2022
ACG / FGS ANNUAL SPRING SYMPOSIUM
MARCH 11-13, 2022 | In-Person
HYATT REGENCY COCONUT POINT • NAPLES, FLORIDA

COURSE DIRECTORS:
Tolga Erim, DO and Joel E. Richter, MD, MACG

2022
ACG / LGS REGIONAL POSTGRADUATE COURSE
MARCH 18-20, 2022 | In-Person
HILTON NEW ORLEANS RIVERSIDE | NEW ORLEANS, LOUISIANA

COURSE DIRECTORS:
James D. Morris, MD, FACG and Eric P. Trawick, MD
International GI Training Grants

GRANT AWARDS: $10,000 | DEADLINE MARCH 31, 2022

Whether you live in the U.S. or another country, you may be eligible!

Acquire or develop new cognitive knowledge or technical skill to improve patient care in your geographic area. The grant is to be used for travel to and from the training center and to the ACG Annual Meeting as well as for incidental expenses related to the training.

Visit gi.org/trainees/gi-training-grants for more information.
ACG AWARDS

Nominate a Colleague by April 15th!

2022 Award Categories:
- New! NP/PA Award for Clinical Excellence
- Berk/Fise Clinical Achievement Award
- Community Service Award
- Distinguished Mentorship & Teaching Award
- Diversity, Equity & Inclusion Award
- International Leadership Award
- Master of the American College of Gastroenterology
- Samuel S. Weiss Award

Nominations for these awards will be presented at the College’s Annual Scientific Meeting in Charlotte, NC on October 22, 2022.

gi.org/about/awards

---

On the Occasion of Lynch Syndrome Awareness Day

State of the Art in Colorectal Cancer Prevention for Lynch Syndrome Patients

Presented by:
Swati Patel, MD, MS

Moderated by:
Carol Burke MD, FACP
Anu Chittenden MS, LGC

📅 Tuesday March 22, 2022
クロック 8:00 PM EST 5:00 PM PT
**TUNE IT UP: A CONCERT TO RAISE COLON CANCER AWARENESS**

ACG Virtual Community Event in honor of March Colorectal Cancer Awareness Month

Thursday, March 31, 2022 at 8 pm EDT

Hosted by Dr. Benjamin Levy and ACG Public Relations Committee

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.
How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

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

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 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, 2023 for this activity.

MOC QUESTION

If you plan to claim 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
Join us for upcoming Virtual Grand Rounds!

Week 11
CRC Survivor & Advocate Allison Rosen on the Patient Journey: What GI Clinicians Need to Know Now
Allison Rosen
March 17, 2022 at Noon Eastern and NEW! 8pm Eastern!

Visit gi.org/ACGVGR to Register

Week 12
Endoscopic Submucosal Dissection: What Gastroenterologists Need to Know
Moamen Gabr, MD, MS
March 24, 2022 at Noon Eastern and NEW! 8pm Eastern!

Visit gi.org/ACGVGR to Register

ACG SPECIAL Grand Rounds
Join us for upcoming Virtual Grand Rounds!

March 16, 2022 at 8:30pm Eastern!
Career Edition: Ergonomics
Speaker: Rabia A. de Latour, MD

March 22, 2022 at 8:00pm Eastern!
Lynch Syndrome Awareness Day!
State of the Art in Colorectal Cancer Prevention for Lynch Syndrome Patients
Speaker: Swati G. Patel, MD, MS

Visit gi.org/ACGVGR to Register
Disclosures:

Speaker:
Joseph K. Lim, MD, FACG
Gilead: Grant/Research Support

Moderator:
Paul Y. Kwo, MD, FACG
Aligos: Consultant
Antios: Consultant
Assembly: Research Grant
Bristol Myers Squibb: Research Grant
Eiger: Research Grant
Enanta: Consultant
Gilead: Consultant, Research Grant

*All of the relevant financial relationships listed for these individuals have been mitigated

Diagnosis and Management of HBV Reactivation

American College of Gastroenterology
Virtual Grand Rounds

Joseph K. Lim, M.D.
Professor of Medicine
Director, Clinical Hepatology
Vice-Chief, Section of Digestive Diseases
Yale University School of Medicine
Lecture Objective

- Summarize key concepts and evidence-based guidelines in the evaluation and management of hepatitis B reactivation in patients undergoing immunosuppressive drug therapy – implications for gastroenterology, hepatology, oncology, rheumatology, dermatology

HBV Reactivation: Questions

- What is HBV reactivation?
- Who is at risk and should be screened?
- What tests should I screen with?
- How do I stratify risk for reactivation?
- Who do I treat?
- What do I treat with?
- How long do I treat?
**HBV**

Global Prevalence: 292 million; US Prevalence: 2 million

<table>
<thead>
<tr>
<th>Country</th>
<th>HBsAg+ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>5.3–12²</td>
</tr>
<tr>
<td>South Korea</td>
<td>2.6–5.1²</td>
</tr>
<tr>
<td>India</td>
<td>2.4–4.7²</td>
</tr>
<tr>
<td>Taiwan</td>
<td>10–13.8²</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>5.7–10²</td>
</tr>
<tr>
<td>Japan</td>
<td>4.4–13³</td>
</tr>
<tr>
<td>Africa</td>
<td>5–19⁴</td>
</tr>
<tr>
<td>Russia</td>
<td>1.4–8⁴</td>
</tr>
<tr>
<td>Europe</td>
<td>0.3–12²</td>
</tr>
</tbody>
</table>


**HBsAg Prevalence (%)¹**

- >8: High
- 2–8: Intermediate
- <2: Low

**Epidemiology of HBV Infection**

- HBV is 50 to 100 times more infectious than human immunodeficiency virus type 1 (HIV-1)¹
- 2 billion worldwide have been infected with HBV (2/3 are Asian)²
  - Up to 350 million CHB globally ²,³
  - approximately 2-3 million CHB in US ²,³
- Significant morbidity/mortality
  - 25% of carriers die of liver disease or liver cancer
  - 1 million deaths/yr³¹ – 5000/yr (US), 500k/yr (China)
- Increased prevalence of CHB is found in Asian-American populations (~ 10%)⁴
  - ~1 of 8 Vietnamese Americans
  - ~1 of 10 Chinese Americans
  - ~1 of 12 Korean Americans

Prevalence of HBV in U.S.

National HBV Data
- NHANES 2011-2014
  - 0.34% chronic HBV = 1.13 million
  - Asian (2.74%) NH Black (0.64%)
- NHANES 1999-2016
  - 0.35% chronic HBV = 1.15 million
  - US-born (0.15%) Foreign-born (1.28%)
- Consensus conference 2019
  - U.S. CHB prevalence estimate of 1.25-2.49 million
- National U.S. VA CDW
  - 21,419 chronic HBV
- National U.S. VA CCR (HCV)
  - 34.7% HBV exposure (58,415)
  - 1.4% HBV infection (1,431)

VA HBV Data


Natural History of HBV Infection

Early Childhood > 95%

HBeAg-
Chronic
Hepatitis B

HBeAg+
Chronic
Hepatitis B

Inactive
Carrier

Immune
Tolerance

Adulthood < 5%

HCC

Natural History of Chronic HBV Infection

- **Immunotolerance**
  - HBV DNA
  - HBeAg+
  - HBsAg+

- **Immune Clearance**
  - ALT
  - HBeAg-
  - HBsAg-

- **Immune Control (Nonreplicative)**
  - HBsAb+

Most Oncology Patients
- Normal ALT
- Low/undetectable HBV DNA
- HBsAg+ and HBeAg-
  - or HBsAg-, anti-HBc+

Do You Ever Really Get Rid of HBV?

- Immune control—not clearance
- "Resolved HBV" a misnomer—still HBV DNA in liver


Immune Suppression

- Immune control can be lost
- Immune-mediated liver damage with immune reconstitution

What is HBV Reactivation?

**Definition**
- Loss of HBV immune control in a patient with inactive or "resolved" HBV infection
- Abrupt reappearance or increase in viral replication with liver damage occurring during and/or following immune reconstitution

**Clinically**
- Range from subclinical to severe/fatal hepatitis
- Rise in HBV DNA ± return of HBeAg
- ALT increase (may be mild or very dramatic)
- May progress to liver failure/death despite antiviral therapy


Consequences of Delayed Recognition of HBV Reactivation

**Hepatitis**
- May be associated with severe histologic injury/inflammation
- May be associated with progressive liver fibrosis
- May present with hepatic decompensation
- Antiviral therapy may be too late to bring hepatitis under control – fatal reactivation with fulminant liver failure

**Interruption of chemotherapy**
- Potential for poorer cancer-related outcome


Who is at Risk and Should be Screened?

**AASLD Guidelines:**
- Persons born in countries with ≥2% HBsAg prevalence
- US born persons not vaccinated as infants whose parents were born in regions with ≥8% HBsAg prevalence
- Persons with behavioral exposures to HBV (IVDU, MSM, etc.)
- Partners of persons who are HBsAg-positive or at risk for HBV
- Persons needing immunosuppressive therapy
  - Chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders
- Persons undergoing HCV therapy with direct acting antivirals (DAA)
- Persons with elevated serum LFTs of unknown etiology

Who is at Risk and Should be Screened?

AASLD Guidelines:

- Persons born in countries with ≥2% HBsAg prevalence
- US born persons not vaccinated as infants whose parents were born in regions with ≥ 8% HBsAg prevalence
- Persons with behavioral exposures to HBV (IVDU, MSM, etc.)
- Partners of persons who are HBsAg-positive or at risk for HBV
- **Persons needing immunosuppressive therapy**
  - Chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders
- Persons undergoing HCV therapy with direct acting antivirals (DAA)
- Persons with elevated serum LFTs of unknown etiology


Who is at Risk and Should be Screened?

- CDC – all persons undergoing IDT including chemotherapy, immunosuppression related to organ transplantation or for rheumatologic or gastroenterologic disorders
- ASCO/NCCN – all patients undergoing systemic anti-cancer therapy
- AASLD/EASL/APASL – all patients undergoing IDT
- AGA – patients undergoing IDT with moderate or high risk for HBVr
- American College of Rheumatology – patients undergoing rituximab, bDMARD (methotrexate, leflunomide) or tsDMARD (apremilast, tofacitinib, filgotinib)
- American Academy of Dermatology – patients who are candidates for biologics (e.g. anti-TNF, IL inhibitors)

What Tests Should I Screen With?

- Screening high-risk individuals requires recognition of high-risk population
- **HBsAg and HBCAb should be tested in all individuals**, with follow-up HBV DNA in HBsAg-positive patients
- Role of HBsAb testing less clear; recommendations from various societies mixed
  - EASL: HBsAg, HBCAb, and HBsAb\(^1\)
  - AASLD: HBsAg and HBCAb\(^2\)
  - CDC: HBsAg, HBCAb, and HBsAb\(^3\)
  - ASCO: HBsAg and HBCAb \(^4,5\)
  - AGA: HBsAg and HBCAb \(^6\)
  - APASL: HBsAg, HBCAb, and HBsAb \(^7\)
- My clinical practice: HBsAg, HBCAb, HBsAb


Low Rates of Screening in Cancer Patients at Risk for HBV Reactivation

- U of Toronto-Canada (2010): 14% tested for HBsAg (n=208)
- MD Anderson-USA (2012): 17% tested for HBsAg and HBCAb (n=10,729)
- Sichuan University-China (2013): 17.1% tested for HBsAg and HBCAb (n=6646)
- Mayo Clinic-USA (2015): 16% tested for HBsAg (n=8005)
- National Cancer Center-Japan (2016): 19.9% tested for HBsAg and HBCAb (n=3302)
- Yale-USA (2017): 15.5% tested for both HBsAg and HBCAb (n=11,959)
- Veterans Health Administration-USA (2016): 53% tested for HBsAg (n=19,304 undergoing anti-CD20 therapy)

### How do I stratify risk for reactivation?

<table>
<thead>
<tr>
<th>High-risk (HBVr &gt; 10% cases)</th>
<th>Moderate Risk (HBVr 1-10% cases)</th>
<th>Low Risk (HBVr &lt;1% cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBSAg+ or HBsAb+ alone:</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B-cell depleting agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rituximab, ofatumumab,</td>
<td>HBSAg+ or HBsAb+ alone:</td>
<td></td>
</tr>
<tr>
<td>obinutuzumab, ocrelizumab</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>High-risk HBVr</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate Risk HBVr</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low Risk HBVr</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TNF-α inhibitor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>etanercept, adalimumab,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>certolizumab, infliximab</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Traditional immunosuppressive agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AZA, 6-mercaptopurine,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>methotrexate</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cytokine or integrin inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>abatacept, ustekinumab,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>natalizumab, vedolizumab</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intra-articular corticosteroids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral corticosteroid for ≤ 1 week</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroid for ≥ 4 weeks</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proteasome inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bortezomib</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Immune checkpoint inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-1, PDL-1, CTLA-4: nivolumab,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pembrolizumab, atezolizumab,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ipilimumab</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tyrosine kinase inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>matinib, nilotinib,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>erlotinib, ibritinib, dasaatinib</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Immune checkpoint inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-1, PDL-1, CTLA-4: nivolumab,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pembrolizumab, atezolizumab,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ipilimumab</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+ or HBsAb+ alone:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tyrosine kinase inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>matinib, nilotinib,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>erlotinib, ibritinib, dasaatinib</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### How do I stratify risk for reactivation?

<table>
<thead>
<tr>
<th>High-risk (HBVr &gt; 10% cases)</th>
<th>Moderate Risk (HBVr 1-10% cases)</th>
<th>Low Risk (HBVr &lt;1% cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>HbsAg+ or HBcAb+ alone:</td>
<td>HbsAg+ or HBcAb+ only:</td>
</tr>
<tr>
<td>B-cell depleting agents (rituximab, ofatumumab, obinutuzumab)</td>
<td>High potency TNF α inhibitor (adalimumab, certolizumab, infliximab, golimumab)</td>
<td>Traditional immunosuppressive agents (AZA, 6-mercaptopurine, methotrexate)</td>
</tr>
<tr>
<td>HbsAg+</td>
<td></td>
<td>Low Potency TNF α inhibitor (etanercept)</td>
</tr>
<tr>
<td></td>
<td>Anthracyclic derivative (doxorubicin, epirubicin)</td>
<td>Cytokine or integrin inhibitors (abatacept, ustekinumab, natalizumab, vedolizumab)</td>
</tr>
<tr>
<td>HbsAg+</td>
<td></td>
<td>Intra-articular corticosteroids Oral corticosteroid daily for ≤ 1 week</td>
</tr>
<tr>
<td>Moderate (10-20 mg prednisone daily) or High-dose (&gt;20 mg prednisone daily)</td>
<td>Proteasome inhibitors (bortezomib)</td>
<td>Low dose (&lt;10 mg of prednisone) Corticosteroid for ≥ 4 weeks</td>
</tr>
<tr>
<td>Hematopoietic stem cell transplantation</td>
<td>HbsAg+</td>
<td>Low Potency TNF α inhibitor (etanercept)</td>
</tr>
<tr>
<td></td>
<td>Immunocologic inhibitors (PD-1, PDL-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
<td>HbsAg+ alone:</td>
</tr>
<tr>
<td>HbsAg+</td>
<td>Moderate (10-20 mg prednisone daily) or High-dose (&gt;20 mg prednisone daily) for ≥ 4 weeks Anthracyclic derivatives</td>
<td>Immune checkpoint inhibitors (PD-1, PDL-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
</tr>
<tr>
<td>Tyrosine kinase inhibitors (matinib, nilotinib, erlotinib, ibrutinib, dasatinib)</td>
<td></td>
<td>Tyrosine kinase inhibitors (matinib, nilotinib, erlotinib, ibrutinib, dasatinib)</td>
</tr>
</tbody>
</table>


### How do I stratify risk for reactivation?

<table>
<thead>
<tr>
<th>High-risk (HBV &gt; 10% cases)</th>
<th>Moderate Risk (HBVr 1-10% cases)</th>
<th>Low Risk (HBVr &lt;1% cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>B-cell depleting agents (rituximab, ofatumumab, obinutuzumab, ocrelizumab)</td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High potency TNF α inhibitor (adalimumab, certolizumab, infliximab, golimumab)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
<tr>
<td></td>
<td>Low Potency TNF α inhibitor (etanercept)</td>
<td></td>
</tr>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>Anthracycline derivative (doxorubicin, epirubicin)</td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cytokine or integrin inhibitors (abatacept, ustekinumab, natalizumab, vedolizumab)</td>
</tr>
<tr>
<td>Moderate (10-20 mg prednisone daily) or High-dose (&gt;20 mg prednisone daily)</td>
<td>Proteasome inhibitors (bortezomib)</td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
<tr>
<td>Corticosteroid for ≥4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>Hematopoietic stem cell transplantation</td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
<tr>
<td></td>
<td>Low dose (&lt;10 mg prednisone daily)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Corticosteroid for ≥4 weeks</td>
<td></td>
</tr>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>Immune checkpoint inhibitors (PD-1, PDL-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
<td>Moderate (10-20 mg prednisone daily) or High-dose (&gt;20 mg prednisone daily) for ≥4 weeks</td>
</tr>
<tr>
<td>Immune checkpoint inhibitors (PD-1, PDL-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
<td>Immune checkpoint inhibitors (PD-1, PDL-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>Tyrosine kinase inhibitors (matinib, nilotinib, erlotinib, ibritinib, dasatinib)</td>
<td>HBsAg+ or HBcAb+ alone:</td>
</tr>
</tbody>
</table>


How do I stratify risk for reactivation?

<table>
<thead>
<tr>
<th>High-risk (HBVr &gt; 10% cases)</th>
<th>Moderate Risk (HBVr 1-10% cases)</th>
<th>Low Risk (HBVr &lt;1% cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>HBsAg+ or HBcAb+ only:</td>
</tr>
<tr>
<td></td>
<td>High potency TNF α inhibitor (adalimumab, certolizumab, infliximab, golimumab)</td>
<td>Traditional immunosuppressive agents (AZA, 6-mercaptopurine, methotrexate)</td>
</tr>
<tr>
<td></td>
<td>HBsAg+: Low Potency TNF α inhibitor (etanercept)</td>
<td></td>
</tr>
<tr>
<td>HBsAg+:</td>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>HBcAb+ only:</td>
</tr>
<tr>
<td>Anthracine derivative (doxorubicin, epirubicin)</td>
<td></td>
<td>Intra-articular corticosteroids Oral corticosteroid daily for ≤ 1 week</td>
</tr>
<tr>
<td></td>
<td>HBsAg+ or HBcAb+ alone:</td>
<td></td>
</tr>
<tr>
<td>Moderate (10-20 mg prednisone daily) or High-dose (≥20 mg prednisone daily)</td>
<td>Proteasome inhibitors (bortezomib)</td>
<td>Low dose (&lt;10 mg of prednisone)</td>
</tr>
<tr>
<td>Corticosteroid for ≥ 4 weeks</td>
<td></td>
<td>Corticosteroid for ≥ 4 weeks</td>
</tr>
<tr>
<td>HBsAg+ or HBcAb+ alone:</td>
<td>HBcAb+ only:</td>
<td></td>
</tr>
<tr>
<td>Hematopoietic stem cell</td>
<td>Low dose (&lt;10 mg prednisone daily)</td>
<td>Low Potency TNF α inhibitor (etanercept)</td>
</tr>
<tr>
<td>transplantation</td>
<td>Corticosteroid for ≥ 4 weeks</td>
<td></td>
</tr>
<tr>
<td>HBsAg+ :</td>
<td>HBcAb+ only:</td>
<td></td>
</tr>
<tr>
<td>Immune checkpoint inhibitors</td>
<td>Moderate (10-20 mg prednisone daily) or High-dose (≥20 mg prednisone daily) for ≥ 4 weeks</td>
<td>Immune checkpoint inhibitors (PD-1, PD-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
</tr>
<tr>
<td>(PD-1, PDL-1, CTLA-4): nivolumab, pembrolizumab, atezolizumab, ipilimumab</td>
<td>Anthracine derivatives</td>
<td></td>
</tr>
<tr>
<td>HBsAg+ :</td>
<td>HBcAb+ only:</td>
<td></td>
</tr>
<tr>
<td>Tyrosine kinase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(matinib, nilotinib, erlotinib, brustinib, dasatinib)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBcAb+ only:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Cytokine/Integrin Inhibitors

- **TNF-alpha**: infliximab, adalimumab, certolizumab, golimumab (moderate except possibly etanercept)
- **Anti-interleukin 17 (IL-17)**: secukinumab, ixekizumab, brodalumab (moderate)
- **Anti-interleukin 12/23 (IL-12/IL-23)**: ustekinumab (moderate)
- **Co-stimulation inhibitors (CD80/CD86)**: abatacept, belatacept (moderate)
- **Anti-CD52**: alemtuzumab (moderate)
- **Integrin inhibitors**: natalizumab, vedolizumab (moderate)
- **Chemokine inhibitors (CCR4)**: mogamulizumab (limited data)
- **Anti-interleukin 23 (IL-23)**: guselkumab, tildrakizumab (limited data)
- **Other anti-interleukin inhibitors (IL-1/IL-6)**: canakinumab, rilonacept, anakinra, tocilizumab, sarilumab (limited data)

Other IDT Classes

- **Calcineurin inhibitors**: cyclosporin, tacrolimus (low)
- **mTOR**: everolimus (limited data)
- **JAK inhibitors/C5 inhibitors**: tofacitinib, eculizumab, ravulizumab, ruxolitinib, baricitinib (limited data)
- **CART**: anti-CD22/anti-CD19 (limited data)
- **Platinum/antimetabolites**: FOLFOX/FOLFIRI (limited data)
- **EGFR/VEGF/FGFR inhibitors (solid tumors)**: sorafenib, cetuximab, bevacizumab, lenvatinib, sunitinib, panitumumab (limited data)


Who do I treat?

- Consider pre-emptive antiviral therapy for all patients who are classified as **moderate or high risk** for HBV reactivation

  - **AASLD**: prophylactic antiviral therapy recommended for **all HBsAg+ carriers** at the onset of cancer chemotherapy or immunosuppressive drug therapy (IDT)
  - **EASL**: prophylactic antiviral therapy recommended for **all HBsAg+ patients** receiving chemotherapy or IDT – **HBsAg+/HBCAb+ patients** should receive prophylaxis if at **high risk** for HBV reactivation
  - **ASCO**: prophylactic antiviral therapy recommended for **all HBsAg+ patients** undergoing IDT; **HBCAb+ only patients undergoing high risk IDT** (anti-CD20 and stem cell transplantation)
  - **AGA**: antiviral prophylaxis recommended for **HBsAg+ and HBsAg-and HBCAb+ patients undergoing high risk (>10%) or moderate risk (1-10%) IDT**
  - **APASL**: prophylactic antiviral therapy recommended for: 1) **all high-risk**; 2) **moderate-risk (HBsAg+)**; 3) **moderate-risk (HBCAb+ alone with F3/F4)**; 4) **low-risk (HBsAg+ or HBCAb+ alone with F3/F4)**

What Do I Treat With?

- **Entecavir or tenofovir preferred agents** for pre-emptive HBV therapy for patients undergoing immunosuppressive drug therapy:
  - **AASLD**: entecavir or tenofovir (TDF/TAF) preferred over low resistance barrier agents
  - **EASL**: entecavir or tenofovir (TDF/TAF) recommended
  - **AGA**: 3rd generation nuc analogues (entecavir or tenofovir) recommended over 1st or 2nd generation agents (lamivudine or telbivudine)
  - **ASCO**: consult specialist who is expert in management of HBV
  - **APASL**: entecavir, tenofovir (TDF/TAF) recommended

How Long Do I Treat?

- Pre-emptive HBV therapy should be continued for **at minimum 6-12 months following end of treatment** (or longer if high risk)
  - **AASLD**: ≥ 6 months following completion of IDT (≥ 12 months after anti-CD20 therapy)
  - **EASL**: 12 months after cessation of IDT and 18 months after cessation for rituximab-based regimens
  - **AGA**: ≥ 6 months after discontinuation of IDT for high and moderate risk patients (except B cell depleting agents); ≥12 months for patients on B cell depleting agents (e.g. rituximab)
  - **ASCO**: 6 months after stopping chemotherapy; patients undergoing anti-CD20: 12 months after stopping chemotherapy
  - **APASL**: 6 months after stopping chemotherapy
How Should I Monitor Patients During & After Immunosuppressive Drug Therapy?

- Patients should be monitored throughout IDT plus a minimum of 6 months with ALT, HBsAg and/or DNA every 1-3 months

- **AASLD**: ALT, HBsAg, DNA every 1-3 months (up to 12 months after IDT cessation)
- **EASL**: HBsAg and/or DNA every 1-3 months
- **AGA**: no recommendation
- **ASCO**: HBsAg, ALT every 3 months
- **APASL**: LFTs every 3 months


HBVr Guidelines

- How should gastroenterologists reconcile the differences in the guidelines?
  - AGA 2015
  - APASL 2021
  - My approach
AGA HBVr Guideline: High Risk

**HIGH RISK (REACTIVATION RISK >10%)**

- HBsAg-positive/anti-HBc-positive or HBsAg-negative/anti-HBc-positive
  - Patients taking B cell depleting agents (e.g., rituximab, atalustimab)
  - Patients taking antiviral prophylaxis for at least 12 months after discontinuation of immunosuppressive therapy
- HBsAg-positive/anti-HBc-positive
  - Patients taking antiviral prophylaxis for at least 6 months after discontinuation of immunosuppressive therapy

GRADE - strong recommendation, moderate quality of evidence

AGA HBVr Guideline: Moderate Risk

**MODERATE RISK (REACTIVATION RISK 1–10%)**

- HBsAg-positive/anti-HBc-positive or HBsAg-negative/anti-HBc-positive
  - Patients taking TNF-α inhibitors (e.g., etanercept, adalimumab, certolizumab, infliximab)
  - Patients taking other cytokine or mesenchymal stem cells inhibitors (e.g., abatacept, ustekinumab, certolizumab, vedolizumab)
- HBsAg-positive/anti-HBc-positive
  - Patients taking low-dose (<10 mg prednisone daily or equivalent corticosteroids daily for >4 weeks)
  - Patients taking moderate-dose (10–20 mg prednisone daily or equivalent high dose (>20 mg prednisone daily or equivalent) corticosteroids daily for >4 weeks)
- HBsAg-negative/anti-HBc-positive
  - Patients taking antiviral prophylaxis for at least 6 months after discontinuation of immunosuppressive therapy

GRADE - weak recommendation, moderate quality of evidence

*Patients who place a higher value on avoiding the long-term use of antiviral therapy and cost associated with its use and a lower value on avoiding the small risk of reactivation (particularly in those who are HBsAg negative), may reasonably select no prophylaxis over antiviral prophylaxis.

AGA HBVr Guideline: Low Risk

LOW RISK (REACTIVATION RISK < 1%)

- HBsAg-positive/anti-HBc-positive or HBsAg-negative/anti-HBc-positive
  - Patients taking traditional immunosuppressive agents (e.g., azathioprine, 6-mercaptopurine, methotrexate)
  - Patients taking intra-articular corticosteroids. Patients taking any dose of oral corticosteroids daily for duration of < 1 week.
- Suggest not to use routine antiviral prophylaxis in patients undergoing immunosuppressive drug therapy who are at low risk for HBV

GRADE - weak recommendation, moderate quality of evidence


APASL 2021 HBVr Guideline

All patients planned to receive immunosuppressive therapy should be screened for HBsAg, anti-HBc, anti-HBx status.

For HBsAg+ patients, quantitative HBsAg, HBV DNA and liver function test should be considered.

Liver fibrosis assessment

Risk of HBVr

High
- HBsAg+
  - No advanced fibrosis or cirrhosis
- HBsAg+ Anti-HBc+
  - Advanced fibrosis or cirrhosis

Moderate
- HBsAg- Anti-HBc+
  - No advanced fibrosis or cirrhosis
- HBsAg+ or HBsAg- anti-HBc+
  - Advanced fibrosis or cirrhosis

Low
- NUCs
  - Monitor ALT q3m+
  - NUCs
  - Monitor ALT q3m+

Termination of NUCs would be considered 6 months after the completion of IST for those who are HBsAg positive, without advanced liver fibrosis or cirrhosis and with low level of HBV DNA (<2000 IU/mL) before initiation of NUCs and also for those who remain HBsAg negative but anti-HBc positive.

HBV Reactivation: My Approach

• Screen all patients undergoing IDT: HBsAg, HBcAb, HBsAb
• Assess for presence of underlying disease (e.g. alcohol, fatty liver, HCV)
• Obtain baseline labs: LFTs, PT/INR, consider non-invasive fibrosis test
• If abnormal LFTs: pursue liver investigation (√ ACG 2017 guideline)
• If HBcAb+ alone: check HBV DNA to exclude occult HBV
• Patients classified as moderate or high-risk for HBVr should be offered pre-emptive antiviral therapy with ETV, TDF, or TAF
• Continue treatment for ≥ 6 months following IDT (≥ 12 months if undergoing anti-CD20 therapy)
• Untreated patients: HBsAg/HBV DNA + LFTs every 1-3 months
  – High/Moderate Risk: LFTs q month + HBsAg/HBV DNA q 3 months
  – Low Risk: LFTs and/or HBsAg q 3 months

Areas for Future Research

• Standardization of HBVr definitions
• Prospective observational cohort studies → stronger evidence base
• Emerging biologic/immunotherapy classes
• Combination regimens involving low-risk IDT classes
• Role of HBsAb in risk for HBVr
• Timing of oral NUC therapy – 1 wk prior vs concurrent vs later
• Role of biomarkers in predicting HBVr – qHBsAg, qHBcAb
• Risk factors: role of underlying liver disease
• Risk factors: variable dosing in oncology, GI, rheumatology, dermatology
• Clinical context of HCC/liver cancer
• HIV/AIDS and immunodeficiency disorders
• Hepatitis C
• QI intervention to improve screening, monitoring, and treatment
• Harmonization of guidance in HBVr evaluation and management
HBV Reactivation: Conclusions

- Immunosuppressive drug therapy (IDT) is increasingly common in both oncology and nononcology fields
- Both chronic HBV and resolved HBV remain underdiagnosed
- HBV reactivation (HBVr) may occur in patients who are HBsAg (+) or HBsAg (-)/HBcAb (+) independent of HBsAb status
- HBVr is associated with significant morbidity and mortality, and may lead to fatal reactivation flares due to fulminant liver failure
- All patients undergoing IDT should be screened: HBsAg, HBcAb, HBsAb
- Patients undergoing moderate or high-risk IDT should undergo pre-emptive antiviral therapy to reduce risk of HBVr
- ETV, TDF, and TAF are preferred agents for pre-emptive treatment of HBVr, and should be continued for ≥ 6-12 months following IDT
- Additional research is needed to further clarify risk factors and optimal treatment strategies for patients at risk for HBVr

Thank You