



**Title: Vaccinations For Paediatric Patients Treated With Standard-Dose Chemotherapy And Haemopoietic Stem Cell Transplantation (HSCT) Recipients**

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## 1. INTRODUCTION: VACCINATIONS FOR PAEDIATRIC PATIENTS TREATED WITH STANDARD-DOSE CHEMOTHERAPY AND HAEMOPOIETIC STEM CELL TRANSPLANTION (HSCT) RECIPIENTS

Immunosuppression of varying degree is present in children with cancer, this can range from mild to severe. Cancer itself, particularly leukaemia and lymphoma, can cause suppression of cellular and humoral immune function. However, cytotoxic antineoplastic therapy is the main contributor.

Antineoplastic treatment usually involves chemotherapy, radiotherapy, or a combination of both. The majority of children with cancer are treated with standard-dose chemotherapy, but children with high-risk haematologic malignancies, children with certain solid tumours, and children with disease relapse often require high dose chemotherapy (+/- radiotherapy) followed by haematopoietic stem cell transplant (HSCT). Some treatment regimens include radiotherapy; if the radiotherapy field includes the spleen (with a dose >10 Gy) then functional hyposplenism or asplenia is likely. These different forms of treatment have different influences on the immune system and the degree of immunodeficiency. Immune alteration is reflected by decreases in neutrophils, lymphocytes, immunoglobulin levels, and specific antibodies against previous infections and vaccinations. This results in increased susceptibility to and severity of infections. Most vaccine-preventable diseases (VPD) are now fortunately rare; however, the risk for some remains significant, in part because of increases in migration and travel, and poor vaccine uptake. VPD can be associated with high morbidity and mortality, particularly in immunocompromised patients. In view of the immune deficiency of children treated for cancer, particularly HSCT recipients, it is important to ensure that they are protected against VPD both during and after completion of treatment. This can be achieved by optimising the vaccination strategy in children during immunosuppressive therapy, and after completion of treatment at a time point that balances immune recovery to avoid vaccine side effects (especially for live vaccines) and enable optimal immune responses. In view of the diversity of malignant diseases and their treatment protocols, it is difficult to propose different schedules for each disease. Rather, it is sensible to divide them into children treated with standard-dose chemotherapy and children treated with high-dose chemotherapy followed by allogeneic or autologous HSCT. There are limited published data and little published guidance for children treated with other modalities such as chimeric antigen receptor T-cell therapy (CAR-T) or those receiving B-cell-depleting therapies (e.g. rituximab). The approach to vaccination (or re-vaccination) in a CAR-T recipient should be individualised in consultation with their treatment centre, based on the timing since completion of treatment, and if (and when) the child has previously undergone HSCT which influences whether either a standard chemotherapy booster vaccination or a re-vaccination schedule is recommended. In addition, many CAR-T recipients have ongoing B-cell aplasia with hypogammaglobulinaemia. Such patients will be receiving intravenous immunoglobulin (IVIg). After B-cell depleting therapy, if immunoglobulin concentrations and B cell numbers have recovered it appears reasonable to follow a standard chemotherapy booster approach.

## 2. VACCINATIONS FOR PAEDIATRIC PATIENTS TREATED WITH STANDARD-DOSE CHEMOTHERAPY

### 2.1 Background

Different cancers require treatment with different combinations of chemotherapy agents. Therapy for a single disease is risk-stratified based on patient factors, extent of disease and tumour biology, so there may be variation in intensity of therapy for a single disease type. Therapy regimens that include agents such as cyclophosphamide, purine nucleoside analogues or corticosteroids are immunosuppressive; they particularly have an effect on lymphocyte function. Some treatment regimens include radiation therapy; there are few data on the influence of radiotherapy on immunosuppression. If radiation therapy involves the spleen, functional hyposplenism or asplenia can result which increases susceptibility to infection with polysaccharide encapsulated bacteria.

Depending on the treatment regimen, B- and T-lymphocyte levels decrease during treatment; with an increase in number occurring one month after completion of chemotherapy. Total B- and T-lymphocytes usually recover, quantitatively and functionally, 3- 6 months after completion of chemotherapy. Normalisation of immunoglobulin levels can take up to one year after completion of treatment.

There are published studies demonstrating a significant reduction in specific antibody concentrations at completion of chemotherapy to Hib, Meningococcus C (Men C), tetanus, polio, measles and pneumococcal vaccines. However, there are no/limited published data for this group of patients on immune responses to newer vaccine antigens such as Human Papilloma Virus vaccine (HPV), Meningococcal serogroups A, B, W and Y (Men ACWY), and SARS-CoV2. Until further data are available on immunity to vaccine antigens in specific disease types and treatment regimens, it is wise to follow the same vaccination recommendations for all patients treated with standard-dose chemotherapy. Clinical experience suggests that there is an increased risk for meningococcal infection in children who have been treated for cancer and therefore we have recommended booster vaccine doses for Meningococcus B (Men B) and Men C, and expedite vaccination for Men ACWY rather than waiting until age 14 years per the national schedule.

There is a reduction in vaccine-antigen specific antibody concentrations after completion of chemotherapy. It is therefore wise to follow the same vaccination recommendations for all patients treated with standard-dose chemotherapy.

## **2.2 Vaccinations for patients receiving standard-dose chemotherapy**

Children are immunosuppressed during chemotherapy and are susceptible to invasive infections. This is also a time in which they are less likely to achieve an optimal immune response to vaccination and furthermore, a period in which live vaccines, such as measles-mumps-rubella (MMR), Varicella zoster virus (VZV), Rotavirus vaccine, Bacillus Calmette-Guerin (BCG), and live attenuated influenza vaccine (LAIV) pose the risk of causing vaccine-related infections. Non-live vaccines can be administered during chemotherapy. Studies that have evaluated antibody response to vaccines during chemotherapy have mostly done so during the maintenance phase of ALL therapy. Antibody responses during chemotherapy are usually impaired. Even so, non-live vaccines should be given according to the national childhood vaccination schedule, provided the child's general health is stable and avoiding periods of more intensive chemotherapy and steroid pulses. This is particularly important for primary vaccinations to ensure at least some immunity in an otherwise nonimmune child. The seasonal inactivated influenza vaccine (SIIV) is recommended annually provided the patient is well and has a neutrophil count above  $0.5 \times 10^9/L$ . The latter is to avoid children with vaccine-associated fever being unnecessarily treated with antibiotics. Ideally, it would not be given within two weeks of more intensive chemotherapy or steroid pulses as the immune response may be sub-optimal.

## **2.3 Vaccination schedule for patients after completion of standard-dose Chemotherapy**

In view of the reduction in vaccine-antigen specific antibody levels as a result of chemotherapy, booster vaccinations should be given after completion of chemotherapy. In terms of timing, the aim is to balance safety and efficacy. Vaccination after completion of chemotherapy results in good immune responses, with most recipients achieving protective antibody levels following a single dose of vaccine. Generally, 3 to 6 months after completion of treatment should be safe and elicit good antibody responses. A booster dose of each routine childhood vaccine is recommended from three months after completion of chemotherapy: heptavalent vaccine (Hib-conjugate [Hib], diphtheria/tetanus/acellular pertussis [DTaP], inactivated poliovirus [IPV] and Hepatitis B), meningococcal B-conjugate, meningococcal ACWY-conjugate, 13-valent pneumococcal-conjugate vaccine (PCV13), HPV, and MMR (if only one dose was given prior to diagnosis and treatment then two booster doses should be given). Surveillance suggests that there is an increased risk for meningococcal infection in children who have been treated for cancer and therefore we recommend booster vaccine doses for Men B, as well as vaccination against Men ACWY. SIIV should be offered for the first six months after completion of treatment. The BCG vaccine should only be considered for children considered to be at high risk of tuberculosis.

In summary, vaccination during treatment should be avoided during the period that the patient is receiving intensive chemotherapy and/ or steroids (as the immune response will be suboptimal) or when the patient is neutropenic (neutrophil count  $<0.5 \times 10^9/L$ ), but otherwise all routine non-live vaccines should be considered according to the childhood vaccination programme. SIIV and SARS-COV-2 vaccines should also be offered during treatment and within six months of completion of treatment (then as per

national guidance). A booster dose of all routine childhood vaccinations should be offered from three months after completion of treatment (Table 1). MMR is a live vaccine, there are not much data on theoretical risk of infection transmission, clinician can decide on individual patient basis regarding the timing (from 3 months with the other vaccinations, or wait until 6 months after completion of treatment). Subsequent routine booster vaccine doses will not be necessary if scheduled to be given within one year. If patient has not received full vaccination schedule prior to diagnosis and treatment, then complete the vaccination schedule.

**Table 1: Vaccination schedule after completion of standard-dose chemotherapy**

Time after EOT	Age under 10 years  Vaccine	Age 10 years and over  Vaccine
<b>From 3 Months</b>	SIIV in first 6 months DTaP/IPV/Hib/HepB Men ACWY-conjugate PCV13 Men B MMR <sup>1</sup> SARS-CoV-2 vaccine (as per national Guidance)	SIIV in first 6 months dTaP / IPV Hib/ Men C Men ACWY-conjugate PCV13 Men B MMR <sup>1</sup> HPV <sup>2</sup> SARS-CoV-2 vaccine (as per national guidance)

[Vaccines: dT = Low dose Diphtheria/ Tetanus/ acellular Pertussis, DTaP = Diphtheria/ Tetanus/ acellular Pertussis, Hib = *H.influenzae* b conjugate, HepB =Hepatitis B, HPV = Human papillomavirus, IPV = Inactivated polio virus, Men B = Meningococcal B conjugate, Men ACWY = Meninococcal ACWY conjugate, MMR = Measles/Mumps/Rubella, PCV13 = 13 valent Pneumococcal conjugate, SIIV = Seasonal inactivated influenza vaccine]

<sup>1</sup> If patient did not receive MMR prior to starting chemotherapy give 2 doses MMR, if patient only received 1 dose of MMR prior to starting chemotherapy then should receive 2 doses of MMR after completion of chemotherapy. The 2<sup>nd</sup> dose should be given 6 months after the 1<sup>st</sup> dose. The 2<sup>nd</sup> dose can be given 3 months after the 1<sup>st</sup> dose or can be considered even earlier (1 month after 1<sup>st</sup> dose) in measles outbreak.

<sup>2</sup> HPV vaccine should be offered to girls and boys ≥12 years old: 2 doses of HPV vaccine should be given at 0 and 6 months from starting vaccination. For girls and boys that did complete the course, a booster dose should be given.

## **2.4 Vaccination of close contacts of patients receiving standard-dose chemotherapy (or within 3-6 months of completion)**

The following live vaccines can be administered to siblings/ close family contacts of patients on chemotherapy or within 3-6 months following completion of chemotherapy.

- MMR Vaccine should be given to contacts as per the national vaccination schedule.
- Varicella zoster virus (VZV) vaccine should be offered to healthy susceptible siblings (and adult family members who are VZV seronegative) of VZV seronegative patients. There is theoretical risk of transmitting the attenuated vaccine virus to a susceptible individual; as a precautionary measure, any person who develops a vesicular rash after receiving VZV vaccine should avoid direct contact with the patient until the rash is dry and crusted.
- Herpes zoster (Shingles) vaccine: Is offered to adults over 60 years old, so the patient's parents or grandparents may be offered this vaccine. There are two types of vaccine, if the live vaccine is given then rarely the transmission of vaccine virus may occur between those vaccinated (who develop a varicella-like rash) and susceptible contacts. As a precautionary measure, any person who develops a vesicular rash after receiving the vaccine should avoid direct contact with the patient until the rash is dry and crusted.
- Rotavirus vaccine: Is given to infants aged 6-24 weeks; it should not be given to the patient but can be given to siblings. There is potential for transmission from the infant to immunocompromised contacts through the faecal-oral route for at least 14 days post-vaccination. However, vaccination of the infant will offer protection to household contacts from wild-type rotavirus disease and outweigh any risk from transmission of vaccine virus to any immunocompromised close contacts. Good personal hygiene should be observed following administration.
- Live attenuated influenza vaccine (LAIV): Consideration should also be given to giving LAIV to household contacts that are eligible for LAIV; other household contacts should be given SIIV. Siblings that are due should be given LAIV; there is a theoretical potential for transmission of live attenuated influenza virus from LAIV to immunocompromised contacts for one to two weeks following vaccination so assess each individual case.

### 3. VACCINATIONS FOR CHILDREN TREATED WITH HIGH DOSE CHEMOTHERAPY AND HAEMOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

#### 3.1 Background

HSCT recipients are profoundly immunocompromised for months, even years, after transplant. This places them at increased risk of morbidity and mortality from infection. The components of the new immune system develop and mature at different rates; immune reconstitution after autologous HSCT occurs faster than after allogeneic HSCT. Innate immune function recovers earlier than adaptive immune function, within weeks to months after transplant. Prolonged immune deficiency arises from a deficiency of the more specialised functions of the adaptive immune system, in particular, the reconstitution of CD4 lymphocytes. B-lymphocytes reach age-matched levels 3 to 6 months after transplant. Immunoglobulin isotypes start normalising 6 months after transplant in accordance with the sequence seen in normal immune ontogeny. Whilst total IgG levels may be normal, IgG subclass imbalance can occur with low IgG2 levels for 18 months or more after transplant. Antibody responses to previously encountered antigens can be elicited from 3 to 6 months after transplant. T-lymphocyte reconstitution occurs in two stages: first the thymus-independent pathway, followed by the thymus-dependent pathway. During the first 6 months after transplant, T-lymphocytes are predominantly repopulated through peripheral expansion of mature T-lymphocytes, with recovery starting 1 to 2 months after transplant and peaking at 3 to 6 months. This pathway is responsible for the rapid reconstitution of memory T-lymphocytes which are of limited repertoire diversity. At 6 to 12 months after transplant the generation of naïve T-lymphocytes is evident. Knowledge of the sequence of immune reconstitution guides the timing of re-vaccination after HSCT. Allogeneic HSCT recipients are at particularly increased risk of infection with polysaccharide encapsulated bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and *Neisseria meningitidis*. This increased susceptibility is related to a number of host factors: functional hyposplenism, low serum IgG2 levels, and impaired opsonisation by specific antibodies.

#### 3.2 Vaccination schedule for haematopoietic stem cell transplant recipients

Following HSCT there is loss of natural and vaccine immunity that was acquired pretransplant. Therefore, HSCT recipients should be considered 'never vaccinated' and should be offered re-vaccination with the full national childhood vaccination schedule. A number of factors influence antibody levels to previous vaccinations and immunogenicity of vaccines post-HSCT: autologous or allogeneic HSCT, time after HSCT, presence of chronic-GvHD, recipient age, the number of vaccine doses, and donor vaccination status. Studies of antibody response to vaccination post-HSCT show that the time elapsed after transplantation and the number of vaccine doses are particularly important. Although the loss of vaccine immunity is likely to be less profound for autologous than allogeneic HSCT recipients, it is difficult to predict this in individual patients, and therefore it is wise to revaccinate both groups with the same schedule.

International and national revaccination guidelines for HSCT recipients are based on a combination of expert opinion and published data and recommend that autologous and allogeneic HSCT recipients should

receive all primary routine childhood vaccines, together with annual SIIV vaccine. In view of the difficulty in predicting the extent of immune suppression and immune recovery, a pragmatic approach is to recommend re-vaccination of all recipients of allogeneic and autologous HSCT.

In summary, the aim in HSCT recipients is to commence re-vaccination as soon as it is safe and a protective immune response can be reliably achieved. The routine use of markers of immune reconstitution to guide timing of vaccination is not recommended. Re-vaccination from 6 months post-HSCT is recommended provided there are no contraindications or reasons to defer vaccination (i.e. no evidence of active chronic GvHD, off all immunosuppressive treatment, ideally for at least 6 months, but (killed) vaccines may be given earlier depending on the individual's circumstances and risk of infection. For live vaccines deferral should be for at least 12 months, off intravenous immunoglobulin [IVIg] for at least 3 months). Given the risk of vaccine induced disease, live vaccines should be avoided until 24 months post-HSCT. *BCG vaccine* is not recommended for HSCT recipients.

Vaccines recommended and their timing post-HSCT detailed in Table 2.

### **3.3 General Principles**

Re-Vaccination should commence:

- From 6 months after any HSCT (transplant team can review this on case by case basis)
- Live vaccines should be avoided until 24 months post-HSCT

*Providing that:*

- No evidence of active chronic GvHD
- Off all immunosuppressive treatment, ideally for at least 6 months, but (killed) vaccines may be given earlier depending on the individual's circumstances and risk of infection. For live vaccines deferral should be for at least 12 months
- Off IVIg for at least 3 months

### **3.4 Vaccinations for Household Contacts of Children Treated with HSCT**

To protect immunocompromised patients from VPD, immunocompetent family members and household contacts should be encouraged to receive all age-appropriate vaccinations as per the national vaccination schedule, with the following caveats:

- SIIV annually. LAIV should not be administered to household contacts of HSCT recipients within two months of transplant or if the HSCT-recipient has active GvHD
- Avoid Rotavirus vaccine in household contacts within two months of transplant or if the HSCT recipient has active GvHD
- VZV vaccine should be offered to healthy susceptible siblings (and adult family members who are VZV seronegative) of VZV seronegative HSCT-recipients.

- Herpes zoster (Shingles) vaccine: Is offered to adults over 60 years old. There are two types of vaccine, if the live vaccine is given then rarely the transmission of vaccine virus may occur between those vaccinated (who develop a varicella-like rash) and susceptible contacts. As a precautionary measure, any person who develops a vesicular rash after receiving the vaccine should avoid direct contact with the patient until the rash is dry and crusted.

**Table 2: Vaccination Schedule for HSCT Recipients**

	Pathogens Protected Against	Vaccine	Trade Name (Equivalent alternative may be used)
Annually from 6 months (consider from 3 months if within a peak transmission period)	Seasonal Influenza SARS-COV-2	SIIV SARS-COV-2 vaccine (as per national recommendations)	Various Various
6 months	Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae b</i> , Hepatitis B  Meningococcal B  <i>Streptococcus pneumoniae</i>  Human Papillomavirus <sup>1</sup>	DTaP/IPV/Hib/HepB (dose 1)  MenB (dose 1)  PCV13 (dose 1)  Quadrivalent HPV (dose 1)	Infanrix hexa or Vaxelis  Bexsero  Prevenar 13  Gardasil
7 months	Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae b</i> , Hepatitis B  <i>Streptococcus pneumoniae</i>  Human Papillomavirus	DTaP/IPV/Hib/HepB (dose 2)  PCV13 (dose 2)  Quadrivalent HPV (dose 2)	Infanrix hexa or Vaxelis  Prevenar 13  Gardasil
8 months	Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae b</i> , Hepatitis B  Meningococcal B  Meningococcal ACWY <sup>2</sup>  <i>Streptococcus pneumoniae</i>	DTaP/IPV/Hib/HepB (dose 3)  MenB (dose 2)  Men ACWY (dose 1)  PCV13 (dose 3)	Infanrix hexa or Vaxelis  Bexsero  Nimenrix or Menveo  Prevenar 13
12 months	Human Papillomavirus	Quadrivalent HPV (dose 3)	Gardasil
18 months	Meningococcal ACWY <sup>2</sup>  Meningococcal B  <i>Streptococcus pneumoniae</i>  <i>Haemophilus influenzae b</i>	Men ACWY (dose 2)  MenB (Booster)  PPSV23 PCV13 (If GvHD)  A Hib containing vaccine	Nimenrix or Menveo  Bexsero  Pneumovax Prevenar 13  -
24 months	Measles, Mumps, Rubella <sup>3,4</sup>	MMR (dose 1) <i>live vaccine</i>	MMR VaxPro or Priorix
30 months	Measles, Mumps, Rubella	MMR (dose 2) <i>live vaccine</i>	MMR VaxPro or Priorix
3 years	Diphtheria, tetanus, pertussis and polio	DTaP/IPV	Repevax or Boostrix IPV
14 years	Diphtheria tetanus, polio	Td/IPV	Revaxis

[Vaccines: DTaP = Diphtheria/ Tetanus/ acellular Pertussis, dT = Low dose Diphtheria/ Tetanus, Hib = *H.influenzae b* conjugate, HepB =Hepatitis B, HPV = Human papillomavirus, IPV = Inactivated polio virus vaccine, Men B = Meningococcal B conjugate, Men C = Meningococcal C conjugate, Men ACWY = Meninococcal ACWY conjugate, MMR = Measles/Mumps/Rubella, PCV13 = 13 valent Pneumococcal conjugate, PnPS 23 = 23 valent pneumococcal polysaccharide, SIIV = Seasonal inactivated influenza vaccine]

<sup>1</sup>HPV vaccine, For paediatric patients >12 years, 3 dose schedule is recommended for immunocompromised patients with 2 doses at a monthly interval and then a third dose 4-6 after the first dose. <sup>2</sup> HSCT Patients at risk from meningococcal disease therefore first dose of quadrivalent conjugate vaccine recommended at 8 months post HSCT. <sup>3</sup> Criteria for administration of live vaccines. i) 24 months post HSCT ii) No active GvHD iii) No Immune suppressive therapy for 12 months iv) No IVig in last 3 months. <sup>4</sup> If criteria for live vaccines met can consider vaccinating from 18 months post HSCT if community outbreak of Measles 24 months post-HSCT, Consider two doses of Live attenuated Varicella vaccine (Varivax or Varilrix) administered 2 months apart if all criteria for administration of live vaccines are met and VZV seronegative. BCG vaccine is not recommended for HSCT recipients.

**Appendices below are for circulation to GPs - to notify vaccination schedule for each patient.**

## References:

- Avanzini MA, Carra AM, Maccario R, et al (1995). Antibody response to pneumococcal vaccine in children receiving bone marrow transplantation. *J Clin Immunol*; 15: 137-144.
- Chiarucci M, Paolasini S, Isidori A, Guiducci B, Loscocco F, Capalbo M *et al*. Immunological Response Against SARS-COV-2 After BNT162b2 Vaccine Administration Is Impaired in Allogeneic but Not in Autologous Stem Cell Transplant Recipients. *Frontiers Oncol* 2021; 11: 737300.
- Cordonnier C, Ljungman P, Juergens C, *et al*. Immunogenicity, Safety, and Tolerability of 13-Valent Pneumococcal Conjugate Vaccine Followed by 23-Valent Pneumococcal Polysaccharide Vaccine in Recipients of Allogeneic Hematopoietic Stem Cell Transplant Aged 2 Years: An Open-Label Study. *Clin Infect Dis* 2015; 61: 313-323.
- Engelhard D, Cordonnier C, Shaw PJ, et al. Infectious disease working party of the European bone marrow transplantation (2002); Early and late invasive pneumococcal infection following stem cell transplantation: a European Bone Marrow Transplant survey. *Br J Haematol*. 2002; 117: 444-450.
- Feldman S, Lott L (1987). Varicella in children: impact of antiviral therapy and prophylaxis. *Pediatrics*; 80: 465-72.
- Guinan EC, Molrine DC, Antin JH, et al (1994). Polysaccharide conjugate vaccine responses in bone marrow transplant patients. *Transplantation*; 57: 677-684.
- Hoyle C, Goldman (1994). Life-threatening infections occurring more than 3 months after BMT. 18 UK Bone Marrow Transplant Teams. *Bone Marrow Transplant*; 14: 247-252.
- Kaplan LJ, Daum RS, Smaron M, McCarthy CA (1992). Severe measles in immunocompromised patients. *JAMA*; 267: 1237-1241.
- Li Volti S, Mauro L, Di Gregorio F, et al (1994). Immune status and immune response to diphtheria-tetanus and polio vaccines in allogeneic bone marrow transplanted thalassemic patients. *Bone Marrow Transplant*; 14: 225-227.
- Ljungman P, Cordonnier C, Einsele H, *et al*. Vaccination of hematopoietic cell transplant recipients. *Bone Marrow Transpl* 2009; 44: 521-526.
- Ljungman P, Duraj V, Magnus L (1991). Response to immunisation against polio after allogeneic marrow transplantation. *Bone Marrow Transplant*; 7(2): 89-93.
- Ljungman P, Wiklund-Hammarsten M, Duraj V, et al (1990). Response to tetanus toxoid immunisation after allogeneic bone marrow transplantation. *J Infect Dis*; 162: 496-500.
- Machado CM, Cardoso MR, da Rocha IF, et al (2005). The benefit of influenza vaccination after bone marrow transplantation. *Bone Marrow Transplant*; 36: 897-900.
- Miesel R, Kuypers L, Dirksen U, et al. Pneumococcal conjugate vaccine provides early protective antibody responses in children after related and unrelated allogeneic hematopoietic stem cell transplantation. *Blood* 2007; 109: 2322-2326.
- Miller PDE, Patel SR, Skinner R, et al. Joint Consensus Statement on the Vaccination of Adult and Paediatric Haematopoietic Stem Cell Transplant Recipients. Prepared on Behalf of the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT), the Children's Cancer and Leukaemia Group (CCLG), and British Infection Association (BIA). *Journal of Infection* 2023; 86: 1-8.
- Parkkali T, Stenvik M, Ruutu T, Hovi T, Volin L, Ruutu P (1997). Randomised comparison of early and late vaccination with inactivated poliovirus vaccine after allogeneic BMT. *Bone Marrow Transplant*; 20: 663-668.
- Patel SR, Ortin M, Cohen BJ, Borrow R, Irving D, Sheldon J, Heath PT. Re-immunization of children after completion of standard chemotherapy for acute leukemia. *Clin Infect Disease* 2007;44(5):635-642.
- Patel SR, Ortin M, Cohen BJ, Borrow R, Irving D, Sheldon J et al. Revaccination with measles, tetanus, poliovirus, Haemophilus influenzae type B, meningococcus C, and pneumococcus vaccines in children after hematopoietic stem cell transplantation. *Clin Infect Dis* 2007; 44: 625-634.
- Redjoul R, Bouter AL, Beckerich F, Fourati S, Maury S. Antibody response after second BNT162b2 dose in allogeneic HSCT recipients. *Lancet Lond Engl* 2021; 398: 298-299.
- RCPC: Immunisation of the immunocompromised child. February 2002.

Schutze GE, Mason EO, Wald ER, et al (2001). Pneumococcal infections in children after transplantation. *Clin Infect Dis*; 33: 16-21

Sheridan JF, Tutschka PJ, Sedmak DD, Copelan EA (1990). Immunoglobulin G subclass deficiency and pneumococcal infection after allogeneic bone marrow transplantation. *Blood*; 75: 1583-1586.

Winston DJ, Schiffman G, Wang D, et al (1979). Pneumococcal infections after human bone-marrow transplantation. *Annals of Internal Medicine*; 91: 835-841.

Witherspoon RP, Storb R, Ochs HD, et al (1981). Recovery of antibody production in human allogeneic marrow graft recipients: influence of time post transplantation, the presence or absence of chronic graft-versus-host disease, and antithymocyte globulin treatment. *Blood*; 58: 360-368.

## Appendix 1



### Vaccination schedule for patients after completion of Standard-dose Chemotherapy

**Patient name and DOB:**

**Date vaccinations will be due:**

Time after EOT	Age under 10 years Vaccine	Age 10 years and over Vaccine
<b>From 3 Months</b>	SIIV in first 6 months DTaP/IPV/Hib/HepB Men ACWY-conjugate PCV13 Men B MMR <sup>1</sup> SARS-COV-2 vaccine (as per national Guidance)	SIIV in first 6 months dTaP / IPV Hib/ Men C Men ACWY-conjugate PCV13 Men B MMR <sup>1</sup> HPV <sup>2</sup> SARS-COV-2 vaccine (as per national guidance)

[Vaccines: DTaP = Diphtheria/ Tetanus/ acellular Pertussis, Hib = *H.influenzae* b conjugate, HepB =Hepatitis B, HPV = Human papillomavirus, IPV = Inactivated polio virus vaccine, Men B = Meningococcal B conjugate, Men ACWY = Meninococcal ACWY conjugate, MMR = Measles/Mumps/Rubella, PCV13 = 13 valent Pneumococcal conjugate, PnPS 23 = 23 valent pneumococcal polysaccharide, SIIV = Seasonal inactivated influenza vaccine]

<sup>1</sup> If patient did not receive MMR prior to starting chemotherapy give 2 doses MMR, if patient only received 1 dose of MMR prior to starting chemotherapy then should receive 2 doses of MMR after completion of chemotherapy. The 2<sup>nd</sup> dose should be given 6 months after the 1<sup>st</sup> dose. The 2<sup>nd</sup> dose can be given 3 months after the 1<sup>st</sup> dose or can be considered even earlier (1 month after 1<sup>st</sup> dose) in measles outbreak.

<sup>2</sup> HPV vaccine should be offered to girls and boys ≥12 years old: 2 doses of HPV vaccine should be given at 0 and 6 months from starting vaccination. For girls and boys that did complete the course, a booster dose should be given.

## Appendix 2



### Vaccination schedule for Bone Marrow Transplant recipients

**Patient name and DOB:**

**Date vaccinations will be due:**

	Pathogens Protected Against	Vaccine	Trade Name (Equivalent alternative may be used)
Annually from 6 months (consider from 3 months if within a peak itransmission period)	Seasonal Influenza  SARS-COV-2	Seasonal inactivated Influenza vaccine SARS-COV-2 vaccine (as per national recommendations)	Various  Various
6 months	Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae b</i> , Hepatitis B  Meningococcal B  <i>Streptococcus pneumoniae</i>  Human Papillomavirus <sup>1</sup>	DTaP/IPV/Hib/HepB (dose 1)  MenB (dose 1)  PCV13 (dose 1)  Quadrivalent HPV (dose 1)	Infanrix hexa or Vaxelis  Bexsero  Prevenar 13  Gardasil
7 months	Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae b</i> , Hepatitis B  <i>Streptococcus pneumoniae</i>  Human Papillomavirus	DTaP/IPV/Hib/HepB (dose 2)  PCV13 (dose 2)  Quadrivalent HPV (dose 2)	Infanrix hexa or Vaxelis  Prevenar 13  Gardasil
8 months	Diphtheria, tetanus, pertussis, polio, <i>Haemophilus influenzae b</i> , Hepatitis B  Meningococcal B  Meningococcal ACWY <sup>2</sup>  <i>Streptococcus pneumoniae</i>	DTaP/IPV/Hib/HepB (dose 3)  MenB (dose 2)  Men ACWY (dose 1)  PCV13 (dose 3)	Infanrix hexa or Vaxelis  Bexsero  Nimenrix or Menveo  Prevenar 13
12 months	Human Papillomavirus	Quadrivalent HPV (dose 3)	Gardasil
18 months	Meningococcal ACWY <sup>2</sup>  Meningococcal B  <i>Streptococcus pneumoniae</i>  <i>Haemophilus influenzae b</i>	Men ACWY (dose 2)  MenB (Booster)  PPSV23 PCV13 (If GvHD or IST)  A Hib containing vaccine	Nimenrix or Menveo  Bexsero  Pneumovax Prevenar 13  -
24 months	Measles, Mumps, Rubella <sup>3,4</sup>	MMR (dose 1) <i>live vaccine</i>	MMR VaxPro or Priorix
30 months	Measles, Mumps, Rubella	MMR (dose 2) <i>live vaccine</i>	MMR VaxPro or Priorix
3 years	Diphtheria, tetanus, pertussis and polio	DTaP/IPV (Booster 1)	Repevax or Boostrix IPV
14 years	Diphtheria tetanus, polio	Td/IPV (Booster 2)	Revaxis

[Vaccines: DTaP = Diphtheria/ Tetanus/ acellular Pertussis, dT = Low dose Diphtheria/ Tetanus, Hib = *H. influenzae b* conjugate, HepB =Hepatitis B, HPV = Human papillomavirus, IPV = Inactivated polio virus vaccine, Men B = Meningococcal B conjugate, Men C = Meningococcal C conjugate, Men ACWY = Meninococcal ACWY conjugate, MMR = Measles/Mumps/Rubella, PCV13 = 13 valent Pneumococcal conjugate, PnPS 23 = 23 valent pneumococcal polysaccharide, SIV = Seasonal inactivated influenza vaccine]

<sup>1</sup>HPV vaccine, For paediatric patients >12 years, 3 dose schedule is recommended for immunocompromised patients with 2 doses at a monthly interval and then a third dose 4-6 after the first dose. <sup>2</sup> HSCT Patients at risk from meningococcal disease therefore first dose of quadrivalent conjugate vaccine recommended at 8 months post HSCT. <sup>3</sup> Criteria for administration of live vaccines. i) 24 months post HSCT ii) No GvHD iii) No Immune suppressive therapy for 12 months iv) In remission v) No IVIg in last 3 months. <sup>4</sup> Paediatric patients – If criteria for live vaccines met can consider vaccinating from 18 months post HSCT if community outbreak of Measles 24 months post-HSCT, Consider two doses of Live attenuated Varicella vaccine (Varivax or Varilrix) administered 2 months apart if all criteria for administration of live vaccines are met and VZV seronegative. BCG vaccine is not recommended for HSCT recipients.