Principles of Vaccination in Hematology and Oncology Patients

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Necessity of Vaccination in Cancer Patients

- Vaccination in patients with cancer can reduce the morbidity and mortality associated with infection
- In general, patients with hematologic malignancies have a greater risk for infection than patients with solid tumors.
- HCT patients may lose immunity to pathogens post-transplant.
- Therefore, the vaccination recommendations for these patients are more expansive than the recommendations for the general population of patients with cancer

Safety of Vaccination in Cancer Patients

- In any Immunocompromised patient, live vaccines, including the live attenuated influenza vaccine (LAIV), have the potential to cause disease and should not be administered during chemotherapy or periods of significant immunosuppression such as treatment for GVHD.
- The safety of vaccines for patients receiving immunostimulatory drugs has not been established.
- Inactivated vaccines can often be safely administered to patients with cancer.

Vaccination in patients with Cancer

- Patients with hematological malignancy are at high risk of infection due to various mechanism of humeral and cell-mediated immune deficiencies depend on underlying disease and specific therapies.

- Although the immunogenicity of the vaccines may be reduced in Immunocompromised patients, the potential for protection conferred by antigen-derived vaccines, even if incomplete, is better than no protection if the vaccine is withheld

GENERAL PRINCIPLE

- The best time for Serological response to vaccines is between chemotherapy intervals:
  - **7 days after the last chemo or >2weeks before later chemo**
- Live viral vaccines should not be administered during chemotherapy
- Three months after cancer chemotherapy, patients should be vaccinated with inactivated vaccines and the live vaccines for varicella, measles, mumps, and rubella and measles, mumps, and rubella–varicella
- In regimens that included anti–B-cell antibodies, vaccinations should be delayed at least 6 months

Influenza Vaccine

- Annual vaccination with Inactivated influenza vaccine (IIV) is recommended for Immunocompromised patients aged ≥6 months.
- Except for patients who are very unlikely to respond (although unlikely to be harmed by IIV), such as those receiving intensive chemotherapy (strong, low) or those who have received anti–B-cell antibodies within 6 months.
- Live attenuated influenza vaccine (LAIV) should not be administered. In lymphoproliferative diseases (M.M, lymphoma, CLL) LAIVs are contraindicated until at least 3 months after the end of chemotherapy.

Varicella and zoster vaccines

- VAR can be considered for patients without evidence of varicella immunity who are receiving long-term, low-level immunosuppression

- VAR as the single antigen product, not MMRV
- MMRV contains ≥7-fold more VZV than monovalent VAR
- ZOS: aged ≥60 years ≥4 weeks before beginning highly immunosuppressive therapy

ZOS: varicella-positive patients aged 50–59 years ≥4 weeks before beginning immunosuppressive therapy

- History of varicella/zoster infection
- VZV seropositive with no previous doses of VAR

PNEUMOCOCCAL VACCINES

Vaccine	Type of Vaccine	Age
PPSV 23 (Polysaccharide)	**T-independent Vaccine**	**Not effective <2 years**
Prevenar 13 (Polysaccharide Conjugated)	**T-dependent Vaccine**	**Effective in all ages**

- PCV13 should be administered to newly diagnosed adults with hematological or solid malignancies
- PPSV23 should be administered to adults and children aged ≥2 years at least 8 weeks after the indicated dose(of PCV13.

BEST TIME TO VACCINATE

Rev Port Pneumol. 2014;20(2):111–114
revista portuguesa de PNEUMOLOGIA
portuguese journal of pulmonology
www.revportpneumol.org
ELSEVIER DOYMA

CONSENSUS

Consensus document for the prevention of respiratory infections in adults

Table 2 Recommendations for antipneumococcal vaccination in specific circumstances (adapted from[1,13]).

Condition	Vaccination recommendations (individuals not vaccinated)
HIV/AIDS	Early, preferably with lymphocytes TCD4$^+$ $\geq$ 200/mm^3; if TCD4$^+$ < 200/mm^3, vaccinate without waiting for immune reconstruction and consider revaccination after TCD4$^+$ $\geq$ 200/mm^3
Surgical splenectomy	In elective surgery, at least 2 weeks before surgery; in unplanned surgery, vaccinate 2 weeks after surgery
Autoimmune diseases	Early and before starting immunosuppressive therapy
Waiting for a solid organ transplant	Early, at least 2–4 weeks before transplant
Solid organ transplant	Start vaccination 6 months after transplant
Transplant of hematopoietic cells	Start vaccination 3–6 months after transplant
Neoplastic diseases in chemotherapy and/or radiotherapy	10–14 days before treatment or 3 months after finishing chemotherapy or radiotherapy. If the vaccine is administered during the course of chemotherapy consider whether to revaccinate 3 months after finishing treatment

Vaccination of Patients With Cancer

Vaccine	Prior to or During Chemotherapy: Recommendation	Prior to or During Chemotherapy: Strength, Evidence Quality	Starting ≥3 mo Postchemotherapy and ≥6 mo Post Anti–B-Cell Antibodies for Inactivated Vaccines; See Each Live Vaccine for Interval: Recommendation	Starting ≥3 mo Postchemotherapy and ≥6 mo Post Anti–B-Cell Antibodies for Inactivated Vaccines; See Each Live Vaccine for Interval: Strength, Evidence Quality
Haemophilus influenzae b conjugate	U[a]	Weak, low	U	Strong, moderate
Hepatitis A	U[a]	Weak, low	U	Strong, very low
Hepatitis B	U[a]	Weak, low	U R: adults	Strong, moderate Strong, very low
Diphtheria toxoid, tetanus toxoid, acellular pertussis; tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis	U[a]	Weak, low	U: age 0–18 y R: adults with acute lymphoblastic leukemia or lymphoma	Strong, moderate Weak, very low
Human papillomavirus	U: 11–26 y[a]	Weak, very low	U	Strong, very low
Influenza-inactivated (inactivated influenza vaccine)	U[a]	Strong, low-moderate[a]	U[b]	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	X	Weak, very low	U	Strong, low
Measles, mumps, and rubella–live	X[c]	Strong, moderate	Starting at 3 mo: U	Strong, low
Measles, mumps, and rubella–varicella–live	X[c]	Strong, moderate	Starting at 3 mo: U	Weak, very low
Meningococcal conjugate	U[a]	Weak, low	U	Strong, low
Pneumococcal conjugate-13 (PCV13)	R: <6 y R: age ≥6 y[d]	Strong, low Strong, very low	U	Strong, low
Pneumococcal polysaccharide (PPSV23)	R: age ≥2 y	Strong, low	U	Strong, low
Polio–inactivated (inactivated poliovirus vaccine)	U[a]	Weak, low	U	Strong, low
Rotavirus–live	X	Strong, very low	Not applicable	
Varicella–live	X[c]	Strong, moderate	Starting at 3 mo: U[e]	Weak, very low
Zoster–live	X[c]	Strong, very low	Starting at 3 mo: U[e]	Weak, very low

❑Abbreviations: R, recommended, U, usual, , X, contraindicated.

- [a] Administer **inactivated influenza vaccine (IIV)** annually to patients with hematological malignancies or solid tumor malignancies. Administration of indicated inactivated vaccines 2 or more weeks prior to chemotherapy is preferred.
- [b] IIV can be administered ≤3 months after chemotherapy, but response rate may be low.
- [c] MMR vaccines should not be administered unless the vaccine is otherwise indicated based on the annually updated Centers for Disease Control and Prevention recommendations and the patient is not immunosuppressed and there will be an interval of ≥4 weeks prior to initiation of chemotherapy.
- [d] For patients aged ≥19 years with Cancer who have received **PPSV23**, **PCV13** should be administered after an interval of ≥1 year after the last PPSV23 dose.
- [e] Although **measles, mumps, and rubella** vaccine has been given safely 3 months after completion of chemotherapy, data on the safety, immunogenicity, and efficacy of varicella or zoster vaccine after completion of chemotherapy are not available.

AML & MDS

- A single dose of IIV is recommended yearly as long as the patients is considered immunocompromised.
- Pneumococcal vaccination should be done 3-6 months after the end of chemotherapy
- Other inactivated vaccines can be administered 3-6 months after the end of chemotherapy According to age and country recommendation

Lymphoma

- IIV and Pneumococcal vaccines are strongly recommended, except:
- High dose chemotherapy
- receiving anti-CD20 Ab (rituximab) in the previous 6 m.

- other inactivated vaccines should be delayed for at least 6 months after the last dose of anti-CD20 Ab According to age and country recommendation
- HPV vaccine is recommended specially after pelvic radiation in lymphoma.

- LAIVs are contra-indicated until at least 3 months after the end of chemotherapy.

Multiple Myeloma

- A single dose of IIV is strongly recommended yearly as long as the patients is considered immunocompromised.
- Pneumococcal vaccine is recommended, preferably before treatment or during maintenance.
- other inactivated vaccines can be administered 3-6 months after the end of chemotherapy According to age and country recommendation.
- LAIVs are contra-indicated until at least 3 months after the end of chemotherapy.

VACCINATION OF HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS (BMT)

- The HSCT donor should be current with routinely recommended vaccines based on age, vaccination history, and exposure history according to the CDC annual schedule.
- Administration of MMR, MMRV, VAR, and ZOS vaccines should be avoided within 4 weeks of stem cell harvest .
- Vaccination of the donor for the benefit of the recipient is not recommended.
- Prior to HSCT, candidates should receive vaccines indicate for Immunocompotent persons based on age, vaccination history, and exposure history according to the CDC annual schedule if they are not already immunosuppressed and when the interval to start of the conditioning regimen is ≥4 weeks for live vaccines and ≥2 weeks for inactivated vaccine

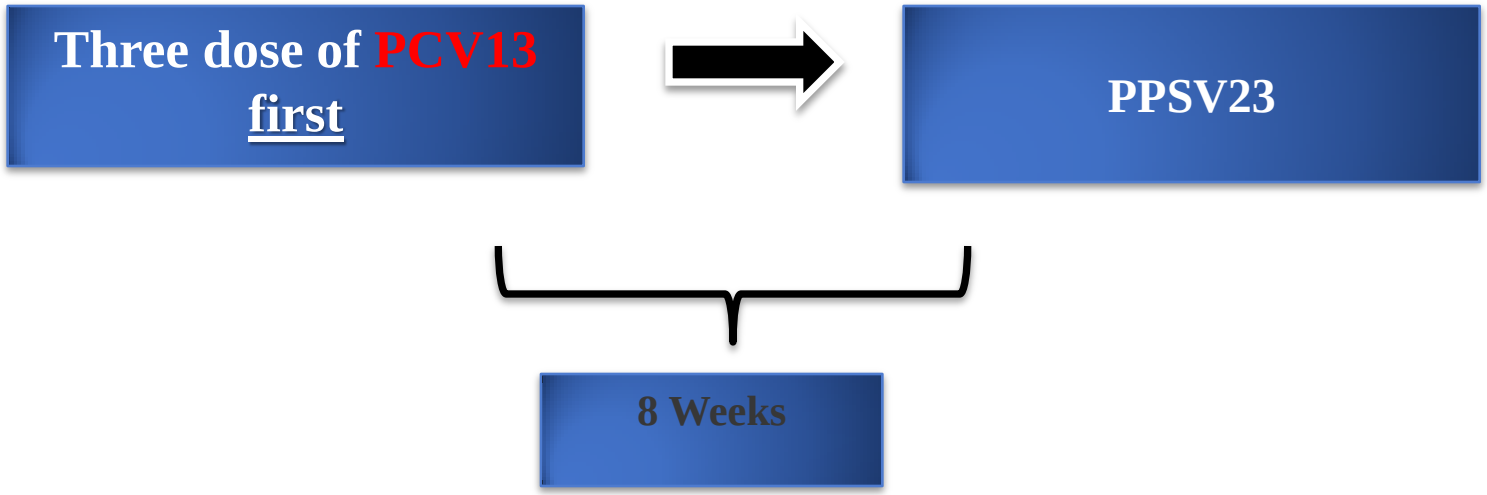
Vaccination of Patients With Allogeneic or Autologous Hematopoietic Stem Cell Transplant

Inactivated Vaccines[nn]	Recommended Timing After HCT	Number of Doses
DTaP (Diphtheria/Tetanus/Acellular Pertussis)	6–12 mo	3
Haemophilus influenzae type b (Hib)	6–12 mo	3
Pneumococcal vaccination • Conjugated 13-valent vaccine • Upon completion of PCV13 series, then PPSV23	 6–12 mo ≥12 mo	 3 1
Hepatitis A[oo] (Hep A)	6–12 mo	2
Hepatitis B[oo] (Hep B)	6–12 mo	3
Meningococcal conjugate vaccine[pp]	6–12 mo	1–2
Influenza (injectable)	4–6 mo	1, annually
Inactivated Polio vaccine	6–12 mo	3
Recombinant zoster vaccine[qq]	50–70 days after autologous HCT May be considered after allogeneic HCT[qq]	2
Human papillomavirus (HPV) vaccine	>6–12 mo For patients up to age 26, consider up to age 45	3

PNEUMOCOCCAL VACCINATION IN RECIPIENTS OF BMT

✓Due to the need for re-immunization after bone marrow transplantation without GVHD, pneumococcal vaccines should be injected for the patients

✓For patients with chronic GVHD, a fourth dose of PCV13 can be given at 12 months after HSCT



Rubin et al. IDSA, 2013, CID 2014:58

HAEMOPHILUS INFLUENZAE TYPE B VACCINE

- Hib vaccine → From 3 m after transplantation,3 doses, at 1 m interval
- Tdap-Hib vaccine → Aternatively, From 6 m after transplantation,3 doses, at 1 m interval

INACTIVATED INFLUENZA VACCINE

- IIV ⟶ From 6 m after transplantation, annually at beginning of flu season
- In severe GVHD ⟶ patients a second dose 3-4 weeks after the first dose
- In the setting of community outbreak IIV: 3 m after transplantation & a second dose 3-4 weeks later

HBV VACCINE

- HBV vaccine ⟶ From 6-12 m after transplantation,3 doses, 0, 1 and 6 m apart

- In patients with (HBsAg - & anti-HBc $^{+}$)
  - ✓ check of anti-HBs titer regularly
  - ✓ Revaccinate with unprotective titers

- If recipients (HBV-) and donor (anti-HBc $^{+}$)
  - ✓ The patient vaccinate before transplant if possible
  - ✓ Additionally receive HBV-IG
  - ✓ 6 m after transplant, should be vaccinated if they lost their immunity at 6 m.

OTHER INACTIVATED VACCINES

- MCV4 ⟶ From 6 m after transplantation,2 doses, at 8 weeks interval

- IPV ⟶ From 6-12 m after transplantation,3 doses, at 1-2 m interval

✓ Booster doses according to country recommendation

- DTap ⟶ From 6-12 m after transplantation,3 doses, at 1-2 m interval

✓ DTap should be preferred over Tdap

✓ Booster doses according to country

LIVE ATTENUATED VACCINES

- LAV can be considered:
  - ✓ at least 24 m after transplantations
  - ✓ in seronegative patients
  - ✓ with no GVHD,
  - ✓ no ongoing immunosuppression,
  - ✓ no relapse of underlying disease,
  - ✓ no treatment of Ig during the previous month

- In case of measles outbreak, MMR vaccination could be considered 12 m after transplantation in patients with low-grade immunosuppression.