UCSF Joint Hepatology/Transplant ID Guidelines for Anti-HBc+ Management in Organ Transplantation and Immunosuppression

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PART I: Management of HBsAg+ anti-HBc+ Patients, Consult Hepatology for Treatment

PART II: Management of HBsAg- anti-HBc+ Patients Receiving Immunosuppression (anti-HBs- or +)

Risk of Reactivation by Type of Immunosuppression[1]	Strategy	Duration of Prophylaxis	Monitoring (HBsAg, HBV DNA, ALT)

High risk (>10%)
• B-cell depleting therapy such as
  ○ Rituximab, obinutuzumab, polatuzumab
  ○ BTK inhibitors
  ○ CAR T-cell therapy
  ○ Plasma cell antibodies (eg. CD38 daratumumab, isatuximab)
  ○ Bi-specific anti- B-cell/plasma cell antibodies
  ○ Alemtuzumab
• JAK inhibitors (e.g. baricitinib)
• HSCT (auto or allo)
• Hematologic malignancy with myelosuppressive chemotherapy
	Prophylaxis	• 2 years after last therapy
		• Consider indefinite ppx for allo-SCT
			q3mo until 1 yr after ppx is stopped

Moderate risk (1-10%)
• Anti-TNF inhibitors
• Cytokine or integrin inhibitors (e.g., abatacept, ustekinumab, natalizumab, vedolizumab)
• Tyrosine kinase inhibitors (e.g., imatinib, nilotinib)
• Steroids (prednisone ≥10mg/d or 2mg/kg/d for pediatrics x ≥4 wks)
• Anthracyclines (e.g.doxorubicin)
• SOT recipients
	Prophylaxis* OR Monitoring
	
	*Factors that favor prophylaxis include logistics of monitoring, hepatotoxicity of concomitant medications or IS that may confound interpretation of LFTs
		• 6 mo after last dose of immunosuppression
		• For SOT recipients:
		  ○ 12 mo for non-liver SOT recipients (Thymoglobulin treatment for rejection should restart the clock. Pulse dose steroids for rejection should extend prophylaxis for an additional 6 months.)
		  ○ No ppx for liver SOT recipients[2]
			Prophylaxis: q3mo until 1 yr after ppx is stopped
			
			Monitoring: 18 months after last dose of immunosuppression

Low risk (<1%) • Immune checkpoint inhibitors • Antimetabolites (e.g. azathioprine, methotrexate) • Alkylating agents (e.g. cisplatin) • <10mg prednisone for ≥4 weeks	Monitoring	n/a	q3mo x 6 mo until after last dose of immunosuppression

[1]Patients on multiple immunosuppressive agents should be considered at risk level higher than based on immunosuppression alone. Persons with HIV receiving immunosuppression are at increased risk of reactivation and risk level should be increased by one level than based on immunosuppression alone

PART III: Management of HBsAg- anti-HBc- Transplant Recipients with HBsAg-, anti-HBc+ Donors

Liver SOT Recipients

All liver SOT recipients of an anti-HBc+ donor receive life-long prophylaxis with entecavir, TDF, or TAF (adjusted for renal function. Lamivudine also acceptable due to its low cost and need for lifelong prophylaxis.

Non-liver SOT Recipients

Recipient Status	Prophylaxis?	Duration	Monitoring (HBsAg, HBV DNA, ALT)
anti-HBc– anti-HBs–	Kidney: yes[1]	At least 1 year[1]	q3mo until 1 yr after ppx stopped
	Heart or lung: no	n/a	q3mo x 1 yr
anti-HBc– anti-HBs+	No	n/a	q3mo x 1 yr (also check for loss of anti-HBs)

[1]Only kidney and liver recipients have been shown to reactivate in this situation. Ultimate duration of ppx depends on results of monitoring labs and patient's net state of immunosuppression.

Note: Pediatric organ transplantation from anti-HBc+ donors is NOT currently recommended due to lack of data for safety in children; if transplantation from an anti-HBc+ donor is being considered under exceptional circumstances, consult with Pediatric ID.

PART IV: General Principles for Prophylaxis

- Entecavir is the preferred antiviral (TDF or TAF are also first line agents, but used less commonly); Lamivudine is considered second line given high risk of resistance. Prophylactic dosing of entecavir is 0.5mg PO daily in patients ≥ 16 years (needs renal dosing adjustment if CrCl <50).
- The presence of anti-HBs is not protective against reactivation and should not influence prophylaxis decisions.
- Prophylaxis, when given, should be started as soon as possible before (when possible) or simultaneously with the onset of immunosuppression.
- For HIV-positive patients requiring prophylaxis: follow DHHS guidelines for the treatment of HIV/HBV coinfection: use tenofovir (TDF or TAF) with FTC or 3TC. If TDF or TAF cannot be used, then use entecavir with a fully suppressive ARV regimen. Do not use 3TC or FTC alone for prophylaxis given the risk of resistance.

References/Guidelines:

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