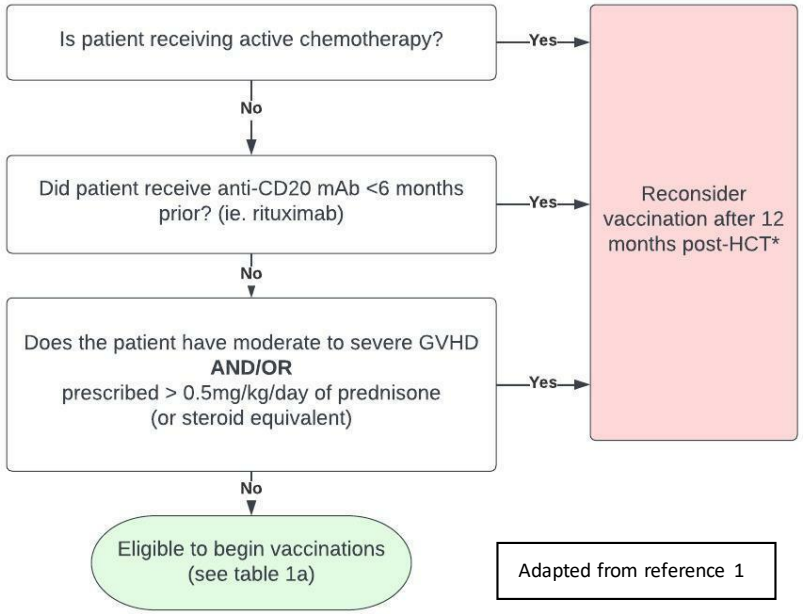
DUKE Adult Hematopoietic Cell Transplant (HCT) Vaccination Protocol

Preamble

- This protocol is intended for adult allogeneic or autologous HCT recipients. Transplant ID should be consulted to guide vaccination strategies for **patients with primary immune deficiencies**.
- Screening for vaccination eligibility should occur **6 months** post-transplant (see Figure 1).
- Vaccines that may be considered before 6 months include:
  - **2023-2024 Formula COVID-19 vaccine (XBB monovalent vaccine)**: All patients should receive at least one dose of the XBB monovalent vaccine (preferentially either Moderna or Pfizer-BioNTech, or Novavax for those intolerant to mRNA vaccines) irrespective of previous vaccinations and no sooner than 3 months following HCT. Patients administered the XBB monovalent vaccine as their first COVID vaccine post-HCT are eligible to receive repeated doses (up to a maximum of 3 doses for Moderna/Pfizer vaccines or 2 doses of Novavax).
  - **RSV vaccine**: Can be given as early as 3 months post-transplant and ideally before the fall/winter RSV season (see glossary for further details).
  - **Influenza vaccine**: Can be given as early as 3 months post-transplant followed by annually thereafter (see glossary for further details).
- Other vaccines not included in this protocol include: **Mpox vaccine** (see glossary).

Figure 1: Screening Questions to Determine Eligibility for Vaccination



*If patients remain ineligible for vaccination at 12 months (based on criteria above) then regularly reassess eligibility every 3 months thereafter.

Vaccination Schedules

Table 1a: Vaccine schedule for 6-month start

Time of initiation post-transplant	Recommended vaccines (Autologous or Allogeneic HCT)	Optional vaccines
≥ 6 months	PCV-20, MCV4, MenB	
≥ 9 months	PCV-20, MCV4, MenB, RZV[A], Pentacel®	
≥ 12 months	PCV-20, RZV[A], Pentacel®, HBV[B]	HPV
≥ 18 months	PCV-20, Pentacel®, HBV[B]	HAV, HPV
≥ 24 months	HBV[B], MMR[C]	HPV, HAV, Varivax®[C]
≥ 26 months		Varivax®[C]
Annual	IIV	

Table 1b: Vaccine schedule for alternate timeline (**at least 12 months post-HCT**)

Time of initiation post-transplant (time of vaccine initiation)	Recommended vaccines (Autologous or Allogeneic HCT recipients)	Optional vaccines
≥ 12 months (month 0)	PCV-20, Pentacel®, MCV4, MenB, HBV[B]	
≥15 months (month 3)	PCV-20, Pentacel®, MCV4, MenB, HBV[B]	HPV
≥18 months (month 6)	PCV-20, Pentacel®, HBV[B], RZV[A]	HAV, HPV
≥24 months (month 12)	PCV-20, MMR[C], RZV[A]	HAV, HPV, Varivax®[C]
≥26 months (month 14)		Varivax®[C]
Annual	IIV	

HAV, hepatitis A virus vaccine; *HBV*, hepatitis B virus vaccine; *HPV*, human papilloma virus vaccine; IIV, Inactive influenza virus, *MBV*, meningococcal B vaccine; *MCV4*, quadrivalent meningococcal vaccine; MenB, serogroup B meningococcal vaccine; *MMR*, measles, mumps and rubella vaccine; *PCV*, pneumococcal conjugate vaccine; RZV, recombinant zoster vaccine (Shingrix®)

[A]Commencement of the RZV series can be modified to earlier or later time points based on the planned duration of ACV prophylaxis. Patients should receive the full 2-dose RZV series prior to cessation of ACV prophylaxis. Current recommendations are to continue ACV prophylaxis at least 4 weeks post administration of RZV dose 2.

[B]2-doses only if Heplisav-B is used. All other formulations require a 3rd dose.

[C]This is a live vaccine and should only be administered in patients ≥ 24-months post HCT, off all immunosuppression, and with CD4 cell count ≥200/mm^3. Live vaccines should also be delayed ≥ 8 months after receipt of IVIg whenever feasible. Criteria for early administration of MMR in local outbreaks are detailed in Table 2.

Optional vaccines:

- **Human papilloma virus** (HPV) vaccine: Should be considered in males and non-pregnant females up to age 50 at the providers' discretion.
- **Varivax®:** Varicella zoster vaccine to be used frontline prior to RZV if fulfilling all 3 criteria: recipient seronegative to VZV, varicella zoster naïve (ie. no history of chickenpox), and no previous vaccination with Varivax. Patient must also meet criteria for receipt of live vaccines.
- **Hepatitis A virus vaccine**: A 2-dose hepatitis A virus (HAV) vaccination series should be considered in high-risk individuals (see criteria under vaccine glossary).

Vaccine Glossary (Alphabetical)

1. Hepatitis A vaccine (HAV): Havrix® or VAQTA® (1 mL IM), 2-dose series, *minimum 6-month interval between doses*; Vaccine indicated in the following "increased risk" groups:
    - Men who have sex with men, persons with chronic liver disease, persons with liver GVHD, concurrent infection with other hepatitis viruses, persons who use injection or non-injection illicit drugs
    - Persons working with HAV-infected primates or with HAV in a research laboratory setting
    - Persons who receive clotting factor concentrates
    - Persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A

2. Hepatitis B virus vaccine (HBV): Heplisav-B® or Engerix-B®, *dosing and intervals brand specific as below*
    - Preferred: **Heplisav-B** (0.5mL IM), 2-dose series, *minimum 1-month interval between doses*
    - Alternative: Engerix-B® (2mL IM), 3-dose series, *minimum 1-month interval between dose 1-2, and 5-month interval between dose 2-3*
    - Check hepatitis B surface antibody (anti-HBs) one month after completion of full vaccination series. If anti-HBs negative, repeat vaccination series

    In patients on hemodialysis, HBV vaccination should be coordinated with and performed by dialysis centers due to possible false positive hepatitis B surface antigen testing early post receipt of HBV vaccine.

3. Human papilloma virus vaccine (HPV): Gardasil-9® Nonavalent vaccine (0.5 mL IM), 3-dose series, minimum *2-month interval between dose 1-2, and 4-month interval between dose 2-3*. Primarily indicated in non-pregnant females and males up to age 26 but series can be initiated in non-pregnant individuals up to age 50 at providers' discretion.

4. Inactivated influenza virus vaccine (IIV): IIV should be administered ≥6 months post-transplant. In epidemics/community outbreaks, IIV can be administered early (e.g., ≥3 months post-transplant) and can be repeated 4-6 weeks later. Recommended formulations for immunocompromised patients and/or those ≥65 years of age include the adjuvanted quadrivalent (Fluad® Quadrivalent, 0.5 mL IM), quadrivalent high dose vaccine (Fluzone® High-Dose Quadrivalent, 0.7 mL IM), or quadrivalent recombinant vaccine (Flublok® quadrivalent, 0.5 mL IM). Patients with accessibility or cost barriers to any of these formulations should receive any available IIV as an alternative.

5. Measles, mumps and rubella vaccine (MMR): M-M-R II® (0.5 mL subQ), 1-dose. This is a live vaccine and should only be administered when all the following criteria are met: 1. ≥ 24 months post-transplant, 2. No active GVHD, 3. Off of all immunosuppressive therapy for ≥ 12 months, and 4. CD4 cell counts ≥ 200/mm^3. Use of MMR vaccine is permissible if IVIG has been administered but should be delayed by 8-months whenever feasible. Other live vaccines can be administered on the same day (e.g. Varivax®), but if not performed on same day, the second live vaccine should be given ≥ 28 days later. Use of MMR vaccine is permissible in patients on maintenance lenalidomide or bortezimib. Early administration of MMR may be recommended in event of local outbreak (see Table 2).

6. (Quadrivalent) Meningococcal vaccine (MCV-4): Preferred: **MenQuadfi®** (0.5 IM); Alternative: Menveo® (0.5mL IM). Both are 2-dose series, *minimum 2-month interval between doses.* For patients on complement inhibitors (ie. eculizumab, ravulizumab) or with continued risks for meningococcal infections including functional asplenia (eg. chronic GVHD), booster doses recommended every 5-years while at-risk.

7. Meningococcal B vaccine (MBV): Bexsero® (0.5 mL IM), 2-dose series, *minimum interval between doses is 1-month*. For patients on complement inhibitors (ie. eculizumab, ravulizumab) or with continued risks for meningococcal infection including functional asplenia (eg. chronic GVHD), booster doses recommended 1-year after 2-dose series followed by every 2-3 years while at risk.

8. Mpox vaccine: Use of Mpox vaccine is permissible in immunocompromised hosts ≥ 18 years of age at high risk for infection. Further details on eligibility and vaccination be found on Duke Custom ID (Mpox).

9. Pentacel® vaccine: Combination vaccine containing diphtheria, tetanus and acellular pertussis (DTaP), *Haemophilus influenzae* B (Hib) and inactivated polio virus (IPV). Pentacel® (0.5 mL IM), 3-dose series, *minimum 2-month interval between doses*. If this combination vaccine cannot be given then individual components can be administered separately (3-dose series): (1) DTaP (0.5 mL IM) – Daptacel® or Infanrix® [alternative Tdap (0.5 mL IM) – Adacel® or Boostrix®], (2) Hib (0.5 mL IM) - ActHIB® or Hiberix®, (c) IPV (0.5 mL IM, subQ) – IPOL®.

10. Pneumococcal conjugate vaccine (PCV-20): Prevnar-20® (0.5 mL IM or subQ), 4-dose series, *minimum interval between doses 1-3 is 1 month, followed by a fourth PCV-20 dose at least 6 months after the 3rd PCV-20 dose, or at least 12 months after HCT, whichever is later.* HCT recipients who have started their pneumococcal vaccine series with another pneumococcal conjugate vaccine (e.g., Prevnar-13 or Prevnar-15) may complete their 4-dose pneumococcal vaccine series with PCV-20.

11. Recombinant zoster vaccine (RZV): Shingrix® (0.5mL IM), 2-dose series, *2-6 month interval between doses*. Used in patients with a previous history of primary varicella infection (chickenpox), pre-transplant seropositivity to VZV and/or documented receipt of Varivax® vaccine prior to transplant. In all other cases, RZV should be deferred and Varivax® series administered ≥ 24 months post-transplant if meeting criteria for live vaccines. Acyclovir prophylaxis should continue until at least 4 -weeks following completion of the RZV vaccine series and off all immunosuppression.

12. Respiratory Syncytial virus vaccine (RSV): Abrysvo™ (Pfizer: 0.5mL IM) or Arexvy® (GSK: 0.5mL IM). Recommended in patients >65 years of age, or patients ≥60 years of age with severe heart or lung disease. Patients <60 years of age may be considered but will incur out-of-pocket costs of ~$250+. Vaccination in this age group should be based on shared clinical decision making.

13. Varicella virus vaccine: Varivax® (0.5 mL subQ), 2-dose series (separated by ≥ 4–8 weeks) is given to patients not meeting criteria for RZV (Shingrix®). Consult transplant infectious diseases team for guidance in all VZV seronegative recipients. Varivax® is a live vaccine and should only be administered in patients ≥ 24-months post-transplant without GVHD and off all immunosuppressive therapy for ≥ 12-months with CD4 cell counts ≥ 200/mm^3. Delay administration of Varivax® for at least 8-months after the receipt of IVIG whenever feasible. LIVE vaccines

can be administered on the same day (e.g., MMR and Varivax®) but if unable to administer the same day the second live vaccine should be given ≥ 28 days later.

Table 2: Criteria recommended for MMR vaccination during local outbreak

- MMR vaccination may be recommended in the case of a local outbreak of measles. Criteria for early administration as below (adapted from reference 10):

Criteria	Allogeneic HCT	Autologous HCT
Timing	> 1 year post transplant	
Immunosuppressive Therapy	Single agent: tacrolimus with serum trough level < 5ng/ml OR cyclosporine with serum trough level < 120ng/ml OR sirolimus with serum trough level of < 2ng/mL	No post-transplant chemotherapy, unless lenalidomide or bortezomib for maintenance therapy
Steroid Use	≤ 5mg prednisone daily (for secondary adrenal insufficiency	
Cell Counts	Total lymphocyte count of ≥ 1 x 10^3 μL or CD4 > 200 cells/mm^3 and CD19 > 20 cells/mm^3	
Immunoglobulin Level	Unsupported IgG > 400mg/dL and measurable IgA > 6mg/dL	
Additional	No active systemic GVHD requiring immunosuppression beyond topical therapy	

If administered early, patients should receive 2 doses of MMR due to reduced rates of seroconversion. Dose 2 to be given no less than 1 month after first dose and at least > 15 months post-transplant.

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