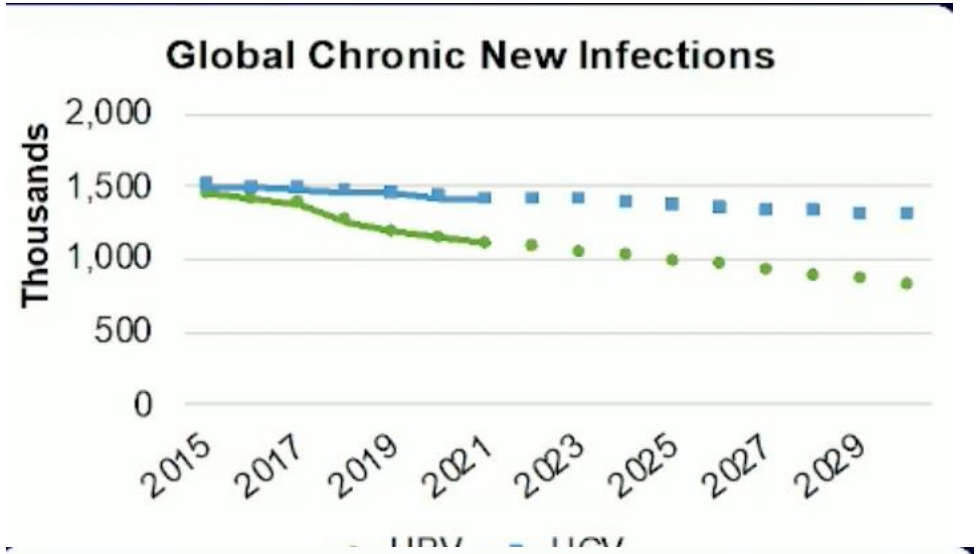
- Worldwide ≈250 million chronic HBsAg carriers[2,3]
- 686,000 deaths from HBV-related liver disease and HCC in 2013[4]

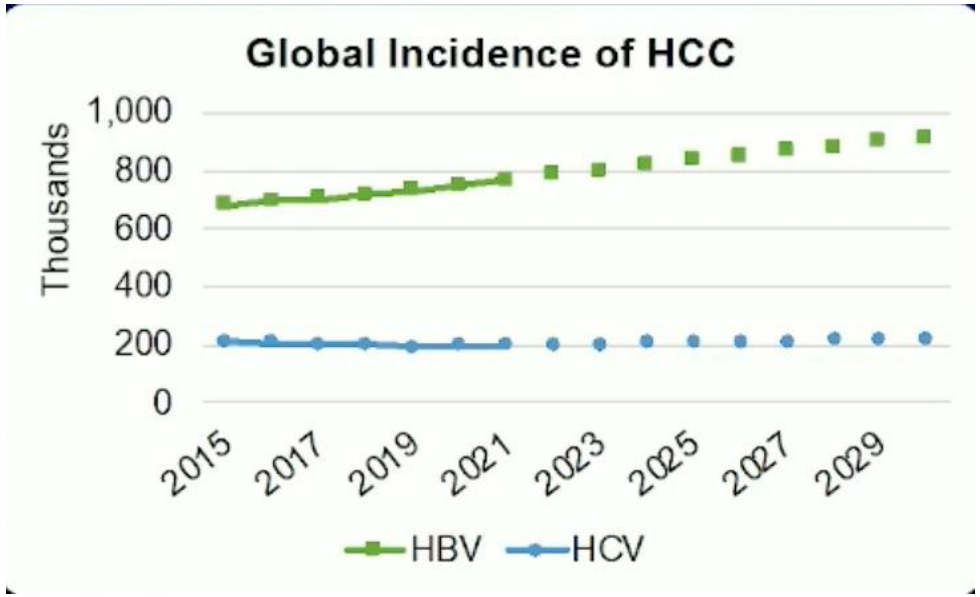


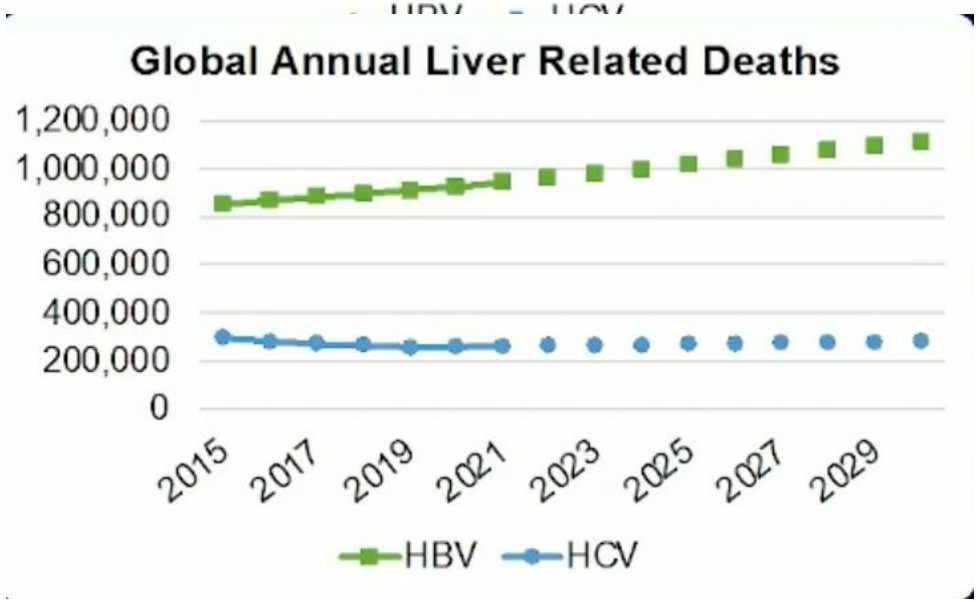
1. EASL CPG HBV. J Hepatol 2017;67:370–98; 2. Schweitzer A, et al. Lancet 2015;386:1546–55;
3. Ott JJ, et al. Vaccine 2012;30:2212–9; 4. GBD 2013 Mortality and Causes of Death Collaborators. Lancet 2015;385:117–71;
5. Coppola N, et al. Euro Surveill 2015;20:30009; 6. Hampel A, et al. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2016;59:578–83;
7. Chen C-L, et al. J Hepatol 2015;63:354–63.

Disease Burden of Hepatitis B and Hepatitis C between 2015 and 2030









Razavi Shearer et al J Hepatol 2022 S050

HBV gestione clinica corrente e prospettive di eradicazione

- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

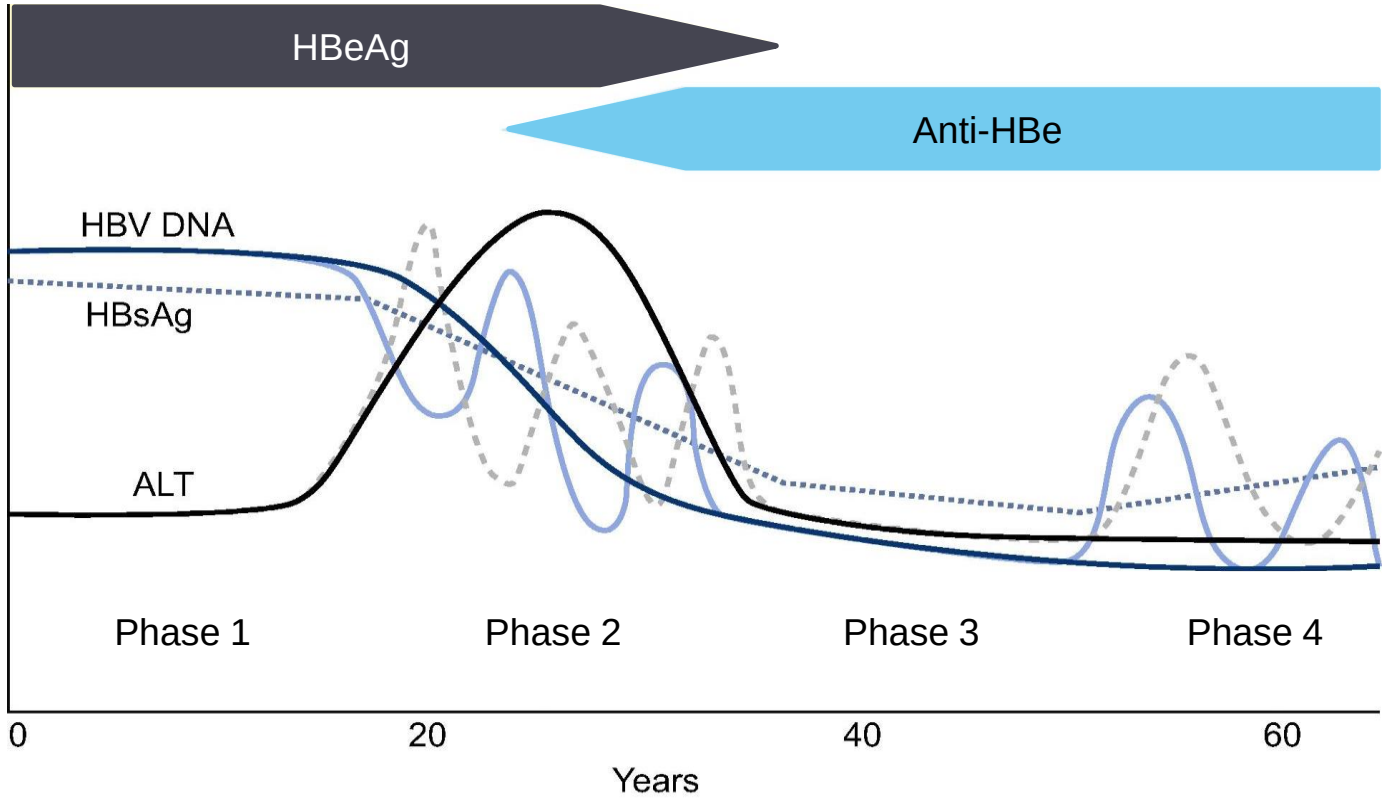
New nomenclature for chronic phases

- The natural history of chronic HBV infection has been schematically divided into five phases

Chronic hepatitis B / Chronic HBV infection	HBeAg positive		HBeAg negative		
	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
	Chronic HBV infection	Chronic hepatitis B	Chronic HBV infection	Chronic hepatitis B	Resolved HBV infection
HBsAg	High	High/ intermediate	Low	Intermediate	Negative
HBeAg	Positive	Positive	Negative	Negative	Negative
HBV DNA	>10^7 IU/mL	10^4–10^7 IU/mL	<2,000 IU/mL*	>2,000 IU/mL	<10 IU/mL‡
ALT	Normal	Elevated	Normal	Elevated†	Normal
Liver disease	None/minimal	Moderate/ severe	None	Moderate/ severe	None§
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis	HBsAg negative /anti-HBc positive

*HBV DNA levels can be between 2,000 and 20,000 IU/mL in some patients without signs of chronic hepatitis;
†Persisitently or intermittently, based on traditional ULN (~40 IU/L). ‡cccDNA can frequently be detected in the liver;
§Residual HCC risk only if cirrhosis has developed before HBsAg loss.
EASL CPG HBV. J Hepatol 2017;67:370–98

Phases of chronic HBV infection[1]



New nomenclature[2]	HBeAg-positive chronic HBV infection	HBeAg-positive chronic hepatitis B	HBeAg-negative chronic HBV infection	HBeAg-negative chronic hepatitis B

1. Lok A, et al. J Hepatol 2017;67:847–61;
2. EASL CPG HBV. J Hepatol 2017;67:370–98

Goals and endpoints of therapy

Goals

- Improve survival and quality of life by preventing disease progression and HCC
- Prevent mother-to-child transmission, hepatitis B reactivation, and prevent and treat HBV-associated extrahepatic manifestations

Recommendations	Grade of evidence	Grade of recommendation
Main endpoint • Induction of long-term suppression of HBV DNA	I	1
Valuable endpoint • Induction of HBeAg loss (± anti-HBe seroconversion) in HBeAg-positive patients with chronic hepatitis B*	II-1	1
Additional endpoint • ALT normalization (biochemical response)†	II-1	1
Optimal endpoint • HBsAg loss (± anti-HBs seroconversion)‡	II-1	1

*Often represents a partial immune control of the chronic HBV infection;
†Achieved in most patients with long-term suppression of HBV replication;
‡Indicates profound suppression of HBV replication and viral protein expression
EASL CPG HBV. J Hepatol 2017;67:370–98

THE INTERNATIONAL LIVER CONGRESS™

Savour science together again

22-26 JUNE 2022 LONDON

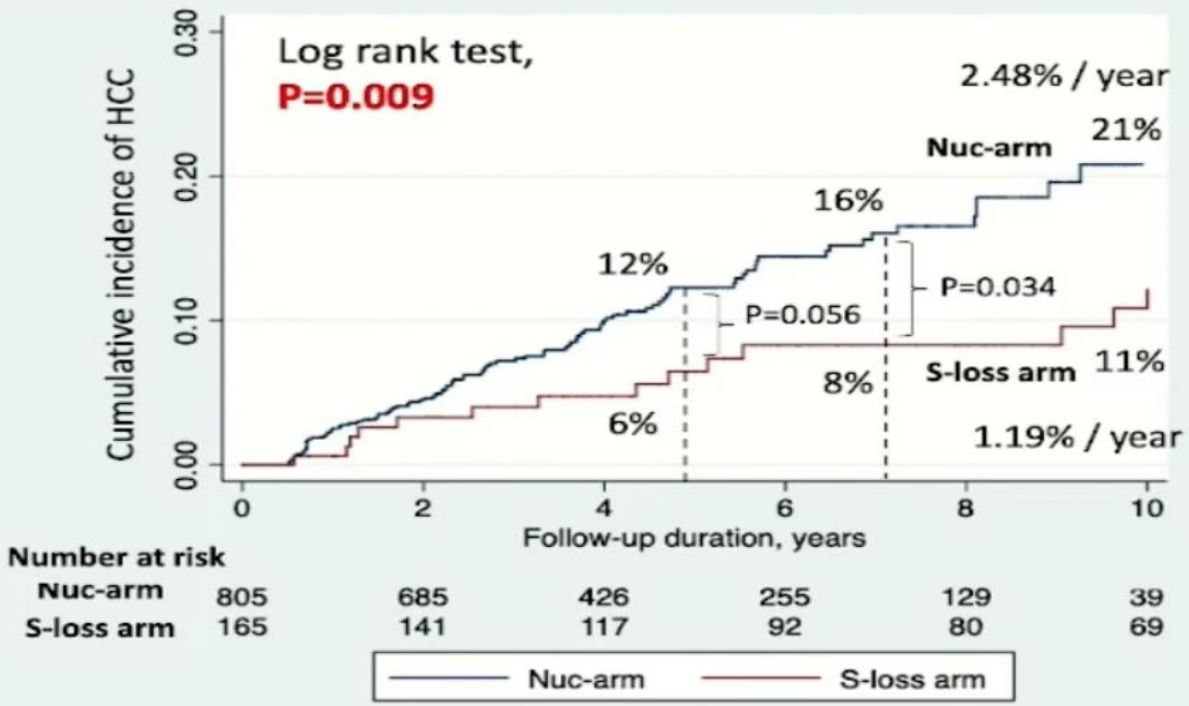
Hepatocellular carcinoma incidence is reduced in cirrhotic chronic hepatitis B patients with HBsAg seroclearance comparing to those with viral suppression

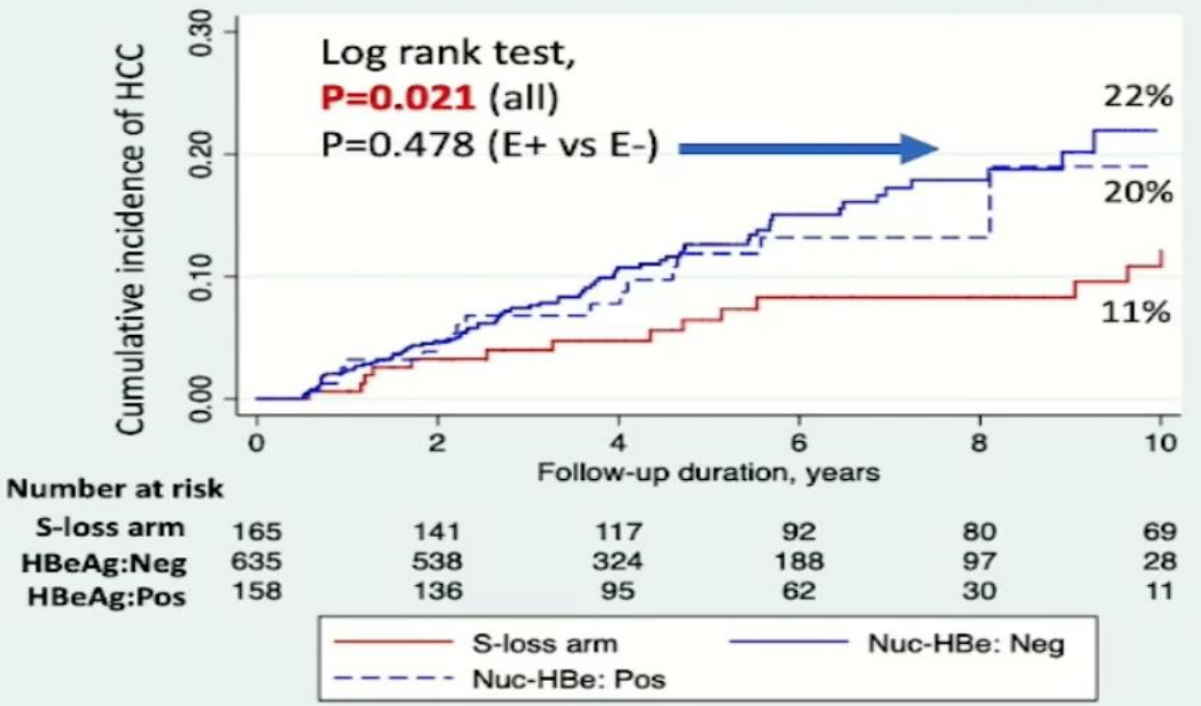
Rachel Wen-Juei Jeng[1,2,3], Chien-Hung Chen[1,4], Hwai-I Yang[5], Yi-Cheng Chen[1,2,3], Yen-Chun Liu[1,2,3], Chia-Ying Wu[2,3], Rong-Nan Chien[1,2,3], Yun-Fan Liaw[1,2,3]

1. College of Medicine, Chang Gung University, Taiwan, 2. Liver research Unit, Chang Gung Memorial Hospital, Linkou Branch, Taiwan, 3. Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Linkou Branch, Taiwan, 4. Division of Hepatogastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, 5. Genomics Research Center, Academia Sinica, Taiwan

EASL™ The Home of Hepatology

Cumulative incidence of HCC is higher in the Nuc-arm
--No difference between HBeAg serostatus





HCC incidence -- spontaneous vs. Nuc related S-loss: P=0.5987 *(after adjusting age, gender, FIB-4)*

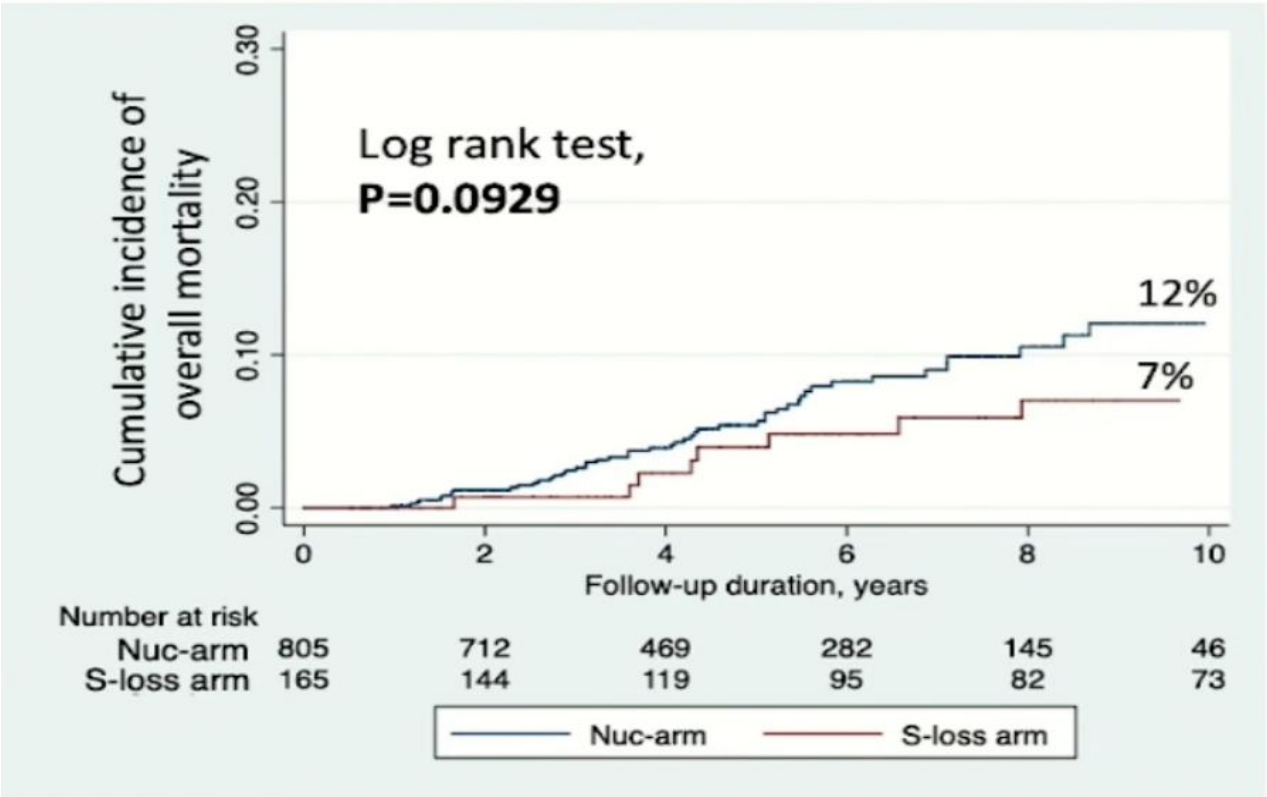
Cox regression analysis for predictors of HCC

Variables		All (N=970)	HCC (N=115)	Crude HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)*	P value
Age, years, mean±SD				1.035 (1.016-1.053)	0.0002	1.037 (1.018-1.055)	<0.0001	1.045 (1.024-1.066)	<0.0001
Gender	Female	236	25	Reference				Reference	
	Male	734	90	1.049 (0.673-1.635)	0.8319			1.231 (0.762-1.990)	0.3950
HBV genotype#	B	538	65	Reference					
	C	393	45	0.850 (0.580-1.243)	0.4016				
ALT, U/L median(IQR)[a]				1.001 (0.997-1.005)	0.7249				
AST, U/L, median (IQR)[b]				1.005 (1.000-1.010)	0.0658				
Platelet, K, median (IQR)[c]				0.999 (0.997-1.002)	0.6403				
FIB-4, median (IQR)[d]				0.999 (0.990-1.008)	0.8416			0.996 (0.986-1.006)	0.4658
Group	Nuc-arm	805	96	Reference		Reference		Reference	
	S-loss arm	165	19	0.468 (0.262-0.833)	0.0099	0.438 (0.244-0.786)	**0.0056**	0.242 (0.089-0.660)	**0.0056**

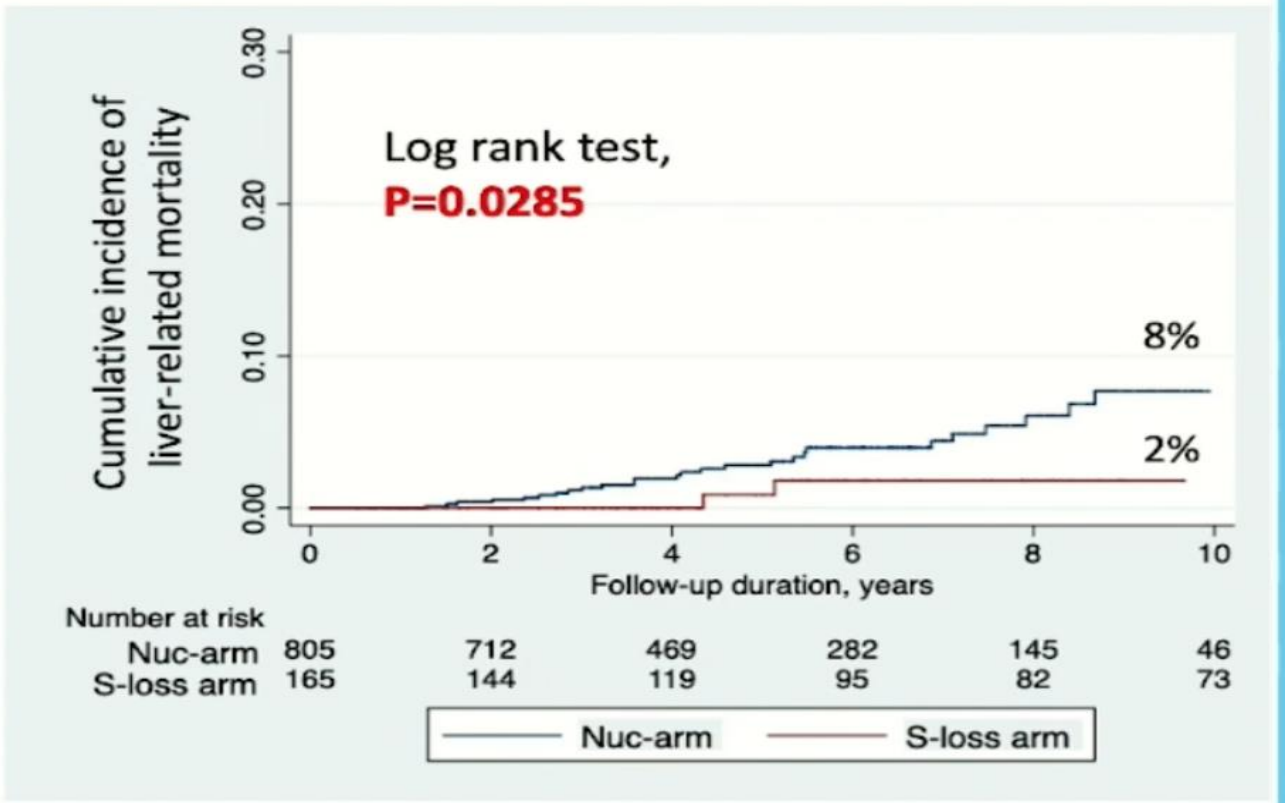
**: Exclusion of REVEAL-HBV cohort and limit in hospital based cohorts*
Missing, a: N=11, b: N=22, c: N=128, d: N=141, #: N=39

The S-loss arm: Lower cumulative incidence of overall and liver related mortality

Overall mortality



Liver-related mortality



Cox regression analysis --Overall and liver related mortality

Overall Mortality

Variables	All (N=970)	Mortality (N=69)	Adjusted HR (95% CI) [A]	P value	Adjusted HR (95% CI) [B]	P value
Age, years, mean±SD			1.070 (1.044-1.096)	<0.0001	1.074 (1.044-1.105)	<0.0001
Group Nuc-arm	805	51	Reference		Reference	
S-loss arm	165	18	0.474 (0.228-0.987)	**0.0460**	0.183 (0.039-0.855)	**0.0309**

Model A: adjusting gender ***Model B: adjusting gender, FIB-4***

Liver-related Mortality

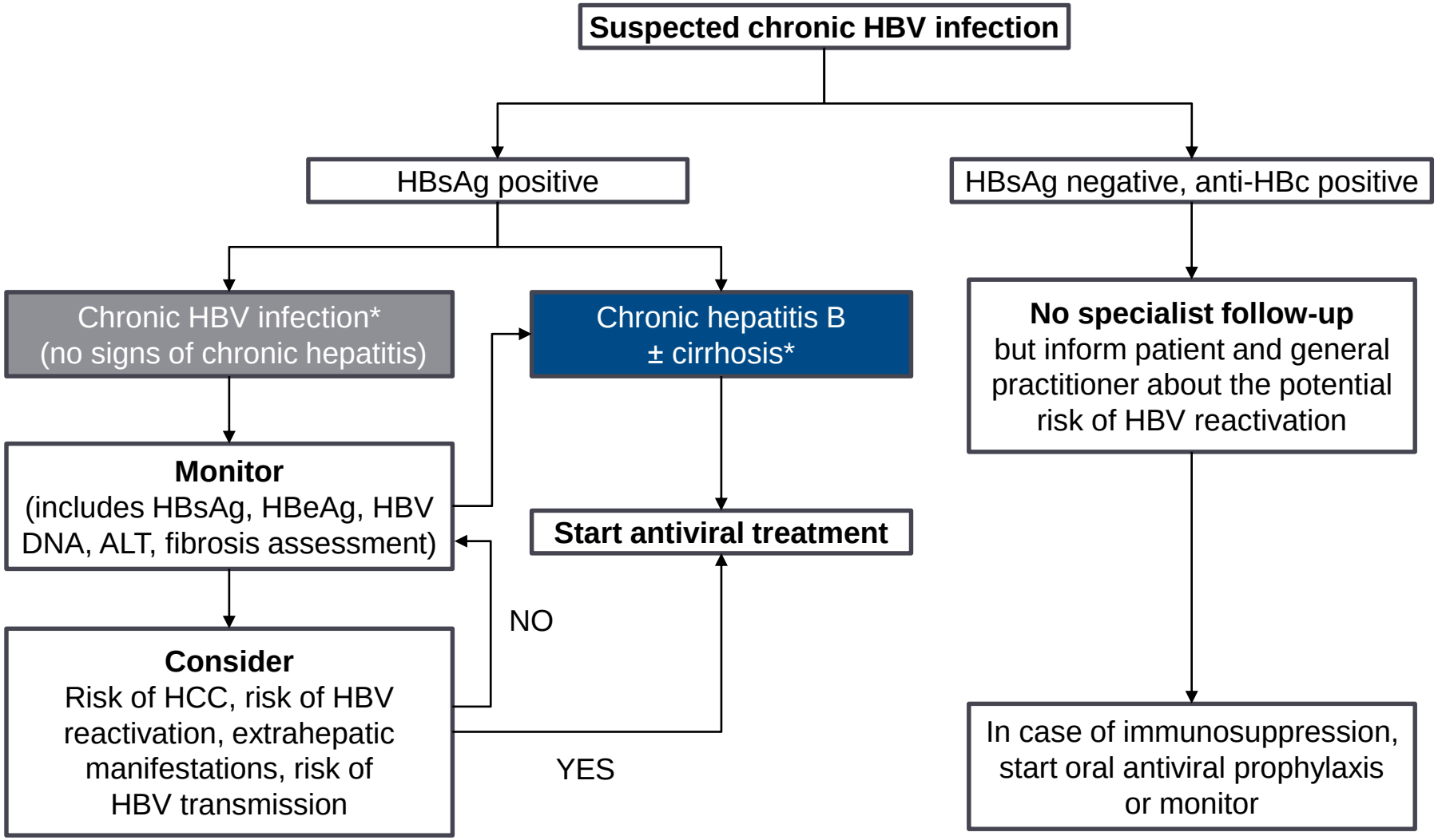
Variables	All (N=970)	Liver-Mortality (N=35)	Adjusted HR (95% CI) [A]	P value
Age, years, mean±SD			1043 (1.008-1.080)	0.0161
Group Nuc-arm	805	27	Reference	
S-loss arm	165	8	0.244 (0.071-0.836)	**0.0248**

Model A: adjusting gender

HBV gestione clinica corrente e prospettive di eradicazione

- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

Algorithm for the management of chronic HBV infection



*See new nomenclature slide.

EASL CPG HBV. J Hepatol 2017;67:370–98

Current treatment strategies for chronic hepatitis B: main concepts and features

Features	PegIFNα	ETV, TDF, TAF
Route of administration	Subcutaneous injections	Oral
Treatment duration	48 weeks	Long-term until HBsAg loss*
Tolerability	Low	High
Long-term safety concerns	Very rarely persistence of on-treatment AEs†	Probably not‡
Contraindications	Many§	None‖
Strategy	Induction of a long-term immune control	Inhibition of viral replication
Level of viral suppression	Moderate	Universally high
Effect on HBeAg loss	Moderate¶	Low in first year, moderate over long term
Effect on HBsAg levels	Variable¶	Low**
Risk of relapse after treatment cessation	Low for those with sustained response 6–12 months after therapy	Moderate if consolidation treatment provided after HBeAg seroconversion. High for HBeAg-negative disease
Early stopping rules	Yes	No
Risk of viral resistance	No	Minimal to none††

*Stopping NAs after some years might be considered in selected cases; †Psychiatric, neurological, endocrinological; ‡Uncertainties regarding kidney function, bone diseases for some NAs; §Decompensated disease, comorbidities etc.; ‖Dose adjustments in patients with eGFR <50 ml/min are required for all NAs except for TAF (no dose recommendation for TAF in patients with CrCl <15 ml/min who are not receiving haemodialysis); ¶Depending on baseline characteristics; **Slowly increases with treatment time in HBeAg-positive patients (a plateau in serological responses has been observed beyond treatment Year 4), usually very low in HBeAg-negative patients; ††So far no TDF or TAF resistance development has been detected

EASL CPG HBV. J Hepatol 2017;67:370–98

NA monotherapy for treatment-naïve patients

- Long-term administration of a potent NA with a **high barrier to resistance** is the treatment of choice
  - Regardless of severity of liver disease

Recommendations	Grade of evidence	Grade of recommendation
Treatment of choice • Long-term administration of a potent NA with high barrier to resistance (regardless of severity of liver disease)	I	1
Preferred regimens • ETV, TDF and TAF as monotherapies	I	1
NOT recommended • LAM, ADV and TBV	I	1

EASL CPG HBV. J Hepatol 2017;67:370–98

Indications for selecting ETV or TAF over TDF*

- In some circumstances ETV or TAF may be a more appropriate treatment choice than TDF

Age	• >60 years
Bone disease	• Chronic steroid use or use of other medications that worsen bone density • History of fragility fracture • Osteoporosis
Renal alteration†	• eGFR <60 ml/min/1.73 m^2 • Albuminuria >30 mg/24 h or moderate dipstick proteinuria • Low phosphate (<2.5 mg/dl) • Haemodialysis

*TAF should be preferred to ETV in patients with previous exposure to NAs; †ETV dose needs to be adjusted if eGFR <50 ml/min; no dose adjustment of TAF is required in adults or adolescents (aged ≥12 years and ≥35 kg body weight) with estimated CrCl ≥15 ml/min or in patients with CrCl <15 ml/min who are receiving haemodialysis

EASL CPG HBV. J Hepatol 2017;67:370–98

Discontinuation of NA treatment

- Long-term therapy with NAs is usually required
  - HBV eradication is not usually achieved

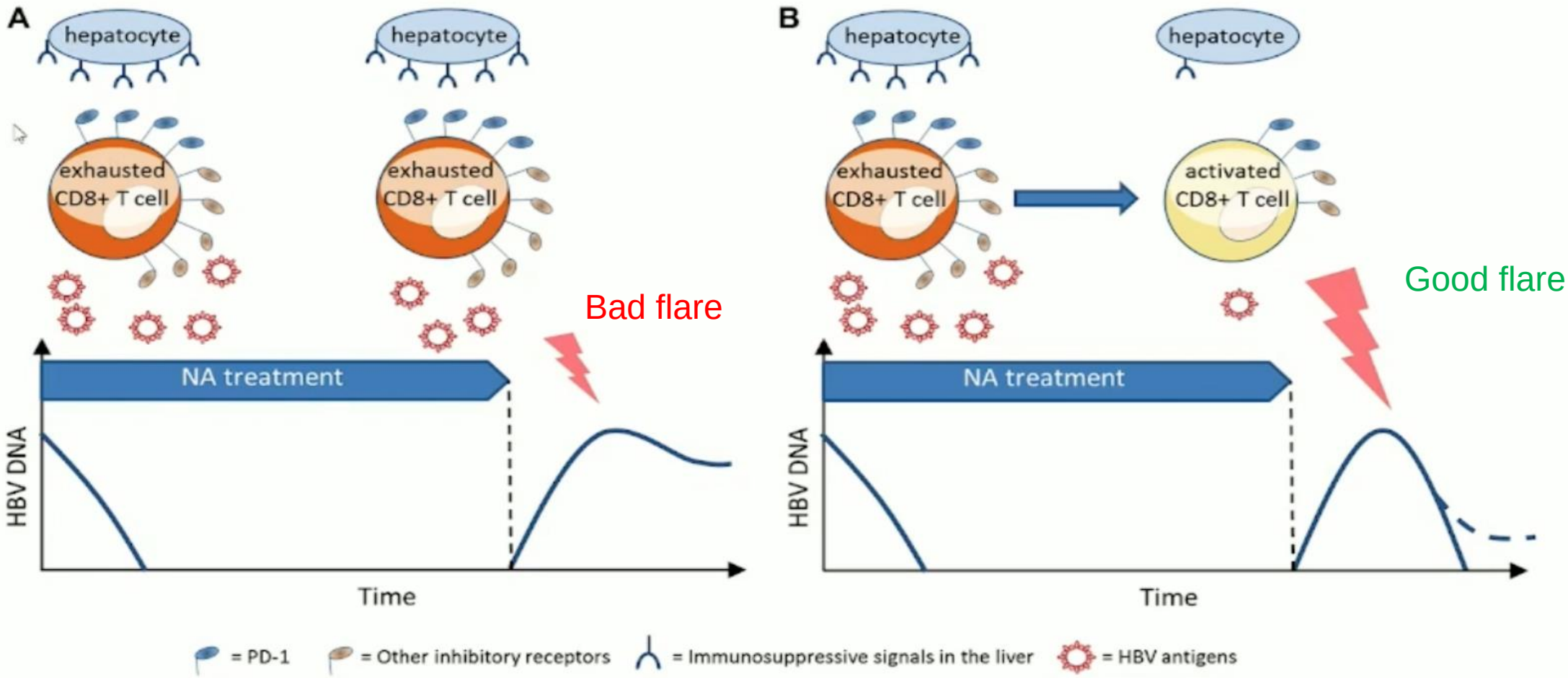
Recommendations	Grade of evidence	Grade of recommendation
NAs <u>should</u> be discontinued • After confirmed HBsAg loss (± anti-HBs seroconversion)	II-2	1
NAs <u>can</u> be discontinued • In HBeAg-positive patients, without cirrhosis, who achieve stable HBeAg seroconversion and undetectable HBV DNA and complete ≥12 months of consolidation therapy **Close post-NA monitoring is warranted**	II-2	2
NAs <u>may</u> be discontinued • In selected HBeAg-negative patients, without cirrhosis, who achieve long-term (≥3 years) virological suppression, **if close post-NA monitoring can be guaranteed**	II-2	2

EASL CPG HBV. J Hepatol 2017;67:370–98

HBV gestione clinica corrente e prospettive di eradicazione

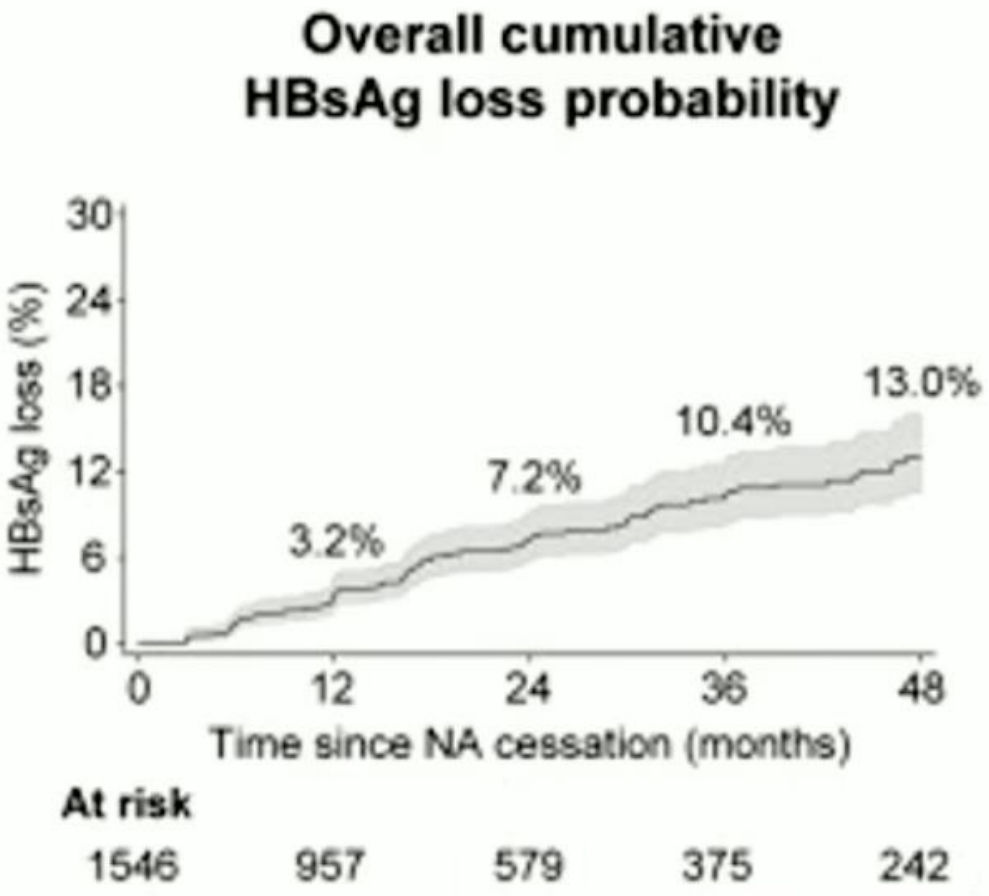
- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell’ HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

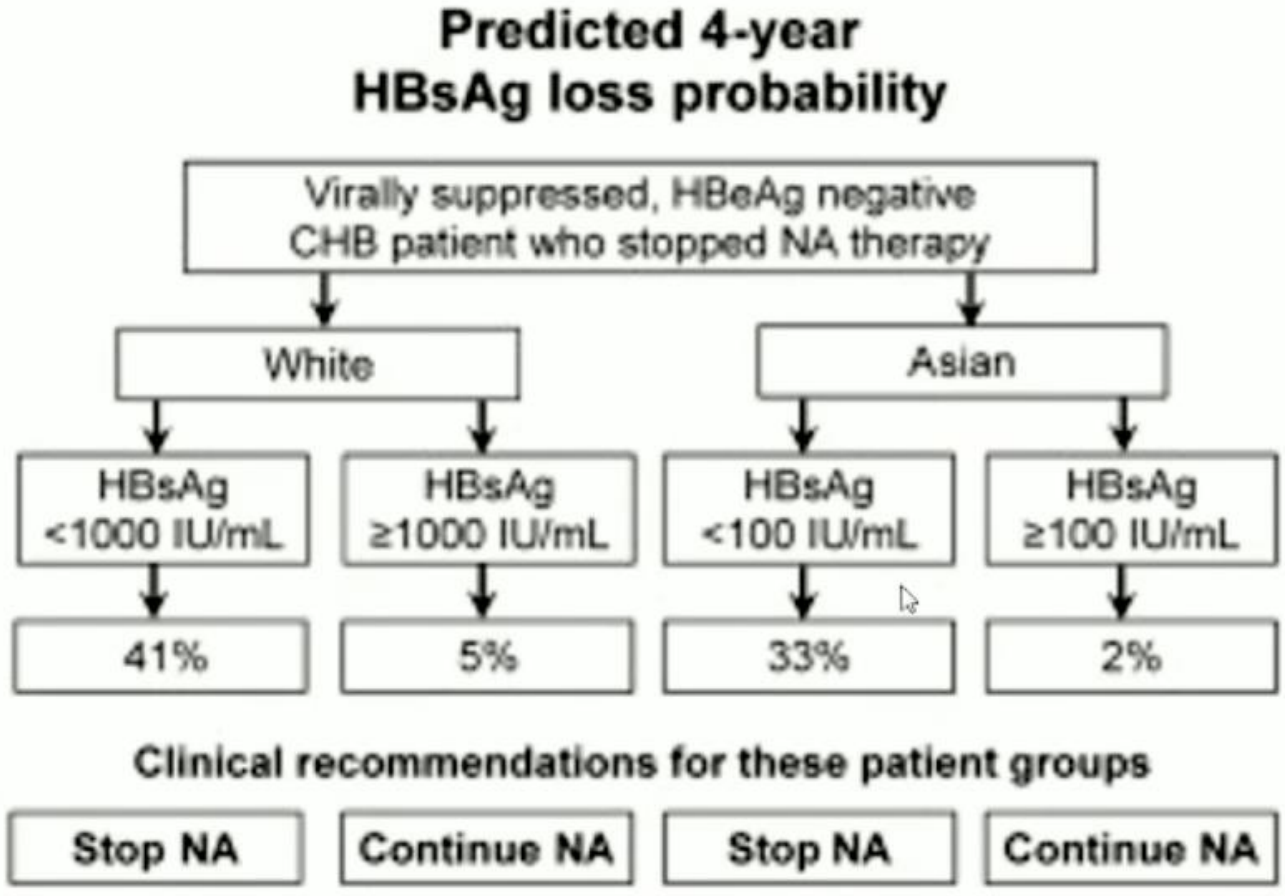
THE CONCEPT OF NUC TREATMENT DISCONTINUATION



Modified from van Bömmel F, Bergt T. Hepatol Comm 2021

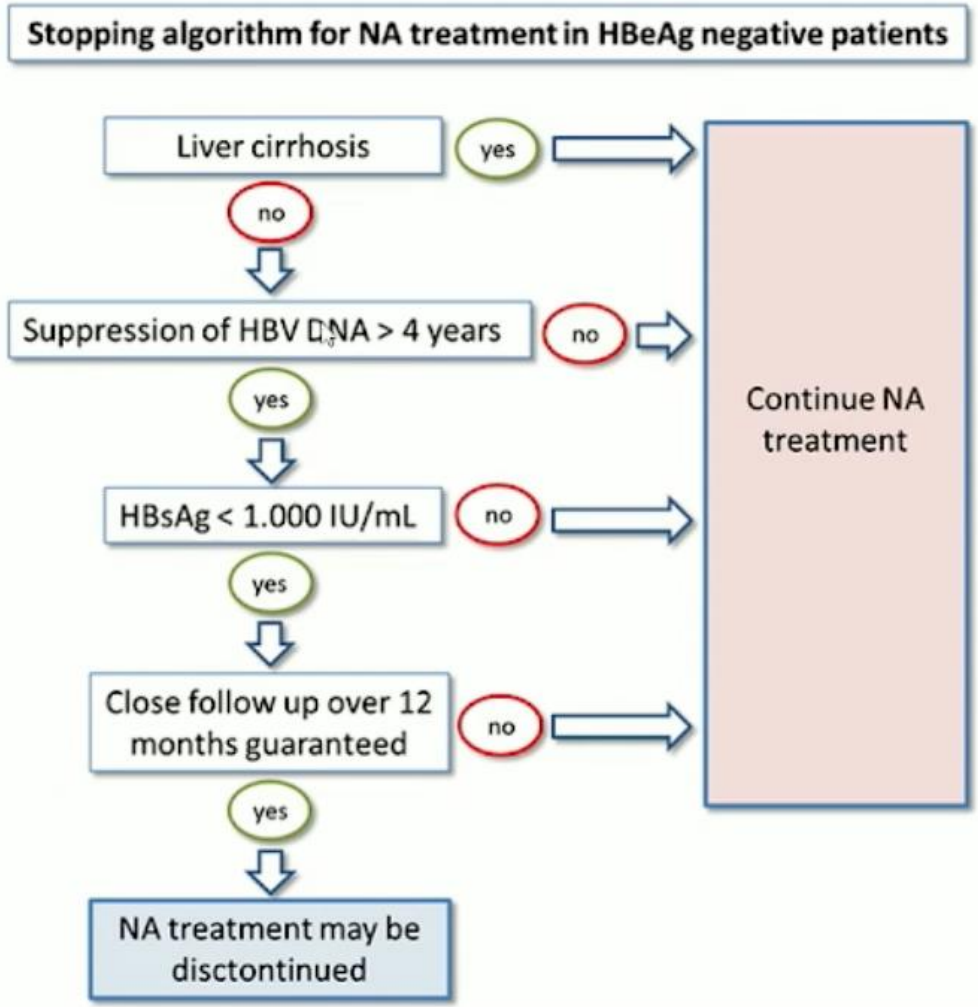
RETRACT – B





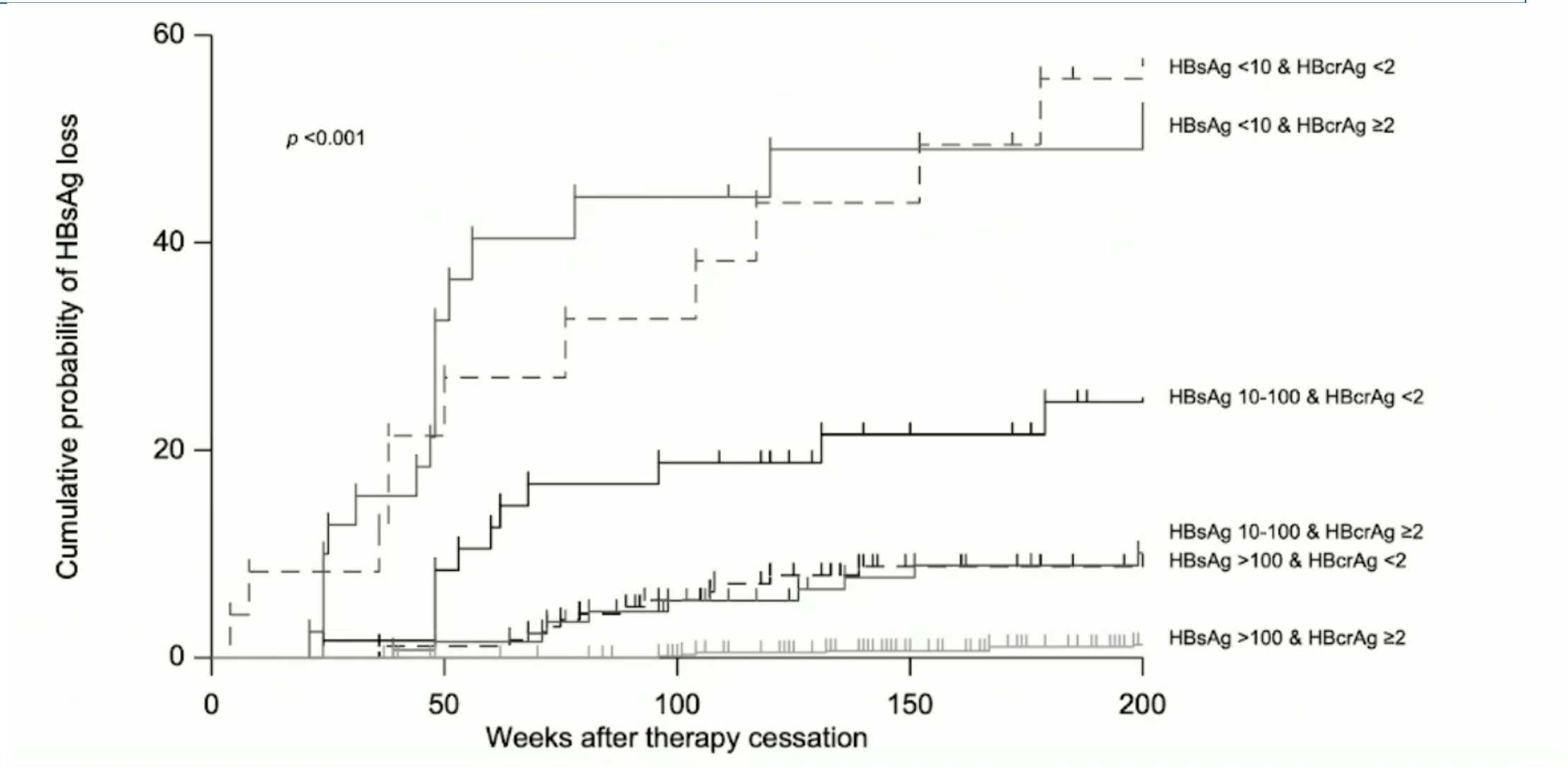
Hirode G, et al. Gastroenterology 2022;162:757-771.

APPROACH TO IDENTIFY PATIENTS FOR NUC DISCONTINUATION



van Bömmel F, Bergt T. Hepatol Comm 2021

ROLE OF BIOMARKERS IN IDENTIFYING PATIENTS WITH BENEFITS FROM NUC DISCONTINUATION

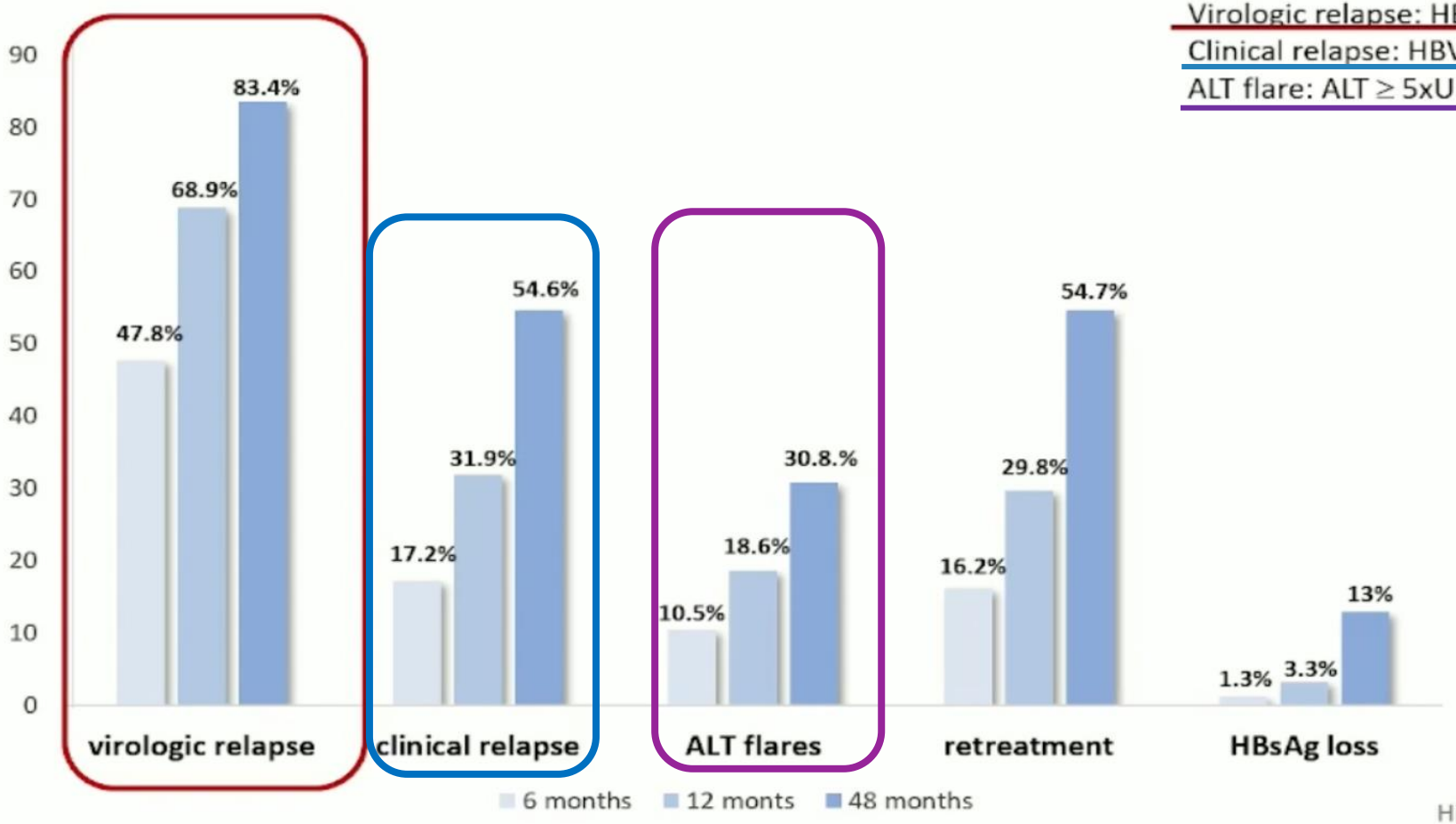


Sonneveld MJ, et al. J Hepatol 2022;76:P1042-1050,

Off-therapy response after NUC withdrawal in patients with CHB: an international, multicentre, multi-ethnic cohort (RETRACT-B study)

- **1552** CHB patients, 87.6% Asian, 84.2% HBeAg neg at NA start
- 63.2% ETV treated, 27.1% TDF
- Median follow-up 18.4 (7.9-39.4) months

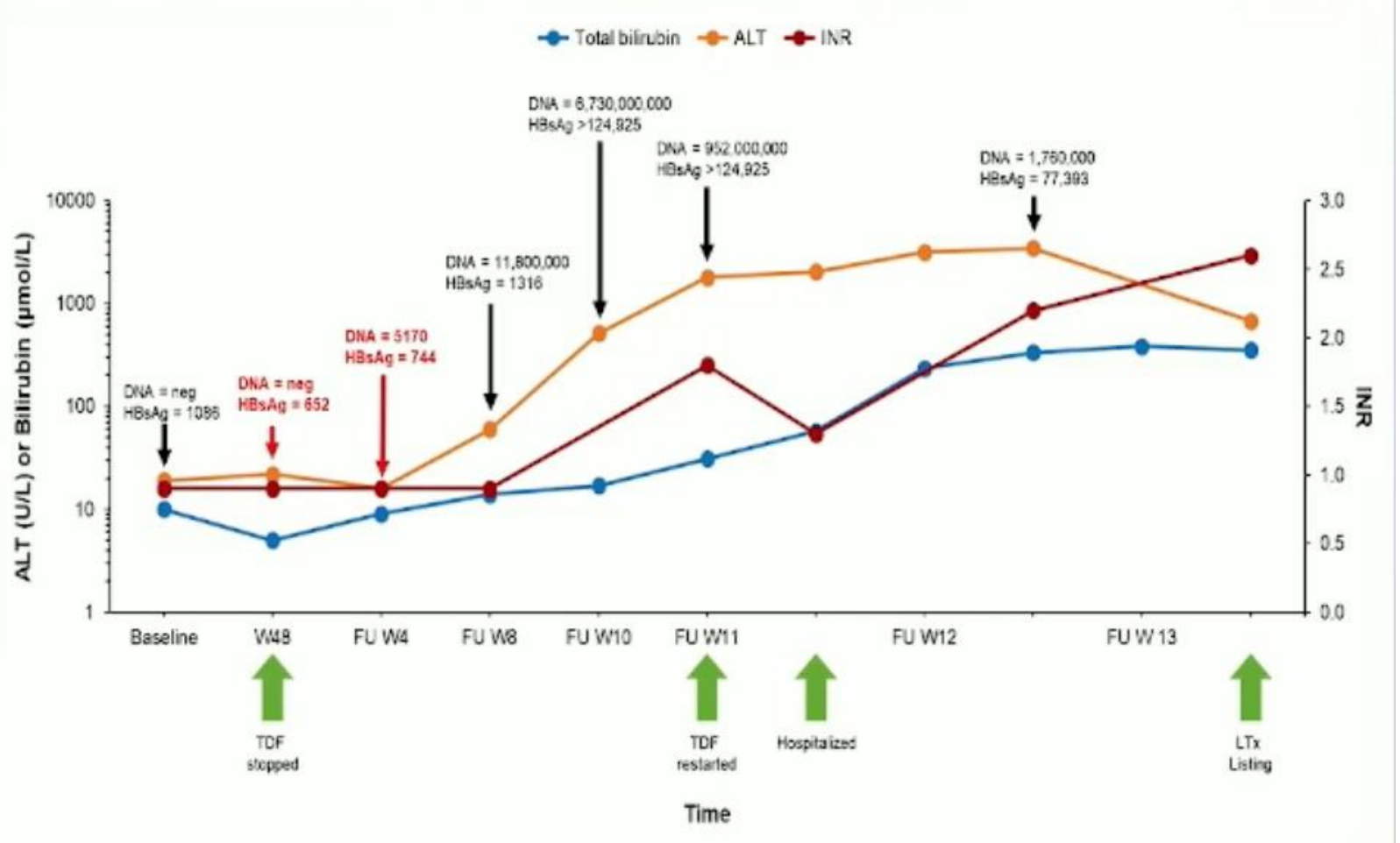
Virologic relapse: HBV-DNA > 2000 IU/ml
Clinical relapse: HBV-DNA > 2000 IU/ml + ALT > 2xULN
ALT flare: ALT ≥ 5xULN



Hirode G et al Gastroenterology 2022

Liver Failure and Transplantation after stopping NUC REEF - 2

One patient in the TDF + placebo arm of the REEF-2 study presenting with liver failure after stopping TDF then requiring liver transplantation



Agarwal et al J Hepatol 2022 Abstract GS 010

STOP NUC PROS and CONS

PROS

- Functional cure is associated with better clinical outcomes
- Actually one of the 2 ways to obtain functional cure
- Quantitative HBsAg and maybe new markers quantitative HBcrAg (or HBVRNA) may help to identify the best candidates
- A management algorithm has already been defined

CONS

- HBV intrahepatic re-expansion after NUC discontinuation may cause the lost of benefit of prolonged suppression of HBV replication (decrease of intrahepatic HBVDNA, liver cell HBcAg, cccDNA)
- Good ALT flares are defined ex post 51% of patients with favourable markers profile show flares w/o HBsAg loss at 48 weeks
- HBsAg levels predicting HBsAg loss are related to ethnicity
- HBcrAg and HBVRNA are still not standardized
- Predictors of HBsAg clearance are still not effective

HBV gestione clinica corrente e prospettive di eradicazione

- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

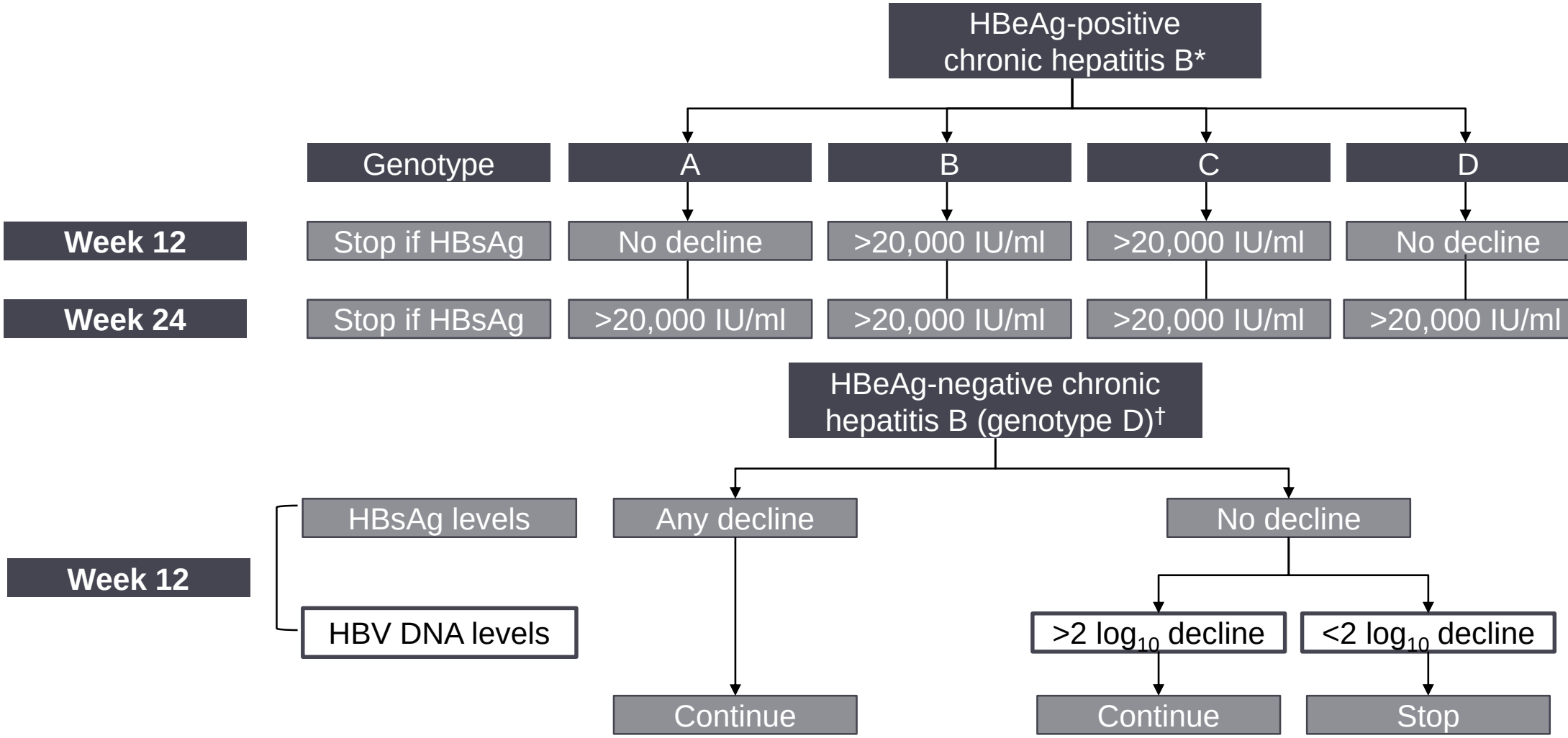
PegIFNα monotherapy

- Only patients with milder disease should generally be considered for treatment with PegIFNα

Recommendations	Grade of evidence	Grade of recommendation
PegIFNα **can be considered as an initial treatment** option for patients with mild-to-moderate HBeAg-positive or -negative chronic hepatitis B	I	2
The standard duration of PegIFNα therapy is 48 weeks	I	1
Extension of PegIFNα therapy beyond Week 48 may be beneficial in selected HBeAg-negative patients with chronic hepatitis B	II-1	2

EASL CPG HBV. J Hepatol 2017;67:370–98

Predictors of PegIFNα response and stopping rules



*Evidence level II-2, grade of recommendation 2; †Evidence level II-2, grade of recommendation 1

EASL CPG HBV. J Hepatol 2017;67:370–98

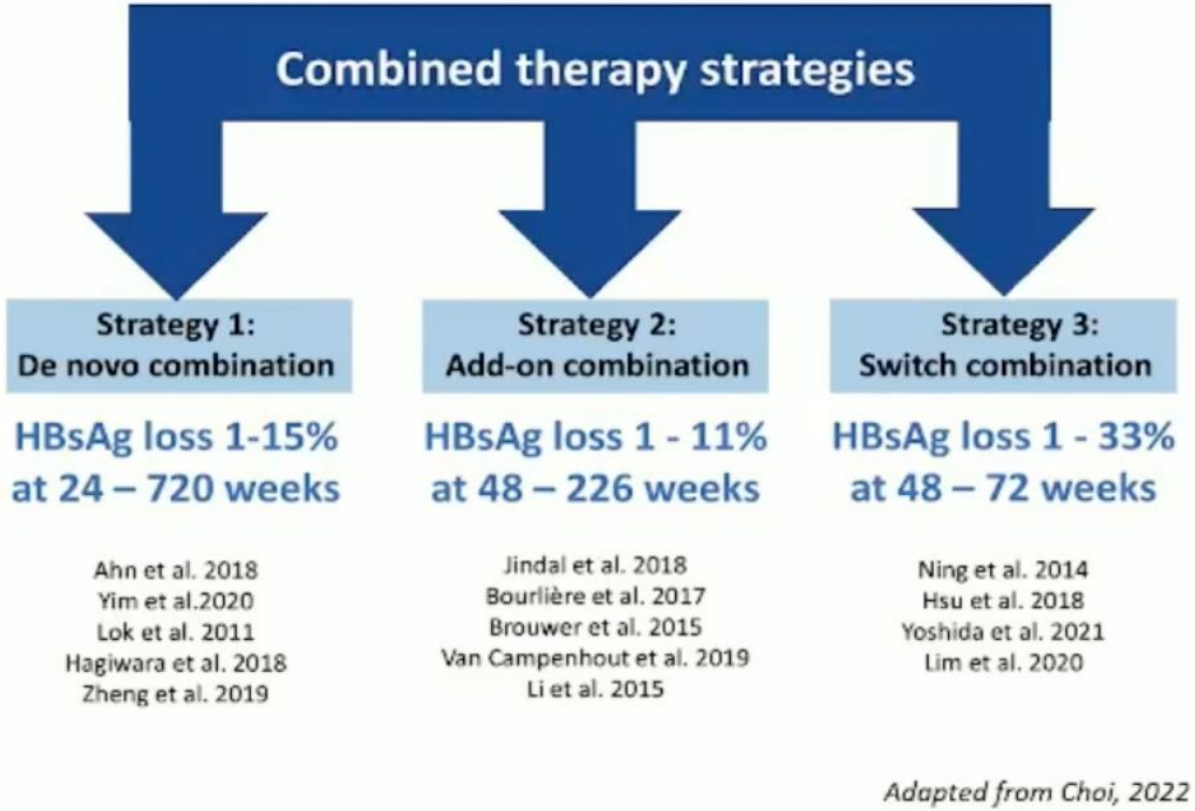
Combination therapy

- Combination therapy is generally not recommended

Recommendations (NA plus NA)	Grade of evidence	Grade of recommendation
NOT recommended • *De novo* combination therapy of two NAs with a high barrier to resistance (ETV, TDF, TAF)	I	1
Drug switch or combination may be considered • In treatment-adherent patients with incomplete HBV suppression reaching a plateau during ETV or TDF/TAF long-term therapy	III	2
Recommendations (NA plus PegIFNα)		
NOT recommended		
• *De novo* combination of NA and PegIFNα	I	1
• Short-term pretreatment with an NA before PegIFNα in treatment-naïve HBeAg-positive patients	II	1
• Adding PegIFNα or switching to PegIFNα in patients with long-term HBV DNA suppression on NA therapy	II	1

EASL CPG HBV. J Hepatol 2017;67:370–98

Combination strategies with approved therapies (NUCs & IFN)



Adapted from Choi, 2022

*Development of improved drugs targeting HBV POL continues:
Besifovir
TDF Exalidex
Pradefovir
ATI-2173
RNaseH inhibitors
…

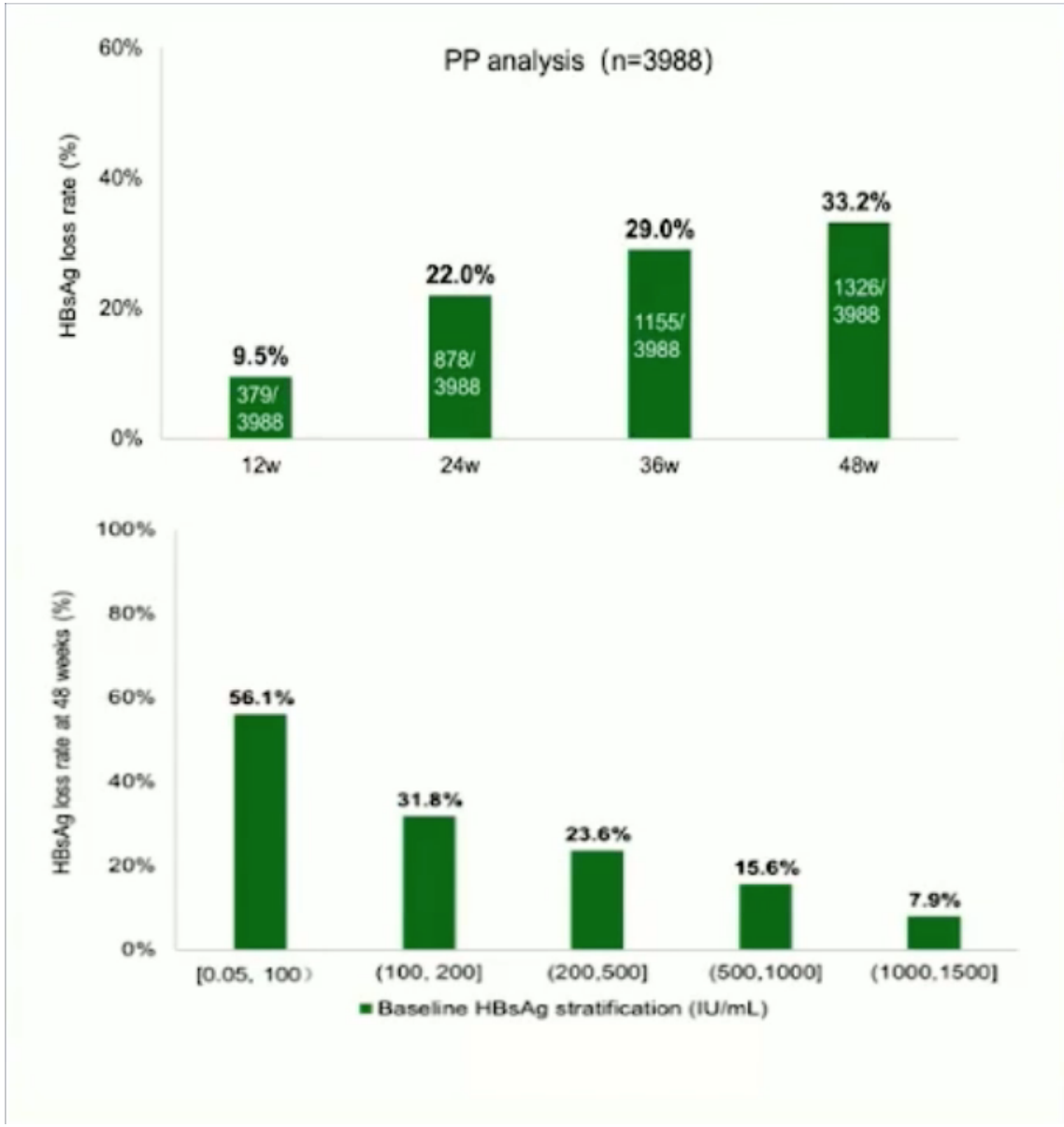
Available studies are heterogenous

Common finding: HBeAg and HBsAg loss are modestly enhanced with PEG-IFNα-based strategies

PegIFNα in NUC-suppressed HBeAg negative patients EVEREST (Real-Life-project)

- Chinese patients with:
  - NUC therapy ≥ 1 year
  - HBVDNA < 100 IU/mL
  - HBeAg negative
  - HBsAg < 1500 IU/mL
- Add on or switch to PegIFNα for 48 weeks or up to 96 weeks and 48 weeks follow up
- mITT population n 5,648
- PP population n 3,988

Conclusion: Functional cure can be achieved in NUC-suppressed HBeAg negative patients by means of pegIFNα strategies

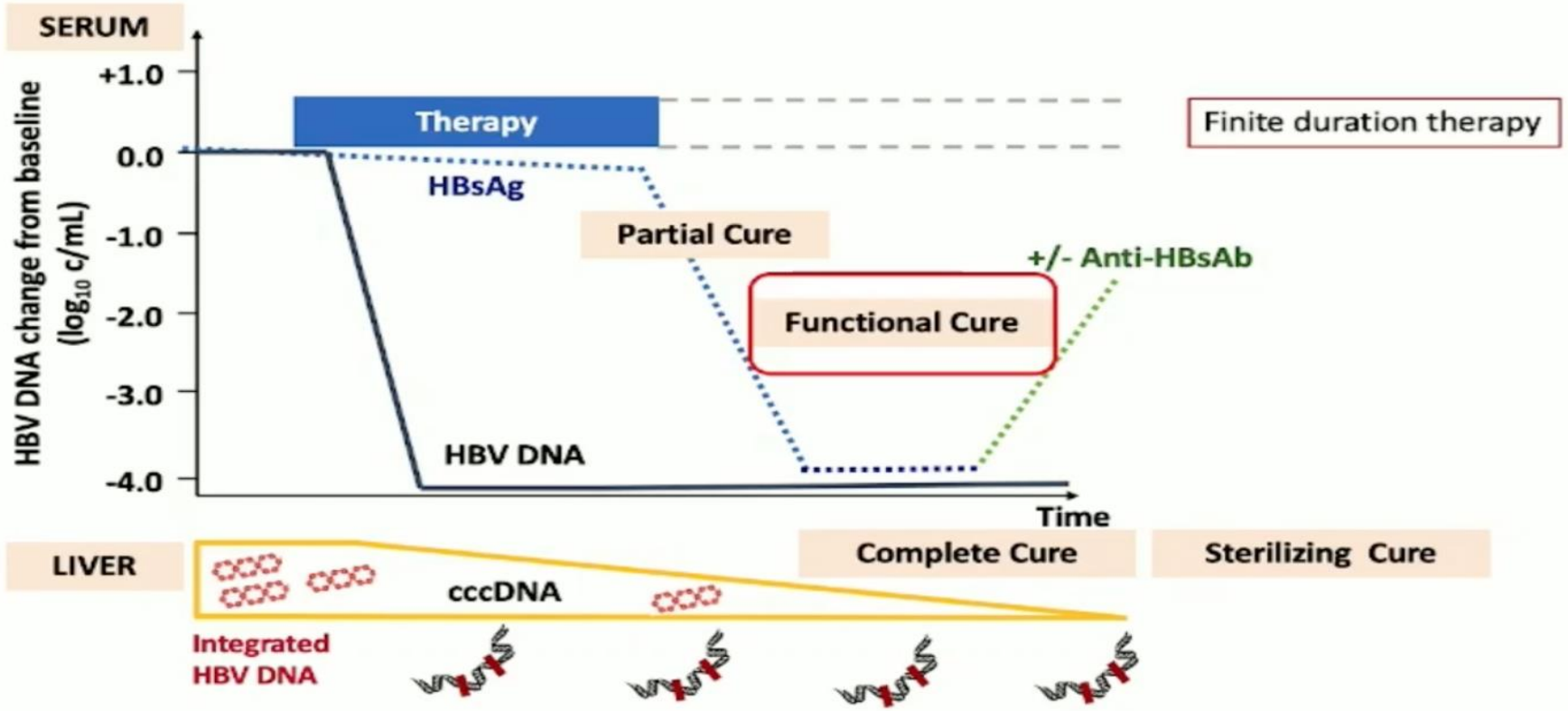


Xie et al J Hepatol 2022 SAT 369

HBV gestione clinica corrente e prospettive di eradicazione

- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

Major goals of current strategies towards « HBV cure »



- Favorable clinical outcome after treatment withdrawal
- Further reduction in HCC risk

Functional Cure

- Sustained loss of serum HBV DNA and HBsAg (+/- anti-HBs)
- Finite course of treatment

- Indication of marked suppression of HBV replication and cccDNA transcription, but HBV still present in the liver!

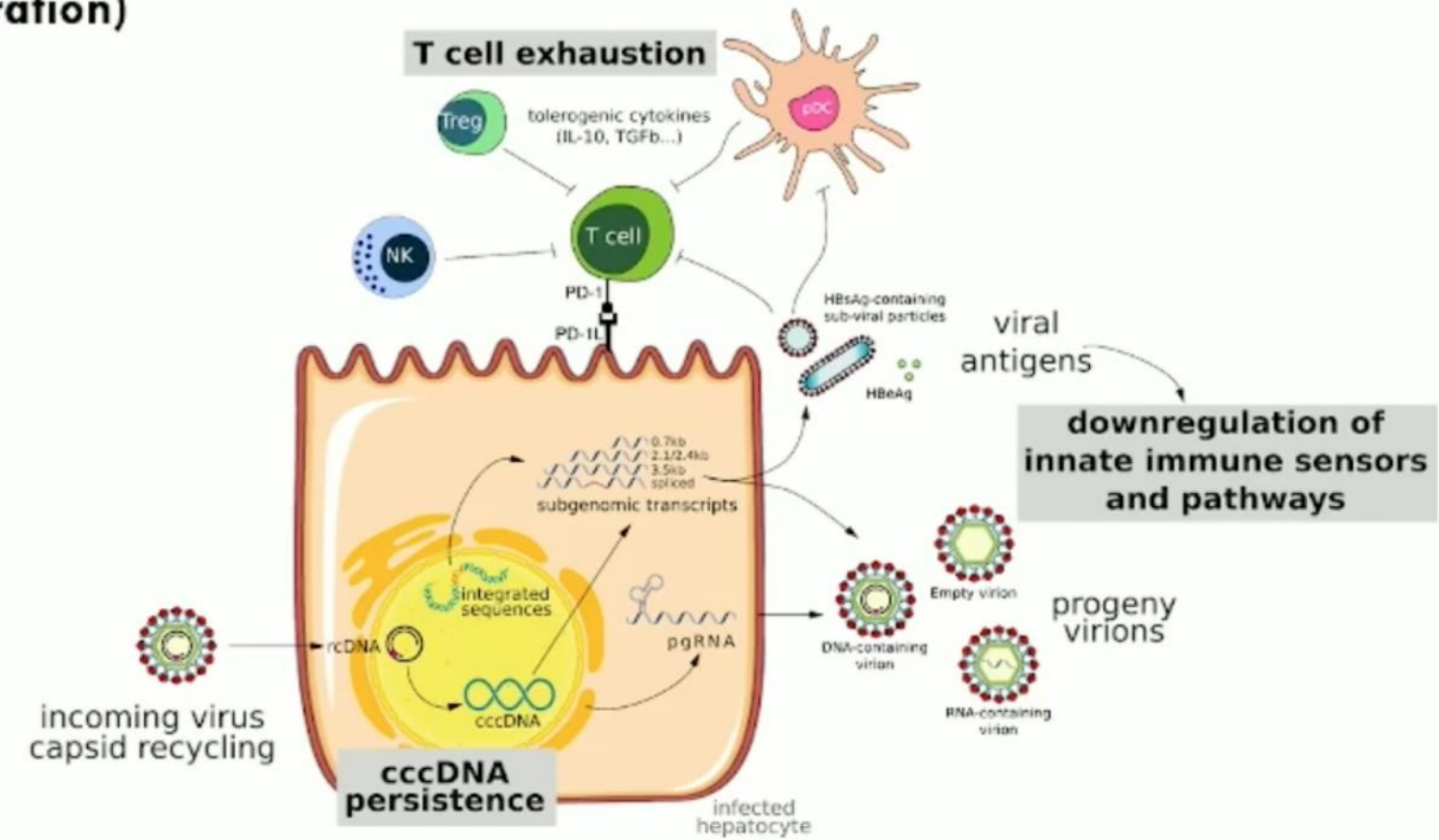
Testoni, 2017; Fanning, 2019; Cornberg, 2020; Martinez, 2021 ...

Obstacles to HBV functional cure

Intrahepatic viral reservoir: long-lived cccDNA (+integration)

High viral antigen load

Defective innate and adaptive immune responses

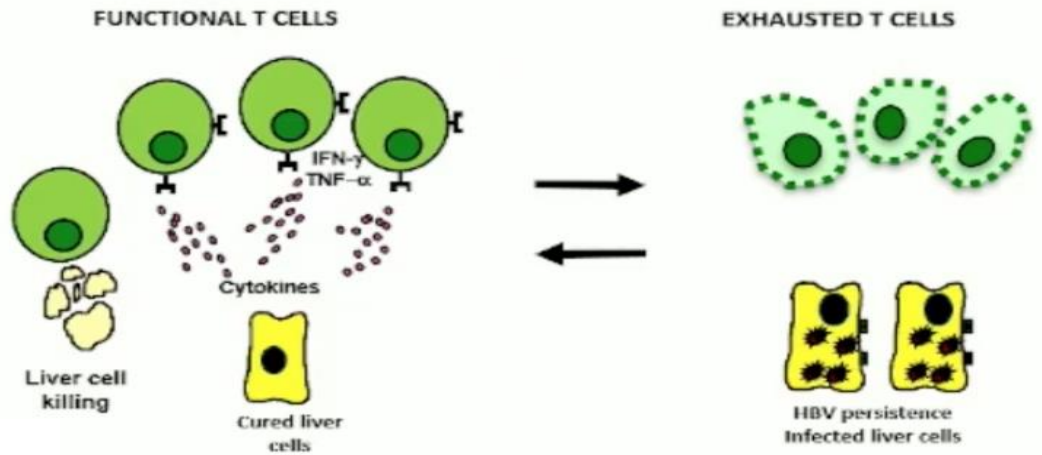


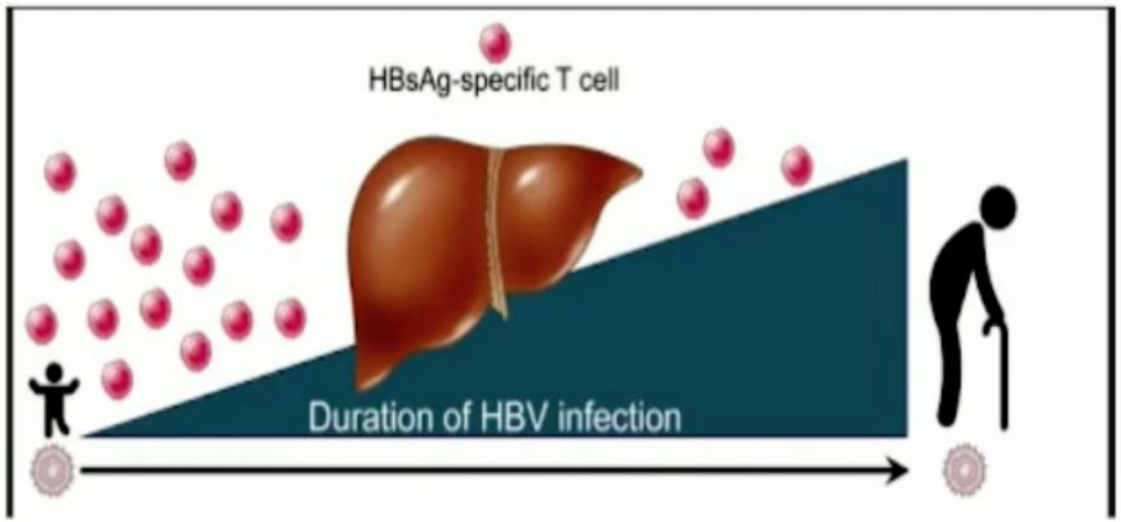
Adapted from Testoni, 2017

Why is HBV cure a difficult task?

- HBV "exhausts" immune responses, promoting chronic infection
- *Immune responses to HBV are defective*
  - *defective CD8+ and CD4+ responses*
  - *defective B cell responses*
  - *inefficient innate response*
- The liver is "immunosuppressive", affecting the ability of the immune system to control HBV

Re-educating the liver microenvironment and *training* the immune system to clear HBV with vaccines or other drugs is difficult to be achieved





› Gastroenterology. 2020 Aug;159(2):652-664. doi: 10.1053/j.gastro.2020.04.019. Epub 2020 Apr 14.

Effects of Hepatitis B Surface Antigen on Virus-Specific and Global T Cells in Patients With Chronic Hepatitis B Virus infection

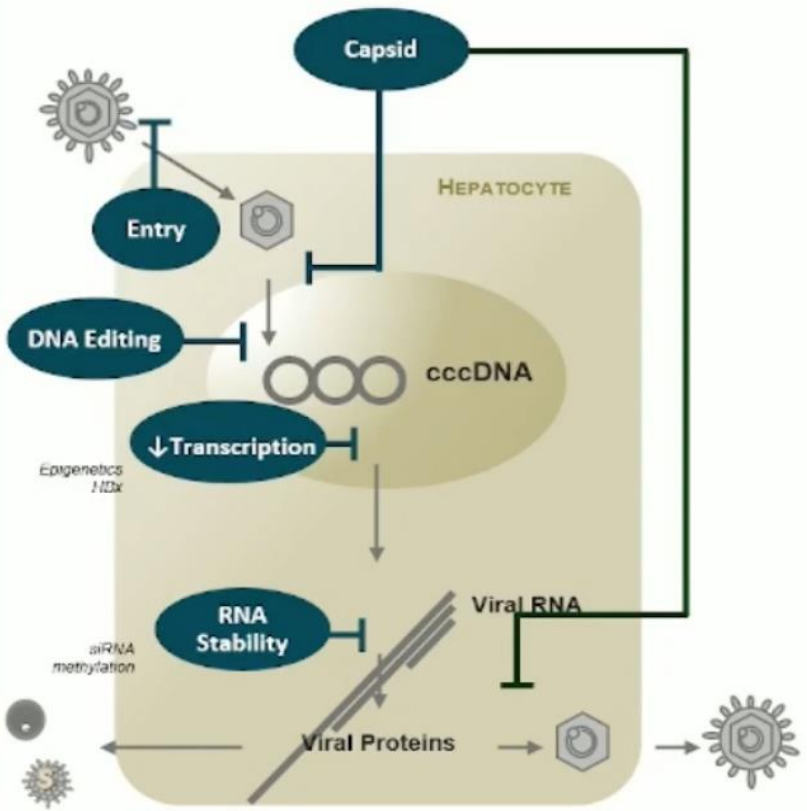
Nina Le Bert [1], Upkar S Gill [2], Michelle Hong [1], Kamini Kunasegaran [1], Damien Z M Tan [1], Raidah Ahmad [1], Yang Cheng [3], Charles-A Dutertre [4], Andreas Heinecke [5], Laura Rivino [6], Anthony Tan [1], Navjyot K Hansi [2], Min Zhang [7], Sujuan Xi [7], Yutian Chong [7], Stefan Pflanz [8], Evan W Newell [3], Patrick T F Kennedy [2], Antonio Bertoletti [9]

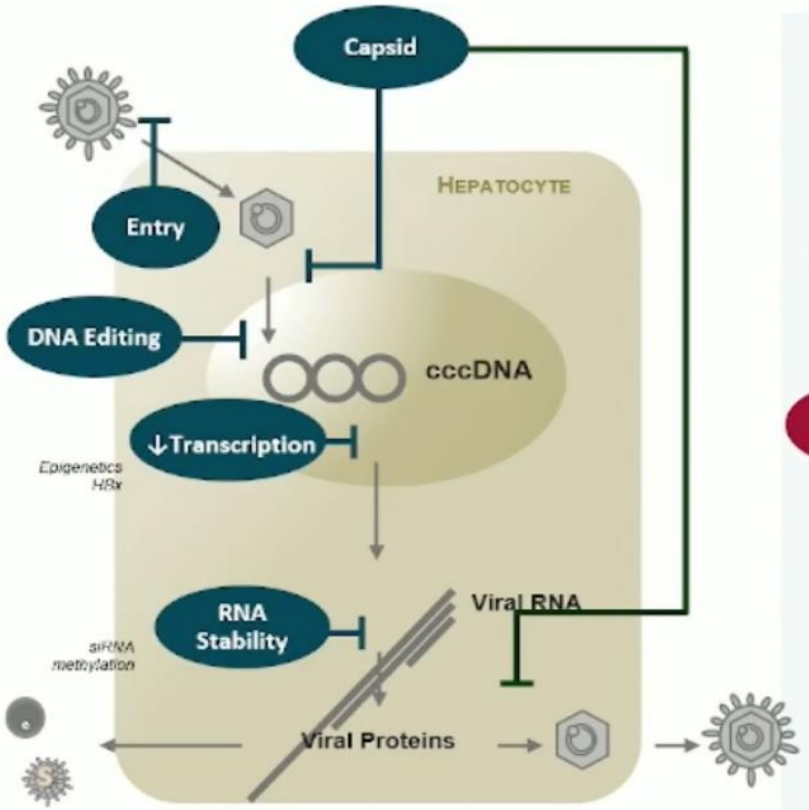
HBV gestione clinica corrente e prospettive di eradicazione

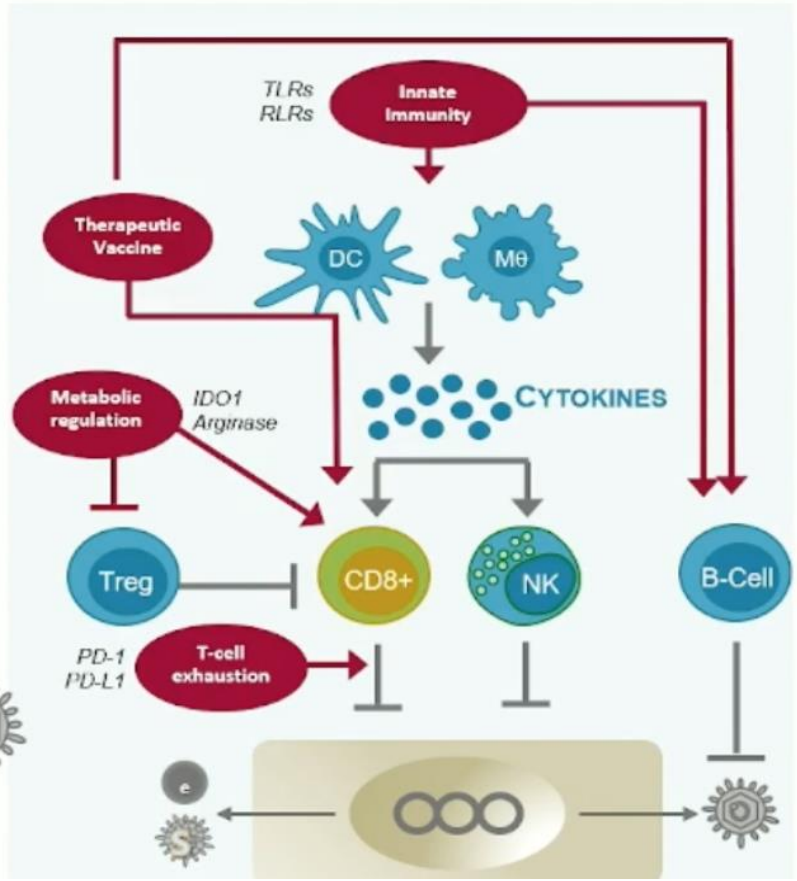
- Disease burden e futuri trends epidemiologici
- Nomenclatura e obiettivi di trattamento: il ruolo della clearance di HBsAg
- Indicazione al trattamento e terapie disponibili
- Sospendere i NUC per ottenere la clearance dell' HBsAg
- Ruolo del Peg IFNα
- Cura funzionale: un obiettivo complesso
- Cura funzionale: strumenti e strategie in valutazione

Therapeutic Approaches to HBV Cure

Inhibit Viral Replication | **Lower Viral Antigen Burden** | **Boost Immune Response**

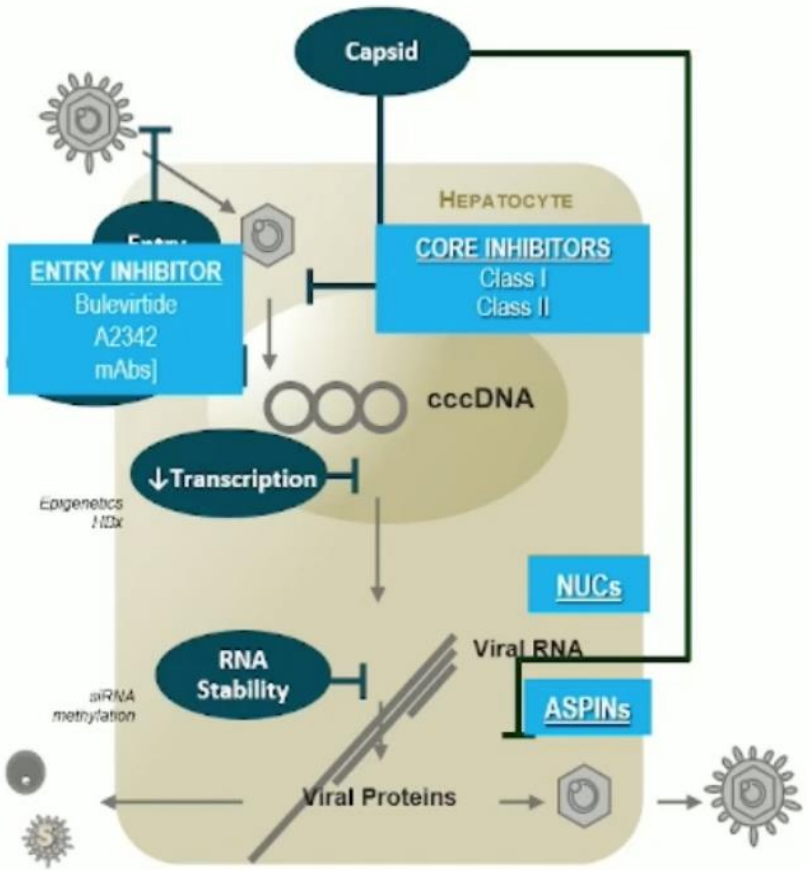






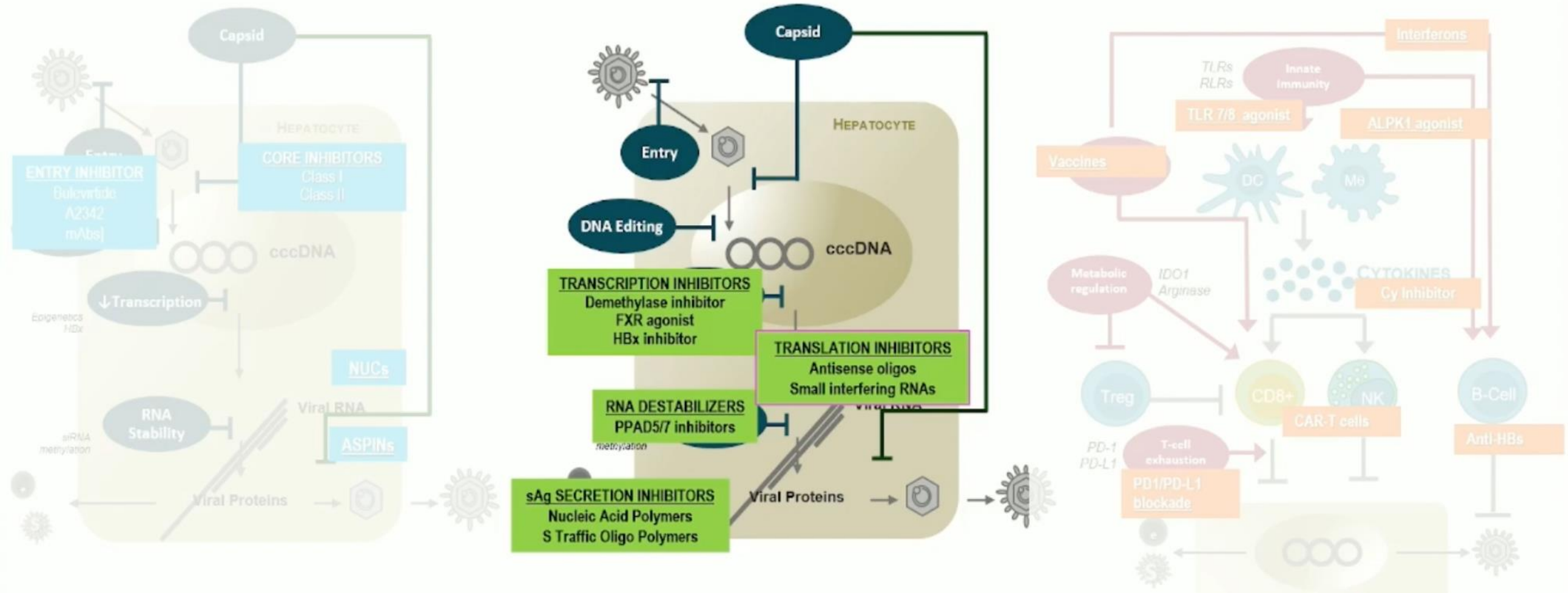
Therapeutic Approaches to HBV Cure

Inhibit Viral Replication | Lower Viral Antigen Burden | Boost Immune Response



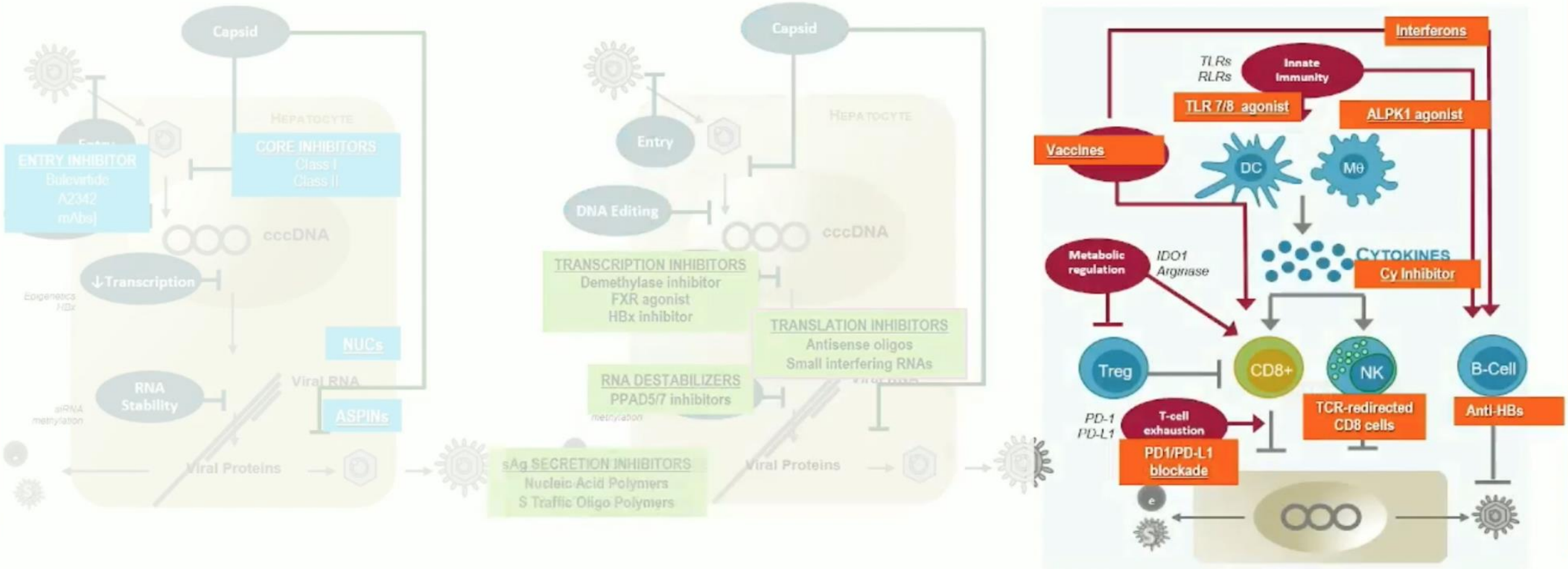
Therapeutic Approaches to HBV Cure

Inhibit Viral Replication	Lower Viral Antigen Burden	Boost Immune Response



Therapeutic Approaches to HBV Cure

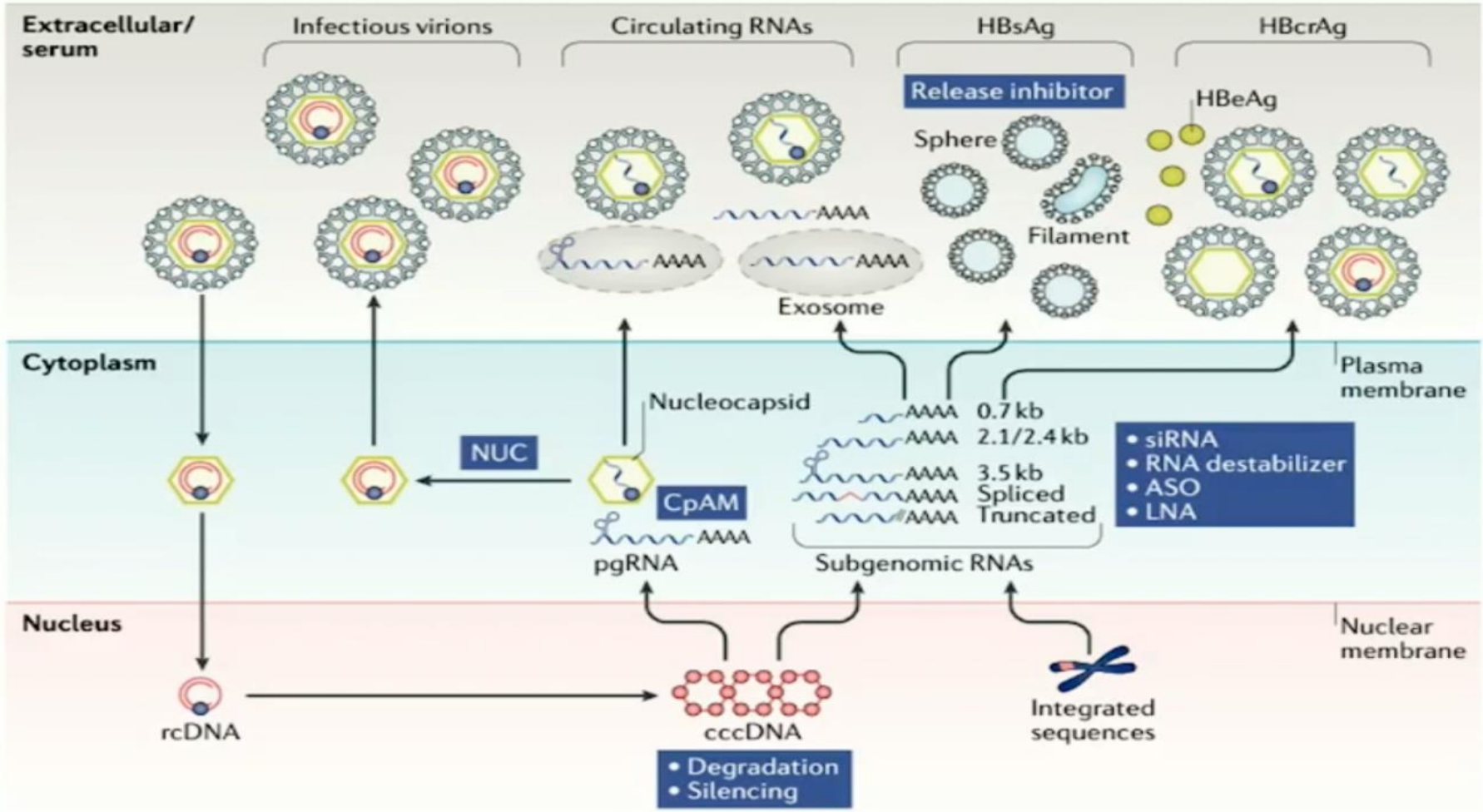
Inhibit Viral Replication | Lower Viral Antigen Burden | Boost Immune Response



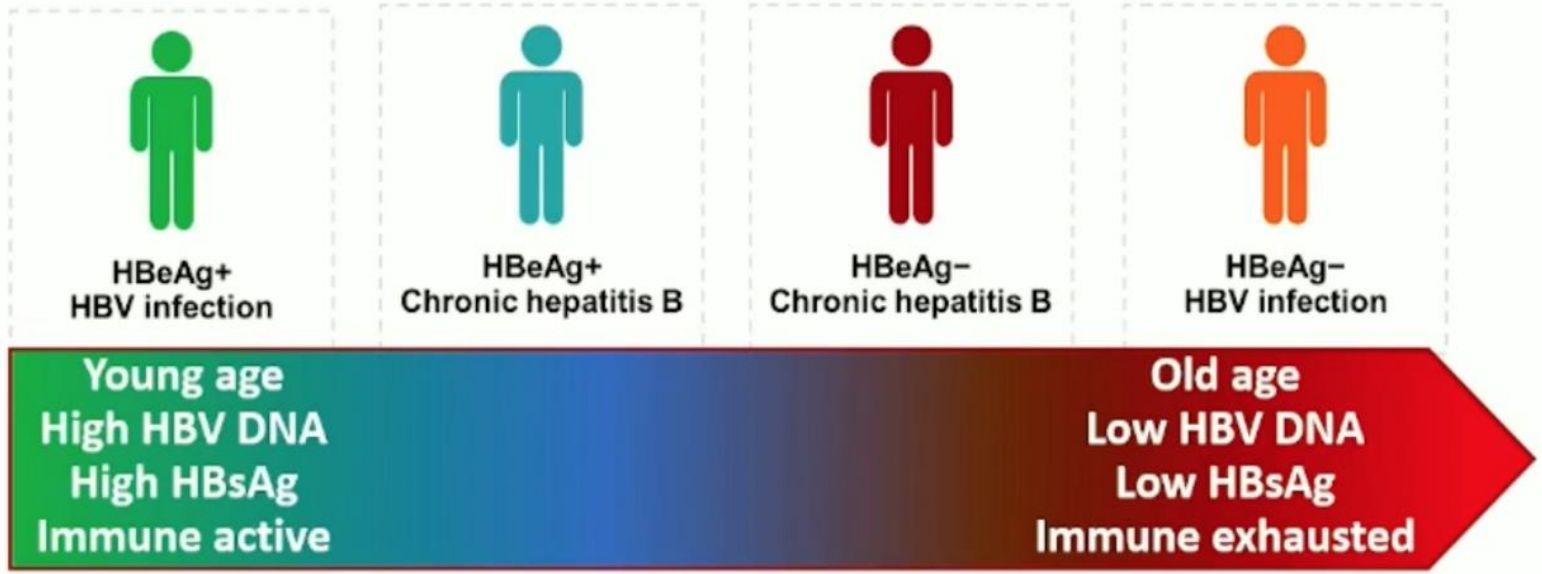
Today we have **many** Novel Therapies to choose from

Inhibit Viral Replication	Lower Viral Antigen Burden	Boost Immune Response
NUC	siRNA	Peg IFN-α
ASPIN	ASO/LNA	RIG-I agonist
CAM	RNA destabilisers	TLR7 agonist
Entry inhibitor	Nucleic Acid Polymers	TLR8 agonist
FXR agonist	S-AgTransport Inhibiting Oligonucleotide Polymers	ALPK1 agonist
Transcription inhibitor		Therapeutic vaccines
HBx inhibitor		Anti-PD-1/L1
		Anti-HBs
		TCR-redirected CD8 cells

HBV biomarkers and new antiviral targets



Fanning GC et al. Nat Rev Drug Discov. 2019



- Should we be trying to cure EVERY patient who is **HBsAg positive** regardless of his/her disease phase?

- Will the future be cccDNA targeting therapies?

INDIRECT APPROACHES

Silencing of cccDNA transcriptional activity

Epigenetic modifiers

KDM5 demethylase inhibitor

FXR agonist

HBx inhibitor

DIRECT APPROACHES

Eliminate/ inactivate cccDNA

±

Eliminate infected cells

Gene-editing CRISPR Cas-9

Base-editing Cas-9

IFN-α

Lymphotoxin -β receptor agonist

Shock & Kill IMC-I109V

Real benefit of functional cure: patients' view

1 pill a day
2 visits / year

pills +/- sc/iv
Weekly-monthly visits for 12 months
Blood tests /Biopsies/FNAs..

HBV gestione clinica corrente e prospettive di eradicazione - Messaggi Chiave

- 250 milioni di soggetti con infezione cronica senza prospettive di decremento
- Nuova nomenclatura → Epatite cronica ed infezione cronica HBeAg+ ed HBeAg-
- Obiettivi del trattamento: dal controllo replicazione virale alla clearance di HBsAg
- La clearance di HBsAg si associa ad un decremento del rischio di HCC ed a maggiore sopravvivenza (nel contesto asiatico) → obiettivo clinico significativo
- Vanno trattate l'epatite cronica HBeAg+ ed HBeAg- e l'infezione cronica HBeAg+ ad alto rischio con terapia long term con NUC o finite con PegIFNα
- Sospendere i NUC per ottenere la clearance dell' HBsAg non è ancora una buona idea→ migliore selezione dei pazienti
- Ruolo del Peg IFNα in combinazione possibile in pazienti selezionati
- Cura funzionale un obiettivo complesso ed ambizioso in funzione dello stato immunologico del paziente, del carico antigenico e del reservoir intraepatico
- I tentative di cura funzionale hanno un triplice bersaglio: replicazione HBV, sintesi e release antigeni e risposta immune → ruolo di strategie di combinazione
- In alcuni pazienti potrebbe essere rilevante una terapia diretta su cccDNA
- Il rapporto costo beneficio di una potenziale cura funzionale va "calato" nella real life