

Vaccination Guidelines

After B-cell and Plasma Cell Targeted CAR T-Cell Therapy

This handout explains vaccine guidelines for patients who had CAR T-cell therapy for B-cell cancers such as leukemia, lymphoma, and multiple myeloma. This handout is written for health care providers and is meant for you to share with your primary care provider (PCP).

Vaccination guidelines

At 6 months post CAR-T therapy, patients may start the re-vaccination process:

- Start by checking these **titers** and **CD19** or **CD20** counts:
 - Streptococcus pneumoniae (23 serotypes) IgG
 - Tetanus toxoid IgG
 - Haemophilus influenza type B (HiB) IgG
 - Hepatitis A (HAV) IgG
 - Hepatitis B (HBV) IgG
- If titers are not seroprotective and CD19/20 counts are > 20 cells/mm³, start inactivated vaccine series. If unable to check CD19/20, fine to proceed with vaccine series. Don't repeat titers until completion of series.
- If CD19 or CD20 counts are < 20 cells/mm³, wait 6 months, repeat CD19/20 and start series when CD19/20 > 20 cells/mm³

Note: If patient is receiving routine IVIG, defer vaccinations until off IVIG for at least 2 months (excluding seasonal influenza and SARS-CoV-2 vaccinations).

Influenza ('flu') vaccine

All patients regardless of CD19 or CD20 blood B-cell count should receive a seasonal high dose influenza vaccine.

- For patients who received seasonal influenza vaccine prior to CAR-T cell therapy:
 - Administer 1 dose of seasonal influenza vaccine starting 3 months post CAR-T, then once yearly thereafter.
- For patients who did not receive seasonal influenza vaccine prior to CAR-T cell therapy:
 - Administer 2 doses of seasonal influenza vaccine, 1 month apart, starting 3 months post CAR-T, then once yearly thereafter.

COVID-19 vaccine

All patients regardless of CD19 or CD20 blood B-cell count should receive full SARS-CoV-2 vaccine series (4 doses).

- Dose 1 of the SARS-CoV-2 vaccination series should be given at ≥ 3 months post CAR-T
- Dose 2 should be given 1 month following (~4 months post CAR-T)
- Dose 3 is given 2 months after dose 2 (~6 months post CAR-T)
- Dose 4 is given 2 months after Dose 3 (~8 months post CAR-T)

Other vaccinations

Patients may need additional vaccines depending on their body's response to the first series of inactivated vaccines, see vaccination schema below. Avoid live vaccines (e.g., MMR) until:

- At least 1 year after CAR T-cell therapy
- At least 2 years after a Hematopoietic Cell Transplant (HCT)

Note: For patients with history of prior HCT and have not completed routine post-HCT vaccinations, the approach is to start over with the whole course of vaccinations when immune function has recovered post CAR-T cell therapy. For vaccination guidelines, please reach out to Bone Marrow Transplant LTFU at (206) 606-4415 or ltfu@fredhutch.org.

For more information and resources

Contact the Fred Hutch Cellular Immunotherapy Long-Term Follow-Up (LTFU) Clinic at:

Phone: (206) 667-5811

Email: imtxltfu@fredhutch.org

Web: FredHutch.org/ltfu-cellular-immunotherapy

Resource

Center for Disease Control (CDC): Vaccines for Moderately to Severely Immunocompromised People: cdc.gov/covid/vaccines/immunocompromised-people.html

Initial vaccination schema in adults and children who received B-cell targeted CAR-T cell therapy with no history of prior HCT or completed last whole series of vaccines post HCT ^{1 †}

Killed/Inactivated Vaccines ¹	Pre-CAR	≥ 3m	~4m	~6m	~6m ³	≥ 6m	≥ 8m	≥ 10m	≥ 12m	≥ 18m	Minimal Time Interval Between Vaccinations
IIV4, Inactivated influenza (Sep-Mar) High Dose Formulation	IIV4 ²	IIV4 ²	IIV4 ²								
Pneumococcal- conjugate (Pevnar 20 [®])				✓ CD19 or CD 20 blood B-cell count	✓ titers	PCV20	PCV20	PCV20	✓ titers ^{4,15}		
Pentacel [®] (DTaP/IPV/Hib) ^{5,6}				✓ CD19 or CD 20 blood B-cell count	✓ titers ⁷	Pentacel [®]	Pentacel [®]	Pentacel [®]	✓ titers ^{7,15}		1-2 months
Hepatitis A				✓ CD19 or CD 20 blood B-cell count	✓ titers ¹⁰	HAV			HAV	✓ titers ^{10,15}	6 months
Hepatitis B ^{8,9}				✓ CD19 or CD 20 blood B-cell count	✓ titers ¹⁰	HBV	HBV	HBV	HBV	✓ titers ^{10,15}	1-2 months
SARS-CoV-2 (Pfizer or Moderna)	COVID ¹³	COVID ¹¹	COVID			COVID ¹²	COVID ¹²				
RSV ¹⁴ (≥ 18 years old to ≥ 50 years old)				RSV							

¹ For inactivated “dead” virus vaccines, vaccination should be at least 2 months post last dose of IVIG.

² If patient has already received seasonal influenza vaccination prior to leukapheresis do not need to give again after leukapheresis and before lymphodepletion chemotherapy. All patients who did not receive seasonal influenza vaccination prior to leukapheresis, administer inactivated influenza vaccine after leukapheresis and ≥ 2 weeks prior to beginning lymphodepletion chemotherapy. All patients who received seasonal influenza vaccine prior to CAR-T cell therapy, a second dose of seasonal influenza vaccine should be given at 3 months post CAR-T cell therapy and thereafter yearly. All patients who did not receive the seasonal influenza vaccination prior to CAR-T cell therapy, two doses of seasonal influenza vaccine should be administered at 3 and 4 months post CAR-T Cell infusion and thereafter yearly.

³ In patients with CD19 or CD20 ≥ 20 cell/mm³, check specific pathogen titers. In patients with CD19 or CD20 blood B-cell count < 20 cells/mm³ DO NOT VACCINATE and repeat CD19 or CD20 blood B-cell count in six months. In patients not able to get CD19 or CD20 blood B-cell count, then check titers.

⁴ Check titers for S. Pneumonia (IgG, 23 serotypes) 2 months after complete series. A positive response to PCV20 is defined: as achieving a seroprotective IgG level against S. pneumoniae in ≥ 15 out of 20 PCV20 serotypes at 1-2 months post-vaccination. If seronegative repeat the whole series of 3 Prevenar and recheck serology.

⁵ Separate component vaccines (shots) may be used instead for DTaP, IPV, and Hib if Pentacel[®] is unavailable.

⁶ If not using Pentacel[®] and DTaP is unavailable, then may use Adacel[®] = Tdap (age ≥ 10 y through 64 y) or Boostrix[®] = Tdap (age ≥10 y).

⁷ Check titers to tetanus and Hib.

⁸ Hepatitis B vaccination is accomplished preferably with Heplisav-B[®] based on data extrapolated from patients with chronic kidney disease or on hemodialysis for ESRF. Alternatively, double (40 mcg/dose = 2 mL total) doses of Engerix-B[®] may be given. Patients who do not respond to the primary vaccine series should receive an additional 1-3 doses of the same vaccine or, alternatively, repeat series with a different vaccine brand (e.g., double doses of Engerix-B[®] if did not respond to Heplisav-B[®] or single doses of Heplisav-B[®] if did not respond to Engerix-B[®]).

⁹ If NOT administering hepatitis B series using Heplisav-B[®], Twinrix[®] can be administered on days when HAV and HBV are given together. (Twinrix[®] approved for age ≥ 18 y)

¹⁰ Hepatitis A & B surface antigen IgG.

¹¹ Dose 1 of the SARS-CoV-2 vaccination series should begin at > to Day + 90.

¹² Dose 3 is preferably given 2 months after dose 2 but may be given as early as 1 month after dose 2 to avoid a missed vaccination opportunity; Dose 4 is 2 months after Dose 3.

¹³ If up to date with SAR-CoV-2 vaccination, before leukapheresis, do not need to give.

¹⁴ Patient should have no evidence of ongoing neurotoxicity. Talk to the patient about pro and cons of getting RSV vaccine. In patients ≥ 50 years, preference is adjuvant RSV vaccine.

¹⁵ If not seroprotective, wait 6-12 months and recheck CD19 or CD20 blood B-cell count and if ≥ 20 cells/mm³ and increased by ≥ 4 fold, then repeat whole antigen specific vaccine series.

Additional vaccinations for adults and children who received B-cell targeted CAR-T cell therapy and are ≥ 17 months post CAR-T cell therapy †

Killed/Inactivated Vaccines¹	≥ 17m	≥ 18m	≥ 20m	≥ 24m	≥ 26m	Minimal Time Interval Between Vaccinations
Meningococcal ACWY (Menactra, Menveo, MCV4) ²		MCV4	MCV4			2 months
Meningococcal Group B (Bexsero®) ^{3,4}				Bexsero®	Bexsero®	≥ 2 months
HPV (Gardasil), 9-45 years		HPV	HPV	HPV		2 m after 1st; 4 m after 2nd dose
Live and Non-Live Adjuvant Vaccines						
Measles/Mumps/Rubella (MMR) ⁵	✓ titers	Only if titers negative, MMR	MMR			
Varicella-Zoster - Varivax (live): <i>VZV seronegative only</i> ^{5,6}	✓ titers ⁸	VZV	VZV			≥ 1 month
Varicella-Zoster - Shingrix® (non-live adjuvant): <i>VZV^{6,7} seropositive only, ⁶ ≥18 years</i>		VZV	VZV			1-2 months

¹For inactivated “dead” virus vaccines, vaccination should be at least 2 months post last dose of IVIG.

²Meningococcal vaccination is recommended for individuals at increased risk for meningococcal infection, such as children between 11 and 18 years of age and certain other groups (college freshmen living in dormitories, individuals traveling to countries where Neisseria meningitidis is hyperendemic or epidemic, patients with terminal complement component deficiencies or anatomic or functional asplenia [i.e. chronic GVHD], and others).

³Recommended for patients ≥ 10 years old with anatomic or functional asplenia condition [i.e. chronic GVHD] or increased environmental risk.

⁴If Bexsero® is not given, Trumenba® can be substituted in patients ≥ 10 years old as 3 doses (0, 2, and 6 months apart).

⁵Not until > 1 year post CAR-T cell therapy, > 2 year post transplant, > 1 year off all systemic immunosuppressive therapy, > 8 months since last dose of IVIG/VZIG or most recent plasma transfusion, and absolute CD4 T cell count ≥ 200 per microliter. Stop acyclovir or valacyclovir a day before starting varivax vaccination.

⁶If patient is VZV seronegative, do not give Shingrix.

⁷Not until ≥ 1 year post CAR-T cell therapy, ≥ 1 year post transplant, ≥ 8 months off all systemic immunosuppressive therapy without GVHD flare up, and absolute CD4 T cell count ≥ 200 per microliter. Continue acyclovir or valacyclovir until 1 month after 2nd Shingrix vaccination.

⁸ If serology titer to VZV is not available from pre-CAR therapy, check VZV titer.