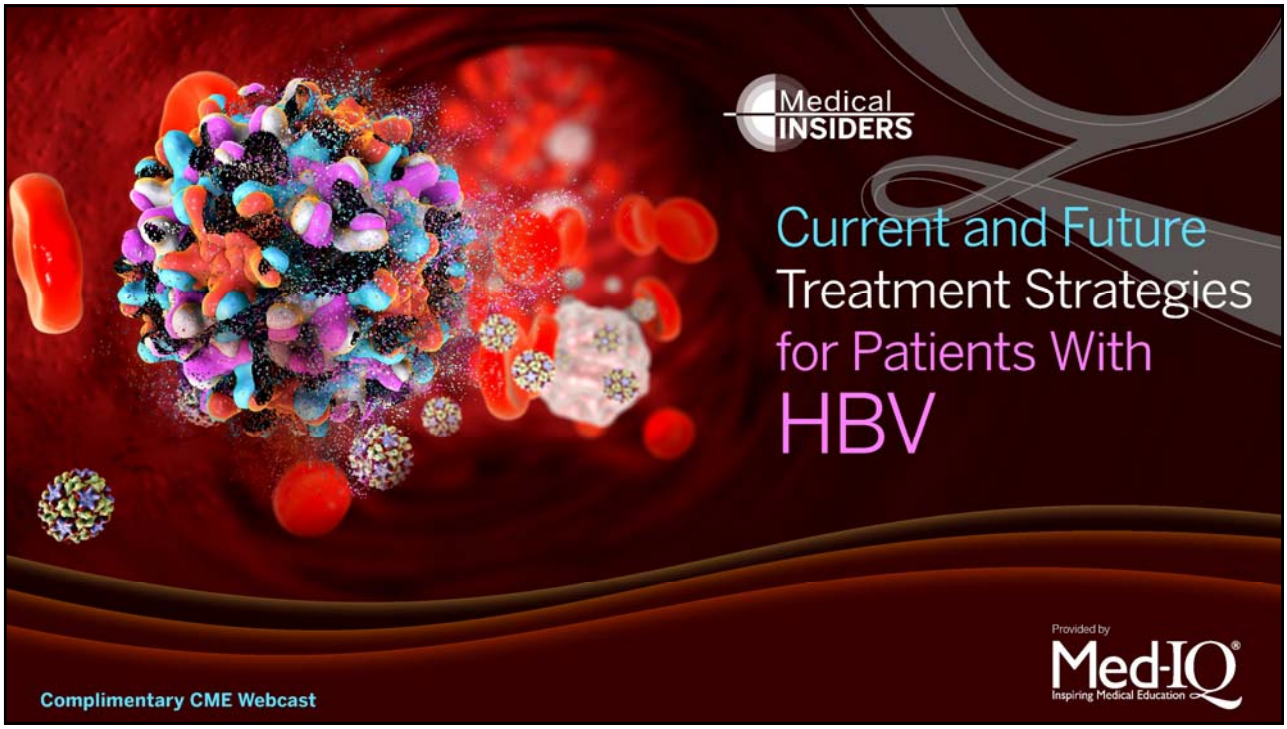


Who to Treat?

Parameter	AASLD	US Algorithm	EASL	APASL
HBV DNA CRITERIA				
HBeAg+	> 20,000 IU/mL	> 2,000 IU/mL	> 2,000 IU/mL	> 20,000 IU/mL
HBeAg-	> 2,000 IU/mL	> 2,000 IU/mL	> 2,000 IU/mL	> 2,000 IU/mL
ALT CRITERIA				
PNALT 1-2 × ULN	Monitor Consider biopsy or elastography	Consider biopsy Treat	Monitor* Treat	Monitor Consider biopsy
> 2 × ULN	Treat	Treat	Treat	Treat
CIRRHOTIC PATIENTS				
Compensated	Treat	HBV DNA detectable → treat	Treat	DNA > 2,000 IU/mL → treat
Decompensated	Treat	Treat	Treat	Treat

*Patients with HBeAg-positive chronic HBV infection who are younger than 30 years and do not fulfill any of the treatment indications should be followed at least every 3-6 months. Patients with HBeAg-positive chronic HBV infection, defined by persistently normal ALT and high HBV DNA levels, may be treated if they are older than 30 years regardless of the severity of liver histologic lesions. Patients with HBeAg-negative chronic HBV infection and serum HBV DNA ≥ 2,000 IU/mL who do not fulfil any of the treatment indications should be followed for 3 months for the first year and every 6 months thereafter.

Terrault NA, et al. *Hepatology*. 2016;63:261-83; Martin P, et al. *Clin Gastroenterol Hepatol*. 2015;13:2071-2087; EASL 2017 Practice Guidelines. www.easl.eu/medias/cpg/management-of-hepatitis-B-virus-infection/English-report.pdf; Sarin SK, et al. *Hepatol Int*. 2016;10:1-98.

Case 1

- A 27-year-old, Korean, male graduate student presents for initial evaluation
- Referred by his PCP for the management of HBV infection
- Diagnosed at age 23 in South Korea
- Has never undergone a liver biopsy or prior antiviral therapy; reports no liver-specific symptoms
- Has been told by prior doctors that his infection is “stable” and does not require treatment
- Reports heightened concern about his liver because his father died last year of HBV-associated liver cancer
- Has one maternal uncle and one paternal uncle who both died of liver cancer (the latter at 38 years old)

Case 1 (cont.)

- The patient is single
- No alcohol or tobacco use
- He takes no medications, including over-the-counter medications, alternative remedies, or herbal remedies
- His physical examination reveals a body mass index of 27 kg/m^2 but is otherwise unremarkable

Case 1 (cont.)

Initial laboratory results reveal:

WBC count	5.4 x 10^9/L
Hb	15.1 g/dL
Platelet count	196,000/mL
Albumin	4.8 g/dL
Total bilirubin	0.9 mg/dL
AST	35 U/L
ALT	41 U/L
Alkaline phosphatase	52 U/L
Creatinine	0.7 mg/dL
Alpha-fetoprotein	2.8 ng/mL
HBsAg	Reactive
HBcAb	Reactive
HBsAb	Nonreactive
HBeAg	Reactive
HBeAb	Nonreactive
HAV Ab total	Reactive
HCV Ab	Nonreactive
HDV Ab	Nonreactive
HBV DNA	> 170 million IU/mL

Case 1 (cont.)

- Liver ultrasonography reveals moderately increased echogenicity and no focal liver mass
- Further testing confirms that he has HBV genotype C, and Fibroscan reveals a median liver stiffness measurement of 4.6 kPa

Case 2

- A 32-year-old Vietnamese woman presents for initial consultation
- Referred by her obstetrician for newly diagnosed chronic HBV infection
- Is currently in her sixteenth week of gestation; her pregnancy has been uneventful
- Reports no chronic medical problems and takes no medications except for folic acid
- Reports a family history of chronic HBV infection in her mother and sister but does not report a known family history of liver cancer
- Does not drink alcohol or smoke tobacco
- Her physical examination reveals no stigmata of advanced liver disease

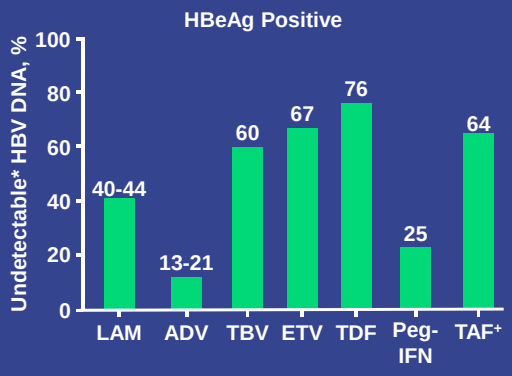
Case 2 (cont.)

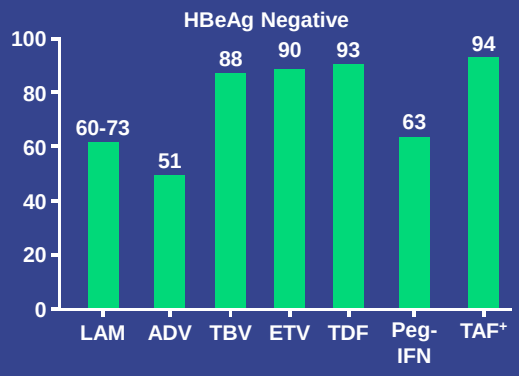
Initial laboratory results reveal:

WBC count	4.9 x 10^9/L
Hb	12.8 g/dL
Platelet count	236,000/mL
Total bilirubin	0.5 mg/dL
AST	14 U/L
ALT	16 U/L
Alkaline phosphatase	61 U/L
HBsAg	Reactive
HBcAb	Reactive
HBsAb	Nonreactive
HBeAg	Reactive
HBeAb	Nonreactive
HAV Ab total	Reactive
HBV genotype B	
HBV DNA	10,269,384 IU/mL

Treatment of Chronic HBV Infection in 2017: Efficacy Data (DNA)

- Not head-to-head trials; different patient populations and trial designs



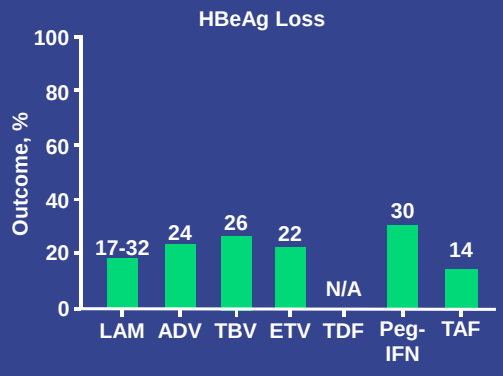


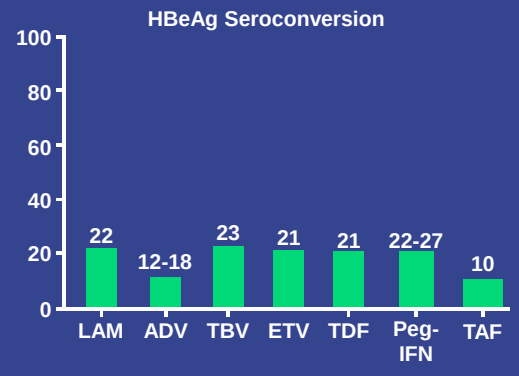
*By PCR-based assay (LLD ~ 50 IU/mL) except for some LAM studies.
+HBV DNA below 29 IU/mL.

Lok AS, et al. *Hepatology*. 2007;45:507-39; Lok AS, et al. *Hepatology*. 2009;50:661-2; Buti M. EASL 2016; April 14, 2016; Barcelona, Spain. Abstract GS06; Chan HYL. EASL 2016; April 15, 2016; Barcelona, Spain. Abstract GS12.

Treatment of Chronic HBV Infection in 2017: Efficacy Data (HBeAg)

- Not head-to-head trials; different patient populations and trial designs

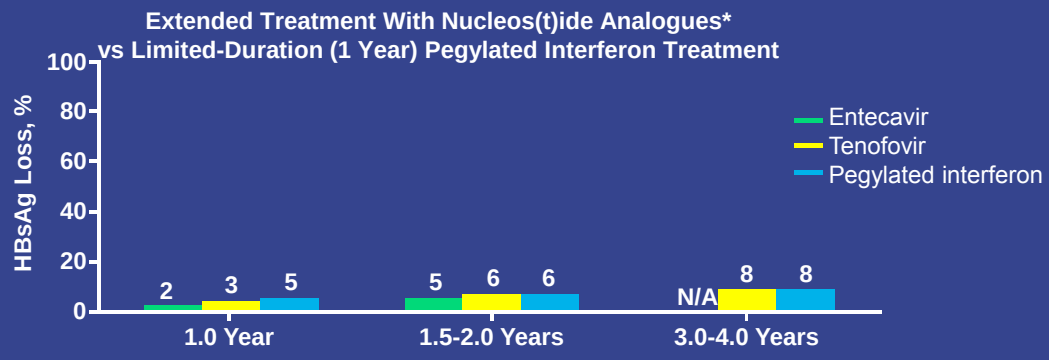




Lok AS, et al. *Hepatology*. 2009;50:1-36; Lau GK, et al. *N Engl J Med*. 2005;352:2682-95; Marcellin P, et al. *N Engl J Med*. 2003;348:808-16; Chang TT, et al. *N Engl J Med*. 2006;354:1001-10; Lai CL, et al. *N Engl J Med*. 2007;357:2576-88; Marcellin P, et al. *N Engl J Med*. 2008;359:2442-55; Janssen HL, et al. *Lancet*. 2005;365:123-9; Chan HYL. EASL 2016; April 15, 2016; Barcelona, Spain. Abstract GS12.

HBsAg Loss Over Time in HBeAg-Positive Patients

- Not head-to-head trials; different patient populations and trial designs



Chang TT, et al. *N Engl J Med*. 2006;354:1001-10; Marcellin P, et al. *N Engl J Med*. 2008;359:2442-55; Buster EH, et al. *Gastroenterology*. 2008;135:459-67; Gish R, et al. *Gastroenterology*. 2007;133:1437-44; Heathcote J. AASLD 2008; October 31-November 4, 2008; San Francisco, CA. Abstract 158; Heathcote J, et al. AASLD 2009; October 30-November 3, 2009; Boston, MA. Abstract 483; Janssen HL, et al. *Lancet*. 2005;365:123-9.

*With sustained undetectable HBV DNA.

When to Stop Nucleos(t)ide Analogues

	AASLD 2016	APASL 2015	EASL 2017
HBeAg+	HBeAg seroconversion and undetectable HBV DNA plus ≥ 12 months' consolidation	HBeAg seroconversion and undetectable HBV DNA plus preferably 3 years' consolidation	Noncirrhotic patients who achieve HBeAg seroconversion and undetectable HBV DNA plus ≥ 12 months' consolidation
HBeAg-	HBsAg loss?	HBsAg loss following either anti-HBs seroconversion or ≥ 12 months' consolidation	May be considered in select noncirrhotic patients who have achieved long-term (≥ 3 years) virologic suppression under nucleos(t)ide analogue(s) if close post–nucleos(t)ide analogue monitoring can be guaranteed
Cirrhosis	Do not stop	May be considered with careful off-therapy monitoring plan	Do not stop

Terrault NA, et al. *Hepatology*. 2016;63:261-83; Sarin SK, et al. *Hepatol Int*. 2016;10:1-98; EASL 2017 Practice Guidelines. www.easl.eu/medias/cpg/management-of-hepatitis-B-virus-infection/English-report.pdf.

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HBV Abbreviations and Acronyms

- Ab = antibody
- ADV = adefovir dipivoxil
- ALT = alanine transaminase
- AST = aspartate aminotransferase
- cccDNA = covalently closed circular DNA
- ETV = entecavir
- FDA = Food and Drug Administration
- HAV = hepatitis A virus
- Hb = hemoglobin
- HBcAb = hepatitis B core antibody
- HBeAb = hepatitis B e antibody
- HBeAg = hepatitis B e antigen
- HBsAb = hepatitis B surface antibody
- HBsAg = hepatitis B surface antigen
- HBV = hepatitis B virus
- HCC = hepatocellular carcinoma
- HCV = hepatitis C virus
- HDV = hepatitis D virus
- LAM = lamivudine
- LLD = lower limit of detection
- N/A = not available
- PCP = primary care provider
- PCR = polymerase chain reaction
- Peg-IFN = pegylated interferon
- PNALT = persistently normal alanine transaminase
- siRNAs = small interfering RNAs
- TAF = tenofovir alafenamide fumarate
- TBV = telbivudine
- TDF = tenofovir disoproxil fumarate
- ULN = upper limit of normal
- WBC = white blood cell