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Vaccination of the Stem Cell Transplant (SCT) recipient and the Hematologic Malignancy patient

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INTRODUCTION

Due to advances in cancer treatment and earlier cancer detection, coupled with the aging and overall growth of the population, the number of cancer survivors in the United States (US) is predicted to reach more than 20 million by 2026[1]. A five-fold increase in number hematopoietic stem cell transplantation (SCT) survivors is expected in the US between 2009 to 2030[2]. The Centers for Disease Control (CDC)-Advisory Committee on Immunization Practices (ACIP) recommends certain vaccines for routine use in all persons, stratified by age and clinical indication[3].

Patients with malignancies affecting the bone marrow or lymphatic system and SCT recipients are both considered severely immunocompromised (high-risk) when it comes to evaluation for travel vaccination[4]. Antibody titers to vaccine-preventable illnesses decline following SCT, so primary re-immunization is required when the immune system has sufficiently reconstituted. Three major societies and consensus groups have published guidelines for SCT recipients: Infectious Disease Society of America (IDSA), American Society of Blood and Bone Marrow Transplantation (ASBMT), and the European Group of Blood and Marrow Transplantation (EBMT)[5,67]. These recommendations, coupled with ACIP recommendations and newly available published data, serve as the basis of this review.

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VACCINE TYPES AND TIMING

Inactivated vaccines are typically protein- or polysaccharide-based. Polysaccharide vaccines are less immunogenic and can be conjugated to proteins to enhance the immune response. Recombinant vaccines consist of genetically-engineered antigens and are typically inactivated but can occasionally be live-attenuated (LAV). Some vaccines contain adjuvants to enhance immunogenicity[8]. LAV uses a weakened but replication competent organism. High-risk patients should not receive LAV until at least two years have elapsed since transplant, no evidence of systemic graft-versus-host-disease (GVHD), and cessation of all immunosuppressive medication[6]. For patients undergoing elective splenectomy as a part of cancer treatment, indicated vaccines should be administered at least 2 weeks prior to the operation[9].

Inactivated vaccines should be administered at least 2 weeks prior to initiation of cytotoxic therapy and/or a pre-transplant conditioning regimen when needed. Consensus guidelines on post-SCT immunization protocols stipulate introduction of immunization with inactivated vaccines at 3–12 months following transplantation and acknowledge the lack of available prospective data to support more specific practices, including assessment of immune parameters before vaccination[5,67]. The recommended immunization schedule after SCT is presented in Figure 1. SCT type, presence of GVHD, and ongoing immunosuppressive therapy may necessitate a delay in vaccine initiation[10].

Special considerations:

Anti-CD-20 therapy: Patients receiving monoclonal anti CD-20 antibody (*Rituximab)* or other B-cell depleting therapies may not develop adequate antibody response to vaccines. An interval of at least 6 months is recommended between the last rituximab dose and vaccination.

Intravenous immunoglobulin (IVIG): IVIG does not interfere with antibody response to inactivated vaccines. Administration of vaccines at different anatomic sites is permissible. Simultaneous or close administration of antibody containing products and live vaccines can have a neutralizing effect with reduction in vaccine efficacy (serological response). IVIG should therefore not be administered for 8–11 months prior to, and for at least two weeks after, Measles, mumps and rubella (MMR) and varicella vaccination (See sections on zoster and MMR).

Chimeric antigen receptor (CAR) T- cell therapy: In 2017, CAR T-cell therapies were approved by the US (Food and Drug Administration) FDA for treatment of refractory acute lymphoblastic leukemia (ALL) in children and advanced B cell lymphomas[11]. Using a genetic engineering technology, T cells gain ability to recognize and destroy specific antigens on tumor cells. The most developed CAR T cell therapy is targeted towards CD19, an antigen expressed on B cells. Once administered, CD 19 directed CAR T cells destroy not only tumor cells that express CD19 but also normal B cells. Consequently, B cell aplasia and hypogammaglobulinemia occurs. The duration and degree of these effects after CAR-T is highly variable, several individuals require IVIG replenishment. No studies have examined

serological response to the inactivated vaccines in patients treated with CAR-T cell therapy but lack of reliable responses is not entirely unexpected[11].

VACCINES

Inactivated Influenza Vaccine

Patients with hematologic malignancy and SCT recipients are at an elevated risk for influenza-related complications[12–15]. A third of SCT recipients with influenza develop lower airway disease. Overall mortality ranges from 6 to 15%, rising to 28 to 45% when infection has progressed to include lower respiratory tract involvement[14–23]. Response to seasonal influenza immunization is mediated by the generation of neutralizing antibodies against viral antigens and CD4+ and CD8+ specific cytotoxic responses[24].

Clinical effectiveness of the inactivated influenza vaccine in the SCT population is not rigorously studied. Routine strategies may not offer an optimal level of protection, especially early after SCT[14]. Several observational reports suggest reduced risk of lower respiratory tract infection and hospitalization among vaccinated SCT patients[2526–30].

Newer FDA approved influenza vaccines and other novel strategies

To overcome the limitations of standard dose (SD) inactivated influenza vaccine, several strategies have been evaluated to see if they enhance protection from influenza following SCT.

High dose (HD) vaccine contains four times the amount of antigen compared to SD. An early phase randomized study comparing HD vs SD (Table 1) demonstrated superior immunogenicity with HD only for the A/H3N2 component. Local reactions were common with HD (67% versus 31% for SD), although the majority of these were mild[31]. Administration of HD vaccine in patients < 65 years is not recommended[32]. In small-randomized studies, a second vaccine dose within the same season did not substantially improve immune response after SCT[33,34].

Among the adjuvanted vaccines, AS03-[35] and MF59-[36] containing vaccines have been evaluated. MF59-containing vaccine, Fluad (*Seqirus*), is the only adjuvanted influenza vaccine approved in the US for elderly patients[37]. Specifically in SCT, a single randomized trial failed to show superior seroconversion rates with Fluad compared to SD inactivated influenza vaccine (see Table 1)[36]. Patients immunized > 6 months after transplant had higher seroconversion rates, indicating a potential benefit by waiting at least 6 months following SCT.

Pre-transplant donor vaccination is without benefit, but vaccination of the SCT recipient may offer protection, although corroboration by additional studies is desired (see Table 1)[38].

Granulocyte macrophage colony stimulating factor has no role in improving vaccine effectiveness after SCT[39].

Among recently approved vaccines, recombinant (egg free) and cell-based vaccines are promising new advancements. Recombinant vaccine (RIV4-Flublok)[40] retains genetic

fidelity to circulating viruses, offering broader protection with a quadrivalent formulation and containing a high amount of antigen (three times higher compared to SD). These vaccines are now licensed for use in adults over the age of 18[41].

Despite data on clinical superiority in the general population of HD compared to SD inactivated influenza vaccines, no existing studies have compared the recombinant, HD, and adjuvanted vaccines among SCT patients. These vaccines are among the ACIP recommend options for adults ≥ 65 years, plausibly rendering better clinical protection for older transplant recipients. No conclusions can be drawn on the preferential use of one formulation over the other.

Recommendations: There is consensus across existing guidelines recommending seasonal influenza vaccination regardless of transplant type[29,6]. The key recommendations are:

- Administer > 6 months after transplant but may begin at 4 months if influenza activity has begun. Influenza activity in US peaks between December and February in 8 out of every 10 seasons.
- Two doses administered one month apart for children < 9 years of age.
- LAIV is contraindicated.

Inactivated Influenza vaccination in patients with hematologic malignancy

Despite reduced effectiveness when compared to the general population, annual vaccination of patients with hematologic malignancy is an important preventive strategy[6,30]. Clinical studies in persons with hematologic malignancy show only marginal benefit with second doses[42,43].

Efficacy of inactivated influenza vaccine with certain malignancy treatment agents is specifically addressed in each of the following two paragraphs:

Rituximab: Antibody responses to adjuvanted influenza vaccine (AS03) were entirely subdued in a cohort of 67 patients vaccinated within 6 months after rituximab (71 % on R-CHOP)[44]. A second vaccine is not helpful in boosting the immune response.

Ibrutinib—Ibrutinib is an immunomodulatory drug currently being used in the treatment of chronic lymphocytic leukemia (CLL), B-cell lymphomas, and Waldenström's macroglobulinemia. It acts by inhibition of Bruton tyrosine kinase (BTK). Disruption in B-cell signaling, maturation, and immunoglobulin synthesis following BTK inhibition causes agammaglobulinemia[45]. Two studies on serological response after inactivated influenza vaccine in ibrutinib-treated patients showed mixed results[46,47]. There are currently inadequate data to determine if inactivated influenza vaccination is ineffective in a certain subset of patients on treatment with this agent.

Pneumococcal conjugate (PCV-13) and polysaccharide vaccines (PPSV-23)

Patients with hematologic malignancy and SCT recipients are at a 45–55 times higher risk (annual incidence 217–266 / 100,000 persons) of developing invasive pneumococcal disease (IPD) than the general population, primarily due acquired hypogammaglobulinemia[48,49]. Multiple Myeloma carries the greatest risk of IPD.

Conjugated vaccines induce early T-cell–dependent responses after SCT and elicit long-term immune memory. Since the introduction of conjugate vaccines for universal immunization, IPD rates have declined in high-risk patients[49,50]. The FDA approved conjugated pneumococcal vaccines starting in early 2000's with the seven valent PCV-7, followed by expanded coverage to 13 serotypes with FDA-approval of PCV- 13 in 2010, including the virulent serotype 19 A[51].

Prospective studies established the superior immunogenicity of conjugated pneumococcal vaccines when given 6–12 months after SCT[52]; 74.4% of pediatric recipients achieve seroprotection[53]. Vaccine response as early as 3 months after SCT was first shown in a randomized study with PCV-7 (3 months vs 9 months; 79% vs 82%). Notable findings in early vaccinees (vaccinated at 3 months following SCT) were a trend towards lower antibody concentration at 2 years as well as inferior priming for PPSV-23 when compared to PCV-7[54]. In a long-term follow-up study[55] of 30 surviving patients, persistent antibody response at 8–11 years from SCT was assessed; 10/17 in the late vs 2/13 in early group had PCV-7 antibodies ≥ 50 μg/ml (p=0.03). PPSV-23 booster after the initial series was without any additional benefit. Collectively, these findings suggest that PCV administered at 3 months has the probable benefit of clinical protection against *S. pneumoniae* earlier after SCT, but durable responses may be compromised.

In 2009, ASBMT guidelines were updated to include PCV-7 at 3–6 months after SCT, with consideration for a fourth dose in patients with chronic GVHD, as a substitute to PPSV-23 (although graded as weak evidence). In other guidelines, PPSV-23 is recommended at 1 year[5,56]. Experience with PCV-13 in SCT recipients was reported in 2015 from a multi-center study, when 251 patients were immunized with a 4 dose PCV-13 series at 3- to 6-months following SCT. The fourth dose (booster) was administered at a 6-month interval, and one month before PPSV-23. Significant increase in geometric mean fold rise was observed after the fourth dose, but comparisons with PPSV-23 boost only were not conducted. The fourth dose of PCV-13 was associated with an increase local and systemic reactions[57].

Recommendations: Current guidelines[6] recommend three doses of PCV-13 starting at 3–12 months after SCT, and 1 dose of PPSV-23 at 12 months in patients without GVHD (with an additional fourth dose of PCV-13 instead in those with GVHD). Although common practice, the optimal interval for post vaccine serological monitoring, and the benefit of booster doses beyond the first year, are not known.

Pneumococcal vaccination in patients with hematologic malignancy

PCV-13 is immunogenic in patients undergoing treatment for hematologic malignancy; duration of response can vary with the type of cancer and type of treatment. Patients with myeloma, especially those receiving lenalidomide[58], can mount an immune response. PCV's[59] are superior to PPSV-23 among splenectomized patients with treated Hodgkin's disease. PCV also performs better than PPSV-23 among patients treated with rituximab within the previous year. ACIP recommends starting with PCV-13, followed by PPSV-23 eight weeks later[6,51,60]

Varicella and Zoster vaccines

Adult cancer patients have a higher overall incidence of herpes zoster, compared to age-matched persons without cancer, particularly those with hematological malignancies[61]. Elderly patients with hematologic malignancy have a two-fold higher rates of zoster compared to those with solid tumors (31.0 vs. 14.9 per 1,000 patient-years)[62].

Currently, one varicella vaccine and two zoster vaccines are licensed for use in adults.

The varicella vaccine, *Varivax* (Merck) and the older zoster vaccine, *Zostavax* (Merck), both contain the live-attenuated Oka strain virus and therefore have limited use in high-risk immunocompromised patients. Death following live zoster virus vaccination to a patient with CLL has been reported[62a].

The new recombinant subunit (non-live) vaccine, *Shingrix* (GlaxoSmithKline) is clinically superior to Zostavax. Shingrix was approved by the US FDA on October 20, 2017. The vaccine is a two-dose series licensed for adults age over 50 years, including those with a previous episode of zoster or who previously received Zostavax. Shingrix is the preferred zoster vaccine as stated by ACIP[63].

Studies demonstrate that Shingrix is highly effective in preventing zoster and post-herpetic neuralgia (PHN) in all age groups without immunocompromising conditions, including the elderly (91% in adults ≥ 70 years old, 97% in adults 50–69 years old)[6465]. There are a lack of efficacy data among immunocompromised patients, although clinical trials are ongoing[73, 74]. No current recommendations from ACIP exist for Shingrix use in patients with an active hematologic malignancy[3].

Vaccination against Varicella and Herpes Zoster in SCT recipients

Varicella zoster virus (VZV) reactivation after SCT is reported to be as high as 20 to 53%[66]. Breakthrough and late reactivations occur despite use of anti-viral prophylaxis[67].

Live vaccine (Varivax and Zostavax): The 2009 consensus[7] and 2013 IDSA[6] guidelines recommend initiating Varivax immunization in seronegative recipients who are at least 24 months post SCT, without systemic GVHD or active immune compromise[6, 7]. Because of possible interference by neutralizing antibodies, patients should also be without receipt of IVIG within the preceding 8–11 months[6]. VZV-specific T-cell immunity does not adequately reconstitute in all situations following SCT[68], so preventive strategies that include vaccination of individuals irrespective of serostatus are required[69]. A single

retrospective study assessed the impact of Varivax administration at 24 months after allogenic SCT, in a majority of seropositive recipients, and after antiviral prophylaxis was discontinued[69]. At 5 years, the overall rate of zoster and PHN was significantly lower in the Varivax vs non-vaccinated group (zoster, 17% vs 33%; PHN, 0% vs 8%). Several single center observational studies have demonstrated short-term safety of Zostavax following SCT[70,7172]. The vaccine, which contains 14 times the dose of virus compared to Varivax, remains largely contraindicated in this patient population[63].

Inactivated varicella zoster vaccines (Shingrix and other): Two recent major clinical trials that evaluated inactivated zoster vaccines are summarized in Table 2. De la Serna et al. found significant efficacy of Shingrix when given as early as 50–70 days post-auto transplant; 68% and 89% effective in preventing zoster and PHN respectively[73]. Another Phase 3 trial assessed an investigational heat-inactivated vaccine among autologous SCT recipients, with the first dose given prior to SCT and 3 additional doses given within the first 3 months after SCT. Incidence of zoster was 32.9/1000-person years in the vaccine group vs 91.9/1000-person years in the placebo group, translating to an efficacy of 63.8%[74].

Recommendations: For seronegative patients, Varivax can be given at 24 months post SCT. The inactive subunit vaccine (Shingrix) is the preferred zoster vaccine for immunocompetent adults ≥ 50 years; patients who are no longer considered severely immunocompromised from their hematologic malignancy and/or SCT should be vaccinated. Insufficient data exist to recommend varicella vaccination earlier after transplant, although clinical trials with inactivated varicella vaccine are ongoing.

Tetanus, diphtheria, pertussis vaccines

Various combinations and doses of vaccines exist, including DTaP, DT, Tdap, and Td. Capital letters indicate higher toxoid or antigen amounts. DTaP should be administered to all children ≤ 7 years of age. For patients aged ≥ 7 years of age, the 2013 IDSA guidelines stipulate that DTaP should be considered or alternatively, one dose of Tdap vaccine should be administered followed by 2 doses of DT or Td (Figure 1)[6]. Among the available Tdap vaccinations in the US, *Boostrix* (GlaxoSmithKline) contains 8 mcg of pertussis toxoid in comparison to *Adacel* (Sanofi Pasteur), which contains 2.5 mcg[75] There are scant data to recommend one over the other[76].

Recommendations: SCT recipients should be immunized with 3 doses of tetanus, diphtheria, pertussis-containing vaccines at 6 months post SCT. Patients with hematologic malignancy should receive a dose of Tdap if not previously given in adulthood.

Hepatitis B

Hepatitis B vaccine is administered starting as early as 6 months following SCT. If administered earlier than 1-year following SCT, vaccine anti-HBs titers should be checked, and if negative, the patient should be re-immunized with a second 3-dose series. Higher antigen dose Hepatitis B vaccine[6] is available, and although it is primarily for use in patients on hemodialysis, it can also be used for booster dosing in this setting. Although not discussed in the 2013 guidelines, Hepatitis B vaccine is also available as a co-formulated

vaccine with Hepatitis A (*Twinrix*-GlaxoSmithKline). Twinrix has been given as a 3-dose series following SCT. This option offers the ability to achieve concurrent Hepatitis A seroprotection.

Measles, mumps and rubella vaccine (MMR)

MMR vaccination is only available as a trivalent formulation in the US. It is a LAV and thus is contraindicated in high-risk patients. Vaccine titers to measles, mumps and rubella decline in the years following SCT.[7778] After SCT, the vaccine is given as a 2-dose series (often to measles-seronegative SCT recipients, although there is transplant center variability and some centers may administer to any recipient eligible for live virus vaccination)[6]. The vaccine can be considered after 24 months following SCT (among those without GVHD, as well as 8–11 months after last receipt of IVIG products). Epidemic measles and mumps cases have re-emerged worldwide[79], and vaccine should be administered irrespective of last IVIG use in an outbreak situation.

Other vaccines

Haemophilus influenza B conjugate (Hib) and **Inactivated polio** vaccines should be given to all SCT recipients, starting as early as 6 months.**Human papillomavirus vaccine (HPV)** vaccine should be offered to all immunocompromised adults through 26 years of age if they have not previously received the series. The US FDA recently approved the vaccine for expanded use in adults age 27 to 45 years. **Conjugate meningococcal vaccines** should be given to SCT recipients according to age or at-risk condition. Two doses of MCV4 (serotypes A, C, W-135 and Y) should be administered 6–12 months after SCT to persons aged 11–18 years, with a booster at 16–18 years. Meningococcal B vaccines should additionally be administered to SCT recipients aged 10–25 years with at risk conditions[80]. ACIP recommends either a 3-dose series of MenB-FHbp (Trumenba, Pfizer) or a 2-dose series of MenB-4C (Bexsero, GSK)[80].

OTHER VACCINATION CONSIDERATIONS

Donor vaccination

Pre-transplant donor immunization may enhance early expansion of humoral immunity in the recipient for some but not all vaccines[38,81]. This approach raises unique ethical and practical challenges and is not endorsed by existing guidelines.

Prior to international travel

International travel is common among cancer patients and SCT recipients[82,83]. Routine vaccinations should be up to date prior to travel. Some additional vaccines (Table 3) are specifically considered based on specific epidemiologic and destination(s) based risk[8485].

Vaccination of household contacts (including children) and healthcare workers

All household members of patients with hematologic malignancy or following SCT should receive age-appropriate vaccinations as recommended by the ACIP, including all inactivated vaccines as well as most live-attenuated vaccines (Table 4).

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KEY POINTS

- Patients with hematologic malignancy are at increased risk of morbidity and mortality from certain vaccine preventable illnesses, such as influenza, pneumococcal disease and zoster.
- SCT recipients lose their preexisting immunity over time following SCT and require primary re-immunization strategies once T- and B-cell immunity have sufficiently recovered.
- Newer vaccines appear to be more immunogenic and show promise in terms of clinical efficacy in these vulnerable patient populations.
- Special vaccination considerations are required for household contacts of immunocompromised individuals as well as immunocompromised travelers.

SYNOPSIS

Patients with hematologic malignancy or those who undergo hematopoietic stem cell transplantation (SCT) experience variable degrees of immunosuppression, dependent on underlying disease, therapy received, time since transplant, and complications such as graft versus host disease. Vaccination is an important strategy to mitigate onset and severity of certain vaccine preventable illnesses, such as influenza, pneumococcal disease or varicella zoster infection, among others. This article highlights vaccines that should and should not be used in this patient population and includes general guidelines for timing of vaccination administration as well as special considerations in the context of newer therapies, recent vaccine developments, travel, and considerations for household contacts.

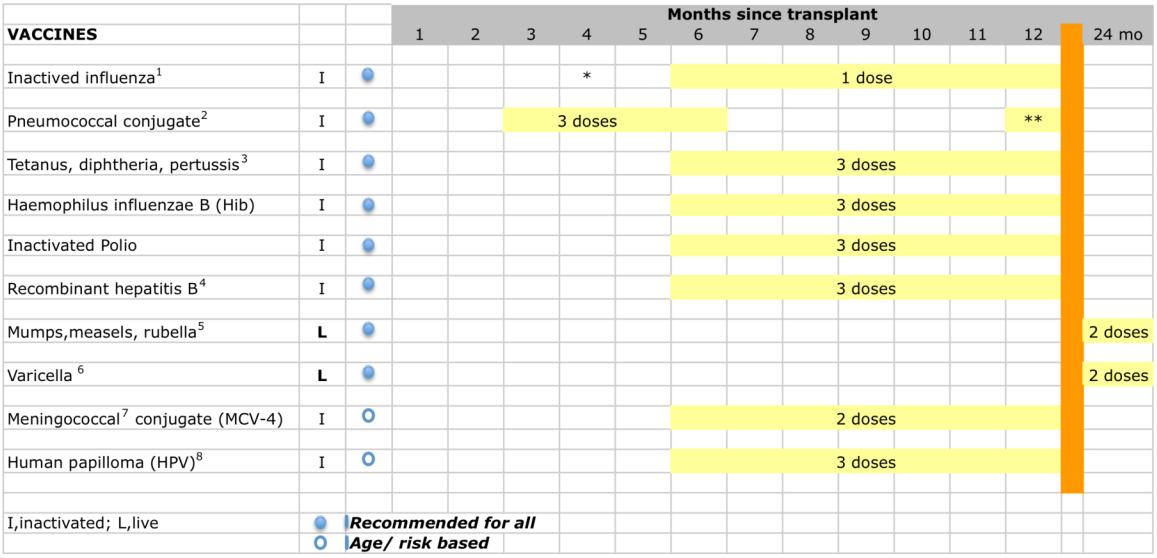

Figure 1.

Immunization schedule for SCT recipients

[1] Inactivated influenza vaccines: For children < 9 years of age, two doses of IIV one month apart. In elderly patients (≥ 65 years of age) consider the following if readily available: High dose (HD-IIV3; Fluzone) or Adjuvanted (aIIV3; Fluad). *May administer vaccine at 4months if widespread influenza in community.

[2]Pneumococcal conjugate vaccine: ** Give fourth dose of PCV-13 if GVHD requiring immunosuppression. For all others, PPSV-23 booster (23 valent polysaccharide vaccine) is given at one year.

[3]Tetanus, diphtheria, acellular pertussis vaccination: Various combinations and doses of vaccines exist, including DTaP, DT, Tdap, Td. Capital letters indicate higher toxoid or antigen amounts. GiveDTaP × 3 doses to all children ≤ 7 years; and can consider for all patients irrespective of age, though DTaP is only license in children < 7 years of age. Alternatively, can give 3 doses of Tdap, or one dose of Tdap followed by 2 doses of Td. Among Tdap vaccines, *Boostrix* contains higher pertussis antigen than *Adacel*. *Boostrix* is preferred in adult's ≥ 65 years.

[4]Recombinant Hepatitis B: check serology after 3 doses, if negative anti-Hbs titer, re-vaccinate with 3 dose series; alternative, one dose booster of either high antigen dose vaccine or standard dose and re-check anti-Hbs titer; if vaccinating with combined Hepatitis A and B vaccine product, must still check anti-Hbs titer, and re-vaccinate with Hepatitis B vaccine if negative.

[5]Measles, mumps, rubella: If measles antibody negative, vaccinate with 2 doses at least one month apart.

[6]Recommended for use in VZV seronegative patients. See text for data on recombinant zoster vaccine (Shingrix) in auto transplant recipients.

[7]MCV-4: Recommended for persons aged 11–18 years, with a booster at 16–18 years. Meningococcal B vaccines should additionally be administered to SCT recipients aged 10–25 years with at risk conditions (asplenia, terminal complement deficiency, laboratory worker, travel, outbreak).

[8]HPV: Now available as 9-valent vaccine. Vaccinate in patients 9–26 years of age; FDA has recently expanded indicated age range to up to 45 years.

Table 1:

Key randomized studies of inactivated influenza vaccines (IIV) in allogeneic SCT recipients

Study	Study population and season	Outcomes assessed	Median time to vaccination	Findings
Halasa et al[31] Phase I randomized safety study. Standard dose (SD) vs High dose(HD); n=15 vs29	Adult allogeneic SCT recipients 2010–11 2011–12	Safety (Primary) Immunogenicity (Secondary)	8.5 mo. (HD) and 7.1 mo. (SD)	• Higher local site reactions with HD (67% Vs31%) • HD had significantly higher seroprotection for A/H3N2 compared with the SD group; 81% versus 36% • No significant difference in seroprotection or seroconversion for A/H1N1 or B viruses
Karras et al[34] Randomized open label. Two doses of TIV 4 weeks apart vs single dose (33 vs32)	Adult allogeneic SCT recipients 2010–2011	Immune response Viral specific T cell responses; Seroprotection; Seroconversion	0.9 (2 doses) and 0.7 (single)	• No significant difference in sero-protection or seroconversion for H3 orH1 N1 • Time from transplants yr. associated with better seroprotection • CD+19 correlated with antibody response
Natori et al[36] Randomized pilot trial. Adjuvanted [Ad]vs Standard dose TIV (35 vs 32)	Adult allogeneic SCT recipients 2015–16	Serological response	19 mo. (Ad) and 10 mo. (SD)	• No significant difference in immunogenicity • Seroconversion to at least 1 antigen 62.9 [Ad] vs 53.1 %[SD] (highest for A/H3N2) • Trend towards higher immunogenicity with adjuvanted among those > 6 mo. post SCT
Ambati et al[38]. Open randomized prospective study of pre SCT vaccination. No vaccine (n=38), Donor (n=44), Recipient (n=40)	2007–2010 Adult and pediatric allogeneic SCT recipients	Seroprotection rate at day 180 after transplant	Pre-transplant and day +180	• Antibody titers against H1 and H3 were highest in the pretransplant recipient vaccination group through day 180 after transplantation. • No beneficial effect of donor vaccination before transplant

SCT, stem cell transplant; SD, standard dose; HD, high dose; TIV, trivalent inactivated influenza vaccine

Table 2:

Summary findings on safety and efficacy of inactivated zoster vaccines in autologous SCT recipients

Study	Study population	Outcomes assessed	Dosing schedule (days in relation to SCT)	Findings
de la Serna et al.[73] Recombinant subunit (RZV) Phase 3 observer-blind, placebo controlled, randomized 1:1 Modified cohort: RZV n=870 placebo n=851 median follow up=21 months	Adult autologous SCT recipients	Clinical Efficacy (Primary) Safety (Primary)	2 doses 1: +50 to +70 2: +80 to +130 (or 30 to 60 days after dose 1)	Incident disease (per person, vaccine vs placebo) • HZ: 49 vs 135 (68.2% efficacy) • PHN: 1 vs 9 (89.3% efficacy)
Winston et al.[74] Heat inactivated VZV vaccine (investigational) Phase 3 double-blind, placebo-controlled, randomized 5:1:5 Vaccine lot n=560 Hi antigen lot n=164 Placebo n=564 Mean follow up=2.4 years	Adult autologous SCT recipients 2010–2013 135 centers	Clinical Efficacy (Primary) Safety (Primary-hi lot group) Immunogenicity (Secondary)	4 doses 1: −5 to −60 2:+30 3:+60 4:+90	Incident disease (per 1000 person-years, vaccine lot vs placebo): • HZ: 32.9/vs 91.9 (63.9% efficacy) • PHN: 2.3 vs 14.6 (83.7% efficacy) VZV-specific responses higher in vaccine group; T cell responses sustained at 3 years; B cell responses plateau after 1 year

HZ, herpes zoster; PHN, post herpetic neuralgia

Table 3:

Vaccination in Immunocompromised Travelers

Safe to give[b]	Unsafe-contraindicated
Hepatitis A[c]	Yellow Fever (YFV)[e,f]
Intramuscular Typhoid[d]	Oral Typhoid
Inactivated Polio (IPV)[e]	Oral Polio (OPV)[g]
Hepatitis B	Oral Cholera
Meningitis (MCV-4)[e]	
Rabies[d]	
Japanese encephalitis[d]	

[a] Country and indication specific vaccine recommendations available through the CDC.[84]

[b] Vaccines are injections unless otherwise indicated.

[c] Can also consider Hepatitis A specific immunoglobulin for short-term pre-exposure prophylaxis if unlikely to mount immune response to vaccination

[d] Immunogenicity not known in immunocompromised recipients.

[e] Proof of vaccine receipt may be required for entry to certain destinations. If YFV cannot safely be given, a waiver letter can be granted from certified YFV providers. Risks of disease at destination vs. benefits of travel should be discussed.

[f] Many clinicians remain reluctant to vaccinate with YFV post HSCT regardless of immune status and time elapsed. One recent study demonstrated immunogenicity and safety in a cohort of 21 allogeneic HSCT recipients who were immunized with YFV, a median of 33 months post HSCT.[85]

[g] Not available in US; give IPV

Table 4:

Safety of live vaccines in household contacts of patients with high-risk immunocompromising conditions[86]

Vaccine	Transmission in high risk household contacts	Recommendation	Special precautions / Comments
MMR	--	Safe	
Varicella	Mild/subclinical disease	Safe	If skin lesions develop, **1** Cover with dressing until scabbed **2** Avoid direct contact
LAIV	--	Do not administer	For patients requiring protective isolation, contacts should receive inactivated vaccine
Rotavirus	Persistent shedding	Safe	Avoid handling diapers for 4 weeks
Oral Polio (outside US)		Do not administer	Use inactivated polio vaccine
Oral Typhoid		Safe	
Yellow fever		Safe	

MMR; measles, mumps and rubella

LAIV; live attenuated influenza vaccine