Singapore Hepatology Conference

Sharp focused updates in Hepatology

UPDATES

LIVE WEBINARS		
Topic: Speaker: Date And Time:	**Prophylaxis for HBV and occult HBV for the immunocompromised** **PROF. SENG GEE LIM** Monday, 2 November 2020 8.00pm – 9.00pm HKT/SGT	
Topic: Speaker: Date And Time:	**Immnotherapy for advanced HCC** **PROF. SENG GEE LIM** Monday, 9 November 2020 8.00pm – 9.00pm HKT/SGT	

ADVANCED LIVER DISEASE WEBINAR SERIES

Topic: Speaker: Date And Time:	**Advanced liver disease - the scope of the problem** **PROF. SENG GEE LIM** Monday, 16 November 2020 7.30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Hepatocyte transplantation - the new frontier?** **PROF. YOCK YOUNG DAN** Monday, 16 November 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Portal hypertension update 2020** **PROF. GUADALUPE GARCIA-TSAO** Monday, 23 November 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Advances in Hepatic encephalopathy** **PROF. RAJENDER REDDY** Monday, 30 November 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Long term albumin replacement: a panacea for decompensated cirrhosis?** **PROF. MAURO BERNADI** Monday, 7 December 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Best Management Practices for Diuretic resistant ascites and Hepatorenal Syndrome** **PROF. SIMONE STRASSER** Monday, 14 December 2020 30 pm – 8.30 pm HKT/SGT	

Housekeeping

- Please mute unless you wish to ask question
- Ask questions through the Q&A button not by raising your hand
- Webinar will last approximately 30mins followed by 10mins of Q&A

National University Health System

Yong Loo Lin School of Medicine • National University Hospital • Faculty of Dentistry

National University Hospital

NUS National University of Singapore

"Prophylaxis in HBV & occult HBV for the Immunocompromised"

SHC-HK ASLD Webinar series

Prof Seng Gee Lim
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National University Health System
Singapore

Disclosures

- Advisory Board
  - MSD
  - Gilead
  - Abbvie
  - Abbott
  - Springbank
  - Roche
  - Arbutus
  - Kaleido Biosciences
- Speaker’s Bureau
  - MSD
  - Abbvie
  - Abbott
  - Gilead

Risk factors for hepatitis B reactivation in patients with current/past hepatitis B infection

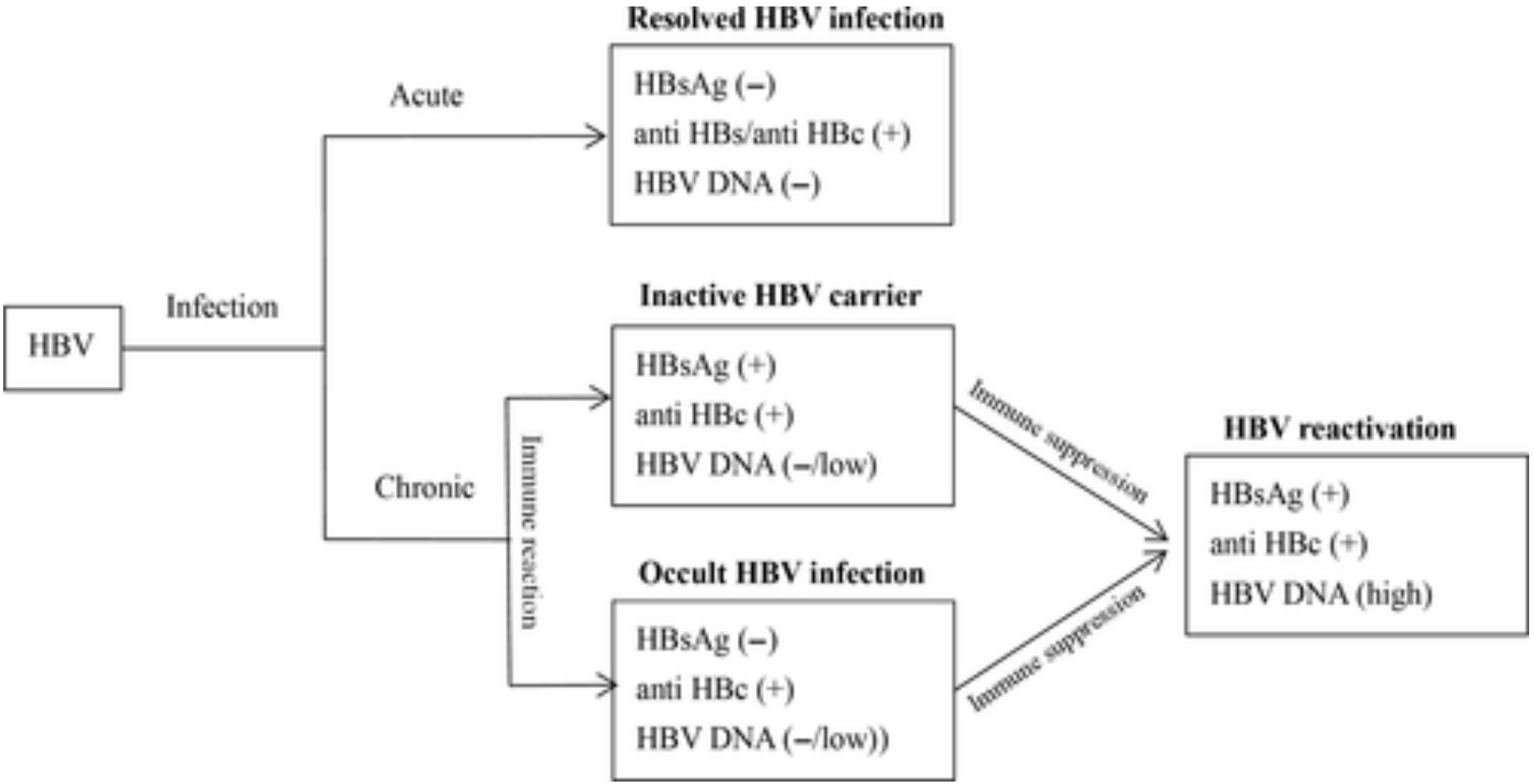
Host
- Male
- Young
- Elevated ALT before IS
- Underlying disease:
  - Solid vs haem malignancy
  - Autoimmune disease
  - Transplant

Drugs: type of immune suppression
- Intensity and duration of IS
- Biologics & Rituximab
- High dose steroids
- Anthracycline
- Stem cell transplantation

Viral
- High HBV DNA load
- HBsAg positive
- HBeAg positive
- Precore mutant
- Core promoter mutant
- Low antiHBs titles (in occult/resolved)

Bessone, World J Hepatol 2016 March 18; 8(8): 385-394

Patients at risk of reactivation



Xu, Eur J Cancer Care (Engl). 2018 Mar;27(2):e12799.

Definitions of Occult HBV Infection (OBI)

- Gold standard: HBV DNA in liver tissue
- Acceptable: Highly sensitive HBV DNA in serum
- Surrogate: anti-HBc positive

Raimondo, Semin Immunopathol (2013) 35:39–52

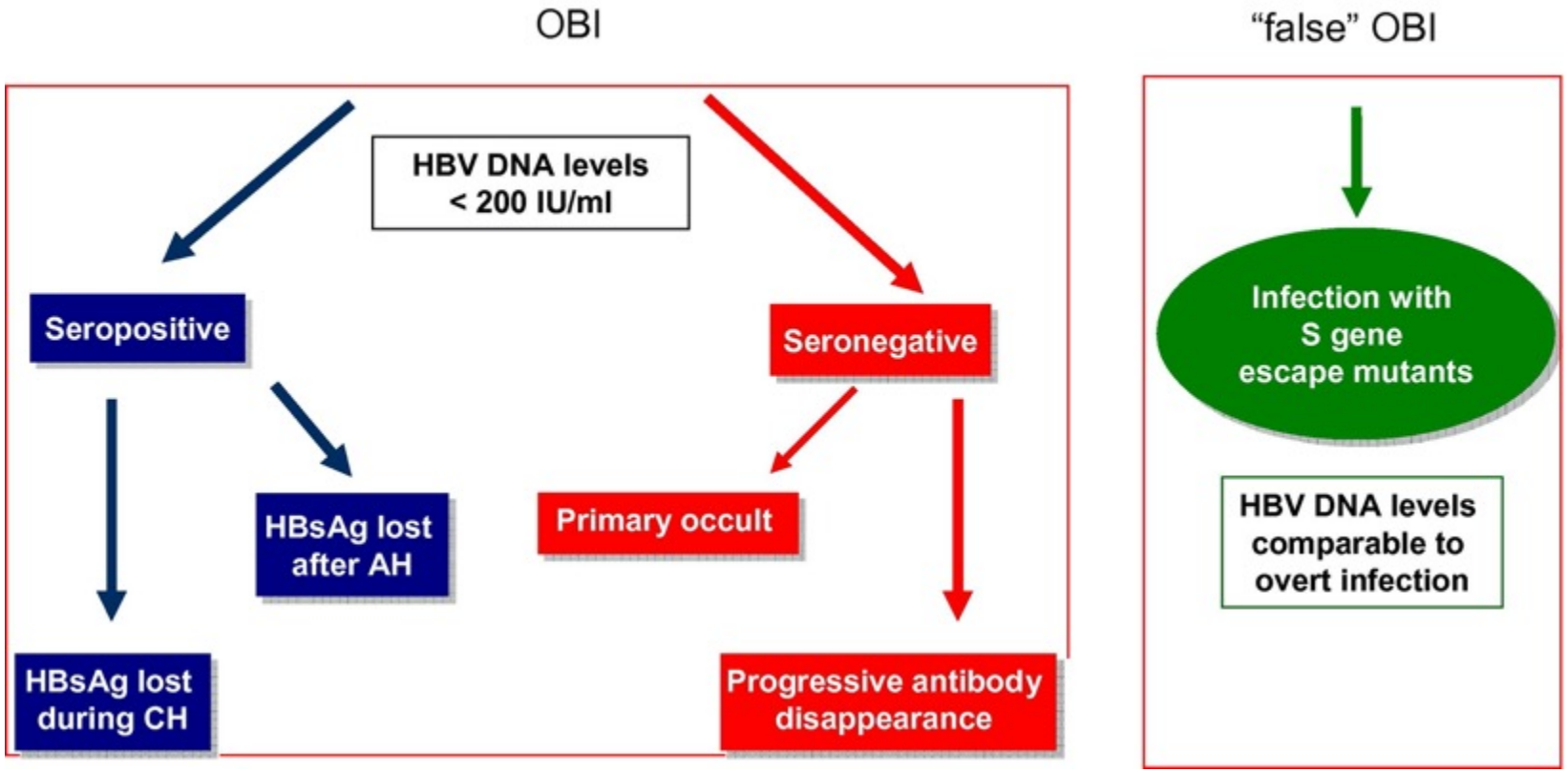
Occult HBV Infection (OBI)

Seropositive

- Anti-HBc or anti-HBs positive

Seronegative

- Anti-HBc and anti-HBs negative



Raimondo et al, Journal of Hepatology 49 (2008) 652–657

Overview of OBI

Prevalence

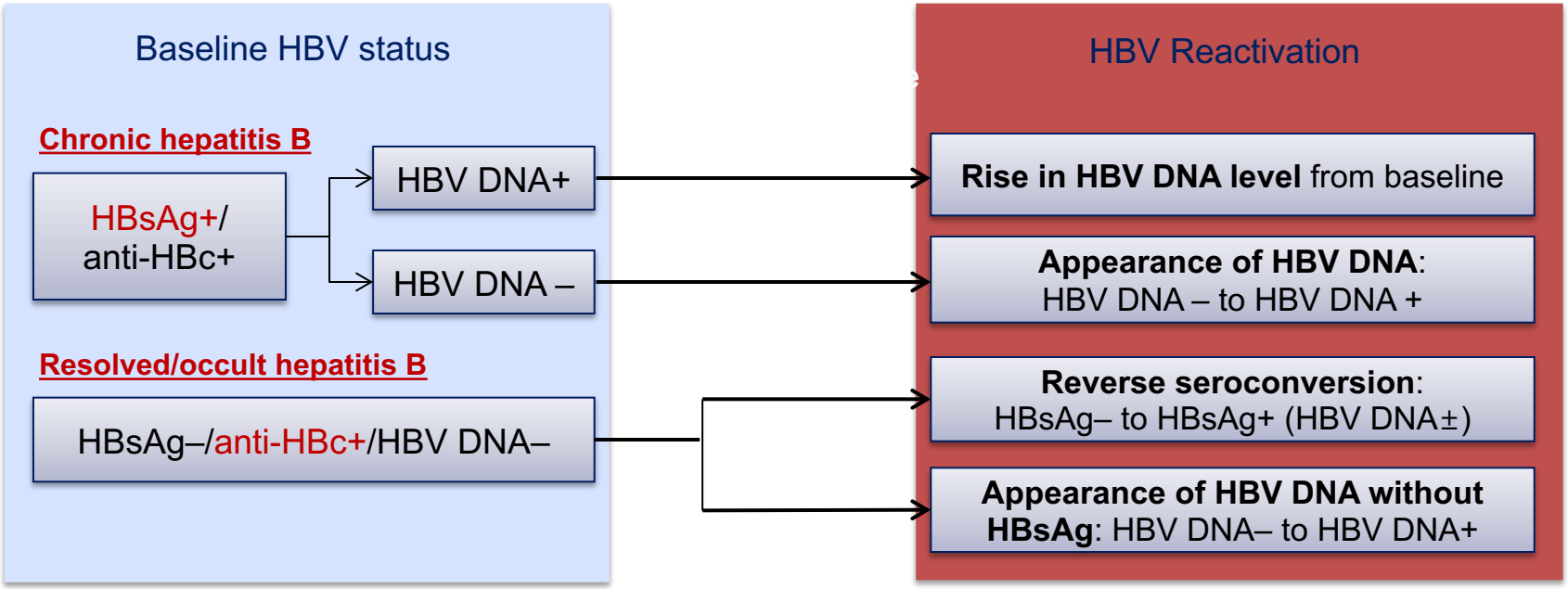
- High risk populations
  - Chronic liver disease (cryptogenic)(20-30%)
  - HCV+ (up to 50%)
  - IVDU (45%)
  - Hemophilia (51%)
  - HIV (41%)
- General populations
  - Canada (18%)
  - China (45%)
  - Taiwan (11% in HBV vaccinated children)

- Prevalence rates depend on the definition
- <20% of anti-HBc positive patients are HBV DNA positive, hence anti-HBc status may over-estimate OBI

Makvandi, World J Gastroenterol 2016 October 21; 22(39): 8720-8734

Definition and Types of HBV reactivation

- Definition: a marked increase in HBV replication (≥2 $\log_{10}$ increase in HBV DNA levels from baseline levels or a new appearance of HBV DNA to a level of ≥ 100 IU/mL) in a person with previously stable or undetectable levels
- **Types**: "exacerbation of chronic hepatitis B" or "reactivation of past hepatitis B"



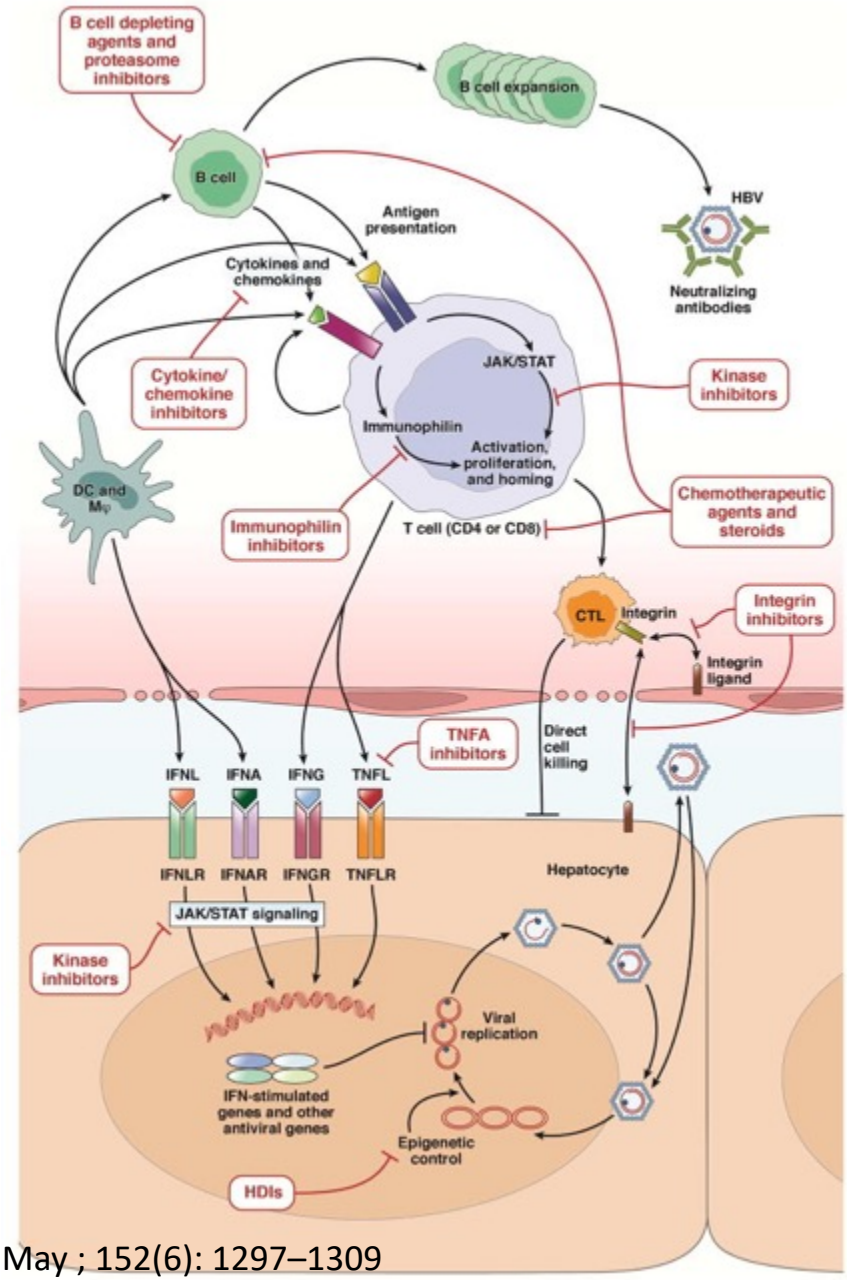
1. Hoofnagle JH. Hepatology 2009;49(5s):S156–65;
2. Hwang J, et al. Nat Rev Gastroenterol Hepatol 2014;11:209–19.

Definitions of HBV Reactivation Based on Society Guidelines

	Reactivation of CHB	HBV Flare	Reactivation of Resolved HBV
Baseline serologies	HBsAg(+), anti-HBc(+)		HBsAg(−), anti-HBc(+)
AASLD 2018 guidelines	Unknown DNA baseline: ≥10,000 IU/mL	ALT≥3x ULN & HBV DNA≥ 100 IU/ml	Detectable DNA
	Known DNA baseline, previously undetectable: ≥1,000 IU/mL		OR
	Known DNA baseline, previously detectable: ≥100-fold↑		Detectable HBsAg
AGA 2015 guidelines	Unknown DNA baseline: not explicitly defined	Not stated	Detectable DNA
	Known DNA baseline, previously undetectable: *de novo* detectable DNA		OR
	Known DNA baseline, previously detectable: ≥10-fold↑		Detectable HBsAg
			OR
			Detectable HBeAg
APASL 2016 guidelines	Unknown DNA baseline: ≥20,000 IU/mL	ALT ≥ 5x ULN	Detectable DNA
	Known DNA baseline, previously undetectable: ≥100 IU/mL	Severe: Abn ALT + coagulopathy (INR>1.5)	OR
	Known DNA baseline, previously detectable: ≥100-fold ↑		Detectable HBsAg
EASL 2017 guidelines	Not explicitly defined	Not stated	Not explicitly defined

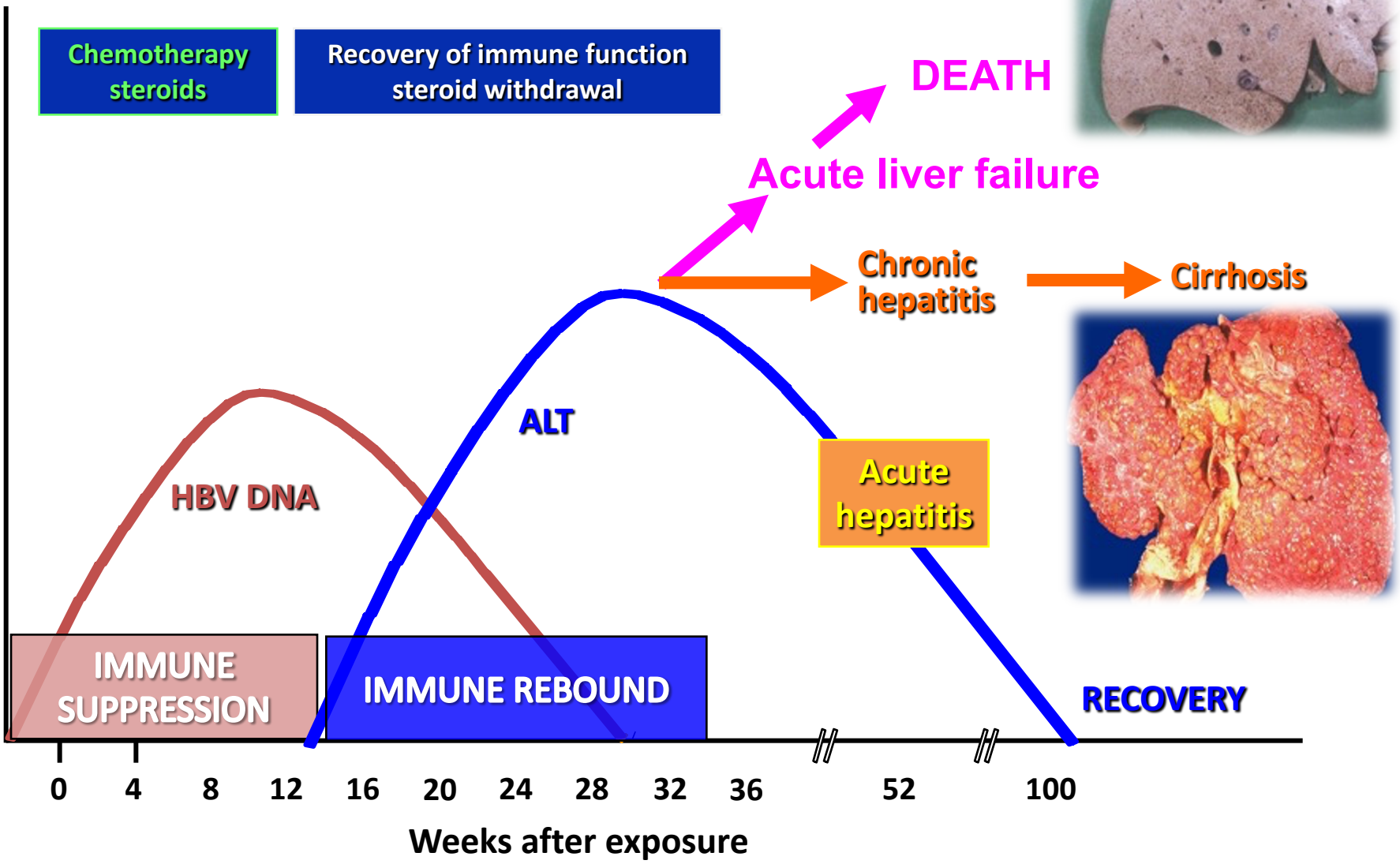
Myint, Clin Liver Dis. 2020 Apr; 15(4): 162–167.

Pathways involved in HBV reactivation



Loomba, Gastroenterology. 2017 May ; 152(6): 1297–1309

Natural history of HBV reactivation during chemotherapy

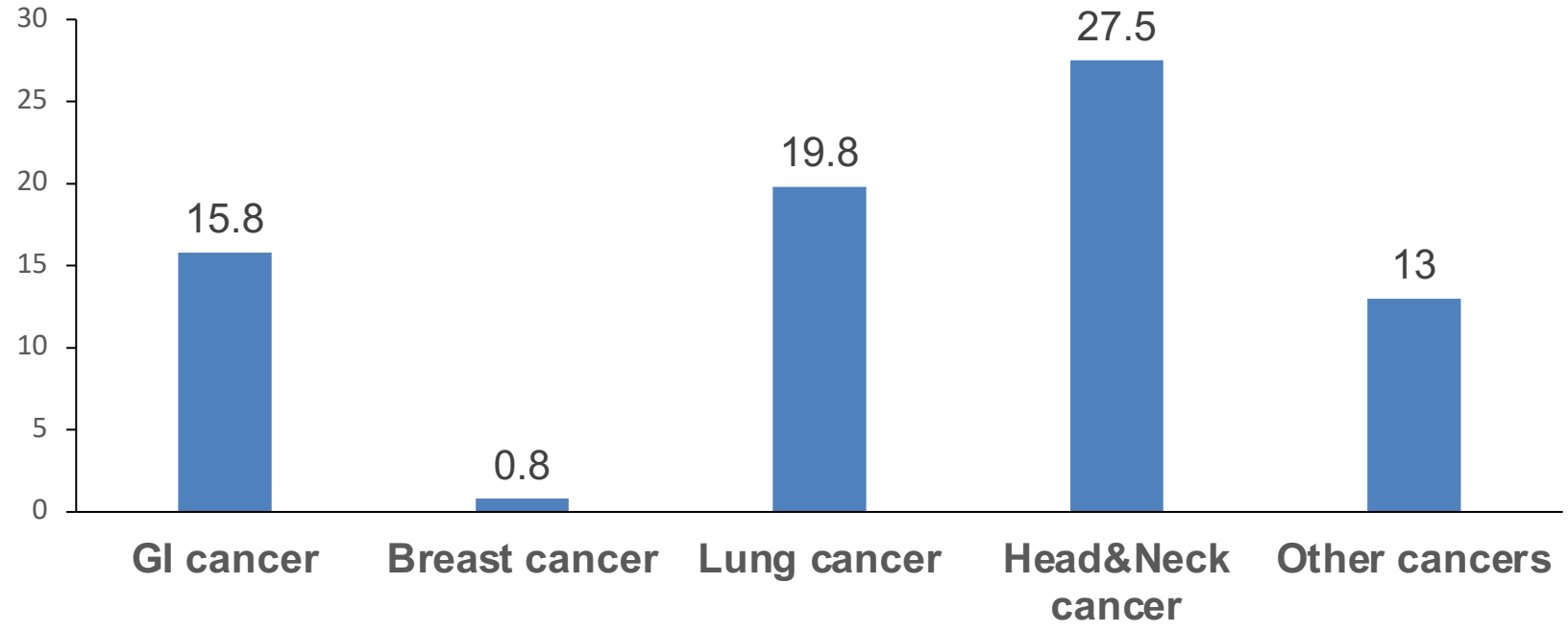


Risk of HBV reactivation

By type of disease

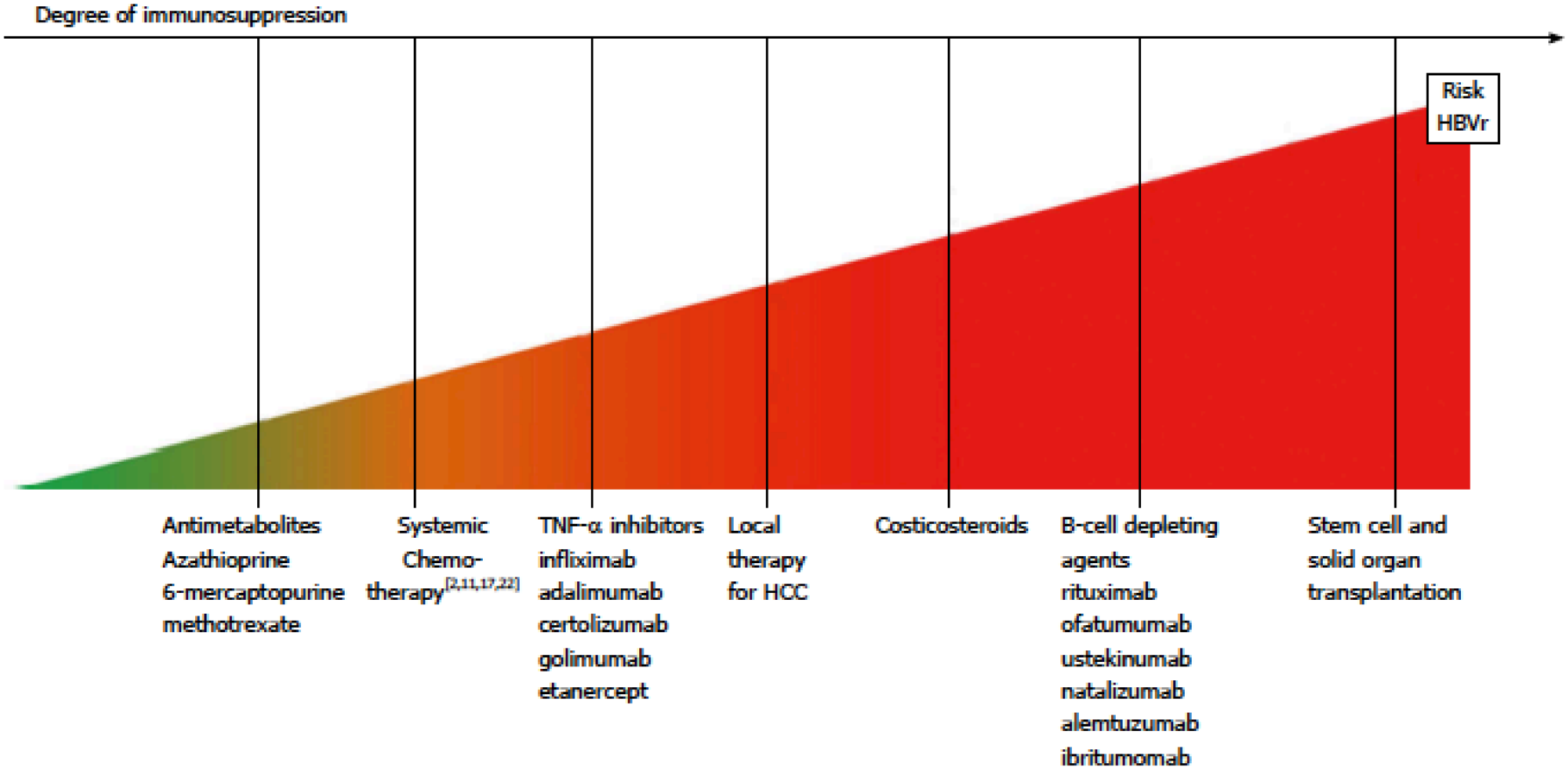
By type of immune suppression

Risk of HBV reactivation by solid tumour type: meta analysis



Paul, Ann Int Med 2016;164(1):30-40.

Risk of reactivation with different classes of immune suppression & chemotherapy



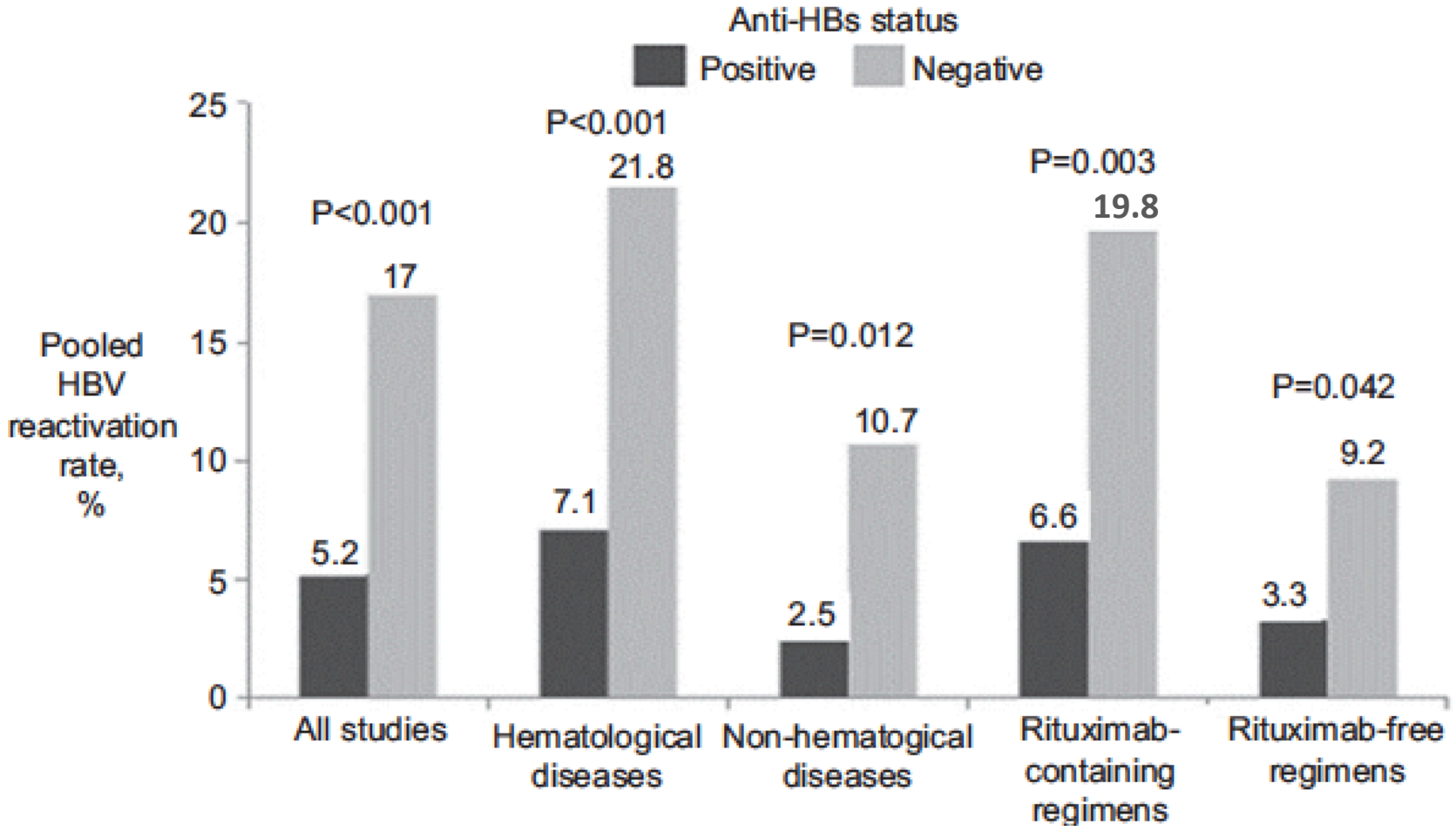
Bessone, World J Hepatol 2016 March 18; 8(8): 385-394

Immunosuppression drug classes and risk of HBV reactivation: AGA Technical Review (Systematic Review)

Drug class	Drug	Risk of reactivation	
		HBsAg pos	HBsAg neg/anti-HBc pos
B-cell depleting agents	• Rituximab (anti-CD20) • Ofatumumab (anti-CD20)	High (30%-60%)	High (> 10%)
TNF-α inhibitors	• Infliximab • Etanercept • Adalimumab	Moderate (1%-10%)	Moderate (1%)
Cytokine inhibitors and integrin inhibitors	• Abatacept (anti-CD80, -86) • Ustekinumab (anti-IL-12, -23) • Natalizumab (binds **α**4-integrin) • Vedolizumab [binds integrin **α**4**β**7 (LPAM-1)]	Moderate (1%-10%)	Moderate (1%)
Tyrosine kinase inhibitors	• Imantinib • Nilotinib	Moderate (1%-10%)	Moderate (1%)
Anthracycline derivatives	• Doxorubicin • Epirubicin	High (15%-30%)	High (> 10%)
Corticosteroids	• High dose, e.g., prednisone ≥ 20 mg for ≥ 4 wk	High (> 10%)	NA
	• Moderate dose, e.g., prednisone < 20 mg for ≥ 4 wk	Moderate (1%-10%)	Moderate (1%-10%)
	• Low dose, e.g., prednisone for < 1 wk	Low (< 1%)	Low (<< 1%)
	• Intra-articular corticosteroids	Low (< 1%)	Low (<< 1%)
Traditional immunosuppression	• Azathioprine • 6-mercaptopurine • Methotrexate	Low (< 1%)	Low (<< 1%)

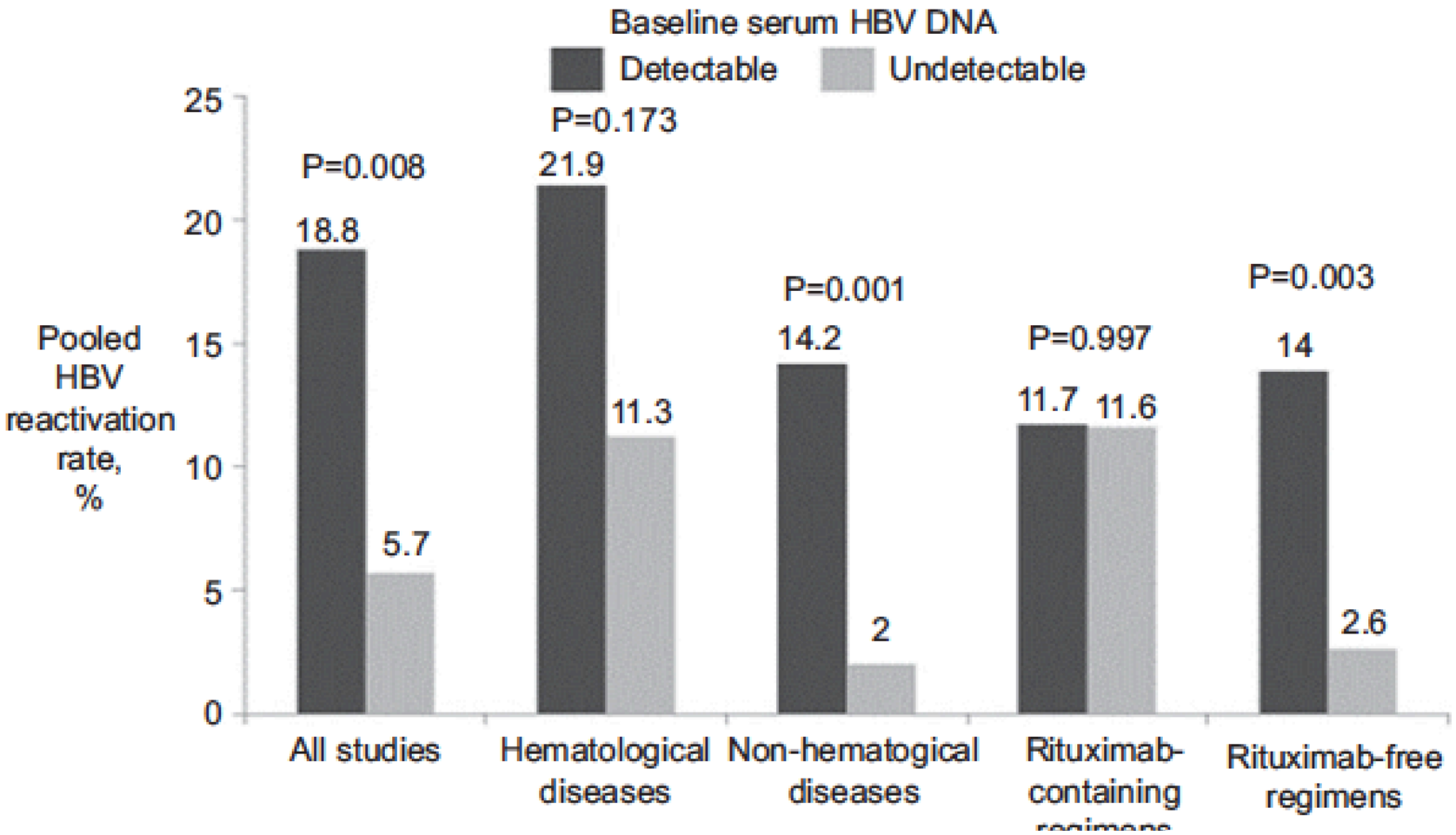
Perillo, Gastroenterology 2015;148(1):221–244

HBV reactivation in those HBsAg neg, based on anti-HBs status



Cholongitas, Annals of Gastroenterology (2018) 31, 480-490

HBV reactivation in those HBsAg neg, based on HBV DNA



Cholongitas, Annals of Gastroenterology (2018) 31, 480-490

Biologics and risk of HBV reactivation: HBsAg positive

Drug class	Risk of reactivation		
	Low(<1%)	Moderate (1-10%)	High (>10%)
TNF-a inhibitors			Infliximab, Adalimumab, Certolizumab, Etanercept, Golimumab
Agents targeting B cells Anti-CD20 Anti-CD38 Anti-CD30 Inhibit B-cell activating factor			Rituximab, Ofatumumab Ocrelizumab, Obinutuzumab, Ibritumomab, Daratumumab, Brentuximab, Belimumab
Direct T-cell activation Anti-CD80/86 Anti-CD2 IL-23 inhibitors IL-17 inhibitors			Belatacept, Abatacept Alefacept, Ustekinumab Guselkumab, Tildrakizumab, Secukinumab, Ixekizumab, Brodalumab
Direct T-cell inhibition and agents targeting T-cell migration and chemotaxis Blocking alpha4-integrin Anti-CD52		Natalizumab Vedolizumab	Alemtuzumab
Interleukin inhibitors IL-1 inhibitors IL-6 inhibitors		Anakinra, Tocilizumab Canakinumab, Rilonacept, Sarilumab	
Checkpoint inhibitors	Ipilimumab, Atezolizumab, Durvalumab, Nivolumab, Pembrolizumab, Cemiplimab, Avelumab		
Tyrosine kinase inhibitors for heme malignancies Bruton tyrosine kinase inhibitors Small-molecule Bcr-Abl tyrosine kinase inhibitors		Ibrutinib, Acalabrutinib, Imatinib, Nilotinib Dasatinib, Bosutinib Ponatinib, Bafetinib	
EGFR inhibitors and other tyrosine kinase inhibitors for solid tumors EGFR tyrosine kinase inhibitors EGFR inhibiting monoclonal antibody Other tyrosine kinase inhibitors VEGF inhibitors VEGF and FGFR inhibitors	Cetuximab, Panitumumab Sorafenib, Sunitinib Bevacizumab Lenvatinib	Gefitinib, Erlotinib Osimertinib, Afatinib Dacomitinib	
Targeting JAK-STAT signaling and complement pathway JAK inhibitors C5 inhibitors	Eculizumab Ravulizumab	Ruxolitinib, Tofacitinib, Baricitinib	

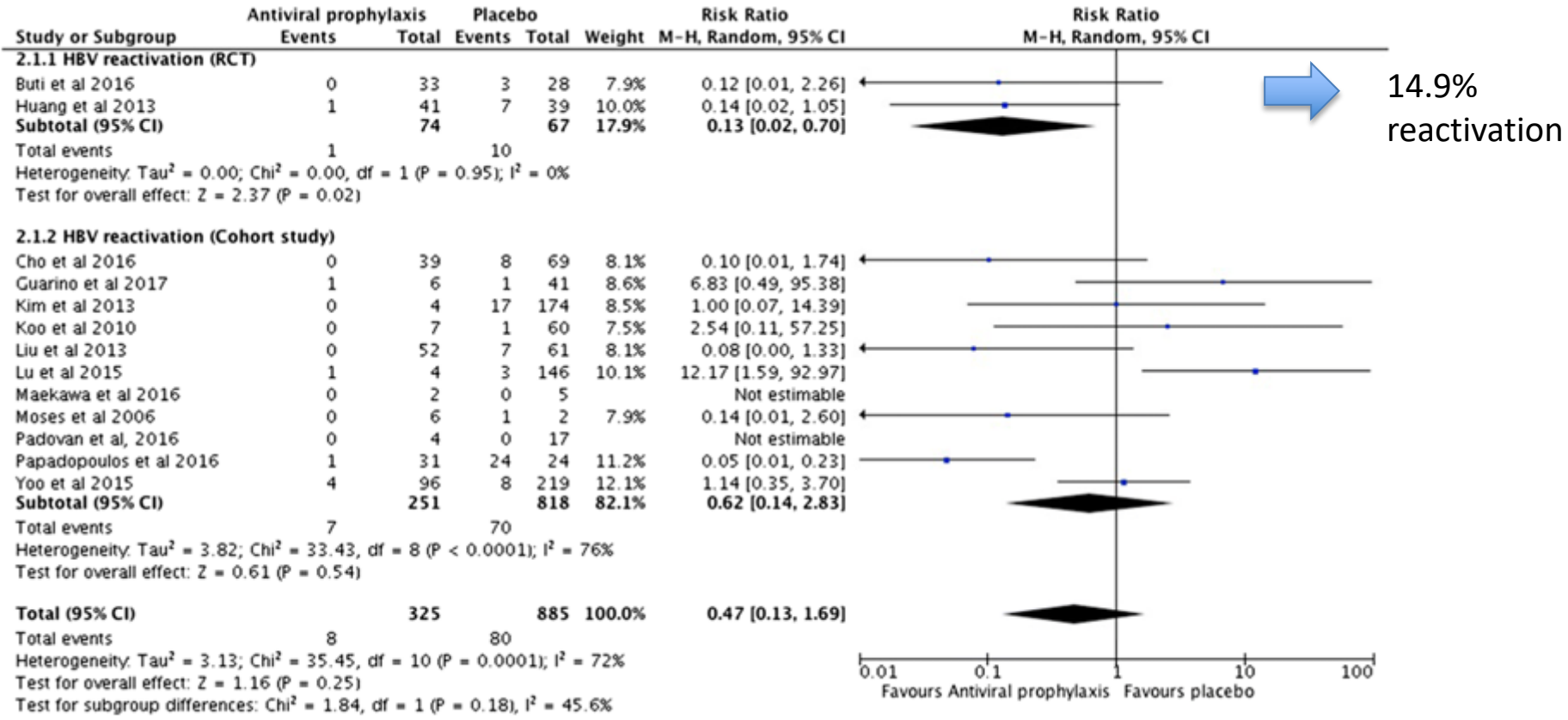
Ogawa et al, Infect Dis Clin N Am 34 (2020) 341–358

Biologics and risk of HBV reactivation: HBsAg(-) anti-HBc(+)

Drug class	Risk of reactivation		
	Low(<1%)	Moderate (1-10%)	High (>10%)
TNF-a inhibitors		Infliximab, Adalimumab, Certolizumab, Etanercept, Golimumab	
Agents targeting B cells Anti-CD20 Anti-CD38 Anti-CD30 Inhibit B-cell activating factor		Daratumumab, Brentuximab, Belimumab	Rituximab, Ofatumumab Ocrelizumab, Obinutuzumab, Ibritumomab
Direct T-cell activation Anti-CD80/86 Anti-CD2 IL-23 inhibitors IL-17 inhibitors		Belatacept, Abatacept Alefacept, Ustekinumab Guselkumab, Tildrakizumab, Secukinumab, Ixekizumab, Brodalumab	
Direct T-cell inhibition and agents targeting T-cell migration and chemotaxis Blocking alpha4-integrin Anti-CD52		Natalizumab Vedolizumab Alemtuzumab	
Interleukin inhibitors IL-1 inhibitors IL-6 inhibitors		Anakinra, Tocilizumab Canakinumab, Rilonacept, Sarilumab	
Checkpoint inhibitors	Ipilimumab, Atezolizumab, Durvalumab, Nivolumab, Pembrolizumab, Cemiplimab, Avelumab		
Tyrosine kinase inhibitors for heme malignancies Bruton tyrosine kinase inhibitors Small-molecule Bcr-Abl tyrosine kinase inhibitors		Ibrutinib, Acalabrutinib, Imatinib, Nilotinib Dasatinib, Bosutinib Ponatinib, Bafetinib	
EGFR inhibitors and other tyrosine kinase inhibitors for solid tumors EGFR tyrosine kinase inhibitors EGFR inhibiting monoclonal antibody Other tyrosine kinase inhibitors VEGF inhibitors VEGF and FGFR inhibitors	Cetuximab, Panitumumab Sorafenib, Sunitinib Bevacizumab Lenvatinib	Gefitinib, Erlotinib Osimertinib, Afatinib Dacomitinib	
Targeting JAK-STAT signaling and complement pathway JAK inhibitors C5 inhibitors	Eculizumab Ravulizumab	Ruxolitinib, Tofacitinib, Baricitinib	

Ogawa et al, Infect Dis Clin N Am 34 (2020) 341–358

HBV reactivation in HBsAg negative, anti-HBc Ab positive patients with Rituximab Therapy



14.9% reactivation

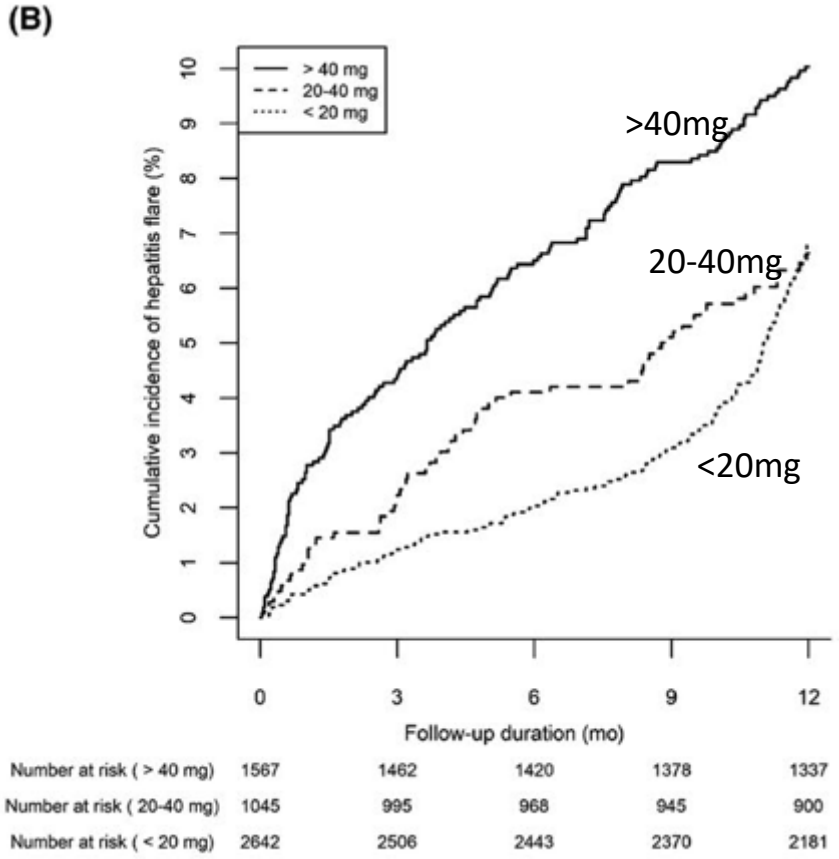
- Blocking B cell function leads to HBV reactivation in ~15% of HBsAg negative patients

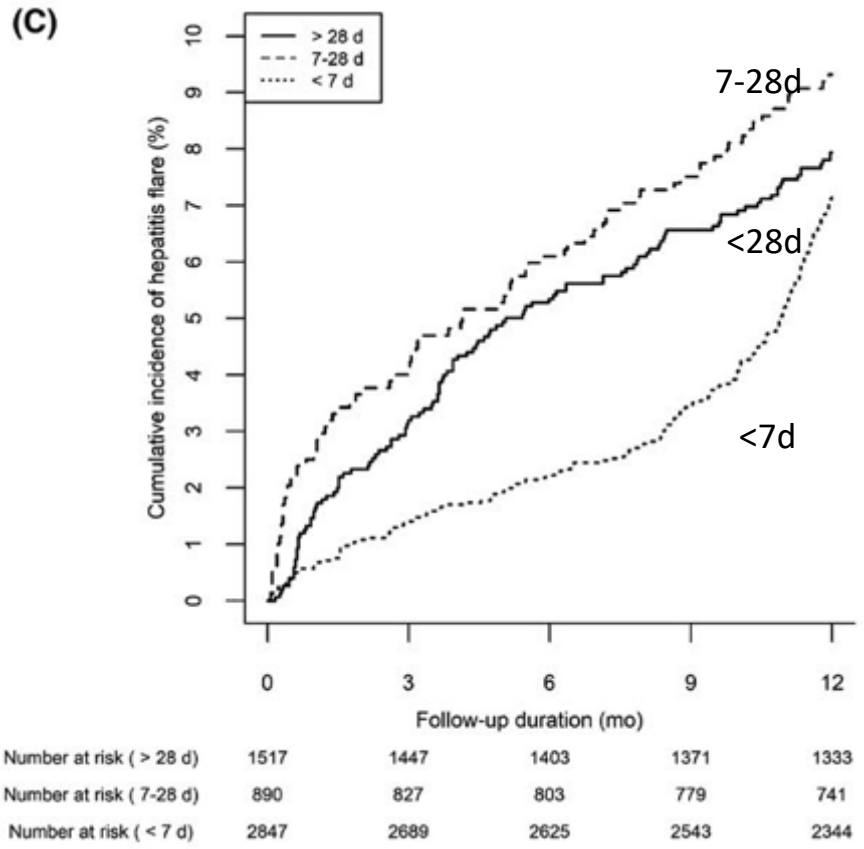
Su, Eur J Clin Pharmacol. 2018 Sep;74(9):1111-1119.

Corticosteroids

Dose and duration of corticosteroids on risk of HBV Flare

- 5254 patients evaluated from HK Hosp Authority database from 2001-2004 (before lamivudine era)
- Highest risk of HBV flare was in those treated with prednisolone >40mg (HR 1.64) and those treated from 7-28d & >28d (HR 1.90, 1.64 respectively)





Wong, Liver International. 2018;1–9.

HBV reactivation with oral prednisone in HBsAg+ patients

- No systematic reviews of HBV reactivation in corticosteroid therapy
  - » Clinical studies show reactivation with prednisolone >30mg, >12w➔reactivation 30-70%

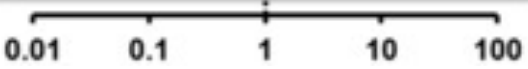
Hwang J and Lok AS. *Nat Rev Gastroenterol Hepatol* 2014;11(4):209–19.

- What is a safe steroid dose? Low risk group:
  - » Low dose (<10 mg/day)
  - » Short course (<4 weeks)
  - » Inhaled
  - » Intra-articular

Perillo, Gastroenterology 2015;148:221–244

Risk factors for HBV reactivation in resolved HBV (HBsAg neg, anti-HBc pos) treated for solid tumours

Factor	Reference	Score χ2	Odds ratio	95% CI	*p*-value
Age	≤ 70	0.71	2.14	0.42-10.9	0.40
Sex	female	0.89	2.77	0.41-18.7	0.35
HBcAb	≥ 8.0 S/CO	0.16	0.69	0.14-3.53	0.69
HBsAb	≥ 10.0 mIU/mL	4.69	5.94	1.15-30.6	0.03
Platinum	No	1.80	5.80	0.55-60.3	0.18
Total DEX	≤ 100.0 mg	0.29	1.63	0.32-8.33	0.59
Daily DEX dose	≤ 1.0 mg/day	5.25	8.69	1.27-58.8	0.02



251 patients had resolved HBV infection (negative for HBs antigen and positive for anti-HBc antibody and/or positive for anti-HBs antibody)

- Cancer types: lung (33%), GI (27%), Gynae (14%), urology (13%), breast (6%)
- Chemotherapy: Platinum based (66.3%), anthracycline based (10%), Dex (83%)

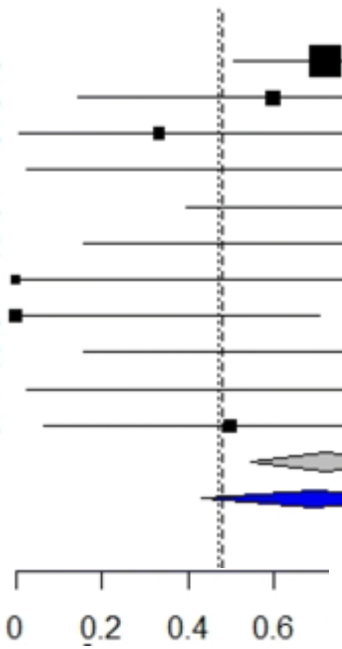
Kotake, Asia Pac J Clin Oncol 2019 Feb; 15(1): 63–68.

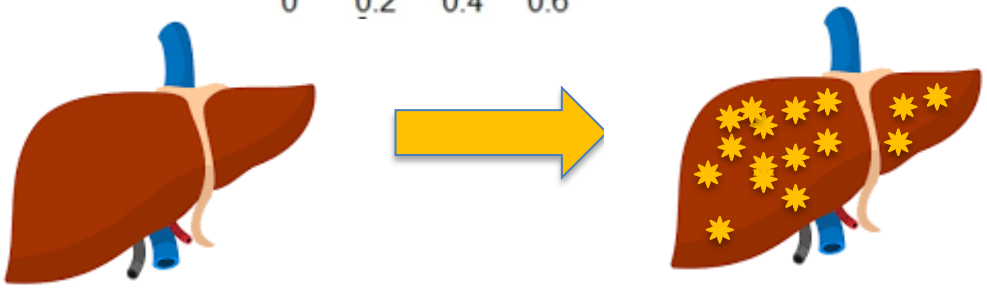
Transplantation

De novo HBV post Liver Transplant: meta analysis

Study	Events	Total	Proportion	95%-CI	Weight (fixed)	Weight (random)
HBcAb negative						
Dodson 1997 [2]	18	25	0.72	[0.51; 0.88]	29.5%	10.3%
Douglas 1997 [3]	3	5	0.60	[0.15; 0.95]	6.4%	7.4%
Rokuharo 2000 [6]	1	3	0.33	[0.01; 0.91]	4.0%	6.1%
Manzabeita 2002 [9]	1	1	1.00	[0.03; 1.00]	1.7%	3.7%
Roque 2002 [11]	4	4	1.00	[0.40; 1.00]	5.2%	6.8%
Chen 2002 [12]	2	2	1.00	[0.16; 1.00]	2.9%	5.1%
Barcena 2006 [19]	0	1	0.00	[0.00; 0.98]	1.7%	3.7%
Prakoso 2006 [21]	0	3	0.00	[0.00; 0.71]	4.0%	6.1%
Kim 2011 [26]	2	2	1.00	[0.16; 1.00]	2.9%	5.1%
Pan 2011 [28]	1	1	1.00	[0.03; 1.00]	1.7%	3.7%
Han 2015 [33]	2	4	0.50	[0.07; 0.93]	5.2%	6.8%
Fixed effect model		**51**	**0.72**	**[0.55; 0.88]**	**65.3%**	--
Random effects model			**0.70**	**[0.43; 0.92]**	--	**64.9%**

Heterogeneity: I^2 = 37%, p = 0.10





Liver Transplant Donor

HBsAg neg
Anti-HBc pos

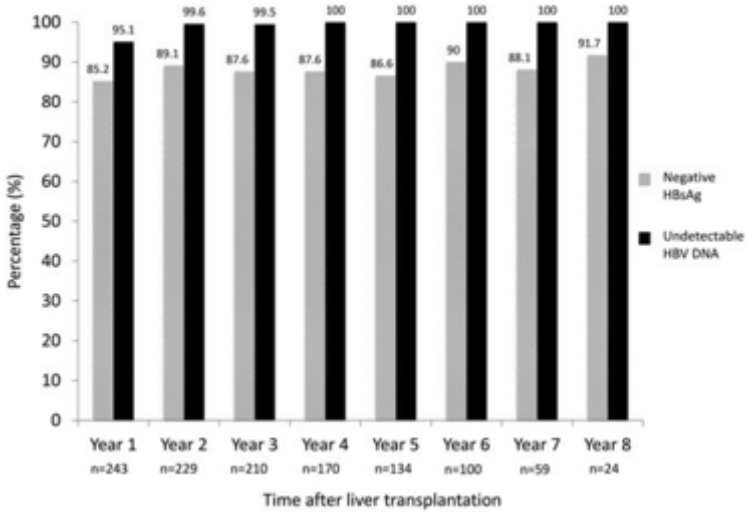
Liver Transplant Recipient

Up to 72% De Novo HBV
In anti-HBc neg recipient

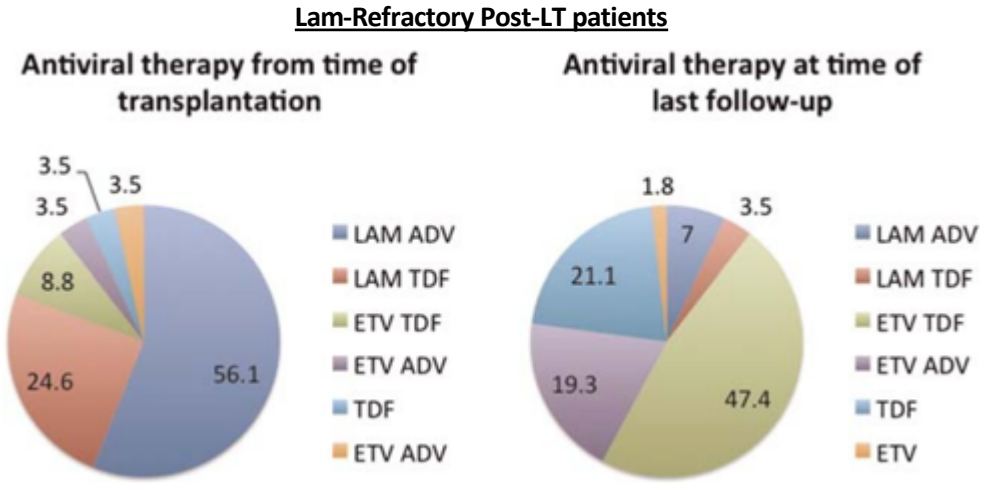
Yang, Hepatol Int 2020 Mar;14(2):202-211.

HBV Prophylaxis after Liver Transplantation without HBIg

- Long-term antiviral prophylaxis is required after liver transplantation for patients with chronic HBV infection to prevent reactivation



J Fung et al. Hepatology 2017



J Fung et al. Transplantation. 2017

Guideline recommendations

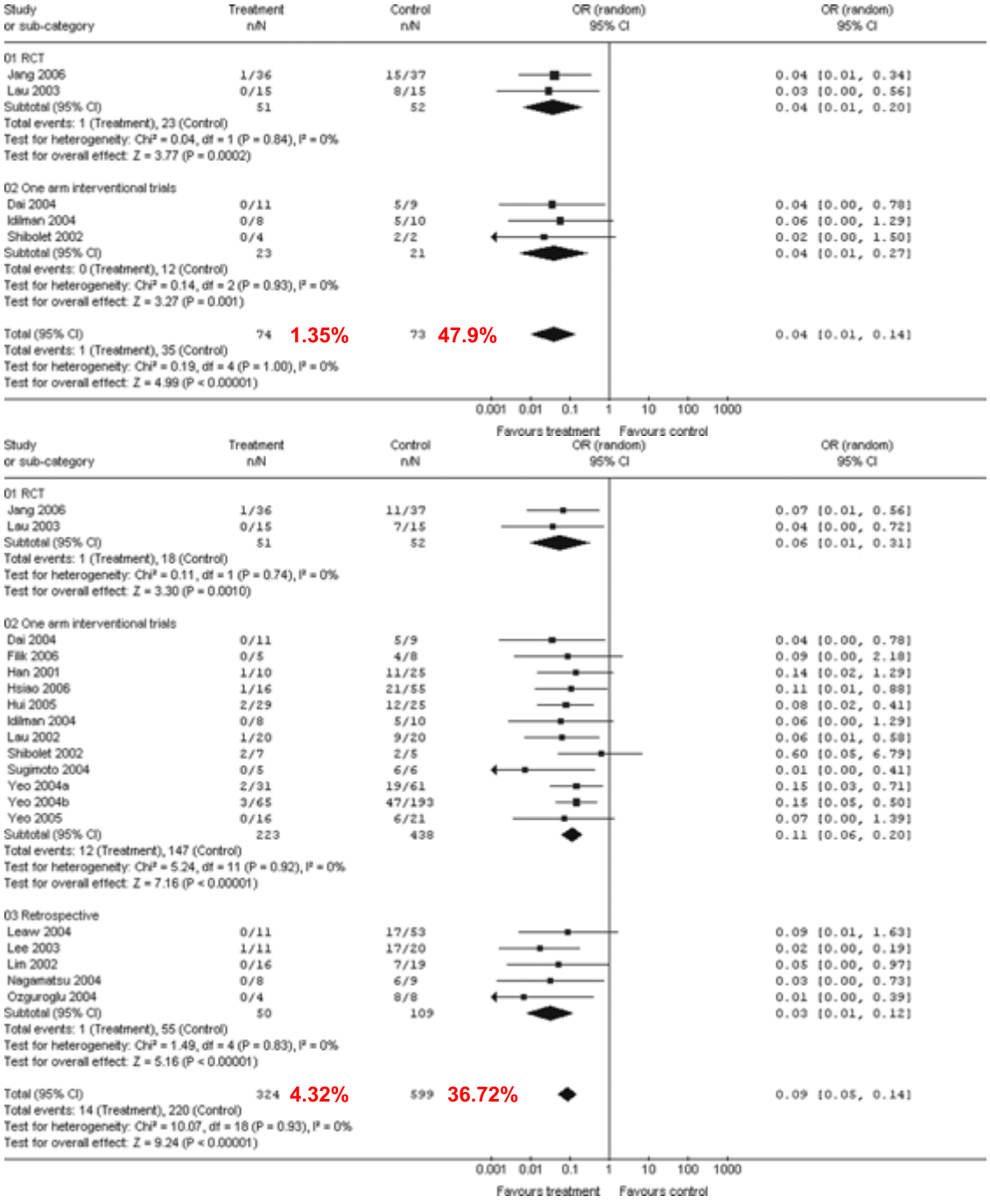
Guideline Recommendations for HBV Screening and Antiviral Prophylaxis

	HBV Screening		Routine Antiviral prophylaxis		
	Population	**Tests**	**Population**	**Duration of prophylaxis**	**Antivirals**
AASLD[1]	**High risk of HBV infection**	**HBsAg, anti-HBc**	**HBsAg+* (regardless of HBV DNA levels)**	**During tx + 6-12 months after cessation of therapy (12m for those on anti-CD20)**	**• High genetic barrier drugs: ETV, TDF, TAF**
			HBsAg- Ant-HBc+	**Only those with lymphoma on anti-CD20 Treatment should be during Tx and 12m after stopping therapy**	**• High genetic barrier drugs: ETV, TDF, TAF**
EASL[2]	**All candidates for chemo- and Immunosuppressive therapy**	**HBsAg, anti-HBc, HBV DNA**	**HBsAg+ (regardless of HBV DNA levels)**	**During Tx + 12 months after cessation of therapy**	**• High genetic barrier drugs: ETV, TDF, TAF**
			HBsAg-/Anti-HBc+/HBV DNA+**	**Those receiving anti-CD20 or stem cell transplant During Tx + 18 months after cessation of therapy**	**• High genetic barrier drugs: ETV, TDF, TAF**
APASL[3]	**All candidates for chemo- and Immunosuppressive therapy**	**HBsAg, anti-HBc**	**HBsAg+**	**During Tx + 12 months after cessation of therapy**	**Nucleoside Analogues**
			HBsAg- Ant-HBc+	**For BM or Stem Cell Transplant – duration uncertain No recommendation for anti-CD20 (monitoring or antivirals unclear)**	**Nucleoside Analogues**

*__HBsAg-/anti-HBc+(regardless of anti-HBs)__ - Monitoring and **pre-emptive therapy** when HBV DNA becomes detectable.
** __HBsAg-/anti-HBc+/HBV DNA- (regardless of anti-HBs)__ – Monitoring and **pre-emptive therapy** upon confirmation of HBV reactivation before ALT elevation.

1. Terrault. *Hepatology* 2018;67:1560; 2. EASL Clinical Practice Guidelines: Management of chronic hepatitis B. *J Hepatol*. 2017; 3. Sarin S, et al. *Hep Int* 2015.

Outcomes of HBV reactivation

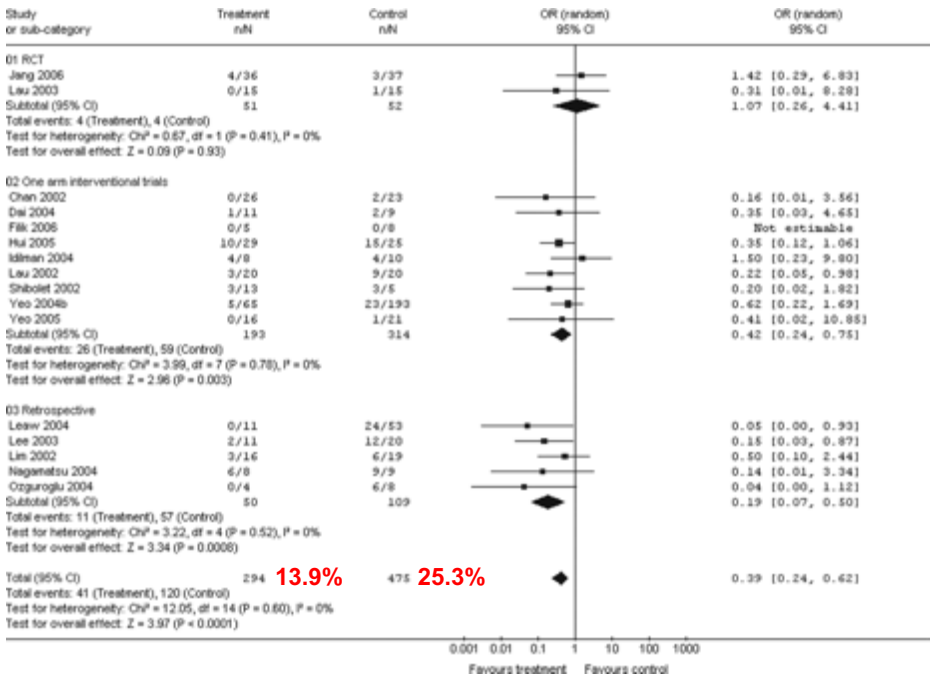


LAM prevents viral & clinical reactivation in immunosuppressed CHB

Viral reactivation 97.2% reduction

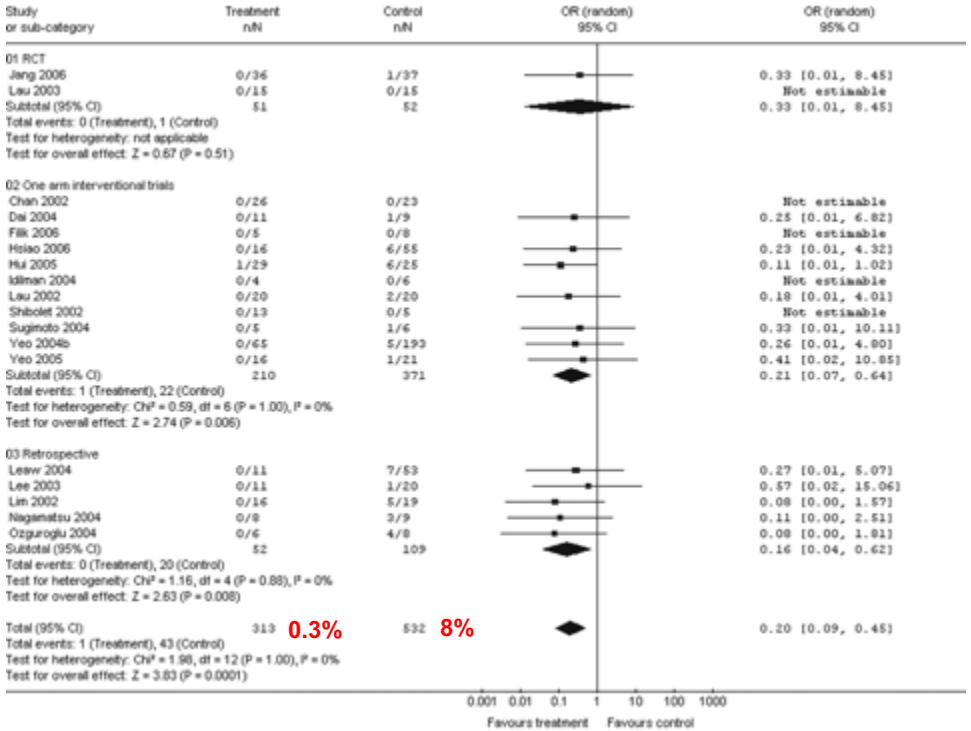
Clinical reactivation 88.2% reduction

Katz, J Viral Hep 2008 Feb;15(2):89-102.



LAM reduces overall & HBV related mortality

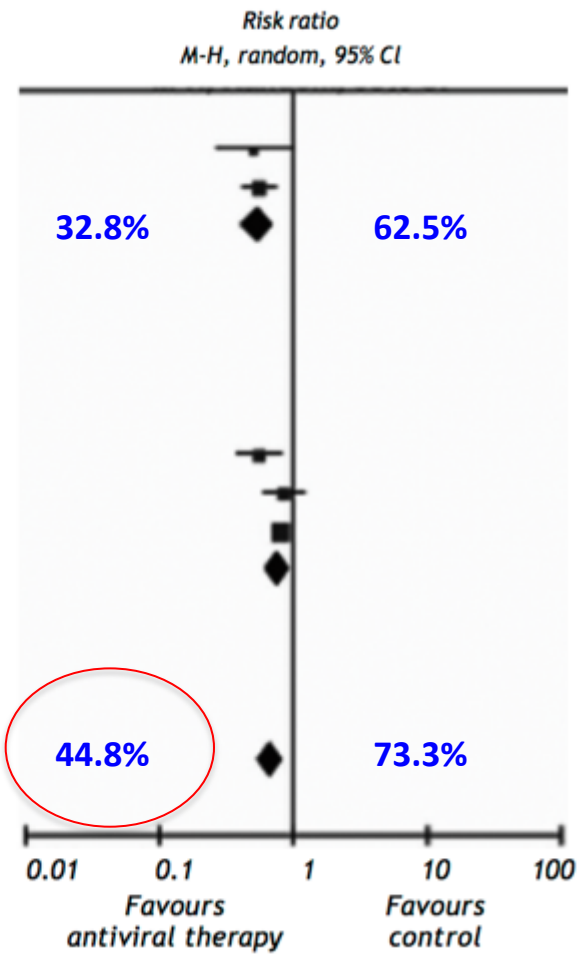
LAM reduces overall mortality by 45%



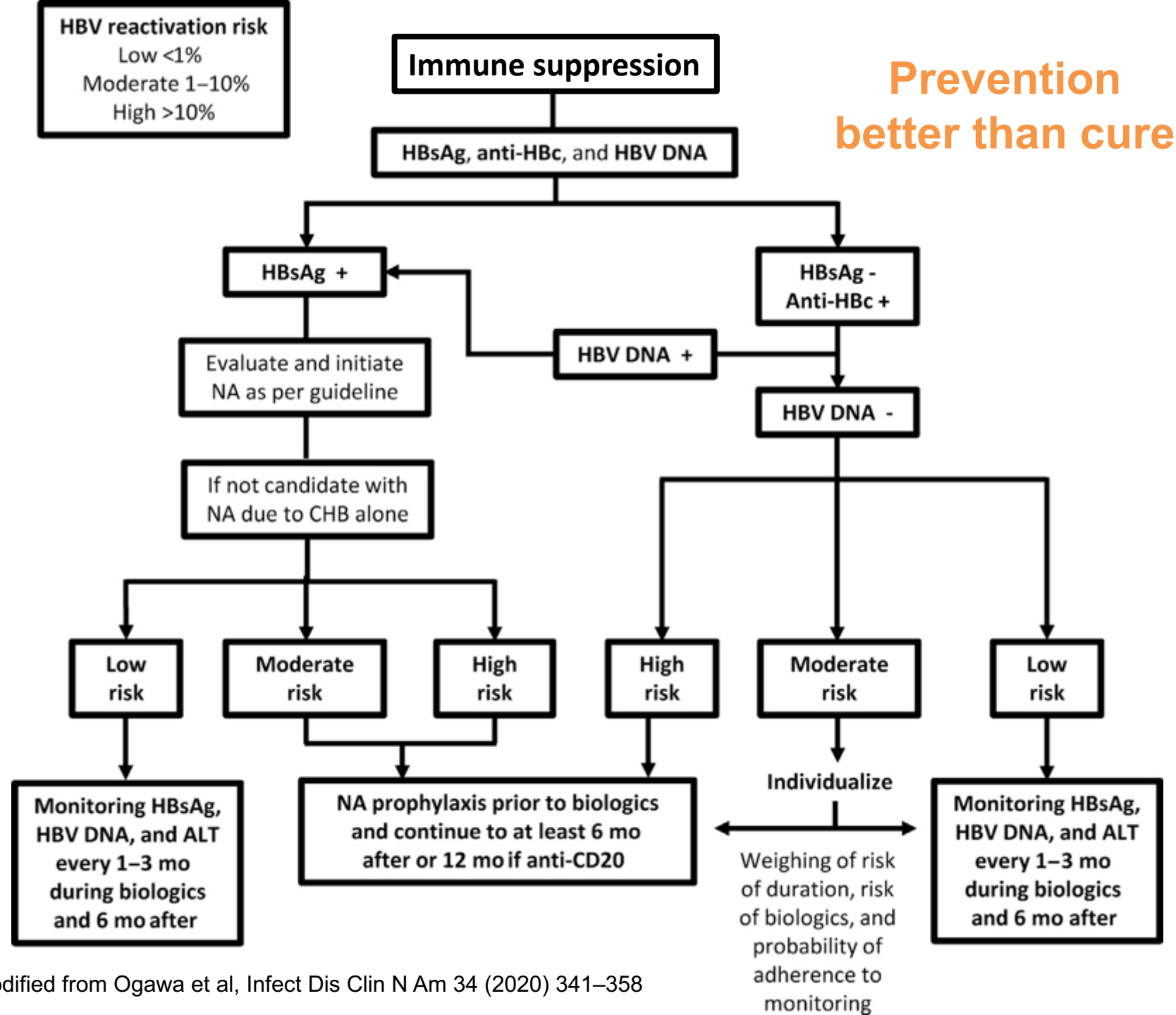
LAM reduces HBV related mortality by 96%

Anti-viral therapy in treatment of HBV induced ACLF

Study of subgroup	Antiviral therapy Events	Total	Control Events	Total	Weight	Risk ratio M-H, random. 95% CI
1.12.1 RCT						
Garg 2011	6	14	11	13	8.8%	0.51 (0.27, 0.97)
Hu 2010	70	218	34	59	22.6%	0.56 (0.42, 0.75)
Subtotal (95% CI)		232		72	31.4%	0.55 (0.42, 0.72)
Total events	76		45			
Heterogeneity: $Tau^2 = 0.00$; $\chi^2 = 0.07$, $df = 1$ ($P = 0.79$); $I^2 = 0\%$.						
Test for overal effec: $Z = 4.43$ ($P < 0.00001$)						
1.12.2 Retrospective cohort						
Chen 2011	26	72	22	34	16.9%	0.56 (0.38, 0.83)
Cui 2010	34	67	22	37	18.9%	0.85 (0.60, 1.22)
Sun 2009	86	124	109	127	32.8%	0.81 (0.70, 0.93)
Subtotal (95% CI)		263		198	68.6%	0.76 (0.62, 0.93)
Total events	146		153			
Heterogeneity: $Tau^2 = 0.01$; $\chi^2 = 3.34$, $df = 2$ ($P = 0.19$); $I^2 = 40\%$						
Test for overall effect: $Z = 2.62$ ($P = 0.009$)						
Total (95% CI)		495		270	100.0%	0.68 (0.54, 0.84)
Total events	222		198			
Heterogeneity: $Tau^2 = 0.03$; $\chi^2 = 9.66$, $df = 4$ ($P = 0.05$); $I^2 = 59\%$						
Test for overall effect: $Z = 3.49$ ($P = 0.0005$)						
Test for subgroup differences: $\chi^2 = 3.63$, $df = 1$ ($P = 0.06$), $I^2 = 72.4\%$						



Shi, Annals Hepatol 2013;12(3):364-372



Modified from Ogawa et al, Infect Dis Clin N Am 34 (2020) 341–358

Conclusions

- Risk for HBV reactivation can be categorised to high (>10%), moderate (1-10%) or low risk (<1%)
- Using HBsAg neg anti-HBc pos as a surrogate for OBI, antiviral prophylaxis should be given for those who are moderate or high risk
- Antiviral prophylaxis generally should use high genetic barrier drugs and for an additional 6-12m after end of immunosuppression
- All patients need to be monitored regularly for potential reactivation
- Reactivation of HBV can rapidly lead to acute on chronic liver failure may not be able to be rescued with antiviral therapy (44% mortality with antiviral therapy)
- If in doubt, risk/benefit ratio is to give prophylaxis as benefit far outweighs the risks.

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UPDATES

LIVE WEBINARS		
Topic: Speaker: Date And Time:	**Prophylaxis for HBV and occult HBV in the immunocompromised** **PROF. SENG GEE LIM** Monday, 2 November 2020 8.00pm – 9.00pm HKT/SGT	
Topic: Speaker: Date And Time:	**Immnotherapy for advanced HCC** **PROF. SENG GEE LIM** Monday, 9 November 2020 8.00pm – 9.00pm HKT/SGT	

ADVANCED LIVER DISEASE WEBINAR SERIES

Topic: Speaker: Date And Time:	**Advanced liver disease - the scope of the problem** **PROF. SENG GEE LIM** Monday, 16 November 2020 7.30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Hepatocyte transplantation - the new frontier?** **PROF. YOCK YOUNG DAN** Monday, 16 November 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Portal hypertension update 2020** **PROF. GUADALUPE GARCIA-TSAO** Monday, 23 November 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Advances in Hepatic encephalopathy** **PROF. RAJENDER REDDY** Monday, 30 November 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Long term albumin replacement: a panacea for decompensated cirrhosis?** **PROF. MAURO BERNADI** Monday, 7 December 2020 30 pm – 8.30 pm HKT/SGT	
Topic: Speaker: Date And Time:	**Best Management Practices for Diuretic resistant ascites and Hepatorenal Syndrome** **PROF. SIMONE STRASSER** Monday, 14 December 2020 30 pm – 8.30 pm HKT/SGT	

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