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Listen using your computer audio. A headset is recommended but not required.

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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ACG will send a link to a CME & ABIM MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.

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MOC QUESTION

If you plan to claim ABIM MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

ACG Virtual Grand Rounds

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Philip O. Katz, MD, MACG
April 23, 2020 at Noon EDT

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Amy S. Oxentenko, MD, FACG
April 30, 2020 at Noon EDT

Visit gi.org/ACGVGR to Register
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Clinical pearls needed by any gastroenterologist on the medicine floor treating COVID-19.

FRIDAY, APRIL 17, 12 NOON EDT

Hosted by:
ACG President Mark B. Pochapin, MD, FACG
ACG President-Elect David A. Greenwald, MD, FACG

Hear from experts in New York, the current U.S. epicenter of COVID-19, with clinical insights in pulmonology, hepatology and the hospitalist’s perspective. Learn how to prepare for the COVID-19 storm and create an army of COVID specialists.

Register Now at gi.org/ACGVGR

Disclosures:

Presenter: Nancy S. Reau, MD, FACG
Research Support: Genfit, Intercept, Shire
Consultant: Abbott, AbbVie, Gilead, Merck

Moderator: Mitchell L. Shiffman, MD, FACG
Advisory Board: AbbVie, Gilead, Intercept, Mallinckrodt, Shionogi
Research Grant: Conatus, CymaBay, Dova, Enanta, Gilead, Intercept
Royalties: Slack
Speakers Bureau: AbbVie, Daiichi Sankyo, Eisai, Gilead, Intercept, Shionogi
Hepatitis B Update

Nancy S. Reau, MD, FACG
Chief, Section of Hepatology
Richard B. Capps Chair of Hepatology
Rush University Medical Center

Agenda

• General overview of HBV Treatment Guidelines
• Highlight treatment conundrums in hepatitis B infection
• Introduce future directions in HBV management
Epidemiology and Public Health Burden

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

<table>
<thead>
<tr>
<th>HBsAg prevalence, adults (19–49 years), 2005(^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2%</td>
</tr>
<tr>
<td>2–4%</td>
</tr>
<tr>
<td>5–7%</td>
</tr>
<tr>
<td>≥8%</td>
</tr>
<tr>
<td>Not applicable</td>
</tr>
</tbody>
</table>

Increasing prevalence in some European countries\(^1,4\)
- Migration from high endemic countries

Decreasing prevalence in some endemic countries, e.g. Taiwan\(^7\)
Possible reasons:
- Improved socioeconomic status
- Vaccination
- Effective treatments

Despite the risk, access to timely diagnosis and treatment is limited globally...

Only 9% of infected individuals globally are diagnosed and only 8% of those start treatment


Current Standard of Care

1. Screening for HBV
2. Goals of therapy
3. Indications for treatment
4. Treatment strategies
5. Endpoints of therapy

Screening:
1. HBsAg + anti-HBs
2. Anti-HBs- Negative should be vaccinated
3. Anti-HBc not routine but has a role with HIV, HD, Donation and Immune suppression
4. Counsel HBsAg positive on transmission
### Groups Recommended for HBV Screening

#### Risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>USPSTF 2014</th>
<th>CDC 2008</th>
<th>AASLD 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Persons born in region with ≥2% prevalence</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>US-born persons not vaccinated as infants whose parents were born in regions with ≥8% prevalence</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>MSM</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PWID</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HIV-positive</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>✓ Household and sexual contacts of HBV-infected persons</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Requiring immunosuppressive therapy</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESRD, including haemodialysis patients</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Persons with elevated ALT or AST</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Persons who are the source of blood or body fluid exposure that might require PEP</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Pregnant women</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Infants born to HBV-infected mothers</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Blood and tissue donors</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Persons with chronic liver disease, e.g. HCV</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persons who are not in a long-term, mutually monogamous relationship</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persons seeking evaluation or treatment for a STD</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At-risk health care and public safety workers</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residents and staff of facilities for developmentally disabled persons</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Travelers to countries with intermediate or high prevalence of HBV infection</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inmates of correctional facilities</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unvaccinated persons with diabetes who are aged 19–59 years</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Including needle-sharing contacts of HBsAg-positive persons;
†Those who are seronegative should receive Hep B vaccine.

---

HBV Serology Interpretation and Management

<table>
<thead>
<tr>
<th>Screening test results</th>
<th>Interpretation</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg Total/IgG anti-HBc Anti-HBs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>-/+ Current infection</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>+ Prior infection with immune control</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>- Prior infection, occult* infection, or false-positive anti-HBc (&lt; 0.2%)</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>+ Immune from prior vaccination</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>- Susceptible</td>
</tr>
</tbody>
</table>

*Occult HBV infection is defined by the presence or detectable HBV DNA in persons who are HBsAg-negative. Patients with occult HBV infection should be managed similarly to those with current infection.
†Consider HBV vaccination for persons not from an area of intermediate or high endemicity, as this may represent a false-positive anti-HBc result. The false-positive anti-HBc is <2/1000, using current assays.
‡Groups at high risk for HBV transmission and immunocompromised persons should be assessed for response to vaccination with a PVST of anti-HBs between 1–2 months after the final dose of the vaccine. A challenge vaccine dose or full vaccine series followed by PVST may be given to persons from high-risk groups with documentation of complete vaccination but not PVST.

Current Standard of Care

1. Screening for HBV
2. Goals of therapy
3. Indications for treatment
4. Treatment strategies
5. Endpoints of therapy
**Goals of Therapy**

- Improve *survival and quality of life* by preventing disease progression and HCC
- Prevent mother-to-child transmission, reactivation, and extrahepatic manifestations

### Recommendations

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

*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.


---

**Current Standard of Care**

1. Screening for HBV
2. Goals of therapy
3. Indications for treatment
4. Treatment strategies
5. Endpoints of therapy
**Nomenclature Differs by Guideline**

<table>
<thead>
<tr>
<th></th>
<th>HBeAg positive</th>
<th>HBeAg negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phase 1</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Chronic HBV</td>
<td>Chronic HBV</td>
<td>Chronic HBV</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>infection</td>
<td>infection</td>
</tr>
<tr>
<td>HBeAg</td>
<td>High</td>
<td>High/intermediate</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>&gt;10^7 IU/mL</td>
<td>10^4–10^7 IU/mL</td>
<td>&lt;2,000 IU/mL</td>
</tr>
<tr>
<td>ALT</td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td>Liver disease</td>
<td>None/minimal</td>
<td>Moderate/severe</td>
</tr>
</tbody>
</table>

1. HBV DNA levels can be between 2,000 and 20,000 IU/mL in some patients without signs of chronic hepatitis.
2. Persistently or intermittently, based on traditional ULN (~40 IU/L).
3. cccDNA can frequently be detected in the liver.
4. Residual HCC risk only if cirrhosis has developed before HBsAg loss.

**Management of CHB in Patients Without Cirrhosis**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA, IU/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBeAg positive</td>
<td>&gt;20,000</td>
<td>&gt;2000</td>
<td>≥2000</td>
<td>&gt;20,000</td>
</tr>
<tr>
<td>HBeAg negative</td>
<td>&gt;2000</td>
<td>&gt;2000</td>
<td>≥2000</td>
<td>≥2000</td>
</tr>
<tr>
<td>ALT</td>
<td>&gt;2 x ULN</td>
<td>&gt;ULN</td>
<td>&gt;ULN</td>
<td>≥2 x ULN</td>
</tr>
<tr>
<td>ULN for males</td>
<td>40 IU/mL</td>
<td>40 IU/L</td>
<td>30 IU/L</td>
<td>35 U/L</td>
</tr>
<tr>
<td>ULN for females</td>
<td>40 IU/mL</td>
<td>40 IU/L</td>
<td>19 IU/L</td>
<td>25 U/L</td>
</tr>
</tbody>
</table>

**May be treated**

- Patients with HBeAg-positive chronic HBV infection† >30 years old, regardless of severity of liver histological lesions

2. EASL. *Hepatol* 2017;67:370.
ELEVATED ALT >ULN SIGNIFICANTLY INCREASES RISK OF LIVER-RELATED COMPlications

<table>
<thead>
<tr>
<th>ALT level (U/L)</th>
<th>Risk of liver-related complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥45</td>
<td>Significantly increases risk of developing cirrhosis and HCC¹,²</td>
</tr>
<tr>
<td>&gt;40</td>
<td>Significantly increases risk of significant liver disease (presence of inflammation and fibrosis) and mortality³</td>
</tr>
<tr>
<td>&gt;30</td>
<td>Significantly increases risk of liver disease mortality (20 for women and 30 for men)⁴</td>
</tr>
<tr>
<td>&gt;20</td>
<td></td>
</tr>
</tbody>
</table>

Recommended ALT ULN

- **USTA 2015**
  - Men: 30 U/L
  - Women: 19 U/L
- **AASLD 2018**
  - Men: 35 U/L
  - Women: 25 U/L


Current Standard of Care

1. Screening for HBV
2. Goals of therapy
3. Indications for treatment
4. Treatment strategies
5. Endpoints of therapy
CHB Therapy Has Changed Over the Years

Because CHB endures, management must account for the changing needs of patients

“In most people... treatment does not cure hepatitis B infection, but only suppresses the replication of the virus. Therefore, most people who start hepatitis B treatment must continue it for life.”

– World Health Organization

1998 LAM
2002 ADV
2005 ADV, Peg-IFN
2006 LdT
2008 TAF
2016 TAF

Because CHB endures, management must account for the changing needs of patients

Prevention of resistance should rely on the use of first-line NAs with a high barrier to resistance

Cumulative incidence of HBV resistance to NAs in pivotal trials in NA-naïve patients with CHB

Preferred regimens: PEG, ETV, TDF and TAF
NOT recommended: LAM, ADV and TBV

*Evidence level I, grade of recommendation 1; †Collation of currently available data – not from head-to-head studies; ‡No evidence of resistance has been shown after 8 years of TDF treatment

EASL CPG HBV. J Hepatol 2017;67:370–88
## Indications for selecting ETV or TAF over TDF*

<table>
<thead>
<tr>
<th>Age</th>
<th>&gt;60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone disease</td>
<td>Chronic steroid use or use of other medications that worsen bone density</td>
</tr>
<tr>
<td></td>
<td>History of fragility fracture</td>
</tr>
<tr>
<td></td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Renal alteration†</td>
<td>eGFR &lt;60 ml/min/1.73 m²</td>
</tr>
<tr>
<td></td>
<td>Albuminuria &gt;30 mg/24 h or moderate dipstick proteinuria</td>
</tr>
<tr>
<td></td>
<td>Low phosphate (&lt;2.5 mg/dl)</td>
</tr>
<tr>
<td></td>
<td>Haemodialysis</td>
</tr>
</tbody>
</table>

* 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

---

## TAF vs. TDF for HBV: Change in eGFR

Median change from baseline in eGFR over 96 weeks TAF 25 mg (n=866) vs. TDF 300 mg (n=432)

- TAF: -1.2
- TDF: -4.8

p<0.001

Agarwal K, et al. J Hepatol 2018;69:672-81
TAF vs. TDF for HBV: change in BMD

Median change from baseline in BMD over 96 week TAF 25 mg (n=866) vs. TDF 300 mg (n=432)

<table>
<thead>
<tr>
<th></th>
<th>Hip</th>
<th>p-value</th>
<th>Spine</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAF</td>
<td>TDF</td>
<td>&lt;0.001</td>
<td>TAF</td>
<td>TDF</td>
</tr>
<tr>
<td>Mean change from baseline (%)</td>
<td>-1.35</td>
<td>-0.15</td>
<td>0.41</td>
<td>0.33</td>
</tr>
<tr>
<td>Time (weeks)</td>
<td>24</td>
<td>48</td>
<td>72</td>
<td>96</td>
</tr>
</tbody>
</table>

Agarwal K, et al. J Hepatol 2018;68:672–81

Monitoring Patients Treated with ETV, TDF or TAF

**Recommendations (monitoring)**

- ALT and serum HBV DNA*
  - All patients treated with NAs q3–4 months for first year then q6 months
- Renal monitoring†
  - Patients at risk of renal disease treated with any NA
  - All patients treated with TDF, regardless of renal risk
- Switch to ETV or TAF‡
  - Should be considered in patients on TDF at risk of development of and/or with underlying renal or bone disease

**Recommendations (long-term surveillance)**

- HCC surveillance recommended
  - All patients under effective long-term NA therapy
- HCC surveillance mandatory
  - All patients with cirrhosis or with moderate or high HCC risk scores at the onset of NA therapy

AASLD: HBsAg-positive adults at high risk for HCC
Asian or black men > 40 yrs of age; Asian women > 50 yrs of age
First-degree relative with history of HCC
Coinfection with HDV

*Liver function tests should be performed every 3–4 months during the first year and every 6 months thereafter. Serum HBV DNA should be determined every 3–4 months during the first year and every 6–12 months thereafter. Frequency of renal monitoring can be every 3 months during the first year and every 6 months thereafter if no deterioration. Closer renal monitoring is required in patients who develop CrCl <60 ml/min or serum phosphate levels <2 mg/dl. Depending on previous LAM exposure.

EASL. J Hepatol 2017;67:370–398
Current Standard of Care

1. Screening for HBV
2. Goals of therapy
3. Indications for treatment
4. Treatment strategies
5. Endpoints of therapy

Discontinuation of NA Treatment

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

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

EASL CPG HBV. J Hepatol 2017;67:370–98
Fewer Relapses With Longer Duration of Consolidation After HBeAg Seroconversion

- **Maintained Response** 2 yrs After Therapy Cessation (%)
  - < 6 mos (n = 47): 29%
  - 6-12 mos (n = 46): 23%
  - > 12 mos (n = 31): 48%

- **Duration of Consolidation**
  - < 12 mos (n = 39): 26%
  - 12-18 mos (n = 41): 39%
  - > 18 mos (n = 21): 71%

*No HBeAg seroreversion or HBV DNA increase to > 10^5 copies/mL. HBeAg seroconversion and undetectable serum HBV DNA.*


Age at HBeAg Seroconversion Predicts Durability of Sustained Response

- **Cumulative Relapse Rate**
  - ≤ 37 yrs
  - > 37 yrs

- **Virologic Recurrence**
  - Group A: ≤ 40 yrs AND ≥ 15 mos consolidation
  - Group B: ≤ 40 yrs OR ≥ 15 mos consolidation
  - Group C: > 40 yrs AND < 15 mos consolidation

Current Conundrums in Standard of Care

1. Do I treat acute HBV?

Acute HBV

- >95% immunocompetent adults recover spontaneously
  - Do not routinely treat symptomatic acute HBV
  - Verify HBsAg loss after 6-12 months

- Severe Acute Hepatitis B: consider therapy with ETV/TdF or TAF
  - Tbili >3 mg/dL, INR >1.5, HE or ascites

- LAM studies: improved HBV DNA but no difference in biochemical improvement or HBsAg loss
  - Hepatic encephalopathy
  - Serum bilirubin >10.0 mg/dL
  - INR >1.6

Current Conundrums in Standard of Care

1. Do I treat acute HBV?
2. How do I prevent MTCT

Recommendations from Association Guidelines for Preventing HBV MTCT

<table>
<thead>
<tr>
<th>Association</th>
<th>Year</th>
<th>Treatment</th>
<th>Gestation Period</th>
<th>HBV DNA Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>EASL 2017</td>
<td></td>
<td>TDF, LdT</td>
<td>Second trimester</td>
<td>&gt;2x10^5 IU/mL, HBsAg levels &gt; 4 logs IU/mL</td>
</tr>
<tr>
<td>AASLD 2018</td>
<td></td>
<td>TDF, LdT</td>
<td>28-32 weeks</td>
<td>&gt;2x10^5 IU/mL.</td>
</tr>
<tr>
<td>APASL 2015</td>
<td></td>
<td>TDF, LdT</td>
<td>28-32 weeks</td>
<td>&gt;10^6-7 IU/mL</td>
</tr>
</tbody>
</table>

TDF Preferred
Algorithm for the Management of Chronic Hepatitis B During Pregnancy

1. **Do I treat acute HBV?**
2. **How do I prevent MTCT**
3. **Role of qHBsAg**
Role of qHBsAg

• HBeAg-negative patients:
  – qHBsAg <1,000 IU/mL and HBV DNA <2,000 IU/mL suggest inactive CHB
  – qHBsAg <1,000 IU/mL predicts spontaneous HBsAg clearance

• Predicts treatment response:
  – Peg-IFN: qHBs @ week 12
    • HBeAg positive: qHBsAg <1,500 IU/mL → 57% for HBeAg seroconversion and 18% for HBsAg loss (no decline high assoc w/ failure)
  – NA: HBeAg negative
    • >1 log decline in qHBsAg predicted increased loss of HBsAg,
    • qHBsAg level <100 IU/mL sustainable off-treatment response after 3+ years consolidation therapy

Current Conundrums in Standard of Care

1. Do I treat acute HBV?
2. How do I prevent MTCT
3. Role of qHBsAg
4. How do I follow patients I don’t have on therapy

Warning: There are a lot of these patients. They get lost to follow-up.

Monitoring Patients Not on Therapy: HBeAg +

Monitoring Patients Not on Therapy: HBeAg (-)

- Normal ALT + HBV DNA < 2,000 IU/mL
  - Test ALT +/- HBV DNA q3 months for a year then 6-12 months
  - Check HBsAg status at 6-12 month intervals
- HBV DNA > 2,000 IU/mL + ALT < 2x ULN
  - Assess histology → treat if F2
  - Treat especially if > 40 yo

Recommendations:

- If ALT < ULN, monitor ALT and HBV DNA every 3-6 months.
- If ALT elevated, assess other causes of ALT elevation and assess disease severity.
- If HBV DNA > 2,000 IU/mL, treat especially if age > 40.

Monitoring in Other Groups

Monitoring Patients Not on Therapy: HBsAg Loss

- ALT and HBV-DNA monitoring no longer required
- HCC screening if cirrhosis, FMHx of HCC or long duration of infection (>40 years for men, >50 years for women if infected at young age)

HBV DNA < 2,000 IU/mL with elevated ALT

- Evaluate for other liver diseases, especially HDV

**NA-Induced HBsAg Loss is Durable**

Retrospective analysis of patients who stopped or continued NA after HBsAg loss
Evaluated incidence of HBsAg sero-reversion and HCC

**Implications for clinical practice:** HBsAg loss is a durable and safe endpoint for stopping therapy

**Current Conundrums in Standard of Care**

1. Do I treat acute HBV?
2. How do I prevent MTCT?
3. Role of qHBsAg
4. How do I follow patients I don’t have on therapy
5. TDF vs ETV
Overview of TDF vs ETV on HCC incidence in CHB Patients: AASLD 2019

HCC Risk Reduction (Hazard Ratios)

<table>
<thead>
<tr>
<th>Study</th>
<th>TDF/ETV (n)</th>
<th>Method</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi, 464 - Global</td>
<td>5591 / 9027</td>
<td>PSM meta-analysis</td>
<td>0.04</td>
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<tr>
<td>Kim, 478 - US</td>
<td>5033 / 5819</td>
<td>Adjusted, propensity-weighted</td>
<td>Significant</td>
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<tr>
<td>Hsu, 456 - Global</td>
<td>520 / 520</td>
<td>PSM</td>
<td>0.77</td>
</tr>
<tr>
<td>Chang, 465 - Taiwan</td>
<td>216 / 876</td>
<td>Multivariable, PS matched</td>
<td>0.0437</td>
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<tr>
<td>Huang, 544 - Taiwan</td>
<td>288 / 452</td>
<td>Multivariable adjusted HR</td>
<td>0.711</td>
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<tr>
<td>Papathodoridou, 454 - Europe</td>
<td>1163 / 772</td>
<td>Multivariable adjusted HR</td>
<td>0.005</td>
</tr>
<tr>
<td>Pol, 187 - France</td>
<td>1073 / 888</td>
<td>Multivariable adjusted HR</td>
<td>nd</td>
</tr>
</tbody>
</table>

All retrospective observational studies
No head-to-head comparison


The Future of HBV

- **Cure**: Elimination of all forms of potentially replicating HBV
- **Functional Cure**: HBV DNA is not detectable after completion of a finite course of treatment with HBsAg loss and decreased risk of HCC
- **Partial Cure**: Detectable HBsAg but HBV DNA negative after completion of finite therapy

Conclusions

- Therapy is recommended for those with chronic hepatitis B (elevated ALT, HBV DNA >2,000 in HBeAg negative and >20,000 IU/mL in HBeAg positive)
- Treatment is also recommended in those at high risk for progression and cancer
- Medications with a high barrier for resistance are recommended as first line therapy
- Regular monitoring for response and adverse events is necessary
- We may start to use the word cure in the discussion of HBV management
How to Receive CME and ABIM MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR
ACG will send a link to a CME & ABIM MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.

ACG will submit MOC points on the first of each month. Please allow 3-5 business days for your MOC credit to appear on your ABIM account.

ABIM MOC QUESTION

If you plan to claim ABIM MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.
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ACG President-Elect David A. Greenwald, MD, FACG

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April 23, 2020 at Noon EDT

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