STI

STPI
Société Tunisienne
de Pathologie Infectieuse

الجمعية التونسية للفرماكولوجيا
Association Tunisienne de Pharmacologie
ATP

Gestion du risque d'HBV sous immunosuppresseurs

Le 08/01/2026

Dr Hana CHAABOUNI
AHU en maladies infectieuses
CHU Hedi Chaker, Sfax

INTRODUCTION

- **Réactivation du virus de l'hépatite B (HBVr) :** Initialement en cas de **lymphome sous chimiothérapie** (1970-1980).

- **Autres contextes :** la néphrologie, la rhumatologie, la gastro-entérologie, la transplantation d'organes ...

- **Sujet d'actualité**

- Plusieurs nouvelles molécules, impossibilité d'éradiquer le VHB

PLAN

- Rappel
- Mécanismes physiopathologiques HBV r
- Définition d’une HBV r
- Facteurs de risque d’une HBV r
- Traitement antiviral et prévention de HBV r
- Comment surveiller un patient à risque de HBV r sous IS?

Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

Gastroenterology 2025;168:267–284

GUIDELINES

AGA Clinical Practice Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation in At-Risk Individuals

Faisal S. Ali,[1] Mindie H. Nguyen,[2,3,4] Ruben Hernaez,[5,6,7] Daniel Q. Huang,[8,9] Julius Wilder,[10,11] Alejandro Piscoya,[12] **Tracey G. Simon,**[13,§] and **Yngve Falck-Ytter**[14,15,§]

---

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Check for updates

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Seminar

Check for updates

JOURNAL OF HEPATOLOGY

Hepatitis B virus reactivation associated with new classes of immunosuppressants and immunomodulators: A systematic review, meta-analysis, and expert opinion

George V. Papatheodoridis[1,†], Vasileios Lekakis[1,†], Thodoris Voulgaris[1,†], Pietro Lampertico[2,3], Thomas Berg[4], Henry L.Y. Chan[5], Jia-Horng Kao[6], Norah Terrault[7], Anna S. Lok[8,*,#], K. Rajender Reddy[9,*,#]

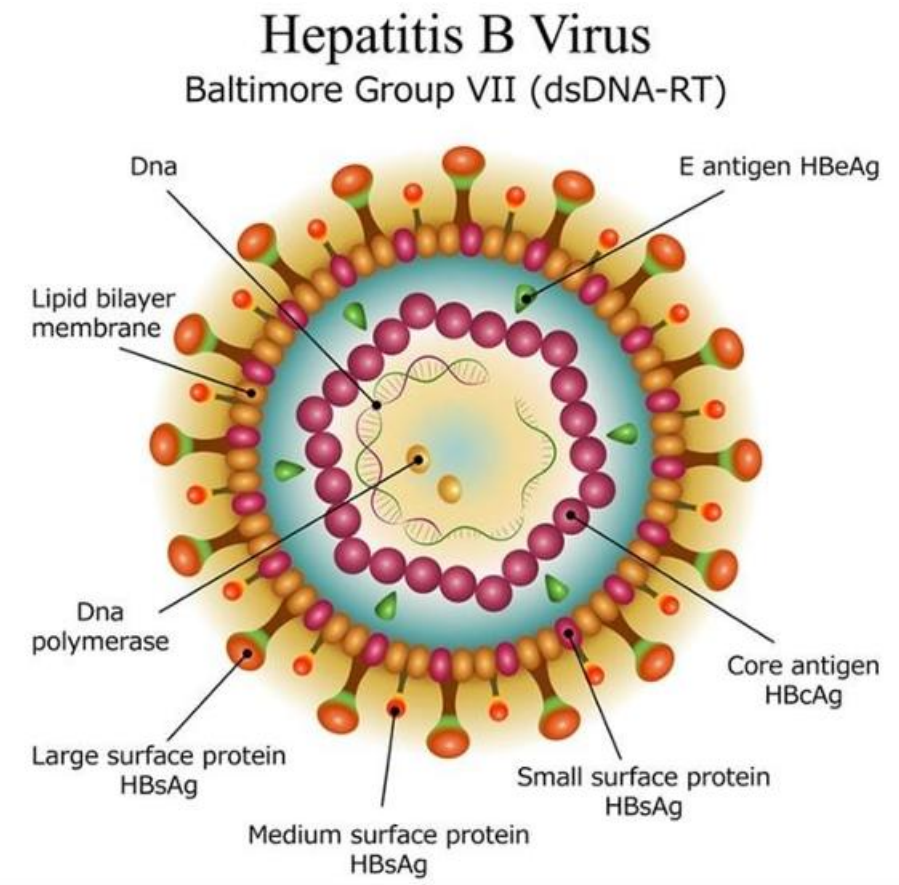
Hepatology International (2021) 15:1031–1048
https://doi.org/10.1007/s12072-021-10239-x

GUIDELINES

Check for updates

APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy

RAPPEL



HbsAg: infection active (aiguë ou chronique)

Anti-Hbs: immunité (naturelle ou post-vaccinale)

Anti-Hbc:

- IgM: hépatite B aigue
- IgG: hépatite B chronique ou ancienne

HbeAg: infection active (marqueur de réplication virale)

Anti-Hbe: hépatite B chronique ou guérie

HBV-DNA: marqueur de réplication virale

RAPPEL

AgHBs	Anti-HBc	Anti-HBs	Interprétation
+	IgM	-	Hépatite B aigue
+	+	-	Hépatite B chronique
-	+	+	Hépatite B résolue
-	+	-	Hépatite B résolue avec perte des anti-HBs Hépatite B occulte, faux positifs
-	-	+	Immunité post-vaccinale
-	-	-	Non immun et non infecté

CYCLE VIRAL

1.Entrée

2. Décapsidation et transport vers le noyau

3. Formation de ccc DNA

4. Transcription

5.Traduction

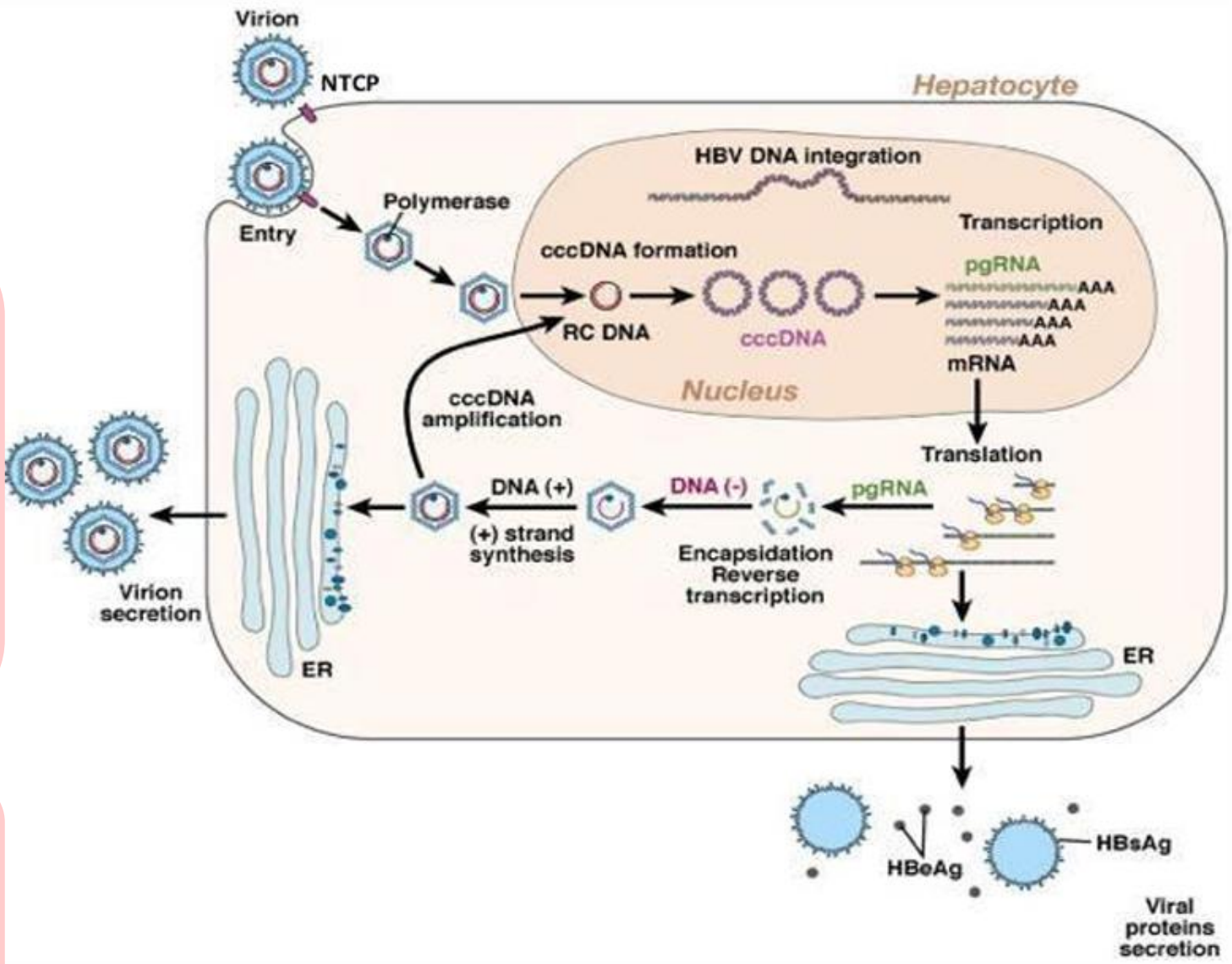
6. Encapsidation et réplication inverse

7. Assemblage et sécrétion

1.cccDNA : Réservoir du virus

2.Pas d'éradication avec les ttt actuels.

3. A l'origine de réactivation



Zoulim et al., Gastroenterology, Volume 137, Issue 5, 1593 – 1608, 2002

HISTOIRE NATURELLE DU VHB

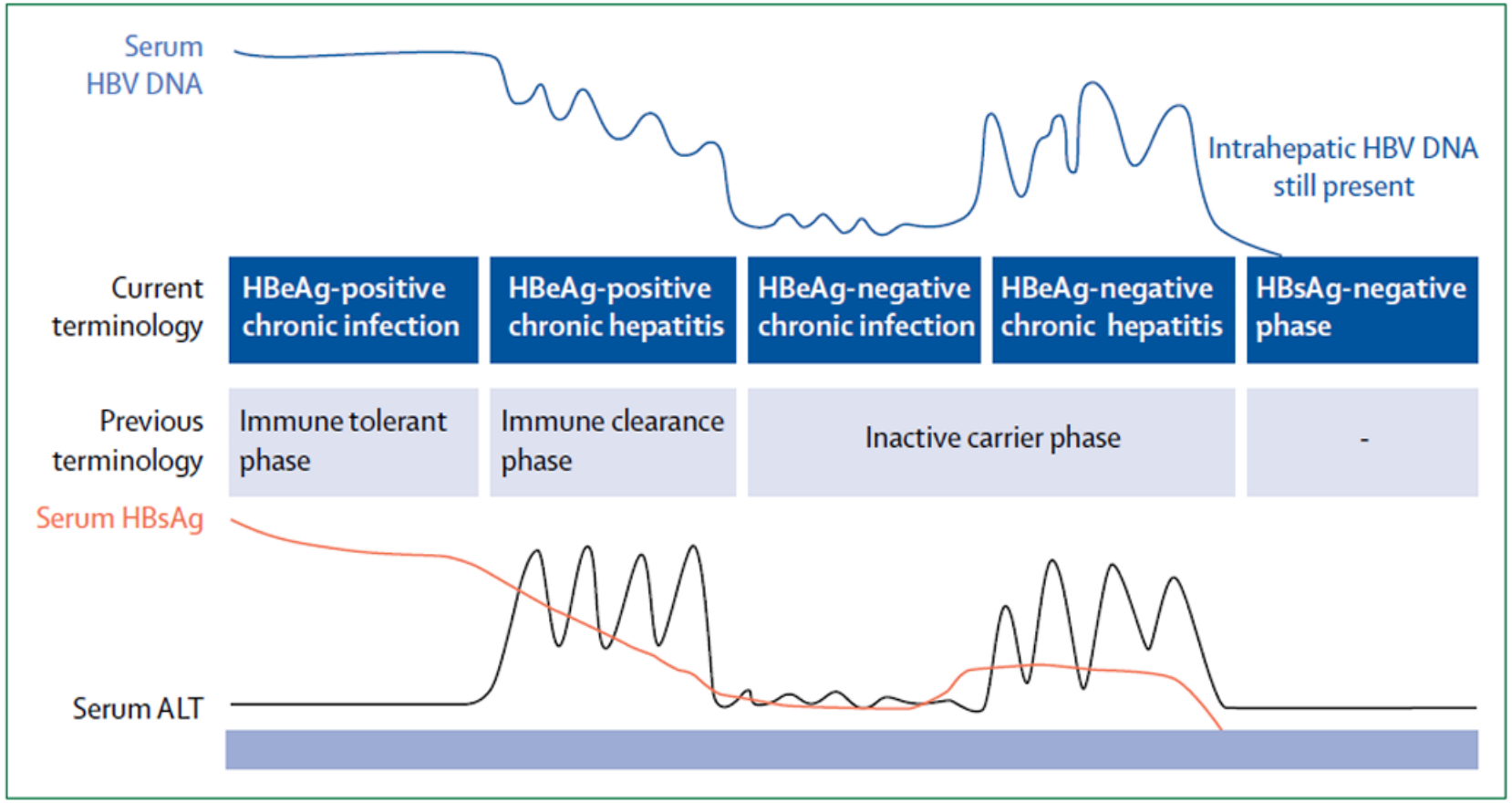
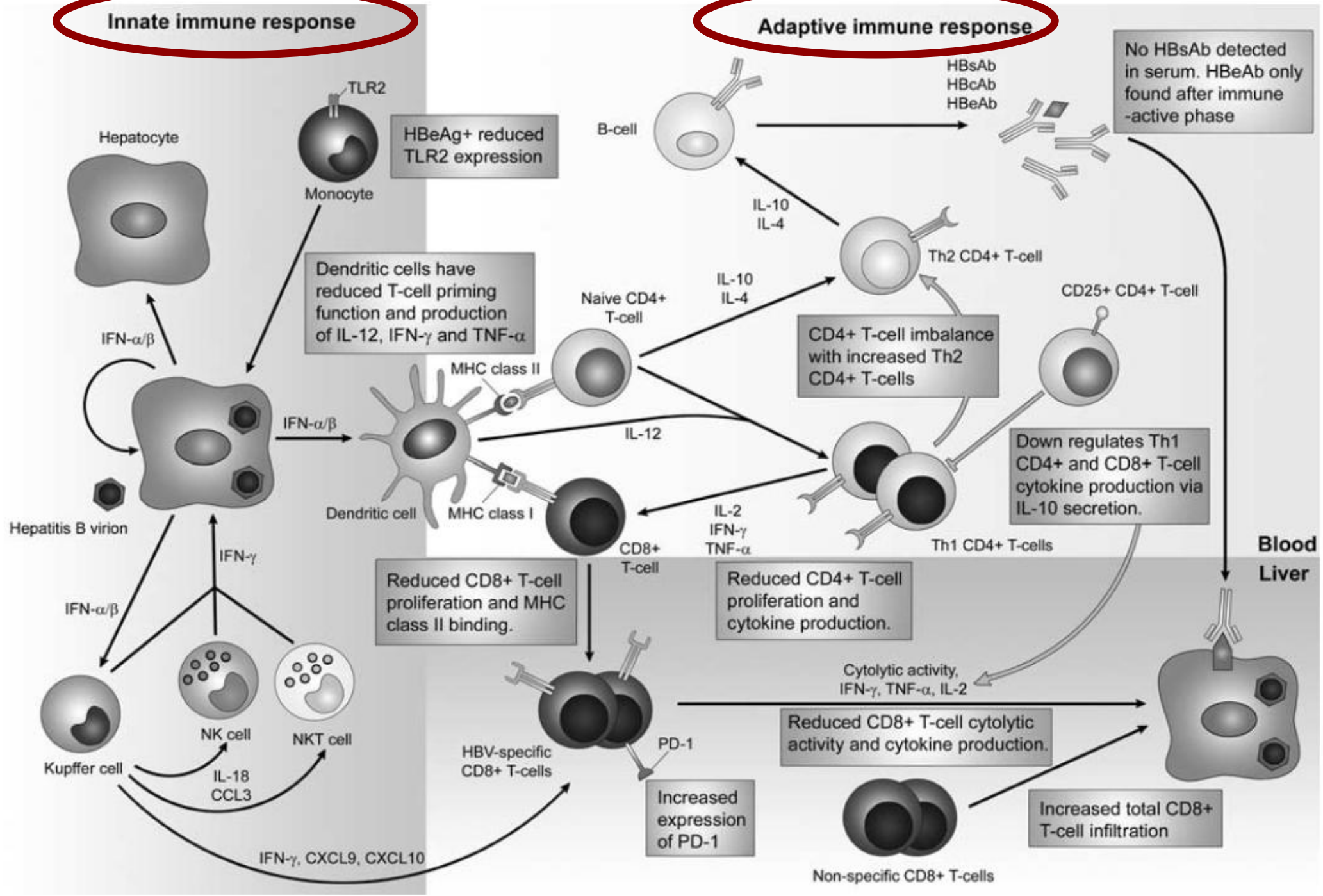


Figure 2: Different phases of chronic HBV infection in relation to the kinetics of serum HBV DNA, HBsAg, and ALT

ALT=alanine aminotransferase. HBV=hepatitis B virus.

Modulées par les interactions le système immunitaire de l'hôte et le virus

Seto, Lancet 2018


Innate immune response
Adaptive immune response
TLR2
HBeAg+ reduced TLR2 expression
Hepatocyte
Monocyte
Dendritic cells have reduced T-cell priming function and production of IL-12, IFN-γ and TNF-α
IFN-α/β
IFN-α/β
Hepatitis B virion
IFN-γ
IFN-α/β
NK cell
NKT cell
Kupffer cell
IL-18
CCL3
IFN-γ, CXCL9, CXCL10
MHC class II
Dendritic cell
MHC class I
Naive CD4+ T-cell
IL-10
IL-4
IL-12
CD8+ T-cell
IL-2
IFN-γ
TNF-α
Reduced CD8+ T-cell proliferation and MHC class II binding.
Reduced CD4+ T-cell proliferation and cytokine production.
B-cell
HBsAb
HBcAb
HBeAb
No HBsAb detected in serum. HBeAb only found after immune -active phase
IL-10
IL-4
Th2 CD4+ T-cell
CD4+ T-cell imbalance with increased Th2 CD4+ T-cells
CD25+ CD4+ T-cell
Down regulates Th1 CD4+ and CD8+ T-cell cytokine production via IL-10 secretion.
Th1 CD4+ T-cells
Blood
Liver
Cytolytic activity, IFN-γ, TNF-α, IL-2
Reduced CD8+ T-cell cytolytic activity and cytokine production.
HBV-specific CD8+ T-cells
PD-1
Increased expression of PD-1
Non-specific CD8+ T-cells
Increased total CD8+ T-cell infiltration

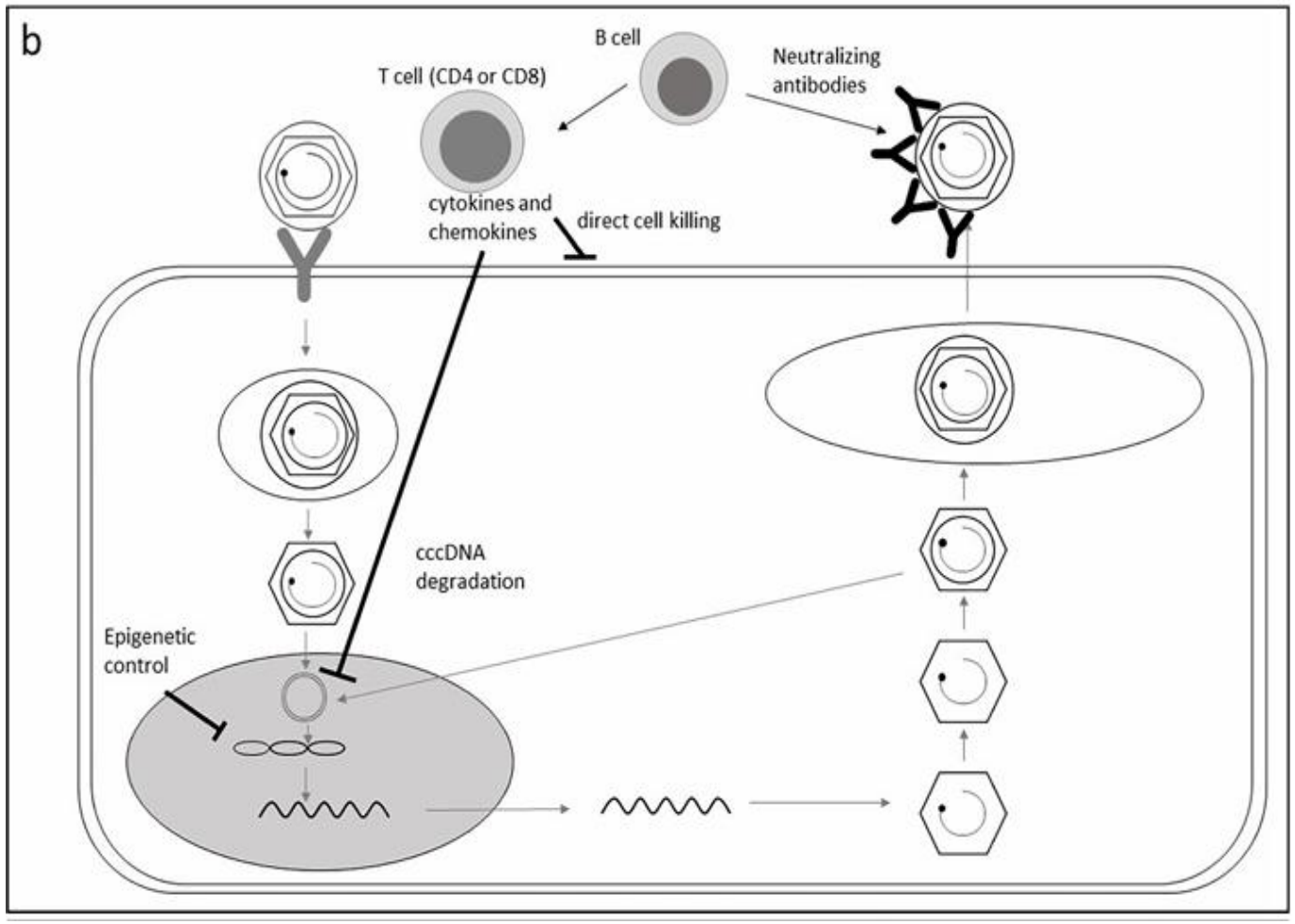
Les LT : mécanismes **cytopathiques** + Suppression de la réplication virale médiées par des **cytokines**

Production d'Ac empêche la propagation virale et élimine les virus.

Les cytokines: réponse antivirale de l'hôte avec **dégradation du cccDNA**

Les chimiokines: réponse inflammatoire locale + activation des LT
→ **Contrôle immunitaire sur réplication intra hépatocytaire** du VHB

Présence d'une histone déacétylase contrôle épigénétique de l'expression des gènes du VHB



Etienne. J Gen Intern Med 2022

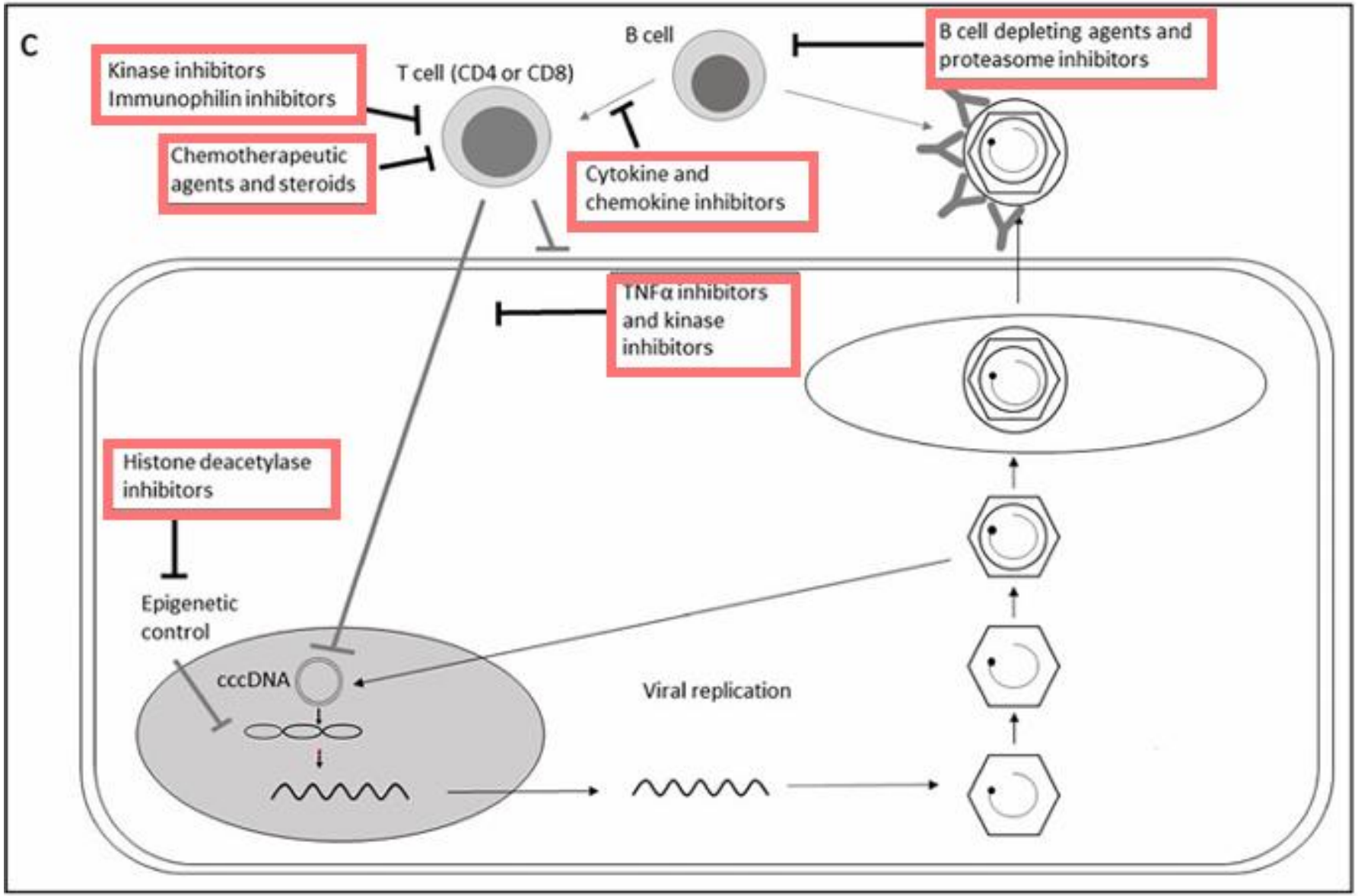
Mécanismes physiopathologiques HBV r

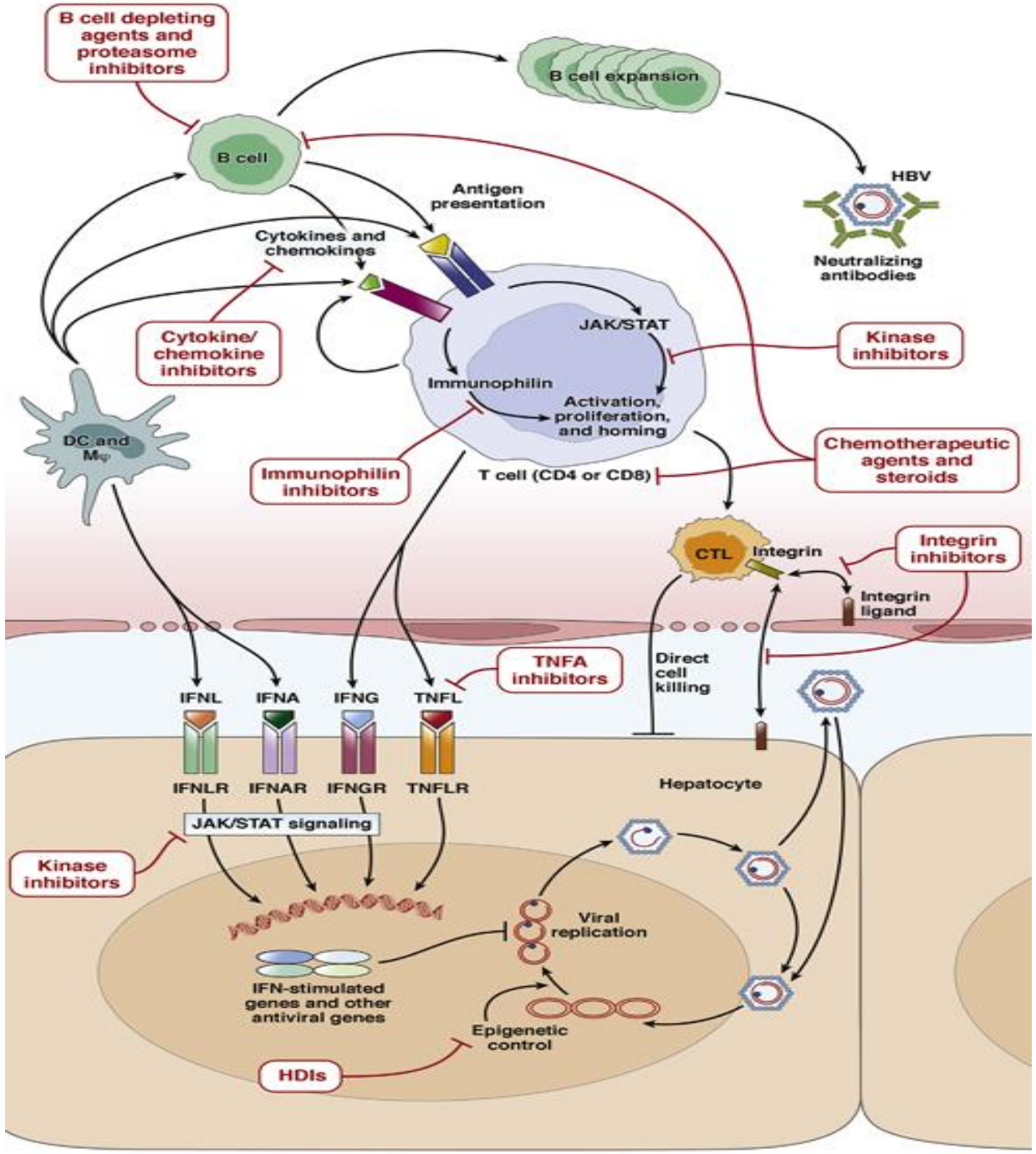
Mécanismes physiopathologiques HBV r

Spontanée

Facteurs déclenchants

Infection par le VIH
Déficit immunitaire
Grossesse
Traitement IS/IM


C
B cell
B cell depleting agents and proteasome inhibitors
Kinase inhibitors
Immunophilin inhibitors
T cell (CD4 or CD8)
Chemotherapeutic agents and steroids
Cytokine and chemokine inhibitors
TNFα inhibitors and kinase inhibitors
Histone deacetylase inhibitors
Epigenetic control
cccDNA
Viral replication



VHB r sous IS : résulte de la perte du contrôle immunitaire à plusieurs niveaux.

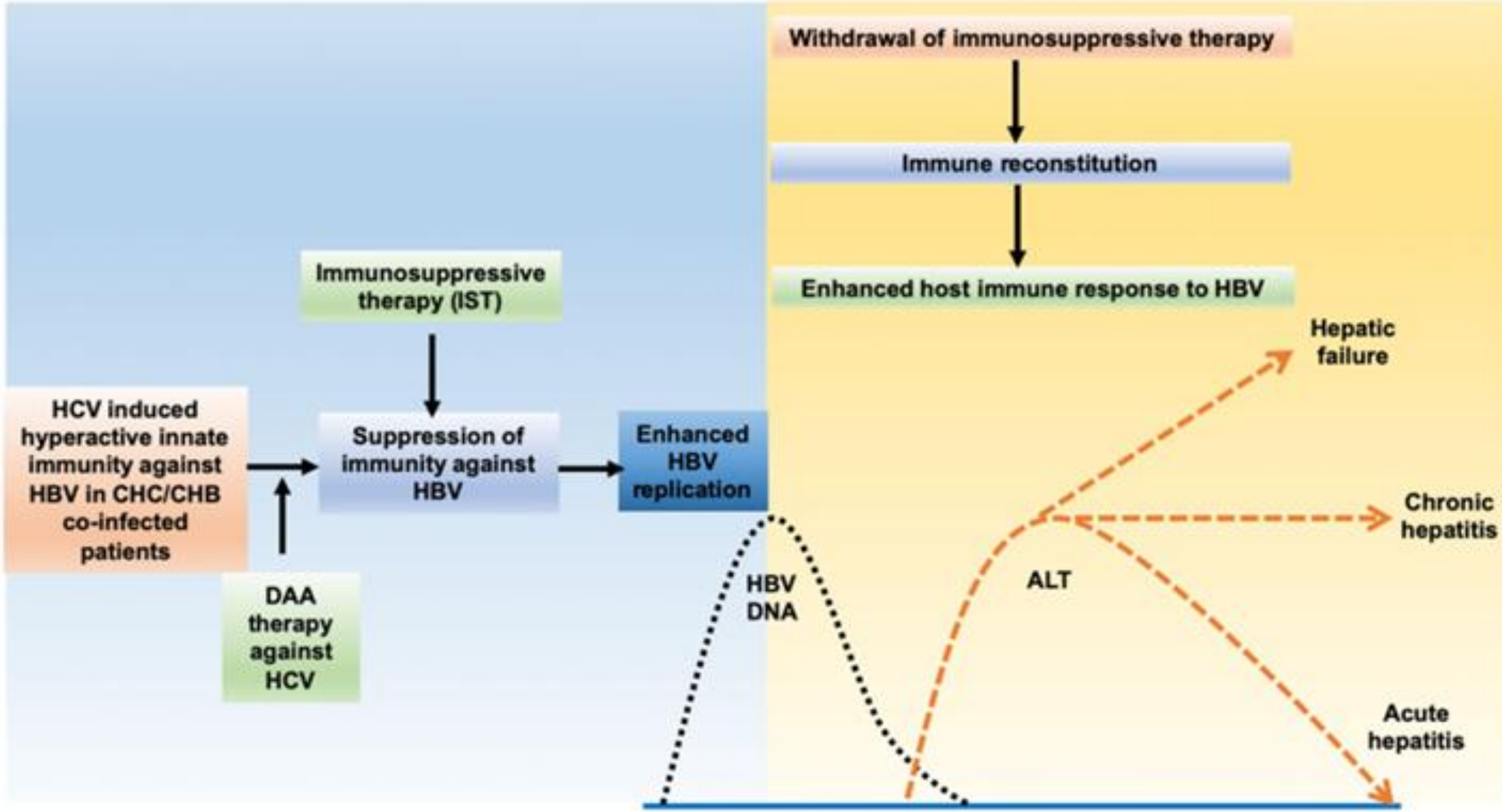
Les agents déplétant les cellules B, suppriment la production d'Ac et la mémoire immunitaire
→ **Risque élevé et tardif de HBVr.**

Les corticoïdes, chimiothérapies et inhibiteurs de kinases altèrent les LT
→ Réduction du contrôle cytotoxique du virus.

Les anti-TNF et inhibiteurs de cytokines bloquent le contrôle médié par les cytokines.

Les inhibiteurs de la voie JAK/STAT empêchent l'action antivirale des INF au niveau de l'hépatocyte → réplication virale à partir du cccDNA.

Loomba R. Hepatitis B reactivation associated with immune suppressive and biological modifier therapies: current concepts, management strategies and future directions. Gastroenterology. Mai 2017


Withdrawal of immunosuppressive therapy
Immune reconstitution
Enhanced host immune response to HBV
Immunosuppressive therapy (IST)
HCV induced hyperactive innate immunity against HBV in CHC/CHB co-infected patients
Suppression of immunity against HBV
Enhanced HBV replication
DAA therapy against HCV
Hepatic failure
Chronic hepatitis
Acute hepatitis
HBV DNA
ALT

Cas clinique

Votre collègue hématologue vous appelle pour un avis concernant une **cytolyse aiguë :**

- Un patient de 48 ans, ATCD d'**hépatite B au jeune âge.**
- Lymphome non hodgkinien de haut grade.
- 6 ème **cure R-CHOP.**
- Dernière cure il y a 10 jours, compliquée d'une neutropénie fébrile, **sous ATB à large spectre**.

Cas clinique

- **Biologie :**
  - NFS 3000/10,1/56000
  - ASAT : 984 UI/mL, ALAT : 1512 UI/mL, GGT: 1769 UI/ml, PAL : 257 UI/Ml, BT 38 UI/mL
  - TP 71%

Étiologies possibles de cette cytolyse ?

Cas clinique

- Hépatite médicamenteuse (CT, ATB)
- Hépatite C aigue
- Hépatite A
- Réactivation du VHB

Quels examens à demander ?

Définition d’une HBVr

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Chronic HBV	+	+	Undetectable	HBV DNA detectable > 1000 IU/mL

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Chronic HBV	+	+	Undetectable	HBV DNA detectable > 1000 IU/mL
	+	+	Detectable	HBV DNA increases > 100-fold or > 2 $\log_{10}$ compared with baseline value

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Chronic HBV	+	+	Undetectable	HBV DNA detectable > 1000 IU/mL
	+	+	Detectable	HBV DNA increases > 100-fold or > 2 $\log_{10}$ compared with baseline value
	+	+	Unknown	HBV DNA >10,000 IU/mL

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Resolved HBV	–	+	Undetectable	Detection of any DNA (even if not quantifiable) -or- HBs Ag (+) (i.e., reverse seroconversion)

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Resolved HBV	−	+	Undetectable	Detection of any DNA (even if not quantifiable) -or- HBs Ag (+) (i.e., reverse seroconversion)
	−	+	Detected but not quantifiable	HBV DNA ≥ 100 IU/mL

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Resolved HBV	−	+	Undetectable	Detection of any DNA (even if not quantifiable) -or- HBs Ag (+) (i.e., reverse seroconversion)
	−	+	Detected but not quantifiable	HBV DNA ≥ 100 IU/mL
	−	+	Detectable and quantifiable	≥ 1 $\log_{10}$ increase in HBV DNA

HBcAb hepatitis B core antibody, *HBsAg* hepatitis B surface antigen, *HBV* hepatitis B virus, *HBVr* hepatitis B reactivation

DEFINITION

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

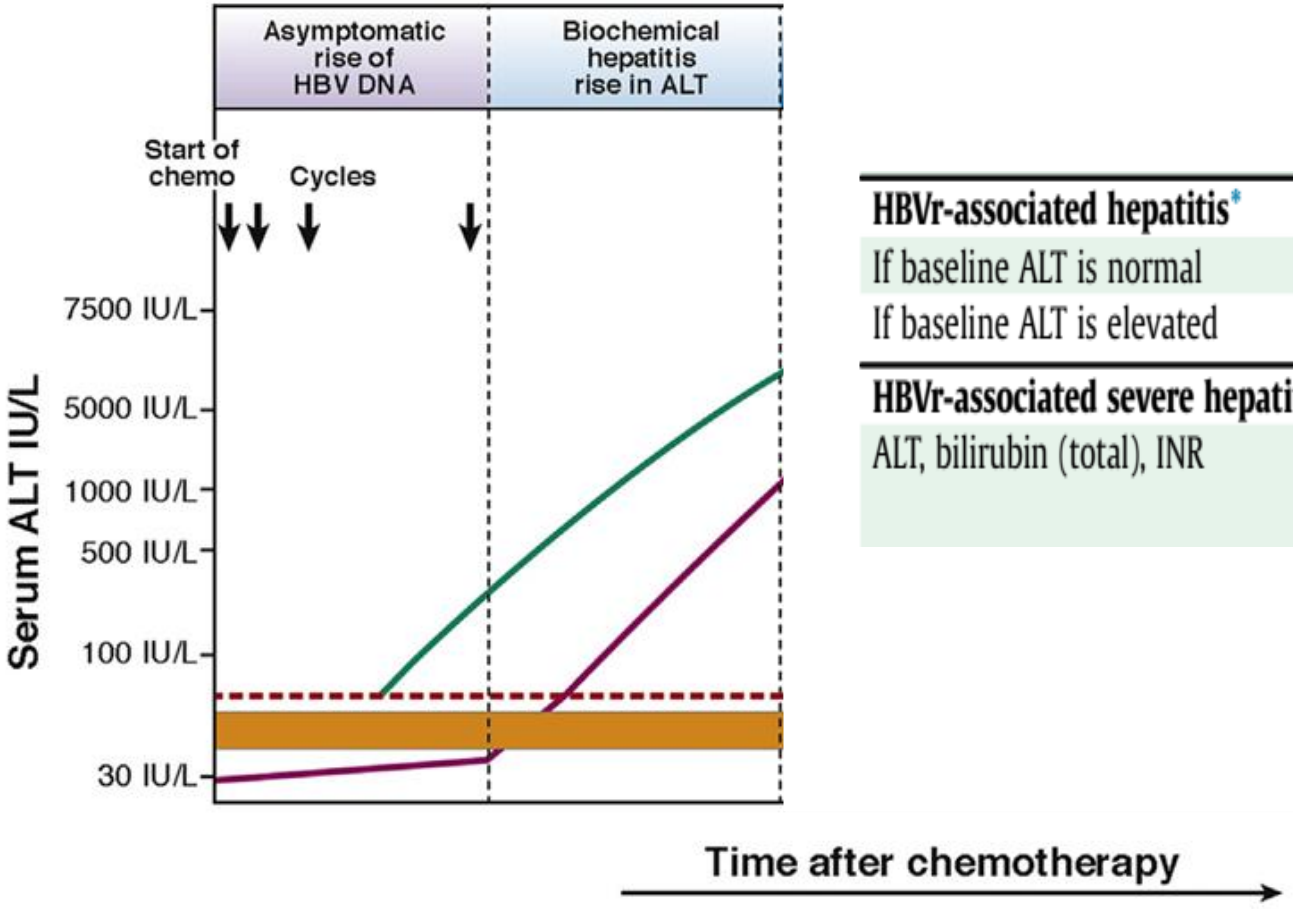
Accepted: 18 January 2024 / Published online: 14 February 2024

Status of HBV infection	Baseline serologies			HBVr diagnostic criteria
	HBsAg	HBcAb	DNA	
Chronic HBV	+	+	Undetectable	HBV DNA detectable > 1000 IU/mL
	+	+	Detectable	HBV DNA increases > 100-fold or > 2 $\log_{10}$ compared with baseline value
	+	+	Unknown	HBV DNA >10,000 IU/mL
Resolved HBV	−	+	Undetectable	Detection of any DNA (even if not quantifiable) -or- HBs Ag (+) (i.e., reverse seroconversion)
	−	+	Detected but not quantifiable	HBV DNA ≥ 100 IU/mL
	−	+	Detectable and quantifiable	≥ 1 $\log_{10}$ increase in HBV DNA

HBcAb hepatitis B core antibody, *HBsAg* hepatitis B surface antigen, *HBV* hepatitis B virus, *HBVr* hepatitis B reactivation

Seuils ≠ en fonction des reco

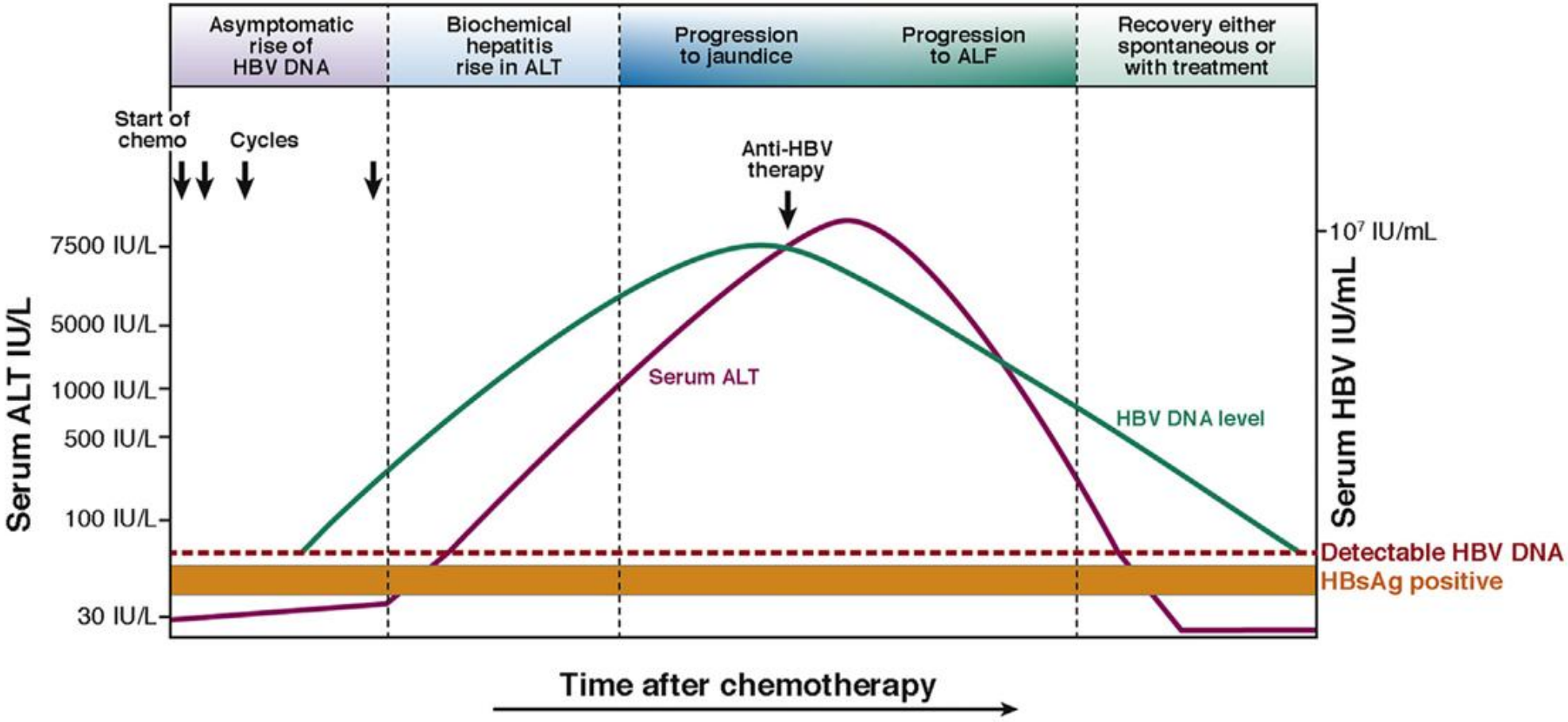
COMPLICATION D'UNE REACTIVATION



HBVr-associated hepatitis*	
If baseline ALT is normal	≥3x ULN
If baseline ALT is elevated	≥3x baseline
HBVr-associated severe hepatitis*	
ALT, bilirubin (total), INR	ALT ≥10x ULN or baseline or ALT ≥3x ULN or baseline AND bilirubin >2x ULN or INR >1.5**

Papatheodoridis, J Hepatol 2022

COMPLICATION D'UNE REACTIVATION



COMPLICATION D'UNE REACTIVATION

Hepatitis B reactivation during cancer chemotherapy: an international survey of the membership of the American Association for the Study of Liver Diseases

J. P. Hwang,[1] A. G. Barbo[2] and R. P. Perrillo[3] [1]Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; and [3]Hepatology Division, Baylor University Medical Center, Dallas, TX, USA

prophylaxie 18/188

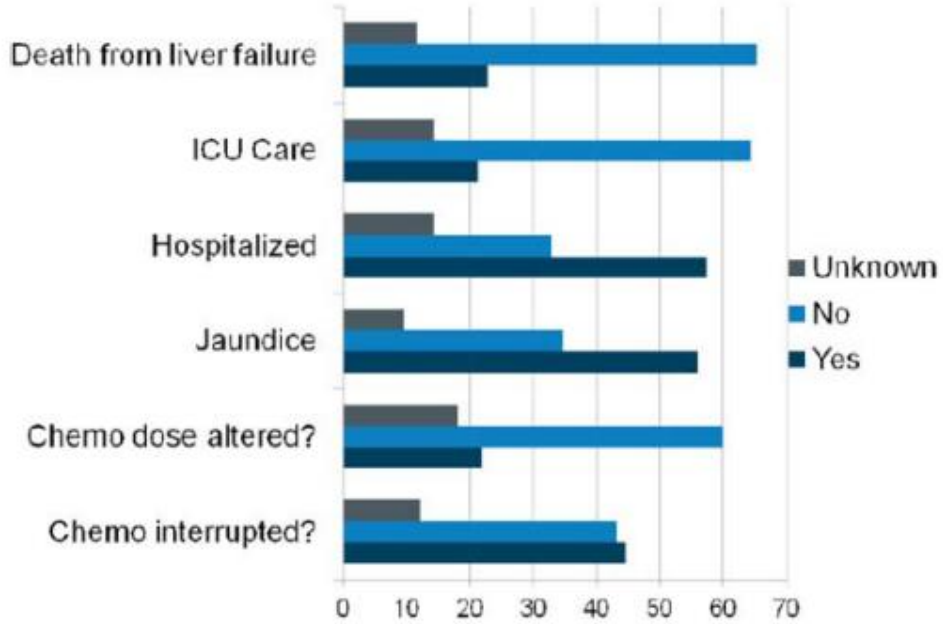


Figure 2. Clinical outcomes of HBV reactivation in 188 patients. This study revealed that interruption of cancer chemotherapy, defined as either delay in initiation or premature discontinuation, was common. Based on data presented in reference 10.

Hwang et al. J Viral Hep 2015

Facteurs de risque d’une HBV r

FACTEURS DE RISQUE DE REACTIVATION

Facteurs liés à l’hôte

Facteurs liés au virus

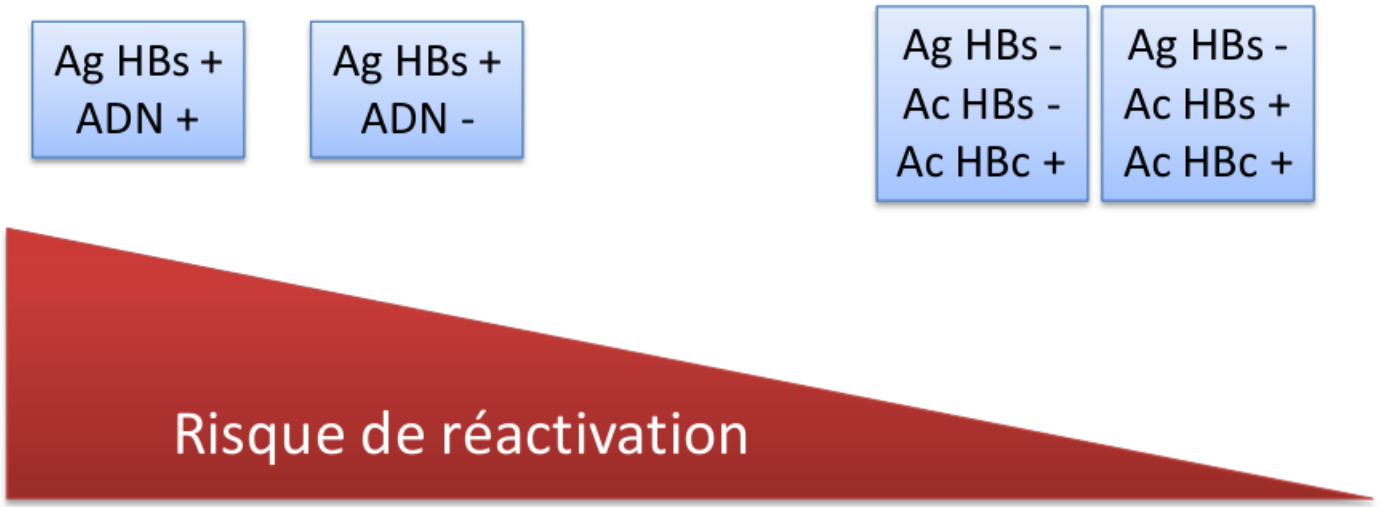
Facteurs liés au traitement

FACTEURS DE RISQUE DE REACTIVATION

Therapy	HBsAg+ patients n/N	HBsAg+ patients Pooled risk (95% CI) or overall percent	HBsAg-/anti-HBc+ patients n/N	HBsAg-/anti-HBc+ patients Pooled risk (95% CI) or overall percent
Anti-TNF		n.a.	16/1564	1% (1-2%)
Immune check point inhibitors	6/56	11% (5-22%)[1]	2/1,006	0% (0-1%)
Tyrosine kinase inhibitors	20/189	11% (7-16%)	0/72	0%*
Cytokine inhibitors	16/45	36% (23-50%)	6/235	3% (1-6%)
T cell-depleting agents	4/42	9.5%*	0/34	0%*
CAR T-cell immunotherapy	-	Unknown[2]	4/112	4% (1-9%)
Corticosteroids	8/72	11%*	41/2138	3% (1-6%)
Anti-proliferative agents	9/50	18%*	0/37	0%*
Alkylating agents	17/133	13%*	0/8	0%*
Calcineurin inhibitors	1/4	25%*	14/137	10%*
mTOR inhibitors	4/26	15%*	-	Unknown
Janus kinase inhibitors	-	Unknown	30/213	14%*

Papatheodoridis, J Hepatol 2022

FACTEURS DE RISQUE DE REACTIVATION



Réactivations	46%
Hépatites	33%
Décompensations	13%
Décès	5%

Loomba, 2008

Réactivations 5%

Lok, 1991 Hui,2006

FACTEURS DE RISQUE DE REACTIVATION

PLOS MEDICINE

RESEARCH ARTICLE

Incidence, risk factors, and clinical outcomes of HBV reactivation in non-liver solid organ transplant recipients with resolved HBV infection: A systematic review and meta-analysis

Saifu Yin[1,2], Fan Zhang[1,2], Jiapei Wu[1,2], Tao Lin[1,2]*, Xianding Wang[1,2]*

1 Department of Urology/Institute of Urology, West China Hospital, Sichuan University, Chengdu City, Sichuan Province, China, **2** Organ Transplantation Center, West China Hospital, Sichuan University, Chengdu City, Sichuan Province, China

* kidney1234@163.com (TL); xiandingwang@outlook.com (XW)

Journal of Hepatology
Volume 69, Issue 2, August 2018, Pages 286-292

Research Article

Quantification of HBV core antibodies may help predict HBV reactivation in patients with lymphoma and resolved HBV infection

Hung-Chih Yang [1 †], Hsiao-Hui Tsou [2 3 †], Sung-Nan Pei [4], Cheng-Shyong Chang [5], Jia-Hong Chen [6], Ming Yao [1], Shyh-Jer Lin [7], Johnson Lin [8], Quan Yuan [9 ‡], Ningshao Xia [9 ‡], Tsang-Wu Liu [10], Pei-Jer Chen [1 11], Ann-Lii Cheng [1 12 13 14], Chiun Hsu [12 13 14], Taiwan Cooperative Oncology Group

Risk factors of HBV reactivation

Nine studies reported crude risk factors of HBV reactivation (S3 Table). Pooled results showed that negative anti-HBs status (random-effects, 34/421 versus 27/1,727; crude odds ratio [OR] 5.05; 95% CI [2.83, 9.00]; $p < 0.001$) was associated with higher risk of HBV reactivation, without heterogeneity ($I^2 = 0\%$; $p_{heterogeneity} = 0.539$) (Fig 5 and S7 Table). Further analyses found that there was no statistically significant difference in the incidence of HBV reactivation in recipients with anti-HBs >100 IU/L compared with those with anti-HBs at 10 to 100 IU/L (random-effects, 1/113 versus 3/96, crude OR 0.28; 95% CI [0.03, 2.71]; $p = 0.270$). ABO blood

HBV reactivation occurred in 24 of the 197 patients enrolled, with an incidence of 11.6/100 person-years. For the 192 patients with enough serum samples for analysis, low anti-HBs (<56.48 mIU/ml) and high anti-HBc (≥6.41 IU/ml) at baseline were significantly associated with high risk of HBV reactivation (hazard ratio [HR] 8.48 and 4.52, respectively; $p < 0.01$). The multivariate analysis indicated that (1) patients with both high anti-HBc and low anti-HBs at baseline (36 of 192 patients) had an HR of 17.29 for HBV reactivation (95% CI 3.92–76.30; $p < 0.001$), and (2) HBV reactivation may be associated with inferior overall survival (HR 2.41; 95% CI 1.15–5.05; $p = 0.02$).

FACTEURS DE RISQUE DE REACTIVATION

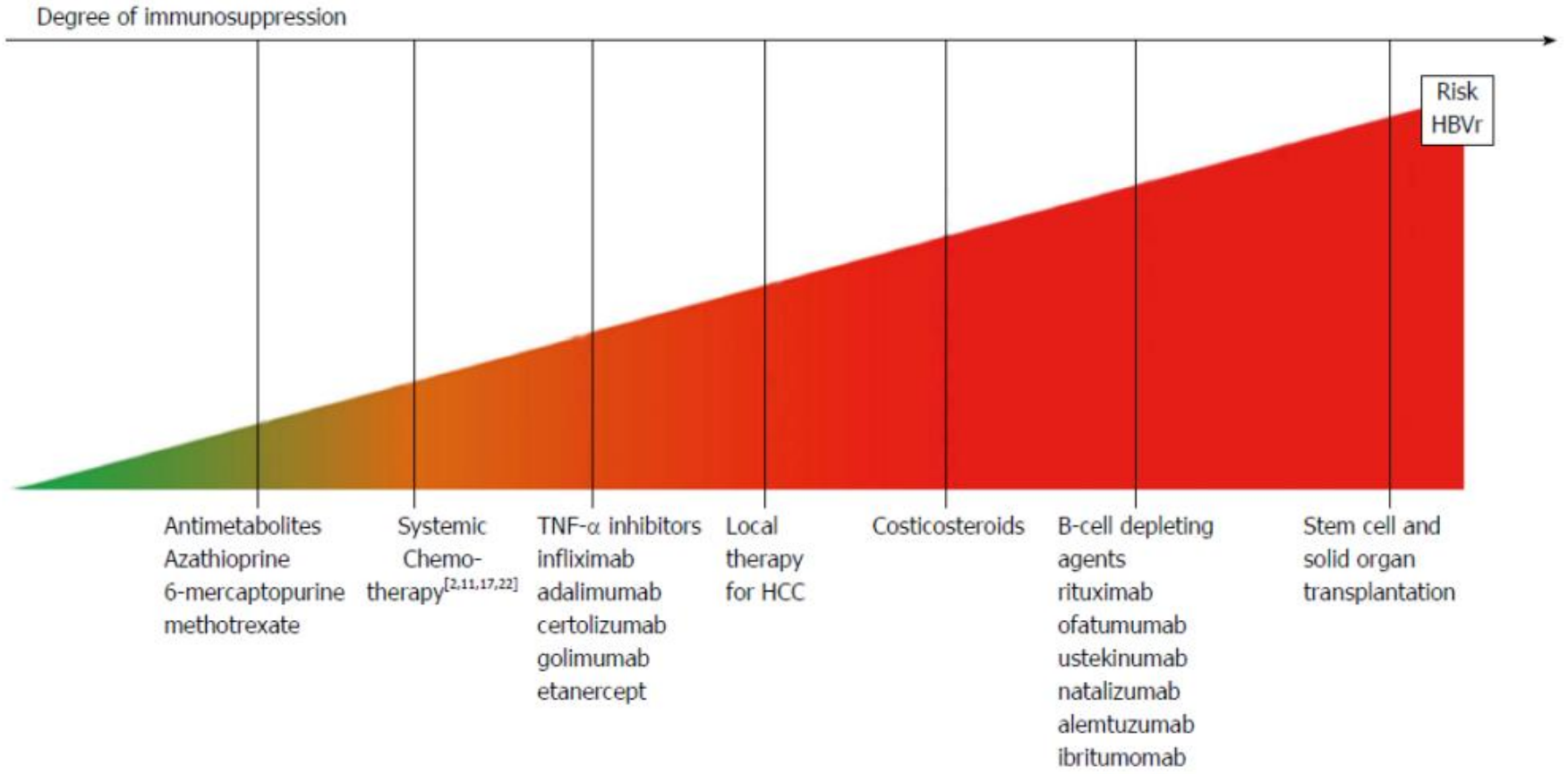


Figure 2 Immunosuppressing agents and related risk of hepatitis B reactivation. HCC: Hepatocellular carcinoma; TNF-α: Tumor necrosis factor-α; HBVr: Hepatitis B virus reactivation.

Bessone and Dirchwolf, WJH 2016

FACTEURS DE RISQUE DE REACTIVATION

Table 1. Incidence of Hepatitis B reactivation due to immunosuppression according to disease

Disease	Incidence of HBV reactivation without HBV prophylaxis		References
	HBsAg positive (%)	HBsAg negative/anti-HBc positive (%)	
Lymphoma	18-73	34-68	6, 10, 33, 51-53
Acute leukaemias	61	2.8-12.5	31, 32
Chronic leukaemias	NA*	NA*	NA*
Multiple myeloma	NA	6.8-8	24, 47
Bone marrow/haematopoetic stem cell transplantation	66-81	6-10	13, 59, 61
Breast cancer	21-41	NA	14, 134, 157, 158
Nasopharyngeal cancer	33	NA	66
Hepatocellular cancer (systemic chemotherapy)	36	11	68, 159
Hepatocellular cancer (trans-arterial chemoembolization)	21-30	9.3	71-73
Rheumatoid arthritis	12.3	3-5	160-163
Psoriasis/psoriatic arthritis	NA*	NA*	NA*
Inflammatory bowel disease	36	0-7*	80, 81
Autoimmune diseases	NA*	17*	92
Renal Transplantation	45-70	0.9	93, 97-99

HBV, hepatitis B virus; NA, not available..
*Case reports or small case series reporting HBV reactivation.

Pattullo, Clin Molec Hepatol 2016

FACTEURS DE RISQUE DE REACTIVATION

Facteurs liés à l'hôte

- Age > 50 ans
- Sexe masculin
- Hémopathie
- Hépatopathie
- GVH chronique
- Incompatibilité ABO
- Rejet de greffe

Facteurs liés au virus

- ADN VHB détectable
- AgHBs +
- Ac anti HBc +
- Ac anti HBs -

Facteurs liés au traitement

- Déplétant les LB
- Anti TNF
- Greffe de CSH

STRATIFICATION

Faible <1%

Modéré 1-10%

Elevé >10%

En fonction du statut sérologique

Molécule IS/IM

EASL 2025, APASL 2021, AGA 2025

Si on revient à notre patient…

- Profil Ac anti-HBc isolés, ADN VHB indétectable.
- Candidat à recevoir un protocole R-CHOP

Quel est le risque de réactivation chez notre patient ?

STRATIFICATION

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Therapy/Medication	Serology	AGA	APASL	EASL
B Cell depleting agents	HBsAg(+)	High risk	High risk [a]	High risk
	HBsAg(−)/ anti-HBc(+)	High risk	High risk [a]	HBV DNA(+): High risk HBV DNA(−): High risk

Rituximab (Rituxan) Obinutuzumab (Gazyva) Ofatumumab (Arzerra)

PR, lupus, vascularite
LLC, lymphome non Hodgkinien

Agent déplétant les LB
Haut risque de HBV r

STRATIFICATION

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Therapy/Medication	Serology	AGA	APASL	EASL
Anti-TNF therapy	HBsAg(+)	High risk	High risk [b]	High
	HBsAg(−)/ anti-HBc(+)	Low risk	Moderate risk [b]	HBV DNA(+): High risk HBV DNA(−): Moderate risk

Infliximab, Adalimumab, Certolizumab et Etanercept

Rhumatologie
Gastro-entérologie
Dermatologie

Gastroenterology 2025;168:267–284

GUIDELINES

AGA Clinical Practice Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation in At-Risk Individuals

Faisal S. Ali,[1] Mindie H. Nguyen,[2,3,4] Ruben Hernaez,[5,6,7] Daniel Q. Huang,[8,9] Julius Wilder,[10,11] Alejandro Piscoya,[12] Tracey G. Simon,[13,§] and Yngve Falck-Ytter[14,15,§]

14 études non-randomisées, 1555 patients

Si anti-HBc + : HBVr : **2 pour 1000**

Si AgHBs + : HBVr **332 pour 1000**

STRATIFICATION

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Therapy/Medication	Serology	AGA	APASL	EASL
Chemotherapy	HBsAg(+)	Anthracyclines addressed and considered high risk	Moderate risk if cytotoxic chemotherapy, except anthracyclines, which are high risk	High risk if high dose combination chemotherapy or anthracyclines
	HBsAg(−)/ anti-HBc(+)	Anthracyclines addressed and considered moderate risk	Low risk if cytotoxic chemotherapy, except anthracyclines and proteasome inhibitors, which are moderate risk	HBV DNA(+): High risk if high dose combination chemotherapy or anthracyclines HBV DNA(−): High risk if high dose combination chemotherapy or anthracyclines
TACE	HBsAg(+)	High risk	High risk	High risk (also radiotherapy, resection, ablation, and systemic therapies)
	HBsAg(−)/ anti-HBc(+)	Moderate risk	Not addressed	HBV DNA(+): High risk (also radiotherapy, resection, ablation, and systemic therapies) HBV DNA(−): High risk in case of TACE therapy.
Tyrosine kinase inhibitor therapy	HBsAg(+)	High risk	High risk [c]	High risk
	HBsAg(−)/ anti-HBc(+)	Moderate risk	Low risk	HBV DNA(+): High risk HBV DNA(−): Moderate risk
JAK inhibitor therapy	HBsAg(+)	High risk	Not addressed	High risk
	HBsAg(−)/ anti-HBc(+)	Moderate risk	Not addressed	HBV DNA(+): High risk HBV DNA(−): Moderate risk

STRATIFICATION

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Therapy/Medication	Serology	AGA	APASL	EASL

Greffe de CSH
Haut risque de HBV r

Allogreffe de CSH : très haut risque +++ (14-78%)
Mortalité : 5-22 % sans prophylaxie
Si Ac anti-HBc isolées : 2,6-42,9%

Autogreffe de CSH : risque moindre
HBV r : **50% si AgHBs + sans ttt**

Stem cell transplantation	HBsAg(+)	Not addressed	High if hematopoietic stem cell transplantation	High risk
	HBsAg(−)/ anti-HBc(+)	Not addressed	High if allogeneic HSCT. Moderate if autologous HSCT.	High risk

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Therapy/Medication	Serology	AGA	APASL	EASL
Azathioprine, methotrexate and mycophenolate mofetil	HBsAg(+)	Low risk [d]	Low risk [d]	Low risk
	HBsAg(−)/ anti-HBc(+)	Low risk [d]	Not addressed	Low risk

Faible risque de HBVr
Azathioprine, MTX, MMF

diseases

MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu

Therapy/Medication	Serology	AGA	APASL	EASL
Steroids therapy	HBsAg(+)	High risk if prednisone dose is ≥10 mg/day ≥ 4 weeks. Moderate risk if the prednisone dose is <10 mg/day ≥ 4 weeks. Low risk at any prednisone dose if for ≤1 week [e]	High risk if prednisone dose is ≥20 mg for ≥4 weeks. Moderate risk if prednisone dose is 10–20 mg/day for ≥4 weeks. Low risk if prednisone dose is <10 mg/day.	High risk if the corticosteroid dose is >20 mg/day for > 4 weeks. Low risk if the corticosteroids dose is <10 mg/day.
	HBsAg(−)/ anti-HBc(+)	Moderate risk if prednisone dose is ≥10 mg/day for ≥4 weeks. Low risk if prednisone dose is <10 mg/day for ≥4 weeks. Low risk at any dose of prednisone if for ≤1 week [e]	Low risk if ≥20 mg prednisone dose.	HBV DNA(+): High risk if the corticosteroid dose is >20 mg for >4 weeks. Low risk if the corticosteroids dose is <10 mg/day. HBV DNA(−): Moderate risk if the corticosteroids dose is >40 mg/day. Low risk if the corticosteroids dose is <40 mg/day for ≤1 week.

La corticothérapie majore le risque de HBV r

Chimiothérapie avec corticoides (26–72%)
Vs
Chimiothérapie sans corticoides (13–26%)

EASL 2025

Risk of reactivation	HBsAg-positive or HBsAg-negative/anti-HBc-positive but HBV DNA-positive	HBsAg-negative/anti-HBc-positive (HBV DNA-negative)*
High >10%	• Immunosuppression in the context of stem cell transplantation[604] • High-dose combination chemotherapy (*e.g.* R–CHOP)[605] • B cell-depleting therapies[606] • CAR-T cell immunotherapy targeting B cells (BCMA, CD19)[577] • HCC therapies (TACE, radiotherapy, resection, ablation, systemic therapies)[598] • Anthracyclines[607] • Anti-TNF therapies[586] • Corticosteroids (>4 weeks, >20 mg/day)[608] • Cyclophosphamide[609] • JAK inhibitors[610] • IL-6 receptor antagonists[594] • Anti-IL-17[610–612] • Tyrosine kinase inhibitors[593,613]	• Immunosuppression in the context of stem cell transplantation[614] • High-dose combination chemotherapy (*e.g.* R–CHOP)[605] • B cell-depleting therapies[595,596] • HCC therapies (TACE)[599,600] • Anthracyclines[588] • T cell-depleting therapy belatacept – 17% in the setting of transplantation[615]
Moderate or intermediate (1-10%)	• Anti-IL-12/23 (*e.g.* ustekinumab)[586] • T cell activation blocking therapies (e.g., abatacept, belatacept)[616] • mTOR inhibitors[617]	• T cell-depleting therapies (*e.g.* abatacept[577]) • CAR-T cell immunotherapy • Corticosteroids (>40 mg)[585] • Anti-TNF therapies[586] • Anti-IL-12/23[586,610] • Anti-IL-17[610] • JAK inhibitors[590,610] • Tyrosine kinase inhibitors (*e.g.* ibrutinib) • Cyclophosphamide[524]
Low (<1%)	• Azathioprine[588] • Methotrexate[588] • Mycophenolate mofetil[588] • Corticosteroids (low-dose <10 mg/day)[608] • Immune checkpoint inhibitors[588]	• Azathioprine[588] • Methotrexate[588] • Mycophenolate mofetil[588] • mTOR inhibitors[617] • Corticosteroids (<40 mg/day) for ≤1 week)[585]

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolisation.
*The classification of moderate/high risk in HBsAg-negative/anti-HBc-positive patients in some cases is based on low-certainty evidence, with safety and prophylaxis decisions balanced against risk assessment.

Traitement antiviral et prévention de HBV r

Si on revient à notre patient…

Ac anti-HBc positifs

Rituximab
Cyclophosphamide
Doxorubicin (**H**ydroxydaunorubicin)
Vincristine (**O**ncovin)
Prednisone

EASL 2025

Risk of reactivation	HBsAg-positive or HBsAg-negative/anti-HBc-positive but HBV DNA-positive	HBsAg-negative/anti-HBc-positive (HBV DNA-negative)*
High >10%	• Immunosuppression in the context of stem cell transplantation[604] • High-dose combination chemotherapy (*e.g.* R–CHOP)[605] • B cell-depleting therapies[606] • CAR-T cell immunotherapy targeting B cells (BCMA, CD19)[577] • HCC therapies (TACE, radiotherapy, resection, ablation, systemic therapies)[598] • Anthracyclines[607] • Anti-TNF therapies[586] • Corticosteroids (>4 weeks, >20 mg/day)[608] • Cyclophosphamide[609] • JAK inhibitors[610] • IL-6 receptor antagonists[594] • Anti-IL-17[610–612] • Tyrosine kinase inhibitors[593,613]	• Immunosuppression in the context of stem cell transplantation[614] • High-dose combination chemotherapy (*e.g.* R–CHOP)[605] • B cell-depleting therapies[595,596] • HCC therapies (TACE)[599,600] • Anthracyclines[588] • T cell-depleting therapy belatacept – 17% in the setting of transplantation[615]
Moderate or intermediate (1-10%)	• Anti-IL-12/23 (*e.g.* ustekinumab)[586] • T cell activation blocking therapies (e.g., abatacept, belatacept)[616] • mTOR inhibitors[617]	• T cell-depleting therapies (*e.g.* abatacept[577]) • CAR-T cell immunotherapy • Corticosteroids (>40 mg)[585] • Anti-TNF therapies[586] • Anti-IL-12/23[586,610] • Anti-IL-17[610] • JAK inhibitors[590,610] • Tyrosine kinase inhibitors (*e.g.* ibrutinib) • Cyclophosphamide[524]
Low (<1%)	• Azathioprine[588] • Methotrexate[588] • Mycophenolate mofetil[588] • Corticosteroids (low-dose <10 mg/day)[608] • Immune checkpoint inhibitors[588]	• Azathioprine[588] • Methotrexate[588] • Mycophenolate mofetil[588] • mTOR inhibitors[617] • Corticosteroids (<40 mg/day) for ≤1 week)[585]

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolisation.
*The classification of moderate/high risk in HBsAg-negative/anti-HBc-positive patients in some cases is based on low-certainty evidence, with safety and prophylaxis decisions balanced against risk assessment.

Comment on aurait pu prévenir cette HBVr

- Prescrire une chimiothérapie moins aplasiante.
- Débuter la chimiothérapie et monitorage rapproché de l’ADN VHB.
- Traitement préemptif avant la chimiothérapie par Interféron.
- Traitement préemptif avant la chimiothérapie par Entécavir.
- Traitement préemptif avant la chimiothérapie par Lamivudine.

diseases

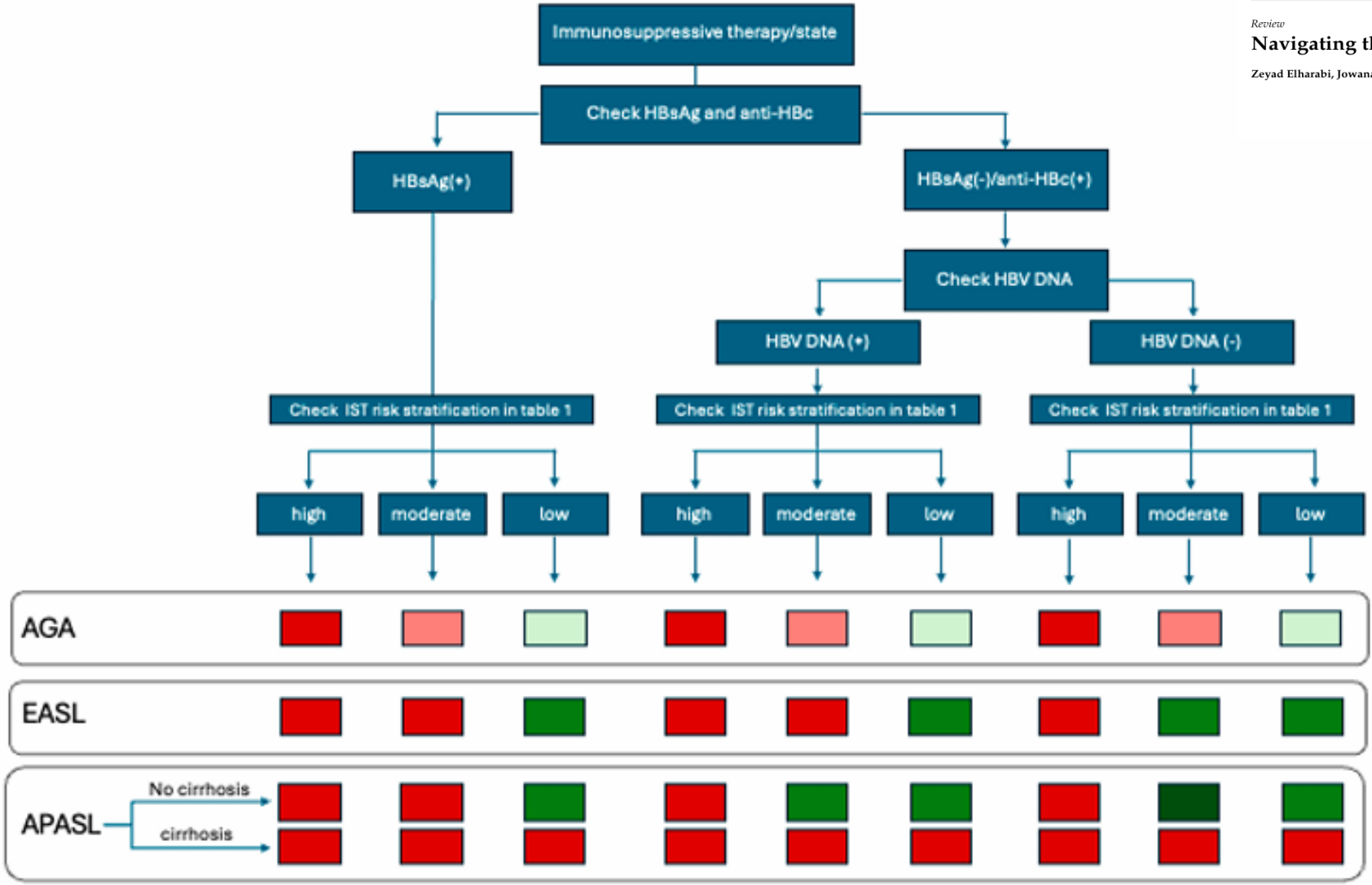
MDPI

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu



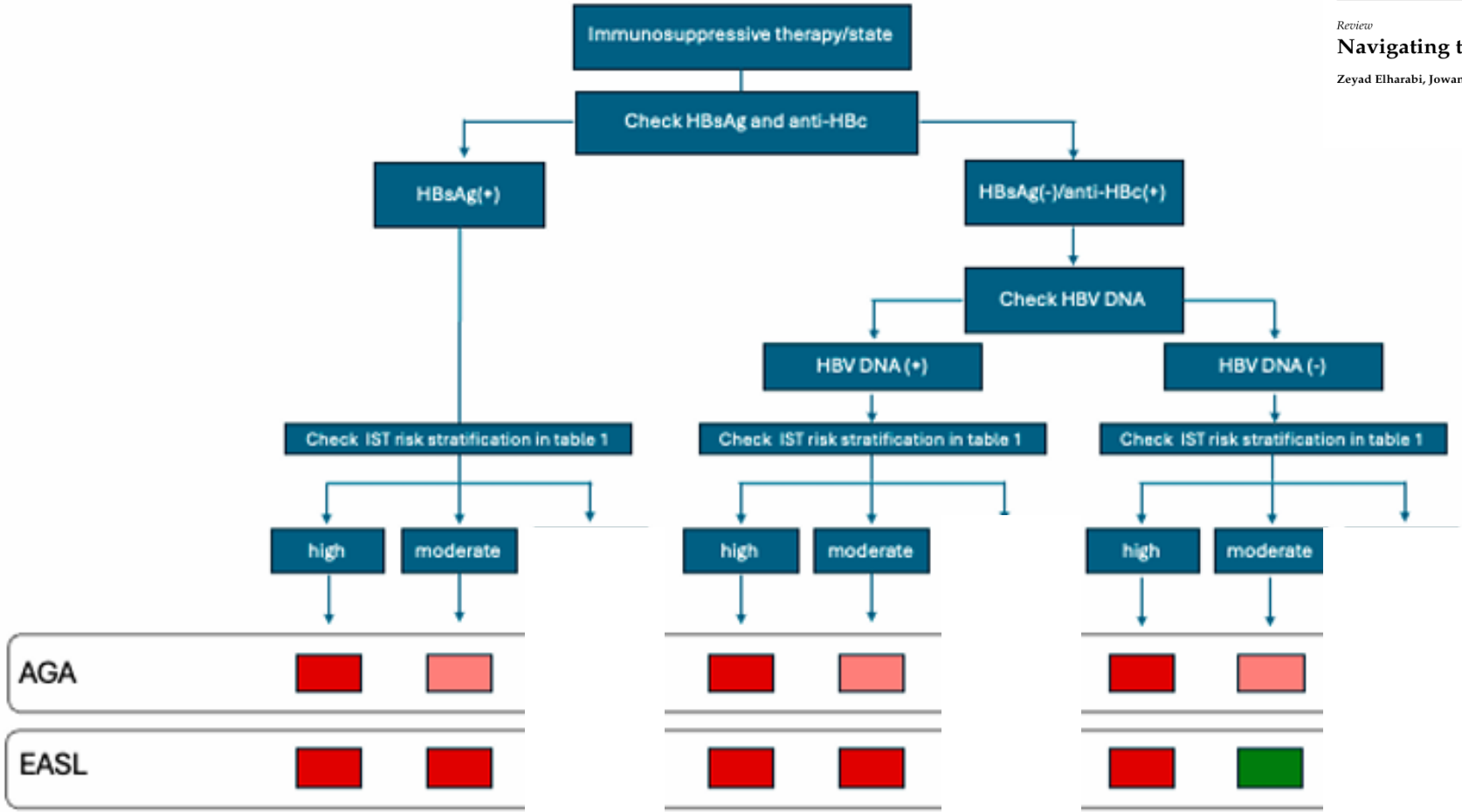
diseases

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu



Color legend:

- Prophylaxis recommended
- Prophylaxis suggested, but monitoring is also reasonable
- Monitoring suggested, but prophylaxis is also reasonable
- Monitoring recommended

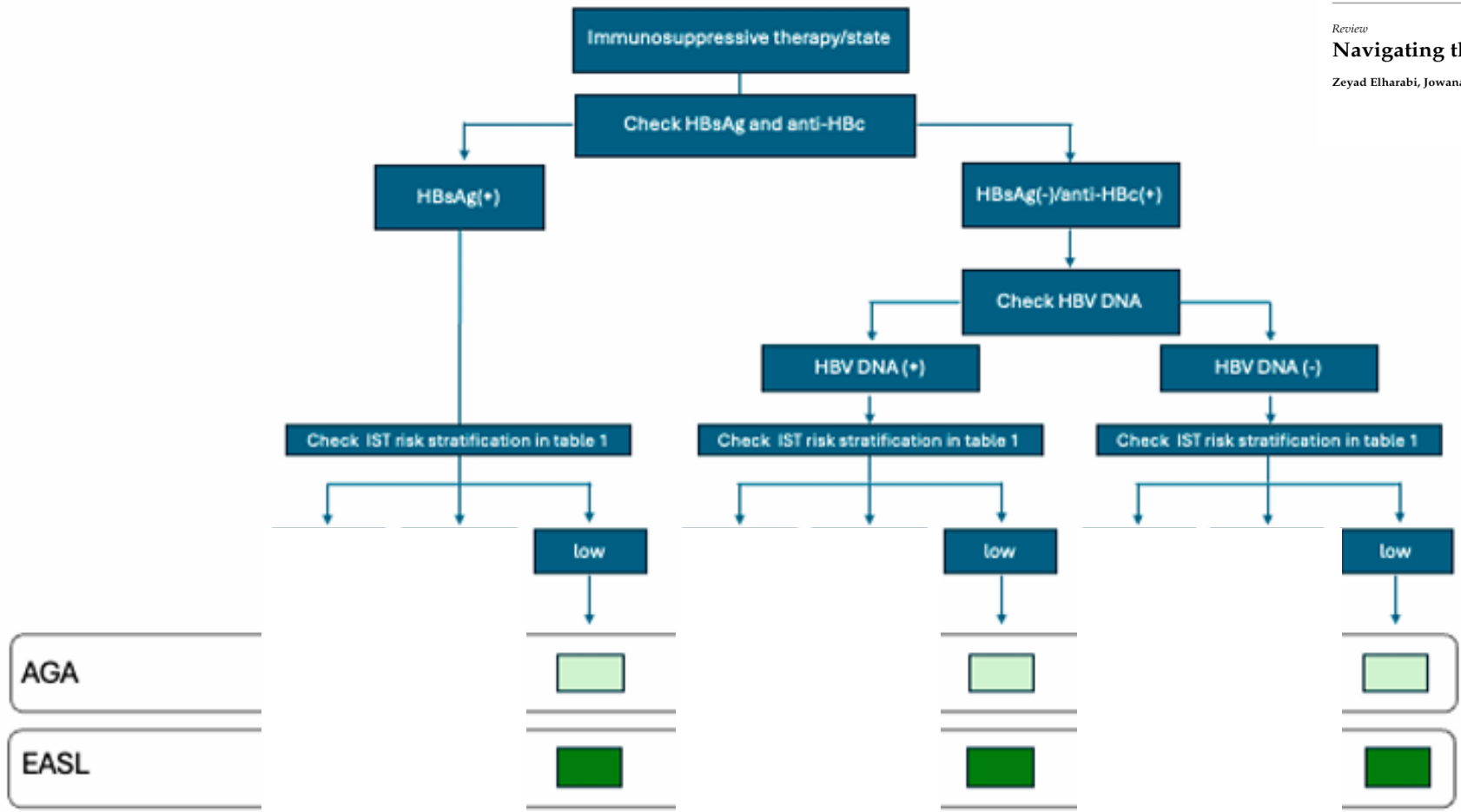
diseases

Review

Navigating the Latest Hepatitis B Virus Reactivation Guidelines

Zeyad Elharabi, Jowana Saba and Hakan Akin *

Division of Gastroenterology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA; zeyad.elharabi@ttuhsc.edu (Z.E.); jowana.saba@ttuhsc.edu (J.S.)
* Correspondence: hakan.akin@ttuhsc.edu



Color legend:

- Prophylaxis recommended
- Prophylaxis suggested, but monitoring is also reasonable
- Monitoring suggested, but prophylaxis is also reasonable
- Monitoring recommended

Transplantation hépatique

Donor HBV Status	Recipient HBV Status	Suggested Management
HBV negative		
	HBsAg positive	- High-barrier NA - HBIG if high risk for reactivation, including detectable HBV DNA at transplant, NA resistance, non-adherence, co-infection with HIV and/or HDV
	Anti-HBs negative/anti-HBc positive	No prophylaxis needed; on-demand NA
HBsAg negative, anti-HBc positive		
	Prior infection with immunity HBsAg negative, anti-HBs positive, anti-HBc positive	No prophylaxis needed; on-demand NA
	HBV naïve, immunity via vaccination HBsAg negative, anti-HBs positive, anti-HBc negative	High-barrier NA
	Prior infection without immunity HBsAg negative, anti-HBs negative, anti-HBc positive	High-barrier NA
	HBV naïve and without immunity HBsAg negative, anti-HBs positive, anti-HBc negative	High-barrier NA
HBsAg positive or HBV DNA positive		
	Any HBV status	High-barrier NA

HBIG: HBV immune globulin; HIV: human immunodeficiency virus; HDV: hepatitis D virus; NA: nucleos(t)ide analog; CHB: chronic hepatitis B.

TOS hors foie

Donor HBV Status	Recipient HBV Status	Suggested Management	Rationale
HBV negative			
	HBsAg positive	High-barrier NA	Prevent HBV reactivation in the setting of immunosuppression
	Anti-HBs negative/anti-HBc positive	High-barrier NA	Prevent HBV reactivation in the setting of immunosuppression
HBsAg negative, anti-HBc positive			
	HBV immune Anti-HBs positive Anti-HBc any status	No prophylaxis needed; on-demand NA	Low risk of de novo HBV infection (<1%)
	HBV non-immune Anti-HBs negative Anti-HBc any status	High-barrier NA	Prevent de novo HBV infection
HBsAg positive or HBV DNA positive			
	HBV immune Anti-HBs positive Anti-HBc any status	High-barrier NA	Prevent de novo HBV infection
	HBV non-immune Anti-HBs negative Anti-HBc any status	High-barrier NA + HBIG	Prevent de novo HBV infection

HBIG: HBV immune globulin; NA: nucleos(t)ide analog.

Quelle molécule prescrire ?

Clinical outcomes, n (%)	LAM, n=89	ETV, n=34
Incidence of hepatitis	24 (27.0)	2 (5.9)
HBV reactivation	18 (20.2)	0
HBV-related hepatitis	11 (12.4)	0
Delayed hepatitis B	8 (9.0)	0
Chemotherapy disruption	18 (20.2)	2 (5.9)
Premature termination	5 (5.6)	2 (5.9)
Delay >8 days	17 (19.1)	2 (5.9)
Mortality	1 (1.1)	0

Li ,J Viral Hep 2011

Quelle molécule prescrire ?

Molécules recommandées dans la prévention de VHB r

- ✓ **Entécavir (ETV 0,5 mg/j)**
- ✓ **Ténofovir disoproxil fumarate (TDF 300 mg/j)**
- ✓ **Ténofovir alafénamide (TAF 10 mg/j)**

Quelle molécule prescrire ?

Indications for using (ETV or TAF) over TDF:

- Aged >60 yrs
- Bone disease
  - Chronic steroids or other meds that affect bone
  - History of fragility fracture
  - Osteoporosis
- Renal abnormalities
  - eGFR <60 mL/min/1.73 m²
  - Albuminuria >30 mg or moderate proteinuria
  - Low phosphatemia (<2.5 mg/dL or <0.81 mmol/L)
  - Hemodialysis

When to prioritize TAF over ETV:

- Previous nucleoside exposure
  - Lamivudine with or without adefovir resistance
- HIV/HBV coinfection
- No dose adjustment for CrCl ≥ 15 mL/min
- Patients' preference due to dosing irrespective of meals

When to prioritize ETV over TAF:

- If less expensive (generic available)
- Dosing guidelines for CrCl <15 mL/min

Sérologie VIH +++

Quelle molécule prescrire ?

- **Insister sur l'observance +++**

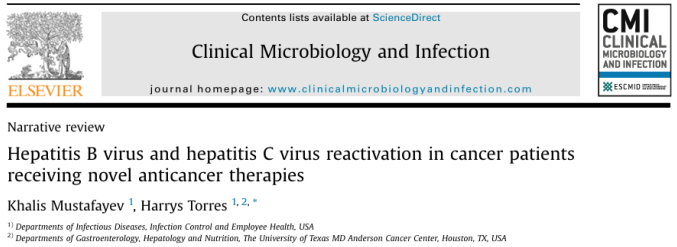
viruses MDPI

Article

Real-World Effectiveness of Antiviral Prophylaxis for Preventing Hepatitis B Virus (HBV) Reactivation in Patients Undergoing Immunosuppressive Therapy

İnci Yılmaz Nakir *, Bilge Çağlar, Esra Zerdali, Rumeysa Gülistan Karaduman and Filiz Pehlivanoğlu

- ✓ **199 patients**
- ✓ ETV 76.4%, TAF 13.1%, TDF 10.5%.
- ✓ **1 seul cas de réactivation**
- ✓ Arrêt volontaire du ttt



Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

ELSEVIER

CMI CLINICAL MICROBIOLOGY AND INFECTION

Narrative review

Hepatitis B virus and hepatitis C virus reactivation in cancer patients receiving novel anticancer therapies

Khalis Mustafayev [1], Harrys Torres [1, 2, *]

[1] Departments of Infectious Diseases, Infection Control and Employee Health, USA
[2] Departments of Gastroenterology, Hepatology and Nutrition, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

- ✓ **3465 patients** sous chimiothérapie pour cancer solide.
- ✓ 511 hépatite B chronique, 2954 hépatite B résolue.
- ✓ **5 cas de HBVr**
- ✓ Pas de prophylaxie (3 cas)
- ✓ Mauvaise observance (1 cas)
- ✓ Arrêt volontaire du ttt (1 cas)

Quand débuter le ttt IS ?

Journal of Cancer 2020, Vol. 11 3559

IVYSPRING INTERNATIONAL PUBLISHER

Journal of Cancer

2020; 11(12): 3559-3566. doi: 10.7150/jca.40154

Research Paper

Optimal timing of antiviral therapy for patients with malignant tumor who presented with hepatitis B reactivation during chemotherapy and/or immunosuppressive therapy

Débuter avant ou au début du ttt IS/IM. Il n'est pas indispensable d'attendre une semaine avant.

Journal of Clinical and Translational Hepatology **2023** vol. 11(6) | 1425–1442
DOI: 10.14218/JCTH.2023.00320

Guideline

Guidelines for the Prevention and Treatment of Chronic Hepatitis B (version 2022)

Hong You[1*], Fusheng Wang[2*], Taisheng Li[3*], Xiaoyuan Xu[4*], Yameng Sun[1], Yuemin Nan[5], Guiqiang Wang[4], Jinlin Hou[6], Zhongping Duan[7], Lai Wei[8], Jidong Jia[1], Hui Zhuang[9] and Chinese Society of Hepatology, Chinese Medical Association; Chinese Society of Infectious Diseases, Chinese Medical Association

Recommendation 22: For patients with pending chemotherapy, targeted therapy, or immunosuppressive therapy, screening for HBV markers (HBsAg, anti-HBs, and anti-HBc) should be recommended (A1). For HBsAg-and/or HBV DNA-positive patients, NAs (ETV, TDF, or TAF) should be initiated at least one week before starting chemotherapy, targeted therapy, or immunosuppressive therapy, or at the same time if necessary (A1). For HBsAg-negative and anti-HBc-positive patients, ETV, TDF, or TAF antiviral treatment is recommended if they have advanced liver fibrosis/cirrhosis, plan to receive B lymphocyte depletion therapy with monoclonal antibody agents, or undergo hematopoietic stem cell transplantation (B1).

Journal of Clinical and Translational Hepatology 2023 vol. 11(6) | 1425–1442

Comment surveiller le patient à risque de HBVr sous IS?

Quel rythme ?

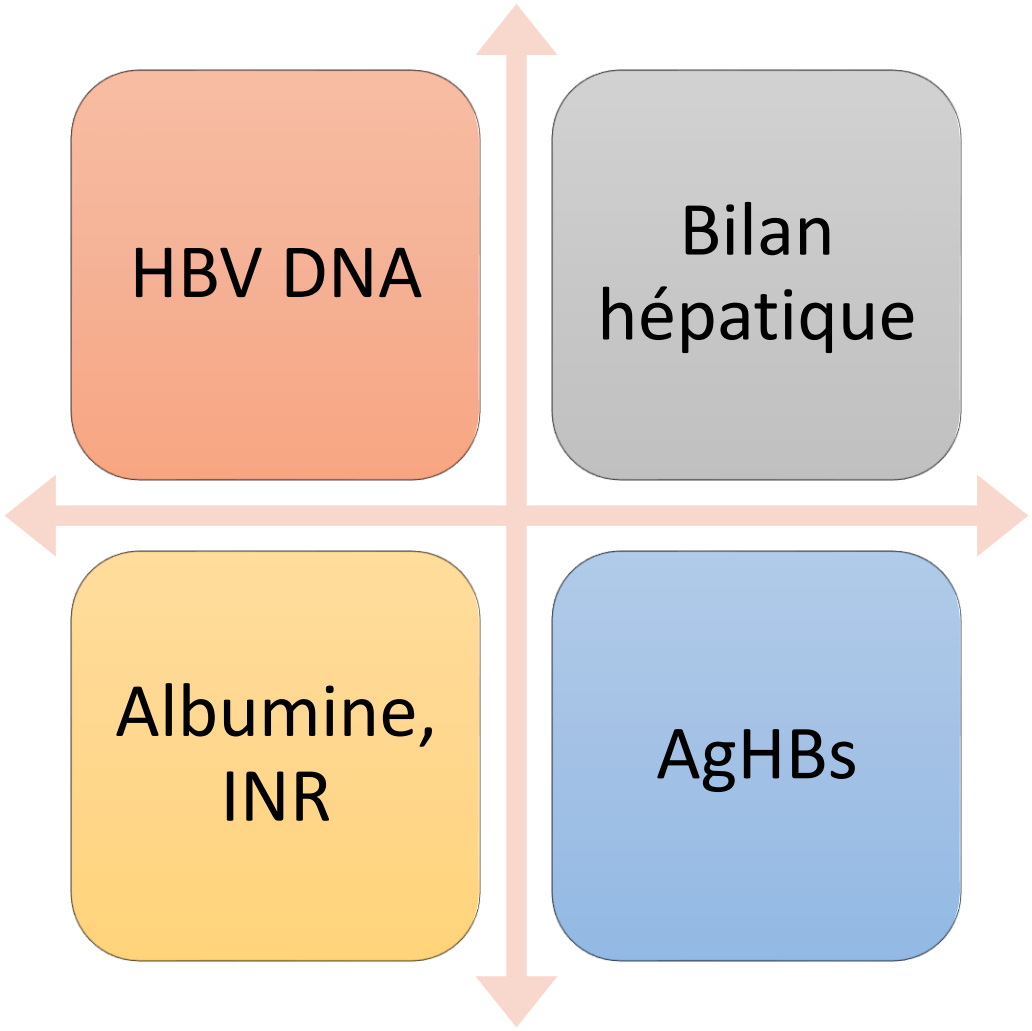
Tous les mois

- **Ag HBs (+), Ac anti HBs (-)**
- **Pas de prophylaxie**
- **TTT à risque élevé, intermédiaire ou inconnu**

Tous les 3 mois

- **Ag HBs (-)**
- **Sous prophylaxie**
- **TTT à risque faible de HBVr**

Comment surveiller le patient à risque de HBVr sous IS?



HBVr suspectée ou confirmée ?

CAT devant une réactivation ou suspicion de HBVr ?

Drug Safety (2024) 47:321–332
https://doi.org/10.1007/s40264-024-01399-4

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

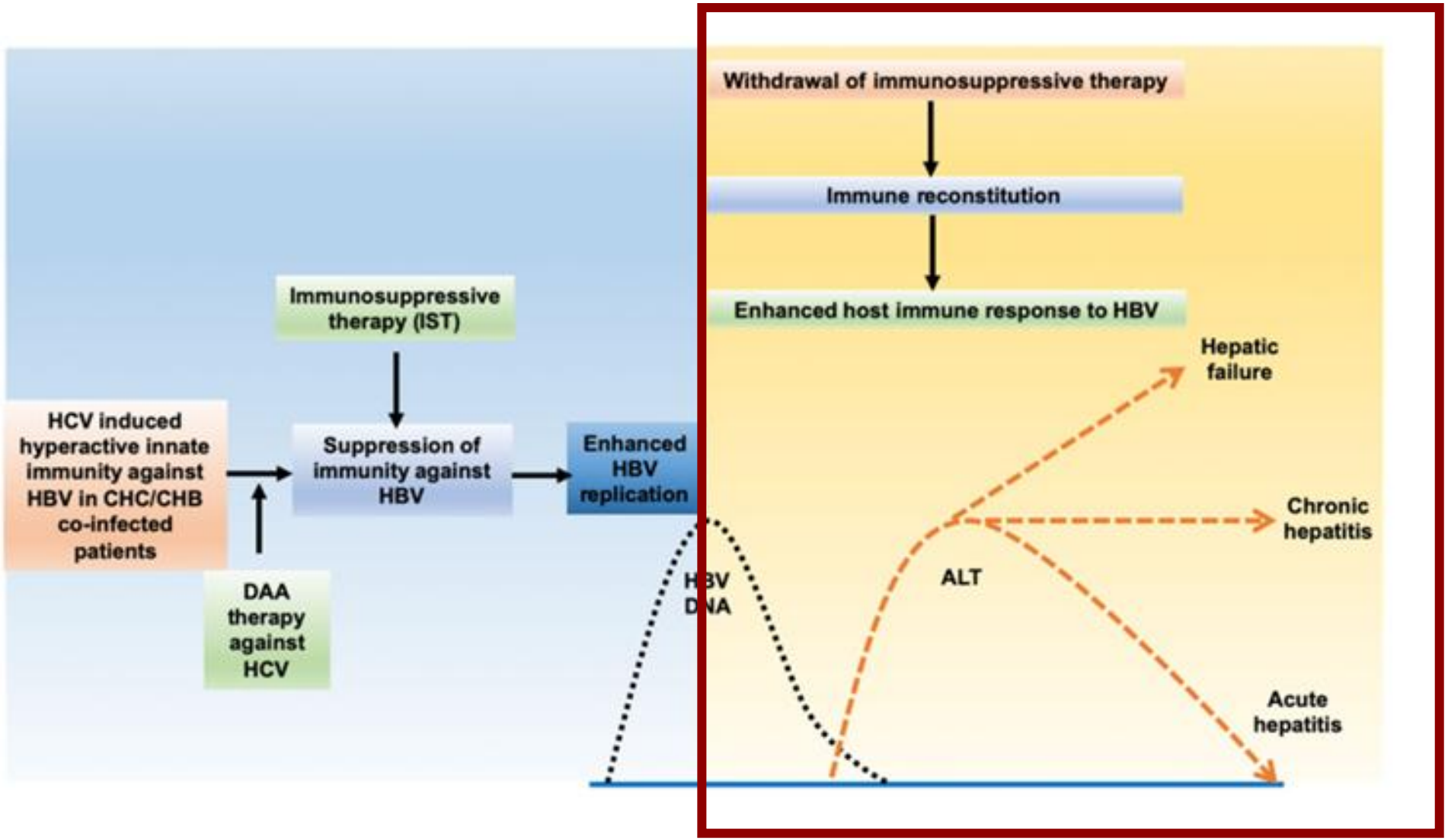
Accepted: 18 January 2024 / Published online: 14 February 2024

Lab scenario	Clinical interpretation	Actions to be taken with IS/IM	Laboratory testing
Criteria for HBVr are met	Confirmed HBVr	Immediately interrupt IS/IM and refer to specialist* Ensure compliance with NA prophylaxis or initiate anti-HBV treatment	Repeat liver biochemical tests (ALT, AST, alkaline phosphatase, total bilirubin, direct bilirubin, INR, and albumin), check HDV RNA if HDV coinfection is considered; repeat HBV DNA in 1–2 weeks to assess clinical course
HBV DNA is detectable but does not meet threshold for HBVr	Possible HBVr	Immediately interrupt IS/IM and refer to specialist Ensure compliance with NA prophylaxis	Repeat liver biochemical tests, HBV DNA in 1–2 weeks; if trending upwards, manage as HBVr
HBV DNA is detectable but not quantifiable	Possible HBVr	Immediately interrupt IS/IM and refer to specialist Ensure compliance with prophylaxis	Repeat liver biochemical tests, HBV DNA in 1–2 weeks; if trending upwards, manage as HBVr
Elevation in ALT but no change in HBV DNA	Not HBVr. Evaluate for other causes of ALT elevation including DILI	Continue IS/IM, unless ALT, AST, or total bilirubin thresholds meet discontinuation criteria for DILI, per study protocol	As per protocol, for elevation in ALT +/− bilirubin

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *DILI* drug-induced liver injury, *HBcAb* hepatitis B core antibody, *HBsAg* hepatitis B surface antigen, *HBVr* hepatitis B reactivation, *HDV* hepatitis delta virus, *INR* international normalized ratio, *IS/IM* immunosuppression/immunomodulation, *NA* nucleos(t)ide analog

*Rapid withdrawal of IS/IM (especially glucocorticoids) in a study patient with signs of inflammatory HBVr could lead to a paradoxical response and cause a flare of clinical and biochemical hepatitis with histopathological evidence of new or worsening HBV hepatitis on liver biopsy. A 'specialist' refers to an individual with recognized expertise in the assessment and management of viral hepatitis and may opt to initiate NA therapy

Durée du traitement prophylactique


Immunosuppressive therapy (IST)
HCV induced hyperactive innate immunity against HBV in CHC/CHB co-infected patients
Suppression of immunity against HBV
Enhanced HBV replication
DAA therapy against HCV
Withdrawal of immunosuppressive therapy
Immune reconstitution
Enhanced host immune response to HBV
Hepatic failure
Chronic hepatitis
Acute hepatitis
ALT
HBV DNA

Modalité de suivi à l'arrêt des immunosuppresseurs

CONSENSUS STATEMENT

Consensus Guidelines: Best Practices for the Prevention, Detection and Management of Hepatitis B Virus Reactivation in Clinical Trials with Immunosuppressive/Immunomodulatory Therapy

Eric B. Cohen[1] · Arie Regev[2] · Anju Garg[3] · Adrian M. Di Bisceglie[4] · James H. Lewis[5] · John M. Vierling[6] · Judith Hey-Hadavi[7] · Klaudia Steplewski[8] · Anna Fettiplace[9] · Chunlin L. Chen[10] · Nonko Pehlivanov[11] · Stuart Kendrick[12] · Mark I. Avigan[13]

Accepted: 18 January 2024 / Published online: 14 February 2024

Table 8 Post-treatment monitoring and management recommendations

Guidelines	Monitoring and management after last dose of IS/IM therapy	
	On NA prophylaxis*	Not on NA prophylaxis
Duration of lab monitoring post-IS/IM**	12 months	6–12 months
Duration of antiviral	3, 6, or 12 months according to perceived risk of HBVr***	N/A
Labs, frequency	HBV DNA and ALT every 1–3 months	HBV DNA and ALT every 1–3 months
Other recommendations	Refer to specialist after completion of clinical protocol if NA treatment is ongoing	Standard follow-up with generalist after completion of clinical protocol

ALT alanine aminotransferase, *HBVr* hepatitis B virus reactivation, *IS/IM* immunosuppression/immunomodulation, *NA* nucleos(t)ide analog

*If antiviral is being given for treatment, not prophylaxis, then patients should continue NA treatment beyond the end of the clinical trial and follow up with a specialist

**May be longer for IS/IM with effect of longer duration

***High-risk, moderate/intermediate-risk, and low-risk categories are defined by treatment-associated HBVr rates of >10%, 1% to 10%, and <1%, respectively

Quand arrêter le traitement ?

AGA 2025	EASL 2025
Au moins 6 mois après l’arrêt des IS Au moins 12 mois si déplétion des LB	Au moins 6-12 mois Au moins 18 mois si déplétion des LB

Quand arrêter le traitement ?

Journal of Infection and Public Health 16 (2023) 1852–1859

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: www.elsevier.com/locate/jiph

Original Article

Long-term comparisons of the durability of 6 months versus 12 months antiviral therapy for hepatitis B after chemotherapy cessation☆

Shih-Yu Yang [1], Tsung-Hui Hu [1], Yeh-Pin Chou, Yuan-Hung Kuo, Ming-Chao Tsai, Kuo-Chin Chang, Yi-Hao Yen, Po-Lin Tseng *

Division of Hepato-Gastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

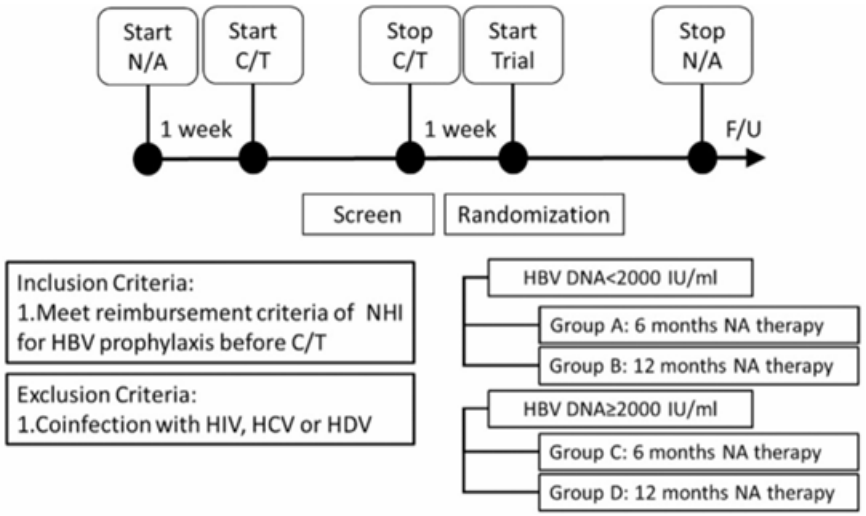


Fig. 1. Study design. C/T: chemotherapy.

Univariate and multivariate cox-regression analysis of virological relapse long-term follow-up after antiviral therapy cessation.

		Univariate		Multivariate	
Variables	Comparisons	Relative risk	*p*-value	Relative risk	*p*-value
Age (years)	≥ 50 vs. < 50	1.16 (0.54–2.53)	0.703		
Gender	Male vs. female	0.76 (0.37–1.60)	0.477		
ALT (U/L)	≥ 40 vs. < 40	1.77 (0.85–3.70)	0.128		
Drug	TDF vs. ETV	2.05 (0.99–4.22)	0.050		
Chemotherapy Duration (weeks)	≥ 24 vs. < 24	0.98 (0.48–2.02)	0.961		
Chemotherapy Regimen (contain anthracycline)	Yes vs. No	1.027(0.49–2.13)	0.942		
Cancer type	Hematological vs. others	1.23 (0.29–5.18)	0.781		
HBeAg	Positive vs. negative	2.69 (1.02–7.11)	0.046		
HBV DNA (IU/ml)	≥ 2000 vs. < 2000	3.15 (1.50–6.61)	0.002	2.98 (1.30–6.82)	0.010
Post chemotherapy ALT	≥ 40 vs. < 40	0.36 (0.14–0.95)	0.039		
End NA therapy HBsAg (IU/ml)	≥ 500 vs. < 500	2.78 (1.25–6.18)	0.012	2.38 (1.05–5.38)	0.037

PREVENTION

Society, year[Ref]	Whom to screen	HBV screening tests
American Gastroenterological Association, 2015[11]	High risk of HBV infection per CDC guidelines Therapies with moderate-high risk of HBVr	HBsAg and anti-HBc HBV DNA if either positive
European Association for the Study of the Liver, 2017[6]	Any immunosuppressive or chemotherapy	HBsAg, anti-HBc, anti-HBs
American Association for the Study of Liver Diseases, 2018[12]	Any immunosuppressive, cytotoxic or immunomodulatory therapy	HBsAg, anti-HBc
American Society of Clinical Oncology, 2020[7]	Any systemic anti-cancer therapy	HBsAg, anti-HBc, anti-HBs
Asian Pacific Association for the Study of the Liver, 2022[8]	Any immunosuppressive therapy	HBsAg, anti-HBc, anti-HBs
European Society of Clinical Microbiology and Infectious Diseases, 2018[10] *	Anti-TNF, anti-CD20, anti-CD52	HBsAg and ant-HBc
American Academy of Dermatology, 2019[9] *	Anti-TNF, anti-IL12, IL13, IL17	HBsAg, anti-HBc, anti-HBs
American College of Rheumatology, 2021[82] *	Disease-modifying antirheumatic drugs	HBsAg and anti-HBc
Authors of current article	Any immunosuppressive or immunomodulatory therapy	HBsAg and anti-HBc HBV DNA if HBsAg+, optional if HBsAg-/anti-HBc+ Anti-HBs optional

Anti-HBC, anti-hepatitis B core antibody; anti-HBs, anti-hepatitis B surface antibody; HBVr, HBV reactivation.
*Recommendations for specific therapies evaluated.

Papatheodoridis, J Hepatol 2022

Dépistage sérologique systématique avant le début de tout traitement immunosuppresseur ou immunomodulateur +++

MESSAGE CLES

1. Dépistage sérologique systématique avant traitement IS/IM.

2. AgHBs+ → Vérifier indication à un ttt curatif ?

3. Les patients séronégatifs doivent être vaccinés avant IS.

4. HBsAg (+) → Risque élevé HBVr , surtout si ADN (+)
   → Prophylaxie avant immunosuppression.

5. TTT par AN à haute barrière génétique de résistance (ETV, TAF, TDF)

MESSAGE CLES

6. Anti-HBc (+) : Risque moins élevé
   A pondérer avec le type d'immunosuppression et la virémie.

7. Poursuite traitement prophylactique après la fin des IS
   (6 à 12 mois voire 12-18 mois si Rituximab)

8. Suivi tests hépatiques et HBV-DNA tous les 3-6 mois pendant le traitement, jusqu'à 12 mois après arrêt de la prophylaxie

CONCLUSION

- Les récentes directives cliniques → Mieux prévoir et gérer la HBVr.
- Nécessité d’adaptation aux préférences du patient et conditions locales.
- Place des nouveaux marqueurs dans la prédiction de la HBVr.

Merci pour votre attention

STI

STPI
Société Tunisienne
de Pathologie Infectieuse

الجمعية التونسية للفرماكولوجيا
Association Tunisienne de Pharmacologie
ATP

Gestion du risque d'HBV sous immunosuppresseurs

Le 08/01/2026

Dr Hana CHAABOUNI
AHU en maladies infectieuses
CHU Hedi Chaker, Sfax