HBV Virus Reactivation

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Disclosures

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Speakers Bureau: Intercept, Clinical Area- NASH
AASLD Guidelines for Screening and Treatment of HBV in Patients Requiring Immunosuppression

• HBsAg and anti-HBc testing should be performed in patients who are to receive immunosuppressive, cytotoxic or immunomodulatory therapy.

• HBsAg-positive, anti-HBc–positive patients should initiate anti-HBV prophylaxis before immunosuppressive or cytotoxic therapy.

• HBsAg-negative, anti-HBc–positive patients could be carefully monitored with ALT, HBV DNA, and HBsAg with the intent for on-demand therapy, except for patients receiving anti-CD20 antibody therapy (e.g., rituximab) or undergoing stem cell transplantation, for whom anti-HBV prophylaxis is recommended.

• LAM can be used if the anticipated duration of treatment is short (≤ 12 months) and baseline serum HBV DNA is not detectable.

• TDF or ETV is preferred if longer duration of treatment is anticipated.

LAM=lamivudine, LdT=telbivudine.
## AGA Guideline on Prevention and Treatment of HBVr During Immunosuppressive Drug Therapy

**AGA recommendation based on risk gradient with different immunosuppressive drugs based on estimates of reactivation**

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>High-risk (&gt;10%)</th>
<th>Moderate-risk (1-10%)</th>
<th>Low-risk (&lt;1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B cell-depleting agents (e.g., rituximab, ofatumumab)</strong></td>
<td>Red</td>
<td></td>
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<tr>
<td>Anthracycline derivatives (e.g., doxorubicin, epirubicin)</td>
<td>Red</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-dose (&gt; 20 mg prednisone daily or equivalent) corticosteroids daily for ≥ 4 weeks</td>
<td>Red</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate-dose (10-20 mg prednisone daily or equivalent) corticosteroids daily for ≥ 4 weeks</td>
<td>Red</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNF alpha inhibitors (e.g., etanercept, adalimumab, certolizumab, infliximab)</td>
<td>Gray</td>
<td></td>
<td></td>
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<tr>
<td>Cytokine or integrin inhibitors (e.g., abatacept, ustekinumab, natalizumab, vedolizumab)</td>
<td>Gray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyrosine kinase inhibitors (e.g., imatinib, nilotinib)</td>
<td>Gray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-dose (&lt; 10 mg prednisone daily or equivalent) corticosteroids for duration of ≥ 4 weeks</td>
<td>Gray</td>
<td></td>
<td>Blue</td>
</tr>
<tr>
<td>Any dose of oral corticosteroids daily for ≤ 1 week</td>
<td>Blue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-articular corticosteroids</td>
<td>Blue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traditional immunosuppressive agents (e.g., azathioprine, 6-mercaptopurine, methotrexate)</td>
<td>Blue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AGA Guideline on Prevention and Treatment of HBVr During Immunosuppressive Drug Therapy

<p>| AGA recommendation based on risk gradient with different immunosuppressive drugs based on estimates of reactivation |
|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Anticipated incidence of HBVr</th>
<th>High-Risk</th>
<th>Moderate-Risk</th>
<th>Low-Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Risk group: HBsAg+/HbcAb+ or HBsAg−/HbcAb+ treated with B cell-depleting agents, or HBsAg+/HbcAb+ treated with anthracycline derivatives, moderate- or high-dose corticosteroids daily for ≥ 4 weeks. Moderate-risk group: HBsAg+/HbcAb+ or HBsAg−/HbcAb+ treated with TNF alpha inhibitors, other cytokine or integrin inhibitors, tyrosine kinase inhibitors, HBsAg+/HbcAb+ treated with low-dose corticosteroids for duration of ≥ 4 weeks, HBsAg−/HbcAb+ treated with moderate- or high-dose corticosteroids daily for ≥ 4 weeks or anthracycline derivatives. Low-risk group: HBsAg+/HbcAb+ or HBsAg−/HbcAb+ treated with traditional immunosuppressive agents, intra-articular corticosteroids, any dose of oral corticosteroids daily for ≤ 1 week, or HBsAg−/HbcAb+ treated with low-dose corticosteroids for ≥ 4 weeks. Reddy KR, et al. Gastroenterology. 2015;148:215–219.</td>
<td>&gt; 10%</td>
<td>1-10%</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>AGA Recommendation</td>
<td>Antiviral prophylaxis during IS &amp; for at least 6-12 months after D/C of IS therapy</td>
<td>Antiviral prophylaxis during IS &amp; for at least 6 months after D/C of IS therapy</td>
<td>No antiviral prophylaxis</td>
</tr>
</tbody>
</table>
Mr. Wang, 79 y/o M, immigrated from Taiwan in the 60's.

History of Chronic Hepatitis B seroconversion.

Developed HCC in late 2019. HCC resected in early 2020 with clean margin.

Lung metastasis discovered in July. Will undergo immunotherapy with atezolizumab and bevacizumab.

Current HBV serology: HBV sAg (-), sAb (+).

Need HBV reactivation prophylaxis before immunotherapy?

Case Study 2

- Ms. Patel, 46 y/o F, born and raised in New Jersey
- Never tested for HBV serology until a few months ago when found to have ovarian cancer and was preparing to undergo chemotherapy
- Current HBV serology HBV cAb (+), sAb (+), sAg (-)
- HBVr risk category? Need sAb titer
- Need HBV reactivation prophylaxis before chemo starts?
Management of Chronic Hepatitis B in Pregnancy: A Case-based Approach
Case Study

• Patient Profile: 32 y/o female with established diagnosis of CHB. 11 weeks pregnant and referred by her OB/GYN for elevated liver enzymes. HBV infection controlled on TDF, which she stopped 3 weeks ago when she found out that she’s pregnant. She has concerns on the fetal exposure to anti-viral and prefers not to be treated.

• Presenting Symptoms: None

• Which tests/labs should be ordered?
Results of Tests/Labs

- Lab Results
  - HBsAg positive, HBeAg negative, HB eAb positive
  - HBV DNA 25,000 IU/ml
  - AST 20
  - ALT 50
  - Albumin 4.5
  - Platelets 225
  - T Bilirubin 0.7
Normal pregnancy

↑Adrenal corticosteroids
Modulation of cytokines

Host immune response

Increase in HBV DNA levels but decrease in ALT

Hepatitis flares at late pregnancy or postpartum

Questions

• Is this patient’s ALT a call for continuing treatment? If you decide not to treat, at what level of ALT and/or viral load you might reconsider treatment?

• What other work up needed for her elevated ALTs and how to monitor it during her pregnancy?
You recommended starting TdF monotherapy, however she deferred the treatment but agreed to a follow up visit in 4 weeks.

She instead returns at gestation week 20, uncomplicated pregnancy. Asymptomatic.

PE: normal exam.

Labs: AST 20, ALT 43.

HBV DNA 280,000,000 IU/mL.

NL Albumin, Platelet count, and T Bilirubin.
• What do you recommend now?
• Any additional information?
### Recommendations From Association Guidelines for Preventing HBV MTCT

<table>
<thead>
<tr>
<th>Association</th>
<th>Year</th>
<th>Treatment</th>
<th>Time of Pregnancy</th>
<th>HBV DNA Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>EASL</td>
<td>2017</td>
<td>TDF, LAM, LdT</td>
<td>Second trimester of pregnancy</td>
<td>$&gt;2 \times 10^5$ IU/mL, HBsAg levels $&gt; 4$ logs IU/mL</td>
</tr>
<tr>
<td>AASLD</td>
<td>2018</td>
<td>TDF, LAM, LdT</td>
<td>28-32 weeks of gestation</td>
<td>$&gt;2 \times 10^5$ IU/mL</td>
</tr>
<tr>
<td>APASL</td>
<td>2015</td>
<td>TDF, LdT</td>
<td>28-32 weeks of gestation</td>
<td>$&gt;10^{6-7}$ IU/mL</td>
</tr>
</tbody>
</table>
Treatment Options

- **Category B**: Telbivudine (HBV), Tenofovir-DF (HBV), Tenofovir-AF (HIV)
- **Category C**: Lamivudine (HBV), Adefovir, Entecavir
- **Pregnancy category B**:  
  - Animal studies do not indicate a risk to the fetus and there are no controlled human studies, or animal studies show an adverse effect on the fetus but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus
- **Pregnancy category C**:  
  - Studies have shown that the drug exerts animal teratogenic or embryocidal effects, but there are no controlled studies in women, or no studies are available in either animals or women

**Not classified for HBV in 2016** Tenofovir alafenamide (TAF)
• If you offer treatment, what are your treatment goals?
  – ALT
  – HBV-DNA
  – Reduction in MTCT

• What would you recommend for Rx?

• After the baby is born, would you consider continuing HBV therapy or would you consider stopping the medication?
• Post Partum what do you recommend?
  – Stop therapy
  – Change therapy
• How do you monitor her?
Patient Follow-Up

• Patient Care
  – Short-term plan
    • Timing including additional labs, procedures, clinic visits
  – Long-term plan
    • Does the patient stay with you? If so, for how long?
    • Do you release back to PCP/OB-GYN? If so, at what point?