CrossMark

ORIGINAL ARTICLE

Infectious diseases in allogeneic haematopoietic stem cell transplantation: prevention and prophylaxis strategy guidelines 2016

Andrew J. Ullmann[1] · Martin Schmidt-Hieber[2] · Hartmut Bertz[3] · Werner J. Heinz[1] ·
Michael Kiehl[4] · William Krüger[5] · Sabine Mousset[6] · Stefan Neuburger[7] ·
Silke Neumann[8] · Olaf Penack[9] · Gerda Silling[10] · Jörg Janne Vehreschild[11] ·
Hermann Einsele[1] · Georg Maschmeyer[12] · on behalf of the Infectious Diseases Working
Party of the German Society for Hematology and Medical Oncology (AGIHO/DGHO)
and the DAG-KBT (German Working Group for Blood and Marrow Transplantation)

Abstract Infectious complications after allogeneic haematopoietic stem cell transplantation (allo-HCT) remain a clinical challenge. This is a guideline provided by the AGIHO (Infectious Diseases Working Group) of the DGHO (German Society for Hematology and Medical Oncology). A core group of experts prepared a preliminary guideline, which was discussed, reviewed, and approved by the entire working group. The guideline provides clinical recommendations for the preventive management including prophylactic treatment of viral, bacterial, parasitic, and fungal diseases. The guideline focuses on antimicrobial agents but includes recommendations on the use of vaccinations. This is the updated version of the AGHIO guideline in the field of allogeneic haematopoietic stem cell transplantation utilizing methods according to evidence-based medicine criteria.

Keywords Infections · Viral · Fungal · Bacteria

Introduction

Infectious complications remain a clinical challenge in the setting of allogeneic haematopoietic stem cell transplantation (allo-HCT). Particular during the early phase after allo-HCT,

✉ Andrew J. Ullmann
   andrew.ullmann@uni-wuerzburg.de

1 Department of Internal Medicine II, Division of Hematology and Oncology, Division of Infectious Diseases, Universitätsklinikum, Julius Maximilian's University, Oberdürrbacher Str. 6, 97080 Würzburg, Germany

2 Clinic for Hematology, Oncology und Tumor Immunology, Helios Clinic Berlin-Buch, Berlin, Germany

3 Department of Hematology/Oncology, University of Freiburg Medical Center, 79106 Freiburg, Germany

4 Medical Clinic I, Klinikum Frankfurt (Oder), Frankfurt (Oder), Germany

5 Haematology and Oncology, Stem Cell Transplantation, Palliative Care, University Hospital Greifswald, Greifswald, Germany

6 Medizinische Klinik III, Palliativmedizin und interdisziplinäre Onkologie, St. Josefs-Hospital Wiesbaden, Wiesbaden, Germany

7 Sindelfingen-Böblingen Clinical Centre, Medical Department I, Division of Hematology and Oncology, Klinikverbund Südwest, Sindelfingen, Germany

8 Medical Oncology, AMO MVZ, Wolfsburg, Germany

9 Hematology, Oncology and Tumorimmunology, Charité University Medicine Berlin, Campus Virchow Klinikum, Berlin, Germany

10 Department of Internal Medicine IV, University Hospital RWTH Aachen, Aachen, Germany

11 Department I of Internal Medicine, German Centre for Infection Research, Partner-site: Bonn-Cologne, University Hospital of Cologne, Cologne, Germany

12 Department of Hematology, Oncology and Palliative Care, Klinikum Ernst von Bergmann, Potsdam, Germany

Springer

mortality rates for infections are high [1, 2]. After the first publication of recommendations from our group in 2003, [3] numerous new results of trials have been published and implemented into daily patient care. With this updated guideline, AGIHO (Infectious Diseases Working Group) of the DGHO (German Society for Hematology and Medical Oncology) pursues a step forward to include the entire patient history up right from the beginning of the preparation of patients through the entire post allo-HCT time period.

This guideline focuses on the adult patient population only and is partitioned into four parts: (a) general precautions and prevention measures, (b) pre-transplantation (screening) phase, (c) prophylactic treatment, and (d) immunization strategies.

Methods

Several steps were undertaken to develop the updated guideline: The first step was defining a group of specialists. They were enlisted by the AGIHO of the DGHO with a designated coordinator. The coordinator was responsible to manage the efforts of the group. The group of authors consisted of 14 certified internists, including 13 certified haematologists, and 5 certified infectious diseases specialists. Four authors are triple certified in internal medicine, infectious diseases, and haematology/oncology.

Predefined topics were elaborated by subgroups and then presented to the entire group for discussions. This included several face-to-face meetings, which were complemented by conference calls. Once the group had consensus with their results, the preliminary recommendations of the group were presented to the entire AGIHO assembly for review, discussions, modification, and final approval. All recommendations were made on the basis of available data providing evidence-based medicine. The guideline utilized the latest version of the strength of recommendation and quality of evidence published by the ESCMID (Table 1) [4]. Specific topics related to cord blood or haplo-identical transplant recipients are not addressed by this guideline.

General precautions

An allo-HCT requires certain assessment procedures, which are basically standardized (e.g. JACIE by the EBMT). Herein, we touch off on a few basic standardized requirements.

Patients' rooms should be equipped with air-filtered systems to keep spore counts low and, thus, preventing nosocomial fungal diseases (BII) [5–9]. Further, nearby construction activities should be kept to a minimum (AII).[10] Isolation of the stem cell recipients in a single hospital room under conditions of laminar airflow or positive pressure HEPA filtration (>12 exchanges per hour) is generally recommended.

However, randomized controlled trials focusing on HEPA filter efficacy against viral infections are lacking. Especially respiratory virus outbreaks, including seasonal pathogens such as respiratory syncytial virus (RSV) and influenza, are not prevented by HEPA filtrations [11]. Genotyping of RSV outbreaks demonstrated that more than two thirds were hospital acquired [12–15]. These results underscored the important necessity of infection control measures (i.e. barrier precautions) to prevent exposure directly at the patients' site (AII).

Some debate usually arises on the topic of appropriate dietary needs for patients after allo-HCT. The rule of thumb "cook it, peal it, or forget it" is easy to understand. However, there is a lack of appropriate literature on this specific topic. On the other hand, the evidence is clearer for the prevention of specific infections, e.g. listeria or other agents

Table 1 Strength of the AGIHO (DGHO) and DAG-KBT recommendation and quality of evidence (modified according to [4])

Strength of a recommendation	
Grade A	AGIHO strongly supports a recommendation for use
Grade B	AGIHO moderately supports a recommendation for use
Grade C	AGIHO marginally supports a recommendation for use
Grade D	AGIHO supports a recommendation against use
Quality of evidence	
Level I	Evidence from at least 1 properly designed randomized, controlled trial
Level II[a]	Evidence from at least 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 centre); from multiple time series; or from dramatic results of uncontrolled experiments
Level III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies

[a] Added index: r: meta-analysis (or systematic review of RCT); t: transferred evidence i.e., results from different patients 'cohorts' or similar immune status situation; h: comparator group: historical control; u: uncontrolled trials; a: published abstract (presented at an international symposium or meeting)

causing infectious diarrhea (BII) [16, 17]. Contact precautions and hand disinfection (incl. repeated teaching on this matter) can prevent nosocomial infection (AII) [18]. Healthcare workers (HCW) with transmissible diseases (e.g. herpes, infectious gastroenteritis, respiratory tract infections) should be restrained from direct patient care to prevent any nosocomial spread of their disease (AIII) [19]. Some hospital facilities have recovered microbes (e.g. *Legionella* spp.) from their drinking water. In order to prevent transmission in high-risk patients, water filters provide a protective solution though regular testing remains a necessity (AII) [20–22].

Pre-transplantation (screening) phase

A comprehensive pre-transplant assessment of the allo-HCT recipient for infectious complications is a valuable tool to identify patients at increased risk for distinct infectious diseases.

Syphilis, tuberculosis, *Toxoplasma gondii*, HIV, hepatitis B and C viruses, and *Herpes viridae* usually persist lifelong in the host after primary infection and can be reactivated under certain conditions. As a consequence, all candidates for allo-HCT should undergo a test for IgG antibodies specific for viral diseases, syphilis, and toxoplasmosis. False negative results particularly could occur in the context of CLL, multiple myeloma, previous antibody treatment (e.g. rituximab), or might be false positive after IVIG application or blood product transfusion. In any case, all patients tested IgG-seronegative strictly remain on preventive measures to avoid de novo infection prior to allo-HCT and afterwards.

Specific viruses

Herpes viridae

All candidates for allo-HCT should be tested for CMV, EBV, and VZV IgG antibodies to determine their risk for reactivation or de novo infection (AIII) [23–25]. Due to the high prevalence of HSV in the patient population, further antibody testing for HSV is not mandatory (CII$_t$) [26].

Hepatitis B

Prior to allo-HCT, besides hepatitis B virus (HBV) antibody panels, additional testing for hepatitis B surface antigen (HBsAg) should be performed [27, 28]. If tested positive for HBsAg or for anti-HBc, further HBV-DNA assessment for active replication is crucial (AII). If considered to be diagnosed with active hepatitis (e.g. viral replication), initiation of antiviral treatment prior to allo-HCT should be considered (AIII) [29].

There is a reported risk of up to 50 % for reverse seroconversion after allo-HCT if a patient is anti-HBc positive but has no detectable viral replication (resolved HBV infection) [30–32]. HBV-vaccination after allo-HCT might alleviate this risk [33].

Hepatitis C

Serologic testing for hepatitis C virus (HCV) is recommended. Serologically positive patients should receive quantitative testing for HCV-RNA viral load (AIII). Patients with chronic hepatitis C should receive a further diagnostic assessment, e.g., fibroscan or a liver biopsy to rule out liver fibrosis or cirrhosis. In case of liver cirrhosis or fibrosis, the conditioning regimen should try to avoid TBI, oral busulfan, or cyclophosphamide to minimize risk of hepatic sinusoidal occlusion syndrome (SOS) (BIII) [34–37].

Hepatitis E

Hepatitis E virus (HEV) is detected in immunocompromised patients. Limited information is available on the real incidence of HEV infection in recipients of allo-HCT [38, 39]. Mostly self-limited reactivation cases are published though chronic forms have been described as well. Serologic testing for HEV prior to allo-HCT is recommended (BIII). HEV should be considered as a differential diagnosis in patients after allo-HCT with elevated liver function tests [39–41].

HIV

HIV testing prior to allo-HCT is recommended. HIV-infected patients should be carefully evaluated for allo-HCT. Though HIV seropositivity per se is not a contraindication for allo-HCT [42]. If allo-HCT seems feasible, a donor screening for CCR5-Delta 32 deletion could be considered in patients with CCR5 tropism to potentially control HIV infection post-allo-HCT (BIII) [43, 44]. Toxicity permitting, antiretroviral therapy should be continued throughout of the post-transplantation phase (AII) [45]. However, recurring interruptions with low drug levels may induce viral resistance, and an interrupted treatment should not be reinstated until the patient has sufficiently recovered to allow stable tablet intake (BIII).

Syphilis

Serologic testing for syphilis is recommended. Frequently TPHA/TPPA or VDRL are utilized. Important are the combinations of nontreponemal (e.g. VDRL) and treponemal tests. If a nontreponemal test is positive, confirmation of infection with treponemal test (e.g. TPPA or TP-EIA) should be performed. In case of an active infection or unclear whether the

patient received an adequate treatment in the past, a treatment with penicillin should be instituted (BIII) [46].

Toxoplasmosis

All candidates for allo-HCT should undergo serologic testing for toxoplasmosis. If the serology testing for toxoplasmosis IgG is positive, patients have a risk of toxoplasmosis reactivation, especially if the donor is serologically negative for toxoplasmosis [47]. Some centres propagate regular PCR testing [48]. Since the incidence in Europe is very low, regular toxoplasmosis DNA through PCR screening is not recommended (DIII). This is of course different in patients with clinical symptoms.

Tuberculosis

Thorough evaluation of the medical history can identify patients at risk for latent or active tuberculosis infection (AIII). As most candidates have received chemotherapy or immunosuppressive treatment prior to evaluation for allo-HCT, a tuberculin skin test might be false negative and therefore cannot be recommended in this setting (DIII). If the medical history is suggestive of prior tuberculosis exposure, an interferon-gamma-release assay (IGRA) can be considered (BIII) [49]. However, a reduced sensitivity in immunocompromised patients has been demonstrated as well [50, 51].

Prophylaxis and prevention

Prevention of bacterial infections (screening for bacterial colonization)

In this era of easy accessibility of antibiotics, clinicians are facing the growing challenge of multi-resistant bacteria (e.g. vancomycin-resistant *Enterococci* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase producing bacteria (ESBL), metallo-β-lactamase-producing bacteria (MBL)). Colonization with certain multi-resistant bacteria is predictive for developing bloodstream infection, and knowledge of colonization status may therefore guide empirical antibiotic treatment, although this strategy has not been demonstrated to improve outcomes [52, 53]. We recommend screening procedures for multi-resistant bacteria, especially in institutions with a known high prevalence (BII) [54, 55]. Since the sensitivity of the screening methods is low, repeated testing (e.g. weekly rectal swabs) would be required [56–58]. Contact precautions between medical staff and patients remain to be necessary and separate sanitary facilities need to be guaranteed to exclude cross-patient transfer of multi-resistant bacteria [59, 60].

Antibiotic prophylaxis (e.g. ciprofloxacin) demonstrated its efficacy by reducing the incidence of Gram-negative sepsis during neutropenia without any significant change in mortality [61, 62]. All-cause mortality was reduced only in meta-analysis [63]. At institutions with a low rate of multi-resistant gram-negative bacteria, antibacterial prophylaxis remains a reasonable choice to reduce the incidence of Gram-negative sepsis during neutropenia (AII$_r$) [62, 64–67]. Encapsulated bacteria such as *Streptococcus pneumoniae* or *Haemophilus influenzae* often cause severe bacterial infections in the late phase after transplantation [68–70]. In patients with chronic GVHD (graft-versus-host disease) on immunosuppressive therapy, antibiotic prophylaxis against these bacteria for disease prevention might be useful until immunizations can be applied (BIII). Antibiotic selection should be guided by local antibiotic resistance patterns. In patients without chronic GVHD, systemic antibiotic prophylaxis is not recommended after reconstitution of the neutrophils (DIII).

The value of selective gut decontamination is frequently debated and the literature points out that sepsis rates are increased and mortality outcomes were significantly worse in patients with lower intestinal diversity; therefore, no recommendation was made [71–74].

Prophylaxis against *Pneumocystis* pneumonia

Pneumocystis jirovecii (previously named *Pneumocystis carinii*) pneumonia has been noted in allo-HCT recipients with an incidence of approximately 5–16 % without adequate prophylaxis and occurred at a median of 9 weeks after allo-HCT. Despite intensive treatment, mortality rates are as high as 89 % during the first 6 months and approximately 40 % after the first 6 months following allo-HCT [75, 76].

Prophylaxis against *Pneumocystis jirovecii* pneumonia is recommended for at least first 6 months after allo-HCT to prevent *Pneumocystis jirovecii* pneumonia-associated death (AII$_t$). However, patients might require prophylaxis for prolonged periods of time. Recommended prophylactic regimens are similar to regimens in HIV/AIDS patients. Therefore, patients on immunosuppressive medications or active GVHD should remain on prophylaxis [77]. Once immunosuppressive medications are discontinued or no active GVHD is noted, prophylaxis may be discontinued assuming a CD4$^+$/CD3$^+$ lymphocyte count of 200/μL or higher (BII$_t$). Thus monitoring of CD4$^+$/CD3$^+$ lymphocytes could be continued until the threshold is confirmed by repeated testing (BII$_t$) [78]. The CD4$^+$/CD3$^+$ lymphocyte count of 200/μL as a discontinuation criterion is not confirmed in the allogeneic setting, and therefore, an individual decision to discontinue can be considered (CIII).

The prophylactic treatment of choice is the fixed combination of trimethoprim (80 mg) and sulfamethoxazole (400 mg) once daily thrice weekly (AII$_t$) [79–82]. In case of intolerance

to the trimethoprim/sulfamethoxazole therapy, aerosolized pentamidine (300 mg) every 4 weeks **(BII$_t$)** or atovaquone (750 or 1500 mg daily) **(BII$_t$)** is recommended [83–89]. Dapsone (100 mg) cannot be recommended **(DII$_t$)** [90]. Protective efficacy against *Pneumocystis* appears to be less with these alternative drugs compared to trimethoprim/sulfamethoxazole [84, 86, 90–93].

Antifungal prophylaxis in allo-HCT

Invasive fungal diseases (IFDs) are severe complications associated with prolonged hospital length of stay, costs, long-term treatment, and high mortality [94]. Approximately two thirds of the IFD develop in allo-HCT patients after leukocyte recovery [95, 96]. Furthermore, intensifying immunosuppression for treatment of transplant rejection or GvHD and CMV infection impose an imminent risk for IFD [97, 98].

The incidence of invasive aspergillosis (IA) varies between reports and may reach 23 % [94, 99]. Primary prophylaxis is highly recommended since diagnostic tools do not present with sufficient sensitivity numbers. This is mirrored in studies with a significant number of post-mortem diagnoses of fungal diseases [100–102]. In patients diagnosed with IA, mortality rates of up to 60 % have been reported despite adequate treatment [103]. Secondary prophylaxis is recommended prior to allo-HCT **(BII)** [104].

Invasive candidiasis, predominantly manifesting as candidemia, is the second most frequent IFD in allo-HCT patients. Invasive candidiasis/candidemia typically manifests in patients with underlying conditions after being exposed to additional risk factors, e.g. intravascular devices, broad-spectrum antibiotic treatment, total parenteral nutrition, or *Candida* colonization [105–107].

The currently largest cohort of IFDs shows an 8 % share of mucormycosis in all IFDs in allo-HCT, followed by a number of other rare mould infections [94]. Approximately half of the patients diagnosed with mucormycosis are patients after allo-HCT [108]. The share of rare IFDs like those caused by the order of *Mucorales* or *Fusarium* spp. appear to be increasing [94, 109]. Newer agents like isavuconazole demonstrated favorable response rates in primary treatment against moulds; however, larger prophylaxis studies are still needed [110–112].

In Table 2, prophylactic recommendations are summarized. Our group recently published recommendations for the treatment (i.e. targeted therapy) of fungal diseases [113].

Herpes simplex virus 1/2 prevention

Herpes viridae persist in the host after primary infection. Up to 80 % of adults are HSV-seropositive and especially during immunosuppression HSV may begin to replicate. Without prophylaxis allo-HCT recipients have a risk of approximately 80 % to reactivate during the early phase mainly during the first 4 weeks after allo-HCT [19, 137, 138]. Dissemination may lead to severe illness with substantial morbidity and mortality. As a consequence, patients should receive acyclovir early on for the prevention of disease to reduce mortality **(AI)** [138–141] (Table 3).

The duration of prophylaxis should last for up to 30 days after allo-HCT **(AI)** [139, 141]. However, exceptions are defined by recurrent episodes of HSV disease or risk of *Varicella zoster* disease. In these situations, duration of acyclovir prophylaxis to prevent disease is prolonged to a year or longer especially during intensified immunosuppressive therapy **(BII)** [142].

Resistance to acyclovir is a rare event and mainly caused by reduced activity or mutations of viral thymidine kinase resulting in reduced activation of acyclovir in infected cells [143, 144]. Breakthrough infections are noted but are usually described as clinically resistant since prophylaxis failure is explainable by decreased bioavailability of acyclovir. In cases of real acyclovir-resistant HSV, foscarnet susceptibility remains, and this agent is considered as an alternative treatment option for acyclovir-resistant disease **(BII)**. However, it cannot be recommended for routine prophylaxis due to its significant toxicity **(DIII)** [145].

It is presumed that valacyclovir and famciclovir are effective for the prevention of HSV reactivation; however, there are no clinical trials in allo-HCT to better support a recommendation **(CIII)** [146, 147].

Varicella zoster virus prevention

Since *Varicella zoster* virus (VZV) is highly contagious, patients with VZV disease should be isolated to prevent nosocomial spreading of viruses until all lesions are crusted **(AIII)** [148, 149]. Patients should be informed of the easy transmission of VZV. Allo-HCT recipients without adequate antiviral prophylaxis are at risk for disease, since up to two thirds develop herpes zoster, which mainly occurs 3 to 12 months after allo-HCT [150]. VZV seronegative family members, healthcare workers, other contact persons of allo-HCT recipients, or children without a history of *Varicella* or immunization, should be advised to receive a vaccination against VZV ideally at least 4 weeks prior to planned allo-HCT **(BIII)** [151].

Primary infection is rare and is associated with a high rate of mortality caused by frequent dissemination (e.g. encephalitis, pneumonia, viscera, or hepatitis) [150, 152, 153]. Therefore, exposure of seronegative recipients to chickenpox, zoster or vaccinated persons who experience a rash after vaccination should be avoided to prevent primary disease or VZV-associated death **(BIII)**. If exposure to persons with chickenpox or zoster

Table 2 Antifungal prophylaxis

Intention	Intervention	SoR	QoE	Comments	Ref
Prevent mould infection in patients without GvHD, day 1–100	Voriconazole 200 mg bid oral or iv[b]	C	I	No difference seen in the trial in comparison to fluconazole	[114]
	Posaconazole (suspension) 200 mg tid[b]	B	II$_t$	Improved overall survival in AML/MDS induction during neutropenia, new formulations (tablet and iv, 300 mg qid) provide a better bioavailability	[115–117]
	Micafungin 50 mg/day	C	I	Only during neutropenia, morbidity advantage	[118]
	Itraconazole suspension 2.5–7.5 mg/kg or capsules	C	I	Administered up to 180 days if GVHD was diagnosed; higher toxicity in comparison to fluconazole, TDM: cutoff at 500 mg/mL (AII)	[119–121]
Prevent invasive *Candida* disease in patients without GvHD, day 1–100	Fluconazole 400 mg/day	A	I	Improved survival, note rising incidence of resistant *Candida* species since studies were published	[122–124]
	Voriconazole 200 mg bid oral or iv[b]	B	II$_t$	Also active against moulds, but no difference seen in the trial between voriconazole and fluconazole	[114]
	Posaconazole (suspension) 200 mg tid[b]	B	II$_t$	Also effective against moulds, new formulations (tablet and iv, 300 mg qd) provide a better bioavailability	[115, 117]
	Micafungin 50 mg/day	B	II$_t$	Also effective against moulds, only during neutropenia, morbidity advantage	[118]
	Itraconazole suspension 2.5–7.5 mg/kg or capsules[b]	C	I	See above	[119–121]
Prevent invasive Aspergillosis during GvHD	Posaconazole (suspension) 200 mg tid[b]	A	I	improved survival (lower attributable mortality), new formulations (tablet and iv, 300 mg qd) provide a better bioavailability	[117, 125]
Prevent fungal disease relapse (previous IFD)	Voriconazole[b]	B	II	considered as secondary antifungal prophylaxis, dosages as above	[126]
	Caspofungin, posaconazole	B	III		[127, 128]
Prevent fungal diseases[a]	Amphotericin B deoxycholate	D	II	Inacceptable toxicity	[129–131]

[a] other formulations and various dosages and application regimens of Amphotericin B have been evaluated with different results in small studies, all would need further evaluation to provide any kind of recommendation [132–134]

[b] Consider TDM, serum levels of efficacy in prophylaxis are still debated, e.g. posaconazole [135]

occurs, passive immunization with anti-VZV hyperimmunoglobulin (Ig) within 96 h after exposure is considered optional (CIII), as efficacy has not been proven [154, 155]. Antiviral therapy with valacyclovir 1 g po tid or acyclovir 800 mg qid should be administered (BIII) immediately to prevent disease in seronegative recipients.

Main antiviral prophylaxis recommendations are summarized in Table 3. Various authors [156–159] noted that even prolonged administration for approximately 1 year or longer is considered safe and there was no higher incidence of disease after drug discontinuation. Longer than 12-month periods appears to be beneficial as long as patients remain on intensified immunosuppressive therapy (BIII).

If resistance to acyclovir is suspected, foscarnet or cidofovir are alternative agents (BIII) [160]. Brivudine is contraindicated in patients receiving 5-fluoropyrimidine derivatives and was not assessed in immunocompromised patients (DIII). (http://www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/EN/RHB/2012/rhb-zostex.html, last accessed May 1, 2016)

CMV disease prevention

All CMV-seronegative recipients ideally should receive a CMV-seronegative donor graft to prevent infection and reduce mortality (AII) [25, 161, 162]. To further prevent disease, CMV-seronegative recipients transplanted from a negative donor should only receive blood products from CMV-seronegative donors upon availability. Blood banks without a sufficient pool of CMV-negative donors should deliver only leukocyte-depleted red blood cells and thrombocytes (AII) [163]. However, data from various studies suggest if blood products are leukocytes reduced, testing for CMV-negative blood products is not needed for HSCT recipients (AII) [163–165]. Noteworthy, irradiation to prevent transfusion-associated GvHD does not inactivate CMV [164, 166–170].

Special risk factors for CMV infection or disease are T cell-depleted graft, HLA-mismatched transplantation, steroid treatment, and acute or chronic GvHD [171–173]. All patients at risk for CMV disease should be screened regularly for pp65 antigenemia or by nucleic acid detection methods after allo-HCT (AII) [174].

Table 3 Antiviral prophylaxis

Intention	Intervention	SoR	QoE	Comments	Ref
HSV					
Prevent HSV disease	Acyclovir 400 mg tid/day	A	II	Up to 30 days post allo-HCT (various dosages)	[139, 141, 233]
	Valacyclovir 500 mg bid /day	A	II		[234]
	Acyclovir any dosage	D	III	Beyond 30 days if patient is also VZV seronegative	
VZV					
VZV disease prevention in VZV seropositive recipients	Acyclovir 800 mg bid	A	I	Up to 1 year after allo-HCT	[156]
	Acyclovir 400 mg/day	B	II		[158, 159, 235]
	Valacyclovir 500 mg bid	B	II		[236, 237]
	Acyclovir 200 mg/day	B	II	More than 365 days if continued on immunosuppressive therapy	[233, 238]
Prevent VZV in seronegative patients	No prophylaxis	C	III		
Prevent VZV in seronegative patients if exposed	Passive immunization	C	II_t	Within 96 h post exposure, optional	[155]
	Acyclovir or other VZV-active antiviral	C	III	If patient is not on acyclovir (or any other VZV active antiviral), a short duration of therapy is an option.	
Prevent VZV disease after exposure	Vaccination	–	–	No data to provide recommendation	
CMV					
Preemptive strategy recommended over prophylaxis/treatment	Ganciclovir, valganciclovir, or foscarnet	A	I		[177, 239–242]
Reduce incidence of CMV infection/disease, if a center does not follow a preemptive strategy	Long term acyclovir 800 mg/day	C	II		[180]
	Valacyclovir 500 mg qid/day	B	I		[182]
	Ganciclovir 2.5–5 mg/kg bid/day	C	II	Caution: myelotoxicity	[243, 244]
	Valganciclovir 900 mg bid	A	II	Caution: myelotoxicity	[177]
	CMV-specific CTLs	C	II	Not available at every site (considered experimental)	[245]
HBV					
Prevent disease in HBsAG seropositive recipients	Lamivudine 100 mg/day	A	II	Monitor HBV DNA closely, duration until anti-HBs is detected (and HBV-DNA is negative)	[210, 246, 247]
	Entecavir 0.5–1.0 mg/day	A	II		[248–250]
	Tenofovir 245 mg/day	C	III		[251, 252]
Prevent disease in HBsAG seropositive recipients with HBsAG seronegative donors	Additionally vaccinate donor	B	III	Requires long term planning	[253]
Prevent reactivation in recipients who are anti-HBcAG seropositive, DNA viral load: positive	Lamivudine 100 mg/day	B	III		[209]
Prevent reactivation and disease in recipients who are anti-HBcAG seropositive, DNA viral load: negative	Lamivudine 100 mg/day	C	III		
	HBV-DNA/HBsAG monitoring	B	III		[254]

The current standard to improve morbidity and lower mortality is the early initiation of a preemptive therapy against CMV **(AII)** [174]. Duration of screening is usually defined by the time period of the application of immunosuppressive agents or GVHD.

Anti-CMV prophylaxis can only be considered as an option. The long-term administration of ganciclovir resulted in a delay of recovery from CMV-specific T cell immunity [175].

Valganciclovir is so far not officially approved in allo-HCT patients but has been applied in randomized trials [176, 177]. In a randomized controlled trial, valganciclovir prophylaxis was not superior in reducing the incidence of CMV disease or death when compared with PCR-guided preemptive therapy. Delay in virus-specific T cell reconstitution was not observed in patients receiving prophylaxis [177]. Administration of human immune

globulins for prophylaxis or therapy of CMV disease is generally not recommended **(DII)** [178, 179]. Some investigators published efficacy of high-dose acyclovir or its prodrug valacyclovir in the prevention of CMV disease [180–183]. However, acyclovir failed to prevent CMV disease in autologous transplantation and therefore, is not recommended for prophylaxis **(DIII)** [184].

Newer antiviral agents have been evaluated mainly in phase II trials. Maribavir, an oral antiviral agent was studied for prophylaxis. Maribavir inhibits the UL97 viral protein-kinase of human CMV. Despite promising results in a phase II study, a phase III study could not confirm a benefit [185–187]. Another antiviral agent named CMX001 is an orally bioavailable lipid acyclic nucleoside phosphonate and is converted intracellularly to cidofovir diphosphate. Brincidofovir (CMX001) is active in vitro against CMV, including ganciclovir-resistant strains and was assessed in a phase II trial with promising results in prophylaxis [188]. Letermovir (previously known as AIC246) is another anti-CMV agent with a novel mechanism of action targeting the viral terminase subunit pUL56, a component of the terminase complex. This agent demonstrated dose-dependent prophylactic efficacy in a phase II trial [189]. If the ongoing phase III trials confirm these results, a paradigm shift may occur in the future.

New DNA-based vaccination strategies against CMV are being evaluated in clinical trials [190].

Main antiviral recommendations are noted in Table 3.

Epstein-Barr virus disease prevention

Factors associated with an enhanced risk for Epstein-Barr virus (EBV) replication and therefore infection after allo-HCT are a selective T cell depletion of the graft, a HLA-mismatched transplantation, the choice of an unrelated donor (especially haploidentical transplant recipients), and the use of T cell depleting antibodies, e.g. alemtuzumab or ATG during conditioning [191, 192]. Early EBV-disease after transplantation is extremely rare. Primary or secondary prophylactic use of antiviral agents is not effective against EBV and therefore not recommended **(DII)** [193, 194]. Close EBV viral load monitoring and rituximab application can be considered as a preemptive therapeutic approach for the prevention of EBV-associated PTLD after allo-HCT in special high-risk patients **(CIII)** [195–197]. Still considered experimental is the application of cytotoxic T cells for

the prevention and treatment of Epstein-Barr virus-induced lymphoma in allogeneic transplant recipients [198, 199].

Toxoplasmosis prophylaxis

Trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis, administered to most transplant patients to prevent *Pneumocystis jirovecii* pneumonia, is also efficacious in preventing toxoplasmosis disease [200, 201].

Clinical reactivation of toxoplasmosis may occur in the late phase after transplantation in seropositive patients under immunosuppression. However, the risk is considerably low and no primary prophylaxis is recommended **(DIII)** [47, 202, 203]. After a successful therapy of toxoplasmosis, secondary prophylaxis should be administered for at least 3 months **(AII$_t$)** [204–206] (Table 4).

Hepatitis A prevention

The incidence of infections due to hepatitis A varies widely. Prevention of hepatitis A by vaccination of seronegative patients or donors follows general vaccination recommendations. A previous exposure to hepatitis A has no impact on transplant-related complications, thus only serologic testing is recommended. In case of IgM seropositivity of the donor and/or recipient, allo-HCT might be postponed since a high risk of transmission or hepatic complications are associated with acute hepatitis A. Additional prevention of infection of the recipient can be achieved by avoiding potentially contaminated food. If exposed, passive immunization has been discussed controversially even in non-transplant patients.

Following patients' post allo-HCT, a continuous loss of acquired hepatitis A antibodies has been described over a median time of 48 months, especially in those older than 18 years. Thus, hepatitis A vaccination should be recommended later in adult transplanted patients at risk **(BII$_t$)** [207].

Hepatitis B prevention (Table 3)

Hepatitis B infection or reactivation contributes to liver-related morbidity and mortality. This is a frequent problem, which occurs in 21–53 % of patients with immunosuppression [208],

Table 4 Secondary prophylaxis after toxoplasmosis disease

Intention	Intervention	SoR	QoE	Comments	Ref
To prevent relapse of CNS toxoplasmosis	Pyrimethamine (25 mg/day)[a] + sulfadiazine (orally, 30 mg/kg/d)	A	II$_t$	Minimum duration for 3 months, many cases longer	[204, 206]
	Pyrimethamine (25 mg/d)[a] + clindamycin (intravenously, 1200 mg/d)	B	II$_t$		[255–257]
	Atovaquone 750 mg qid	B	II$_t$	In patients intolerant to conventional toxoplasmic encephalitis therapies	[206]

[a] Should be combined with folinic acid

especially after conditioning regimens containing alemtuzumab [209]. The goal is to avoid impairment of liver function, fulminant liver failure, hepatic sinusoidal obstruction syndrome (SOS), cirrhosis, or even hepatocellular cancer [210].

Preferably, HBsAG-negative donors should be selected. However, if no other HLA-compatible donor is available, a positive donor for transplantation is not absolutely contraindicated (BIII). Although transplantation of HBV-negative patient with stem cells from an infected donor (HBsAG positive) is associated with a high risk of transmission, some patients develop chronic hepatitis B [210]. Donors with active HBV (DNA detection) should receive antiviral treatment, if possible (AIII).

All HBsAG-positive patients awaiting chemotherapy or immunosuppressive therapy should receive antiviral prophylaxis with a nucleoside analogue, regardless of HBV-DNA levels. In anti-HBc positive patients with no detectable viral replication (resolved HBV infection), there is a serious risk (up to 50 %) of reverse seroconversion after allo-HCT [211]. These patients should be monitored for HBV replication on a regular basis and receive preemptive antiviral treatment with lamivudine (AII) or entecavir (AII) once HBV DNA levels are positive (more details: Table 3). It is recommended that antiviral treatment should be continued until at least 6 months after the cessation of immunosuppression (BIII) [29]. Prophylactic treatment of anti-HBc-positive patients without any viral load during the first months after allo-HCT is optional since no data are published in this patient population (CIII).

Hepatitis C prevention

Patients tested positive for HCV-RNA have a significantly higher risk of developing sinusoidal obstruction syndrome (SOS). Long after allo-HCT they suffer a higher rate of liver fibrosis or cirrhosis [34]. Therefore, patients tested positive for HCV-RNA should be considered (if time permitted) to receive highly active antiviral treatment (BII$_t$) [212]. In allo-HCT, data is lacking; however, Mahale et al. reported that patients who have successfully eliminated HCV are not at risk of reactivation at least after conventional chemotherapy [212]. Detailed therapy recommendations cannot be provided since at this time many promising trials with new drugs are being published demonstrating eradication of HCV [213].

Allo-HCT from an HCV-RNA-positive donor should be avoided since the incidence of transmission remains high (DII). If timing permitted and no alternative donor options are available, the donor should be treated accordingly to prevent hepatic complications (AII$_t$) [214].

Prevention of diseases caused by respiratory viruses

In recent years, an increasing number of reports on respiratory viral infections after allo-HCT are noted, which are in part attributable to improved diagnostic tools and better awareness.

RSV followed by influenza, parainfluenza, metapneumovirus, and adenovirus are the main viruses causing severe diseases [215]. These viruses can contribute significantly to morbidity after allo-HCT; however, mortality rates seem to be mixed due to heterogeneity of various risk situations [216]. The main recommendation is to avoid infections with these viruses through adequate exposure prevention (AIII) [217, 218]. Visitors and staff with signs and symptoms of respiratory infections must avoid visiting the wards to prevent further disease (AIII). Additionally, annual influenza vaccination is strongly recommended for healthcare workers, all persons living with allo-HCT candidates or patients to prevent transmission (AIII) [219]. If vaccination was carried out during an influenza outbreak, a 2-week course of antiviral chemoprophylaxis could follow until immune response is effective (BIII) [19, 220].

There is no published data confirming clinical efficacy of prophylactic administration of respiratory syncytial virus (RSV) immune globulin (RSVIG); therefore, this approach is discouraged (DII) [221].

Intravenous immune globulin for prophylaxis

There is an ongoing controversy about the benefit, dosing, and optimum preparation (hyperimmune or polyvalent) of intravenous immune globulins (IVIG) in allo-HCT [222]. Older studies have demonstrated prevention of infection, interstitial pneumonia (IP), or GVHD [223, 224]. Large meta-analyses demonstrated no clinical benefit, except for a decrease of IP and an increase of sinusoidal obstruction syndrome (SOS) with high-dose IVIG [225, 226].

In a recent multicenter trial, 200 patients received different doses of IVIG or placebo weekly starting day −7 till day +100, but no differences were observed in regards to infections, interstitial pneumonia, treatment-related mortality, and overall survival. However, higher doses of immune globulin were again associated with deleterious SOS [227]. Therefore, the routine prophylactic substitution of immune globulin is not recommended if the IgG level is >4 g/L (DI) [227, 228].

Nevertheless, a retrospective study reported patients with severe hypogammaglobulinemia (e.g. IgG <4 g/L) were to be at risk for decreased survival [229]. This compares well with the IgG substitution recommendations by the IDSA [220] and the guidelines for patients with the common variable immunodeficiency (CVID) syndrome to substitute low-dose immune globulin if IgG <4 g/l [230]. According to an analysis by the Cochrane group, the use of IVIG may be considered in patients with hypogammaglobulinemia associated with CLL or multiple myeloma and recurrent infections. IVIG can significantly decrease the number of infections [225, 226].

Therefore, immune globulin should be replaced in patients with low serum IgG levels and recurrent infections associated with hypogammaglobulinemia to lower the incidence of infections (BII$_t$).

Table 5 Vaccination recommendations for allo-HCT recipients

Intention	Intervention (timing of 1st application after allo-HCT) Vaccine	after day +100	after 6–12 months	after 24 months	SoR	QoE	Comments	Ref
Provide immunity	Pneumococcus (combination of conjugate and polysaccharide vaccines)	X			A	II$_t$	Post allo-HCT 6 months; 3 applications of 13-valent pneumococcal conjugate vaccine (PCV13, 4 weeks apart). After 1 year post allo-HCT use 23-valent polysaccharide pneumococcal vaccine; no data for non-myeloablative, haplo-identical, or DLI protocol regimes	[258, 269–270, 310]
	Pneumococcus (polysaccharide vaccine) 23-valent (PPV23)		(X)		D	II	Alone not recommended as a single vaccine since conjugate vaccine provide a better immune response	[266, 271–276]
	Influenza	X			A	II	Consider to vaccinate patient after 4 weeks again (BII) if still early after transplantation; Include next of kin and healthcare workers (HCW) to receive vaccination as well (AIII). Consider quadrivalent vaccine (BIII).	
	Bordatella pertussis (acellular)[b]		X		A	III	Antibody levels do not reflect effective vaccination.	[276–278]
	Diphtheria and tetanus toxoid[a, b]		X		A	II	First diphtheria and tetanus vaccination after 12 months; only data available beyond 12 months; for diphtheria higher dose possibly better (child dosage) but not approved (BIII)	[279–281, 310]
	TBE[a] (Tick-borne encephalitis)		X		B	II$_t$	Only in endemic areas	[282]
	Poliovirus[a, b]		X		A	II	Inactivated vaccine only	[281, 283–288]
	Haemophilus influenza (HI)[a, b]		X		B	II	Incidence of HI type B (vs. non type B) infections after allo-HCT is relatively low.	[269, 288–295, 310]
	Meningococcal conjugate vaccine against serogroups A, C, W135, Y and Meningococcal vaccine for serogroup B		X		B	II$_t$	Europe, North America and Canada register high rates of meningococcal disease by serogroup B. Therefore, both vaccines are recommended equally.	[295–297]
	Hepatitis A and B (HAV and HBV)[a, b]		X		B	II$_t$	Only in patients at risk for hepatitis. Combination vaccination possible. Patients with a previous history of HBV need to be revaccinated (**AII**).	[33, 207, 298–300]
	MMR (mumps, measles, and rubella; life attenuated vaccine)[a, b]			X	B	II	Live attenuated vaccine after 24 months post allo-HCT and no GVHD or immunosuppressive therapy. Less than 24 months: DIII. Consider occupational risks and household.	[301–303]
	VZV (varizella zoster virus, life attenuated vaccine)[a]			X	B	II	As MMR but no history of VZV disease and seronegative	[304–307]

[a] Consider antibody measurements

[b] Consider combination vaccines

Granulocyte transfusion for prophylaxis

A small matched pair analysis of nine neutropenic patients at high risk for recurrence of a previous fungal infections after allo-HCT demonstrated that prophylactic administration of granulocyte transfusions could reduce the incidence and shorten the duration of fever as well as the duration of neutropenia compared to the control group [231]. Oza et al. performed a "biological randomization" in 151 stem cell recipients dependent on ABO- and CMV-compatibility of their donor. There was a significant decrease in the number of febrile days and the use of intravenous antibiotics; however, no difference in the length of hospital stay or 100-day survival was noted [232]. So far, prophylactic granulocyte transfusion remains an experimental approach and is considered more a therapeutic option.

Immunization (Tables 5 and 6)

Protection against vaccine-preventable infections should be a part of the post-transplantation medical care management. Ideally, trials should provide evidence for the protection against diseases. However, a study powered for protective efficacy is not necessary if a sponsor of a vaccine study can justify the use of immunological data to predict protection against infection [233]. If it is not feasible to perform an efficacy study and there is no immunological correlation of protection, it may sometimes be justifiable to gauge the likely efficacy of a vaccine by comparison of immunological responses with those seen in past studies of similar vaccines with proven protective efficacy (e.g., acellular pertussis vaccines) [233].

In allo-HCT recipients, antibody titers against vaccine-preventable infections decline, leading to an increased risk of developing a disease [259]. For this reason, an early vaccination schedule would be warranted. However, during the first 3 to 6 months after transplantation, a sufficient specific immune system response to vaccination cannot be expected [259]. Depending on different factors such as pre- and post-transplant treatment, age, type of transplantation, or presence of chronic GVHD, recovery of the immune system is delayed [259]. Additionally, limited information about vaccine response exists for patients after reduced-intensity conditioning or with umbilical cord blood grafts. Administration of rituximab can suppress humoral immune response as long as 6 months after the last dose. Delayed vaccination schedules should be considered in these patients (BII$_t$) [260–262].

Table 6 Immunization schedule

Vaccine	SoR/ QoE	Relative to day of allo-HCT				12 months after first vaccination	Refresher	Comments	Ref
		Day +100	Month +6	Month +7	Month +8				
Pneumococcus	AII$_t$	X	X	X		X	Unclear	Start with PCV13, after 12 months after first vaccination the 23 valent polysaccharide vaccine should be used	[269–270, 308]
Influenza	AII	X				X	Annually		[266, 271–276]
Polio inactivated[a]	AII		X	X	X	X	According to local health advisory	[a] Combination vaccine possible	[283–288, 309]
Pertussis (acellular)[a]	AIII		X	X	X	X			[277, 278, 309]
Diphtheria and tetanus toxoid[a]	AII		X	X	X	X			[279–282, 292, 309]
Haemophilus influenzae[a]	BII		X	X	X	X			[269, 284, 288–295, 311, 312]
Meningococcal conjugate 4 valent and serogroup B	BII		X			X	None		[295, 313–315]
TBE	BII$_t$		X	X		X	5 years		[282, 316]
Hepatitis B	CII		X			X	Depending on titer	Combination vaccine possible (together with HAV)	[298–299, 317–320]
Mumps, measles, rubella	BII	Live attenuated vaccine after 24 months accordingly to the rule mentioned in Table 5					Unclear, depending on immune response	One dose is recommended	[301–303, 321, 322]
Varicella zoster virus (VZV)	BII								[304–307, 323]

[a] combination vaccination possible

Pneumococcal and meningococcal immunization with the conjugated vaccine seems to provide a more stable immune response than the polysaccharide-based vaccine in immature or altered immune systems, but comparative trials are still missing [263].

MMR (measles, mumps, rubella) and *Varicella* vaccines are live attenuated vaccines that should not be given within the first 2 years after transplantation or during active GVHD **(DIII)**. A significant risk of disease and side effects in the immunocompromised patient were observed. However, 24 months after transplantation without evidence of chronic GVHD and immunosuppression, MMR vaccine appears safe to be administered **(BIII)**.

Routine VZV-vaccination is currently not indicated in seropositive patients for the prevention of herpes zoster **(DIII)**. A newer inactivated VZV vaccine is being developed providing adequate VZV-specific antibody titers in most patients [264]. This new vaccine has the potential to change this recommendation in the future.

Additional immunizations against hepatitis A virus, human papillomavirus, yellow fever, cholera, typhus, rotavirus, or pre-exposure rabies virus vaccination are not routinely indicated in adults. Decision-making should follow the recommendations of general population and country-specific policy. Degree of immune suppression against live attenuated vaccines especially in the allo-HCT population needs special attention.

Little is known whether vaccinations can induce GVHD, since viral infections are known to do so [265]. On the other hand, clinical data demonstrate response to vaccination despite GVHD [266, 267]. A group of European experts published results of a consensus conference on vaccination in GVHD [268]. The conference attendees were more cautious about immune suppression. In patients receiving prednisone ≥0.5 mg/kg bodyweight per day as part of a combination therapy or a three-agent immunosuppressive treatment is given; vaccination may be postponed until immunosuppression is reduced to a double combination or prednisone <0.5 mg/kg bodyweight daily in order to achieve a better vaccine response **(BIII)** [268].

Antibody titer testing prior to and after immunization can be recommended for many vaccines. Decision-making based on a titer is not recommended for all vaccinations to document efficacy except for VZV, HAV, or HBV. Basically, titer determination provides some insight on vaccination success and should be considered as optional **(CIII)**. Testing for sufficient antibody response after immunization is indicated in hepatitis B one month or later after the third vaccine dose **(BIII)**. Revaccination with a second series of hepatitis B vaccine should be considered in non-responders **(CIII)**.

In review of the available literature, clearly more studies are needed to provide more information on the safety and efficacy of vaccination schedules in allo-HCT.

References

1. Tabbara IA et al (2002) Allogeneic hematopoietic stem cell transplantation: complications and results. Arch Intern Med 162(14): 1558–1566
2. Hiemenz JW (2009) Management of infections complicating allogeneic hematopoietic stem cell transplantation. Semin Hematol 46(3):289–312
3. Einsele H et al (2003) Infectious complications after allogeneic stem cell transplantation: epidemiology and interventional therapy strategies—guidelines of the Infectious Diseases Working Party

(AGIHO) of the German Society of Hematology and Oncology (DGHO). Ann Hematol 82(Suppl 2):S175–S185

4. Ullmann AJ et al (2012) ESCMID* guideline for the diagnosis and management of Candida diseases 2012: developing European guidelines in clinical microbiology and infectious diseases. Clin Microbiol Infect 18(Suppl 7):1–8

5. Cornet M et al (1999) Efficacy of prevention by high-efficiency particulate air filtration or laminar airflow against Aspergillus airborne contamination during hospital renovation. Infect Control Hosp Epidemiol 20(7):508–513

6. Eckmanns T, Ruden H, Gastmeier P (2006) The influence of high-efficiency particulate air filtration on mortality and fungal infection among highly immunosuppressed patients: a systematic review. J Infect Dis 193(10):1408–1418

7. Oren I et al (2001) Invasive pulmonary aspergillosis in neutropenic patients during hospital construction: before and after chemoprophylaxis and institution of HEPA filters. Am J Hematol 66(4):257–262

8. Kruger WH et al (2003) Effective protection of allogeneic stem cell recipients against Aspergillosis by HEPA air filtration during a period of construction—a prospective survey. J Hematother Stem Cell Res 12(3):301–307

9. Vokurka S et al (2014) The availability of HEPA-filtered rooms and the incidence of pneumonia in patients after haematopoietic stem cell transplantation (HSCT): results from a prospective, multicentre, eastern European study. J Clin Nurs 23(11–12):1648–1652

10. Humphreys H (2004) Positive-pressure isolation and the prevention of invasive aspergillosis. What is the evidence? J Hosp Infect 56(2):93–100, quiz 163

11. Hayes-Lattin B, Leis JF, Maziarz RT (2005) Isolation in the allogeneic transplant environment: how protective is it? Bone Marrow Transplant 36(5):373–381

12. McCann S et al (2004) Outbreaks of infectious diseases in stem cell transplant units: a silent cause of death for patients and transplant programmes. Bone Marrow Transplant 33(5):519–529

13. Harrington RD et al (1992) An outbreak of respiratory syncytial virus in a bone marrow transplant center. J Infect Dis 165(6):987–993

14. Whimbey E et al (1995) Combination therapy with aerosolized ribavirin and intravenous immunoglobulin for respiratory syncytial virus disease in adult bone marrow transplant recipients. Bone Marrow Transplant 16(3):393–399

15. Taylor GS, Vipond IB, Caul EO (2001) Molecular epidemiology of outbreak of respiratory syncytial virus within bone marrow transplantation unit. J Clin Microbiol 39(2):801–803

16. McWilliam Leitch EC et al (2001) Dietary effects on the microbiological safety of food. Proc Nutr Soc 60(2):247–255

17. Boyle NM et al (2014) Bacterial foodborne infections after hematopoietic cell transplantation. Biol Blood Marrow Transplant 20(11):1856–1861

18. Allegranzi B, Pittet D (2009) Role of hand hygiene in healthcare-associated infection prevention. J Hosp Infect 73(4):305–315

19. CE1-7 (2000) Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. MMWR Recomm Rep 49(RR-10)1–125

20. Daeschlein G et al (2007) Hygienic safety of reusable tap water filters (Germlyser) with an operating time of 4 or 8 weeks in a haematological oncology transplantation unit. BMC Infect Dis 7:45

21. Zhou ZY et al (2014) Removal of waterborne pathogens from liver transplant unit water taps in prevention of healthcare-associated infections: a proposal for a cost-effective, proactive infection control strategy. Clin Microbiol Infect 20(4):310–314

22. Cervia JS et al (2010) Point-of-use water filtration reduces healthcare-associated infections in bone marrow transplant recipients. Transpl Infect Dis 12(3):238–241

23. Kelsey SM, Newland AC (1989) Cytomegalovirus seroconversion in patients receiving intensive induction therapy prior to allogeneic bone marrow transplantation. Bone Marrow Transplant 4(5):543–546

24. Hamadani M et al (2010) How we approach patient evaluation for hematopoietic stem cell transplantation. Bone Marrow Transplant 45(8):1259–1268

25. Schmidt-Hieber M et al (2013) CMV serostatus still has an important prognostic impact in de novo acute leukemia patients after allogeneic stem cell transplantation: a report from the Acute Leukemia Working Party of EBMT. Blood 122(19):3359–3364

26. Stewart JA et al (1995) Herpesvirus infections in persons infected with human immunodeficiency virus. Clin Infect Dis 21(Suppl 1):S114–S120

27. Liang R, Lau GK, Kwong YL (1999) Chemotherapy and bone marrow transplantation for cancer patients who are also chronic hepatitis B carriers: a review of the problem. J Clin Oncol 17(1):394–398

28. Hammond SP et al (2009) Hepatitis B virus reactivation following allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 15(9):1049–1059

29. Liang R (2009) How I treat and monitor viral hepatitis B infection in patients receiving intensive immunosuppressive therapies or undergoing hematopoietic stem cell transplantation. Blood 113(14):3147–3153

30. Knoll A et al (2004) Reactivation of resolved hepatitis B virus infection after allogeneic haematopoietic stem cell transplantation. Bone Marrow Transplant 33(9):925–929

31. Mikulska M et al (2014) Hepatitis B reactivation in HBsAg-negative/HBcAb-positive allogeneic haematopoietic stem cell transplant recipients: risk factors and outcome. Clin Microbiol Infect 20(10):O694–O701

32. Pompili M et al (2015) Prospective study of hepatitis B virus reactivation in patients with hematological malignancies. Ann Hepatol 14(2):168–174

33. Takahata M et al. (2014) Hepatitis B virus (HBV) reverse seroconversion (RS) can be prevented even in non-responders to hepatitis B vaccine after allogeneic stem cell transplantation: long-term analysis of intervention in RS with vaccine for patients with previous HBV infection. Transpl Infect Dis 16(5):797–801

34. Peffault de Latour R et al (2008) Allogeneic hematopoietic cell transplant in HCV-infected patients. J Hepatol 48(6):1008–1017

35. de Latour Peffault R (2004) Long-term outcome of hepatitis C infection after bone marrow transplantation. Blood 103(5):1618–1624

36. Locasciulli A et al (1989) Predictability before transplant of hepatic complications following allogeneic bone marrow transplantation. Transplantation 48(1):68–72

37. Lee JH et al (2005) Decreased incidence of hepatic veno-occlusive disease and fewer hemostatic derangements associated with intravenous busulfan vs oral busulfan in adults conditioned with busulfan + cyclophosphamide for allogeneic bone marrow transplantation. Ann Hematol 84(5):321–330

38. van der Eijk AA et al (2014) Hepatitis E virus infection in hematopoietic stem cell transplant recipients. Curr Opin Infect Dis 27(4):309–315

39. Versluis J et al (2013) Hepatitis E virus: an underestimated opportunistic pathogen in recipients of allogeneic hematopoietic stem cell transplantation. Blood 122(6):1079–1086

40. le Coutre P et al (2009) Reactivation of hepatitis E infection in a patient with acute lymphoblastic leukaemia after allogeneic stem cell transplantation. Gut 58(5):699–702

41. Bettinger D et al. (2014) Chronic hepatitis E virus infection following allogeneic hematopoietic stem cell transplantation: an important differential diagnosis for graft versus host disease. Ann Hematol 94(2):359–360

42. Hutter G, Zaia JA (2011) Allogeneic haematopoietic stem cell transplantation in patients with human immunodeficiency virus: the experiences of more than 25 years. Clin Exp Immunol 163(3): 284–295

43. Hutter G et al (2009) Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. N Engl J Med 360(7):692–698

44. Hutter G (2014) More on shift of HIV tropism in stem-cell transplantation with CCR5 delta32/delta32 mutation. N Engl J Med 371(25):2437–2438

45. Henrich TJ et al (2013) Long-term reduction in peripheral blood HIV type 1 reservoirs following reduced-intensity conditioning allogeneic stem cell transplantation. J Infect Dis 207(11):1694–1702

46. Au WY, Lie AK, Cheng VC (2005) VDRL screening and haemopoietic stem cell transplantation. Bone Marrow Transplant 35(10):1027–1028

47. Martino R et al (2005) Early detection of Toxoplasma infection by molecular monitoring of Toxoplasma gondii in peripheral blood samples after allogeneic stem cell transplantation. Clin Infect Dis 40(1):67–78

48. Fricker-Hidalgo H et al (2009) Diagnosis of toxoplasmosis after allogeneic stem cell transplantation: results of DNA detection and serological techniques. Clin Infect Dis 48(2):e9–e15

49. Lee YM et al (2014) A prospective longitudinal study evaluating the usefulness of the interferon-gamma releasing assay for predicting active tuberculosis in allogeneic hematopoietic stem cell transplant recipients. J Infect 69(2):165–173

50. Menzies D, Pai M, Comstock G (2007) Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. Ann Intern Med 146(5): 340–354

51. Moon SM et al (2013) Comparison of the QuantiFERON-TB gold in-tube test with the tuberculin skin test for detecting latent tuberculosis infection prior to hematopoietic stem cell transplantation. Transpl Infect Dis 15(1):104–109

52. Biehl LM et al (2014) Colonization and infection with extended spectrum beta-lactamase producing Enterobacteriaceae in high-risk patients—review of the literature from a clinical perspective. Crit Rev Microbiol 42(1):1–16

53. Liss BJ et al (2012) Intestinal colonisation and blood stream infections due to vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBLE) in patients with haematological and oncological malignancies. Infection 40(6):613–619

54. Zirakzadeh A et al (2008) Vancomycin-resistant enterococcal colonization appears associated with increased mortality among allogeneic hematopoietic stem cell transplant recipients. Bone Marrow Transplant 41(4):385–392

55. Dubberke ER et al (2006) Vancomycin-resistant enterococcal bloodstream infections on a hematopoietic stem cell transplant unit: are the sick getting sicker? Bone Marrow Transplant 38(12):813–819

56. Thouverez M, Talon D, Bertrand X (2004) Control of Enterobacteriaceae producing extended-spectrum beta-lactamase in intensive care units: rectal screening may not be needed in non-epidemic situations. Infect Control Hosp Epidemiol 25(10):838–841

57. Blot S et al (2005) Colonization status and appropriate antibiotic therapy for nosocomial bacteremia caused by antibiotic-resistant gram-negative bacteria in an intensive care unit. Infect Control Hosp Epidemiol 26(6):575–579

58. Frere P et al (2004) Bacteremia after hematopoietic stem cell transplantation: incidence and predictive value of surveillance cultures. Bone Marrow Transplant 33(7):745–749

59. Mikulska M (2015) How to manage infections caused by antibiotic resistant gram-negative bacteria - EBMT Educational Meeting from the severe aplastic anaemia and infectious diseases working parties, Naples, Italy, 2014. Curr Drug Targets

60. Mikulska M, Del Bono V, Viscoli C (2014) Bacterial infections in hematopoietic stem cell transplantation recipients. Curr Opin Hematol 21(6):451–458

61. Hammond SP, Baden LR (2007) Antibiotic prophylaxis during chemotherapy-induced neutropenia for patients with acute leukemia. Curr Hematol Malig Rep 2(2):97–103

62. Bucaneve G et al (2005) Levofloxacin to prevent bacterial infection in patients with cancer and neutropenia. N Engl J Med 353(10):977–987

63. Gafter-Gvili A et al (2012) Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy. Cochrane Database Syst Rev 1:CD004386

64. Cullen M et al (2005) Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. N Engl J Med 353(10):988–998

65. Leibovici L et al (2006) Antibiotic prophylaxis in neutropenic patients: new evidence, practical decisions. Cancer 107(8):1743–1751

66. Cruciani M et al (2003) Reappraisal with meta-analysis of the addition of Gram-positive prophylaxis to fluoroquinolone in neutropenic patients. J Clin Oncol 21(22):4127–4137

67. Kimura S et al (2014) Antibiotic prophylaxis in hematopoietic stem cell transplantation. A meta-analysis of randomized controlled trials. J Infect 69(1):13–25

68. Roy V, Ochs L, Weisdorf D (1997) Late infections following allogeneic bone marrow transplantation: suggested strategies for prophylaxis. Leuk Lymphoma 26(1–2):1–15

69. Ochs L et al (1995) Late infections after allogeneic bone marrow transplantations: comparison of incidence in related and unrelated donor transplant recipients. Blood 86(10):3979–3986

70. Kulkarni S et al (2000) Chronic graft versus host disease is associated with long-term risk for pneumococcal infections in recipients of bone marrow transplants. Blood 95(12):3683–3686

71. Mitsui H et al (2003) Analysis of sepsis in allogeneic bone marrow transplant recipients: a single-center study. J Infect Chemother 9(3):238–242

72. Taur Y et al (2014) The effects of intestinal tract bacterial diversity on mortality following allogeneic hematopoietic stem cell transplantation. Blood 124(7):1174–1182

73. Taur Y et al (2012) Intestinal domination and the risk of bacteremia in patients undergoing allogeneic hematopoietic stem cell transplantation. Clin Infect Dis 55(7):905–914

74. Shono Y et al (2016) Increased GVHD-related mortality with broad-spectrum antibiotic use after allogeneic hematopoietic stem cell transplantation in human patients and mice. Sci Transl Med 8(339):339ra71

75. De Castro N et al (2005) Occurrence of Pneumocystis jiroveci pneumonia after allogeneic stem cell transplantation: a 6-year retrospective study. Bone Marrow Transplant 36(10):879–883

76. Tuan IZ, Dennison D, Weisdorf DJ (1992) Pneumocystis carinii pneumonitis following bone marrow transplantation. Bone Marrow Transplant 10(3):267–272

77. Williams KM et al (2016) The incidence, mortality and timing of Pneumocystis jiroveci pneumonia after hematopoietic cell transplantation: a CIBMTR analysis. Bone Marrow Transplant 51(4): 573–580

78. Schneider MM et al (1999) Discontinuation of prophylaxis for Pneumocystis carinii pneumonia in HIV-1-infected patients treated with highly active antiretroviral therapy. Lancet 353(9148): 201–203

79. Hughes WT et al (1987) Successful intermittent chemoprophylaxis for Pneumocystis carinii pneumonitis. N Engl J Med 316(26): 1627–1632

80. Hughes WT et al (1977) Successful chemoprophylaxis for Pneumocystis carinii pneumonitis. N Engl J Med 297(26):1419–1426

81. Stein DS et al (1991) Use of low-dose trimethoprim-sulfamethoxazole thrice weekly for primary and secondary prophylaxis of Pneumocystis carinii pneumonia in human immunodeficiency virus-infected patients. Antimicrob Agents Chemother 35(9):1705–1709

82. Stern A et al (2014) Prophylaxis for Pneumocystis pneumonia (PCP) in non-HIV immunocompromised patients. Cochrane Database Syst Rev 10:CD005590

83. Lyytikainen O et al (1996) Late onset Pneumocystis carinii pneumonia following allogeneic bone marrow transplantation. Bone Marrow Transplant 17(6):1057–1059

84. Vasconcelles MJ et al (2000) Aerosolized pentamidine as pneumocystis prophylaxis after bone marrow transplantation is inferior to other regimens and is associated with decreased survival and an increased risk of other infections. Biol Blood Marrow Transplant : J Am Soc Blood Marrow Transplant 6(1):35–43

85. Green H et al (2007) Prophylaxis for Pneumocystis pneumonia (PCP) in non-HIV immunocompromised patients. Cochrane Database Syst Rev 3:CD005590

86. Colby C et al (1999) A prospective randomized trial comparing the toxicity and safety of atovaquone with trimethoprim/sulfamethoxazole as Pneumocystis carinii pneumonia prophylaxis following autologous peripheral blood stem cell transplantation. Bone Marrow Transplant 24(8):897–902

87. Link H et al (1993) Pentamidine aerosol for prophylaxis of Pneumocystis carinii pneumonia after BMT. Bone Marrow Transplant 11(5):403–406

88. Marras TK et al (2002) Aerosolized pentamidine prophylaxis for Pneumocystis carinii pneumonia after allogeneic marrow transplantation. Transpl Infect Dis 4(2):66–74

89. Chan C et al (1999) Atovaquone suspension compared with aerosolized pentamidine for prevention of Pneumocystis carinii pneumonia in human immunodeficiency virus-infected subjects intolerant of trimethoprim or sulfonamides. J Infect Dis 180(2):369–376

90. Souza JP et al (1999) High rates of Pneumocystis carinii pneumonia in allogeneic blood and marrow transplant recipients receiving dapsone prophylaxis. Clin Infect Dis 29(6):1467–1471

91. Tomonari A et al (2008) No occurrence of Pneumocystis jiroveci (carinii) pneumonia in 120 adults undergoing myeloablative unrelated cord blood transplantation. Transpl Infect Dis 10(5):303–307

92. Hughes W et al (1993) Comparison of atovaquone (566C80) with trimethoprim-sulfamethoxazole to treat Pneumocystis carinii pneumonia in patients with AIDS. N Engl J Med 328(21):1521–1527

93. El-Sadr WM et al (1998) Atovaquone compared with dapsone for the prevention of Pneumocystis carinii pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. Community Program for Clinical Research on AIDS and the AIDS Clinical Trials Group. N Engl J Med 339(26):1889–1895

94. Kontoyiannis DP et al (2010) Prospective surveillance for invasive fungal infections in hematopoietic stem cell transplant recipients, 2001–2006: overview of the Transplant-Associated Infection Surveillance Network (TRANSNET) Database. Clin Infect Dis 50(8):1091–1100

95. Martino R et al (2002) Invasive fungal infections after allogeneic peripheral blood stem cell transplantation: incidence and risk factors in 395 patients. Br J Haematol 116(2):475–482

96. Balloy V, Chignard M (2009) The innate immune response to Aspergillus fumigatus. Microbes Infect 11(12):919–927

97. Zhang P et al (2010) Risk factors and prognosis of invasive fungal infections in allogeneic stem cell transplantation recipients: a single-institution experience. Transpl Infect Dis 12(4):316–321

98. Garcia-Vidal C et al (2008) Epidemiology of invasive mold infections in allogeneic stem cell transplant recipients: biological risk factors for infection according to time after transplantation. Clin Infect Dis 47(8):1041–1050

99. Post MJ et al (2007) Invasive fungal infections in allogeneic and autologous stem cell transplant recipients: a single-center study of 166 transplanted patients. Transpl Infect Dis 9(3):189–195

100. Lewis RE et al (2013) Epidemiology and sites of involvement of invasive fungal infections in patients with haematological malignancies: a 20-year autopsy study. Mycoses 56(6):638–645

101. Sinko J et al (2008) Invasive fungal disease in allogeneic hematopoietic stem cell transplant recipients: an autopsy-driven survey. Transpl Infect Dis 10(2):106–109

102. Chamilos G et al (2006) Invasive fungal infections in patients with hematologic malignancies in a tertiary care cancer center: an autopsy study over a 15-year period (1989–2003). Haematologica 91(7):986–989

103. Cordonnier C et al (2006) Prognostic factors for death due to invasive aspergillosis after hematopoietic stem cell transplantation: a 1-year retrospective study of consecutive patients at French transplantation centers. Clin Infect Dis 42(7):955–963

104. Cordonnier C et al (2010) Voriconazole for secondary prophylaxis of invasive fungal infections in allogeneic stem cell transplant recipients: results of the VOSIFI study. Haematologica 95(10):1762–1768

105. Ostrosky-Zeichner L (2004) Prophylaxis and treatment of invasive candidiasis in the intensive care setting. Eur J Clin Microbiol Infect Dis 23(10):739–744

106. Paphitou NI, Ostrosky-Zeichner L, Rex JH (2005) Rules for identifying patients at increased risk for candidal infections in the surgical intensive care unit: approach to developing practical criteria for systematic use in antifungal prophylaxis trials. Med Mycol 43(3):235–243

107. Wenzel RP, Gennings C (2005) Bloodstream infections due to Candida species in the intensive care unit: identifying especially high-risk patients to determine prevention strategies. Clin Infect Dis 41(Suppl 6):S389–S393

108. Ruping MJ et al (2010) Forty-one recent cases of invasive zygomycosis from a global clinical registry. J Antimicrob Chemother 65(2):296–302

109. Neofytos D et al (2009) Epidemiology and outcome of invasive fungal infection in adult hematopoietic stem cell transplant recipients: analysis of Multicenter Prospective Antifungal Therapy (PATH) Alliance registry. Clin Infect Dis 48(3):265–273

110. Cornely OA et al (2015) Safety and pharmacokinetics of isavuconazole as antifungal prophylaxis in acute myeloid leukemia patients with neutropenia: results of a phase 2, dose escalation study. Antimicrob Agents Chemother 59(4):2078–2085

111. Marty FM et al. (2016) Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case–control analysis. Lancet Infect Dis. doi:10.1016/S1473-3099(16)00071-2

112. Maertens JA et al (2016) Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial. Lancet 387(10020):760–769

113. Mousset S et al (2014) Treatment of invasive fungal infections in cancer patients-updated recommendations of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO). Ann Hematol 93(1):13–32

114. Wingard JR et al. (2010) Randomized double-blind trial of fluconazole versus voriconazole for prevention of invasive fungal infection (IFI) after allo hematopoietic cell transplantation (HCT). Blood 116(24):5111–5118

115. Cornely OA et al (2007) Posaconazole vs. fluconazole or itraconazole prophylaxis in patients with neutropenia. N Engl J Med 356(4):348–359

116. Duarte RF et al (2014) Phase 1b study of new posaconazole tablet for prevention of invasive fungal infections in high-risk patients with neutropenia. Antimicrob Agents Chemother 58(10):5758–5765

117. Cornely OA et al. (2016) Phase 3 pharmacokinetics and safety study of a posaconazole tablet formulation in patients at risk for invasive fungal disease. J Antimicrob Chemother 71(6):1747

118. van Burik JA et al (2004) Micafungin versus fluconazole for prophylaxis against invasive fungal infections during neutropenia in patients undergoing hematopoietic stem cell transplantation. Clin Infect Dis 39(10):1407–1416

119. Marr KA (2004) Itraconazole versus fluconazole for prevention of fungal infections in patients receiving allogeneic stem cell transplants. Blood 103(4):1527–1533

120. Glasmacher A et al (1998) Antifungal prophylaxis with itraconazole in neutropenic patients with acute leukaemia. Leukemia 12(9):1338–1343

121. Glasmacher A et al (1999) Breakthrough invasive fungal infections in neutropenic patients after prophylaxis with itraconazole. Mycoses 42(7–8):443–451

122. Goodman JL et al (1992) A controlled trial of fluconazole to prevent fungal infections in patients undergoing bone marrow transplantation. N Engl J Med 326(13):845–851

123. Marr KA et al (2000) Prolonged fluconazole prophylaxis is associated with persistent protection against candidiasis-related death in allogeneic marrow transplant recipients: long-term follow-up of a randomized, placebo-controlled trial. Blood 96(6):2055–2061

124. Slavin MA et al (1995) Efficacy and safety of fluconazole prophylaxis for fungal infections after marrow transplantation—a prospective, randomized, double-blind study. J Infect Dis 171(6):1545–1552

125. Ullmann AJ et al (2007) Posaconazole or fluconazole for prophylaxis in severe graft-versus-host disease. N Engl J Med 356(4):335–347

126. Cordonnier C et al (2004) Secondary antifungal prophylaxis with voriconazole to adhere to scheduled treatment in leukemic patients and stem cell transplant recipients. Bone Marrow Transplant 33(9):943–948

127. de Fabritiis P et al (2007) Efficacy of caspofungin as secondary prophylaxis in patients undergoing allogeneic stem cell transplantation with prior pulmonary and/or systemic fungal infection. Bone Marrow Transplant 40(3):245–249

128. Gupta S et al (2007) Successful treatment of disseminated fusariosis with posaconazole during neutropenia and subsequent allogeneic hematopoietic stem cell transplantation. Transpl Infect Dis 9(2):156–160

129. Wingard JR et al (1999) Clinical significance of nephrotoxicity in patients treated with amphotericin B for suspected or proven aspergillosis. Clin Infect Dis 29(6):1402–1407

130. Bates DW et al (2001) Mortality and costs of acute renal failure associated with amphotericin B therapy. Clin Infect Dis 32(5):686–693

131. Ullmann AJ et al (2006) Prospective study of amphotericin B formulations in immunocompromised patients in 4 European countries. Clin Infect Dis 43(4):e29–e38

132. Penack O et al (2006) Low-dose liposomal amphotericin B in the prevention of invasive fungal infections in patients with prolonged neutropenia: results from a randomized, single-center trial. Ann Oncol 17(8):1306–1312

133. Behre GF et al (1995) Aerosol amphotericin B inhalations for prevention of invasive pulmonary aspergillosis in neutropenic cancer patients. Ann Hematol 71(6):287–291

134. Luu Tran H et al. (2014) Tolerability and outcome of once weekly liposomal amphotericin B for the prevention of invasive fungal infections in hematopoietic stem cell transplant patients with graft-versus-host disease. J Oncol Pharm Pract 22(2):228–234

135. Cornely OA, Ullmann AJ (2011) Lack of evidence for exposure-response relationship in the use of posaconazole as prophylaxis against invasive fungal infections. Clin Pharmacol Ther 89(3):351–352

136. Kawamura K et al (2014) Prophylactic role of long-term ultra-low-dose acyclovir for varicella zoster virus disease after allogeneic hematopoietic stem cell transplantation. Int J Infect Dis 19:26–32

137. Meyers JD, Flournoy N, Thomas ED (1980) Infection with herpes simplex virus and cell-mediated immunity after marrow transplant. J Infect Dis 142(3):338–346

138. Saral R et al (1981) Acyclovir prophylaxis of herpes-simplex-virus infections. N Engl J Med 305(2):63–67

139. Gluckman E et al (1983) Prophylaxis of herpes infections after bone-marrow transplantation by oral acyclovir. Lancet 2(8352):706–708

140. Wade JC et al (1982) Intravenous acyclovir to treat mucocutaneous herpes simplex virus infection after marrow transplantation: a double-blind trial. Ann Intern Med 96(3):265–269

141. Wade JC et al (1984) Oral acyclovir for prevention of herpes simplex virus reactivation after marrow transplantation. Ann Intern Med 100(6):823–828

142. Ljungman P et al (1986) Long-term acyclovir prophylaxis in bone marrow transplant recipients and lymphocyte proliferation responses to herpes virus antigens in vitro. Bone Marrow Transplant 1(2):185–192

143. Sauerbrei A et al (2011) Novel resistance-associated mutations of thymidine kinase and DNA polymerase genes of herpes simplex virus type 1 and type 2. Antivir Ther 16(8):1297–1308

144. McLaren C, Sibrack CD, Barry DW (1982) Spectrum of sensitivity of acyclovir of herpes simplex virus clinical isolates. Am J Med 73(1A):376–379

145. Piret J, Boivin G (2011) Resistance of herpes simplex viruses to nucleoside analogues: mechanisms, prevalence, and management. Antimicrob Agents Chemother 55(2):459–472

146. Mertz GJ et al (1997) Oral famciclovir for suppression of recurrent genital herpes simplex virus infection in women. A multicenter, double-blind, placebo-controlled trial. Collaborative Famciclovir Genital Herpes Research Group. Arch Intern Med 157(3):343–349

147. Tyring SK, Baker D, Snowden W (2002) Valacyclovir for herpes simplex virus infection: long-term safety and sustained efficacy after 20 years' experience with acyclovir. J Infect Dis 186(Suppl 1):S40–S46

148. Garner JS (1996) Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. Infect Control Hospital Epidemiol 17(1):53–80

149. Josephson A, Gombert ME (1988) Airborne transmission of nosocomial varicella from localized zoster. J Infect Dis 158(1):238–241

150. Koc Y et al (2000) Varicella zoster virus infections following allogeneic bone marrow transplantation: frequency, risk factors, and clinical outcome. Biol Blood Marrow Transplant 6(1):44–49

151. Rumke HC et al (2011) Immunogenicity and safety of a measles-mumps-rubella-varicella vaccine following a 4-week or a 12-month interval between two doses. Vaccine 29(22):3842–3849

152. Han CS et al (1994) Varicella zoster infection after bone marrow transplantation: incidence, risk factors and complications. Bone Marrow Transplant 13(3):277–283

153. Locksley RM et al (1985) Infection with varicella-zoster virus after marrow transplantation. J Infect Dis 152(6):1172–1181

154. Weinstock DM, Boeckh M, Sepkowitz KA (2006) Postexposure prophylaxis against varicella zoster virus infection among

hematopoietic stem cell transplant recipients. Biol Blood Marrow Transplant 12(10):1096–1097

155. Zaia JA et al (1983) Evaluation of varicella-zoster immune globulin: protection of immunosuppressed children after household exposure to varicella. J Infect Dis 147(4):737–743

156. Boeckh M et al (2006) Long-term acyclovir for prevention of varicella zoster virus disease after allogeneic hematopoietic cell transplantation—a randomized double-blind placebo-controlled study. Blood 107(5):1800–1805

157. Erard V et al (2007) Use of long-term suppressive acyclovir after hematopoietic stem-cell transplantation: impact on herpes simplex virus (HSV) disease and drug-resistant HSV disease. J Infect Dis 196(2):266–270

158. Thomson KJ et al (2005) The effect of low-dose aciclovir on reactivation of varicella zoster virus after allogeneic haemopoietic stem cell transplantation. Bone Marrow Transplant 35(11):1065–1069

159. Kanda Y et al (2001) Long-term low-dose acyclovir against varicella-zoster virus reactivation after allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant 28(7):689–692

160. Gilbert C, Bestman-Smith J, Boivin G (2002) Resistance of herpesviruses to antiviral drugs: clinical impacts and molecular mechanisms. Drug Resist Updat 5(2):88–114

161. Kroger N et al (2001) Patient cytomegalovirus seropositivity with or without reactivation is the most important prognostic factor for survival and treatment-related mortality in stem cell transplantation from unrelated donors using pretransplant in vivo T-cell depletion with anti-thymocyte globulin. Br J Haematol 113(4):1060–1071

162. Boeckh M, Nichols WG (2004) The impact of cytomegalovirus serostatus of donor and recipient before hematopoietic stem cell transplantation in the era of antiviral prophylaxis and preemptive therapy. Blood 103(6):2003–2008

163. Thiele T et al (2011) Transmission of cytomegalovirus (CMV) infection by leukoreduced blood products not tested for CMV antibodies: a single-center prospective study in high-risk patients undergoing allogeneic hematopoietic stem cell transplantation (CME). Transfusion 51(12):2620–2626

164. Narvios AB et al (2005) Transfusion of leukoreduced cellular blood components from cytomegalovirus-unscreened donors in allogeneic hematopoietic transplant recipients: analysis of 72 recipients. Bone Marrow Transplant 36(6):499–501

165. Kekre N et al (2013) Is cytomegalovirus testing of blood products still needed for hematopoietic stem cell transplant recipients in the era of universal leukoreduction? Biol Blood Marrow Transplant 19(12):1719–1724

166. Bowden RA et al (1991) Use of leukocyte-depleted platelets and cytomegalovirus-seronegative red blood cells for prevention of primary cytomegalovirus infection after marrow transplant. Blood 78(1):246–250

167. Bowden RA et al (1995) A comparison of filtered leukocyte-reduced and cytomegalovirus (CMV) seronegative blood products for the prevention of transfusion-associated CMV infection after marrow transplant. Blood 86(9):3598–3603

168. Miller WJ et al (1991) Prevention of cytomegalovirus infection following bone marrow transplantation: a randomized trial of blood product screening. Bone Marrow Transplant 7(3):227–234

169. De Witte T et al (1990) Prevention of primary cytomegalovirus infection after allogeneic bone marrow transplantation by using leukocyte-poor random blood products from cytomegalovirus-unscreened blood-bank donors. Transplantation 50(6):964–968

170. Narvios AB, Lichtiger B (2001) Bedside leukoreduction of cellular blood components in preventing cytomegalovirus transmission

in allogeneic bone marrow transplant recipients: a retrospective study. Haematologica 86(7):749–752

171. Zaia JA et al (1997) Late cytomegalovirus disease in marrow transplantation is predicted by virus load in plasma. J Infect Dis 176(3):782–785

172. Nagler A et al (1994) Cytomegalovirus pneumonia prior to engraftment following T-cell depleted bone marrow transplantation. Med Oncol 11(3–4):127–132

173. Schmidt-Hieber M et al (2010) Immune reconstitution and cytomegalovirus infection after allogeneic stem cell transplantation: the important impact of in vivo T cell depletion. Int J Hematol 91(5):877–885

174. Einsele H et al (1991) Polymerase chain reaction to evaluate antiviral therapy for cytomegalovirus disease. Lancet 338(8776):1170–1172

175. Li CR et al (1994) Recovery of HLA-restricted cytomegalovirus (CMV)-specific T-cell responses after allogeneic bone marrow transplant: correlation with CMV disease and effect of ganciclovir prophylaxis. Blood 83(7):1971–1979

176. O'Brien S et al (2008) Valganciclovir prevents cytomegalovirus reactivation in patients receiving alemtuzumab-based therapy. Blood 111(4):1816–1819

177. Boeckh M et al (2015) Valganciclovir for the prevention of complications of late cytomegalovirus infection after allogeneic hematopoietic cell transplantation: a randomized trial. Ann Intern Med 162(1):1–10

178. Ruutu T et al (1997) No prevention of cytomegalovirus infection by anti-cytomegalovirus hyperimmune globulin in seronegative bone marrow transplant recipients. the Nordic BMT Group. Bone Marrow Transplant 19(3):233–236

179. Zikos P et al (1998) A randomized trial of high dose polyvalent intravenous immunoglobulin (HDIgG) vs. Cytomegalovirus (CMV) hyperimmune IgG in allogeneic hemopoietic stem cell transplants (HSCT). Haematologica 83(2):132–137

180. Meyers JD et al (1988) Acyclovir for prevention of cytomegalovirus infection and disease after allogeneic marrow transplantation. N Engl J Med 318(2):70–75

181. Winston DJ et al (2003) Randomized comparison of oral valacyclovir and intravenous ganciclovir for prevention of cytomegalovirus disease after allogeneic bone marrow transplantation. Clin Infect Dis 36(6):749–758

182. Ljungman P et al (2002) Randomized study of valacyclovir as prophylaxis against cytomegalovirus reactivation in recipients of allogeneic bone marrow transplants. Blood 99(8):3050–3056

183. Vusirikala M et al (2001) Valacyclovir for the prevention of cytomegalovirus infection after allogeneic stem cell transplantation: a single institution retrospective cohort analysis. Bone Marrow Transplant 28(3):265–270

184. Boeckh M et al (1995) Failure of high-dose acyclovir to prevent cytomegalovirus disease after autologous marrow transplantation. J Infect Dis 172(4):939–943

185. Winston DJ et al (2008) Maribavir prophylaxis for prevention of cytomegalovirus infection in allogeneic stem cell transplant recipients: a multicenter, randomized, double-blind, placebo-controlled, dose-ranging study. Blood 111(11):5403–5410

186. Avery RK et al (2010) Oral maribavir for treatment of refractory or resistant cytomegalovirus infections in transplant recipients. Transplant Infect Dis 12(6):489–496

187. Marty FM et al (2011) Maribavir prophylaxis for prevention of cytomegalovirus disease in recipients of allogeneic stem-cell transplants: a phase 3, double-blind, placebo-controlled, randomised trial. Lancet Infect Dis 11(4):284–292

188. Marty FM et al (2013) CMX001 to prevent cytomegalovirus disease in hematopoietic-cell transplantation. N Engl J Med 369(13):1227–1236

189. Chemaly RF et al (2014) Letermovir for cytomegalovirus prophylaxis in hematopoietic-cell transplantation. N Engl J Med 370(19):1781–1789

190. Kharfan-Dabaja MA et al (2012) A novel therapeutic cytomegalovirus DNA vaccine in allogeneic haemopoietic stem-cell transplantation: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Infect Dis 12(4):290–299

191. Curtis RE et al (1999) Risk of lymphoproliferative disorders after bone marrow transplantation: a multi-institutional study. Blood 94(7):2208–2216

192. Bertz H et al (2009) A novel GVHD-prophylaxis with low-dose alemtuzumab in allogeneic sibling or unrelated donor hematopoetic cell transplantation: the feasibility of deescalation. Biol Blood Marrow Transplant 15(12):1563–1570

193. Oertel SH, Riess H (2002) Antiviral treatment of Epstein-Barr virus-associated lymphoproliferations. Recent Results Cancer Res 159:89–95

194. Davis CL et al (1995) Antiviral prophylaxis and the Epstein Barr virus-related post-transplant lymphoproliferative disorder. Clin Transplant 9(1):53–59

195. Liu Q et al (2013) Molecular monitoring and stepwise preemptive therapy for Epstein-Barr virus viremia after allogeneic stem cell transplantation. Am J Hematol 88(7):550–555

196. Meerbach A et al (2008) Monitoring of Epstein-Barr virus load after hematopoietic stem cell transplantation for early intervention in post-transplant lymphoproliferative disease. J Med Virol 80(3):441–454

197. Gruhn B et al (2003) Pre-emptive therapy with rituximab for prevention of Epstein-Barr virus-associated lymphoproliferative disease after hematopoietic stem cell transplantation. Bone Marrow Transplant 31(11):1023–1025

198. Rooney CM et al (1998) Infusion of cytotoxic T cells for the prevention and treatment of Epstein-Barr virus-induced lymphoma in allogeneic transplant recipients. Blood 92(5):1549–1555

199. Gerdemann U et al (2012) Rapidly generated multivirus-specific cytotoxic T lymphocytes for the prophylaxis and treatment of viral infections. Mol Ther 20(8):1622–1632

200. Yan J et al (2013) Meta-analysis of prevention and treatment of toxoplasmic encephalitis in HIV-infected patients. Acta Trop 127(3):236–244

201. Ruskin J, LaRiviere M (1991) Low-dose co-trimoxazole for prevention of Pneumocystis carinii pneumonia in human immunodeficiency virus disease. Lancet 337(8739):468–471

202. Bretagne S et al (2000) Prospective study of toxoplasma reactivation by polymerase chain reaction in allogeneic stem-cell transplant recipients. Transpl Infect Dis 2(3):127–132

203. Costa JM et al (2001) Quality control for the diagnosis of Toxoplasma gondii reactivation in SCT patients using PCR assays. Bone Marrow Transplant 28(5):527–528

204. Katlama C et al (1996) Pyrimethamine-clindamycin vs. pyrimethamine-sulfadiazine as acute and long-term therapy for toxoplasmic encephalitis in patients with AIDS. Clin Infect Dis 22(2):268–275

205. Podzamczer D et al (1995) Twice-weekly maintenance therapy with sulfadiazine-pyrimethamine to prevent recurrent toxoplasmic encephalitis in patients with AIDS. Spanish Toxoplasmosis Study Group. Ann Intern Med 123(3):175–180

206. Katlama C et al (1996) Atovaquone as long-term suppressive therapy for toxoplasmic encephalitis in patients with AIDS and multiple drug intolerance. Atovaquone Expand Access Group AIDS 10(10):1107–1112

207. Garcia Garrido HM et al. (2015) Response to hepatitis A vaccination in immunocompromised travelers. J Infect Dis 212(3):378–385

208. Yeo W et al (2000) Frequency of hepatitis B virus reactivation in cancer patients undergoing cytotoxic chemotherapy: a prospective study of 626 patients with identification of risk factors. J Med Virol 62(3):299–307

209. Moses SE et al (2006) Lamivudine prophylaxis and treatment of hepatitis B Virus-exposed recipients receiving reduced intensity conditioning hematopoietic stem cell transplants with alemtuzumab. J Med Virol 78(12):1560–1563

210. Locasciulli A et al (2003) Hepatitis reactivation and liver failure in haemopoietic stem cell transplants for hepatitis B virus (HBV)/hepatitis C virus (HCV) positive recipients: a retrospective study by the Italian group for blood and marrow transplantation. Bone Marrow Transplant 31(4):295–300

211. Knoll A et al (2007) Long-term surveillance of haematopoietic stem cell recipients with resolved hepatitis B: high risk of viral reactivation even in a recipient with a vaccinated donor. J Viral Hepat 14(7):478–483

212. Mahale P, Okhuysen PC, Torres HA (2014) Does chemotherapy cause viral relapse in cancer patients with hepatitis C infection successfully treated with antivirals? Clin Gastroenterol Hepatol 12(6):1051–1054, e1

213. Liang TJ, Ghany MG (2014) Therapy of hepatitis C—back to the future. N Engl J Med 370(21):2043–2047

214. (2013) A SPECIAL MEETING REVIEW EDITION: Advances in the Treatment of Hepatitis C Virus Infection From EASL 2013: The 48th Annual Meeting of the European Association for the Study of the LiverApril 24–28, 2013 * Amsterdam, The NetherlandsSpecial Reporting on:* Simeprevir Plus Peginterferon/Ribavirin Is Associated with a High SVR12 Rate in Treatment-Naive Patients with Genotype 1 Hepatitis C Virus Infection* Addition of Simeprevir to Peginterferon/Ribavirin Is Associated with Faster Resolution of Fatigue in Treatment-Naive Patients* Sofosbuvir Plus Ribavirin Demonstrates Significant Efficacy in Multiple HCV Genotype 2/3 Populations* Daclatasvir Plus Sofosbuvir with or without Ribavirin Yields 100% SVR24 Rate in Genotype 1 Patients Who Fail Telaprevir or Boceprevir* Addition of TG4040 Vaccine to Peginterferon/Ribavirin Increases Sustained Virologic Response Rate at 24 Weeks in Genotype 1 Hepatitis C InfectionPLUS Meeting Abstract Summaries With Expert Commentary by: Ira M. Jacobson, MDJoan Sanford I. Weill Medical College at Cornell UniversityNew York, New York. Gastroenterol Hepatol (N Y) 9(6 Suppl 3): 1–18

215. Raboni SM et al (2003) Respiratory tract viral infections in bone marrow transplant patients. Transplantation 76(1):142–146

216. Roghmann M et al (2003) Active surveillance for respiratory virus infections in adults who have undergone bone marrow and peripheral blood stem cell transplantation. Bone Marrow Transplant 32(11):1085–1088

217. Sullivan KM et al. (2001) Preventing opportunistic infections after hematopoietic stem cell transplantation: the Centers for Disease Control and Prevention, Infectious Diseases Society of America, and American Society for Blood and Marrow Transplantation Practice Guidelines and beyond. Hematol Am Soc Hematol Educ Program 392–421

218. Lehners N et al (2013) Risk factors and containment of respiratory syncytial virus outbreak in a hematology and transplant unit. Bone Marrow Transplant 48(12):1548–1553

219. Ariza-Heredia EJ et al (2015) Influenza vaccination in patients with cancer: factors associated with vaccination practices for patients and their household members. Infect Control Hosp Epidemiol 36(10):1239–1241

220. Dykewicz CA (2001) Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: focus on community respiratory virus infections. Biol Blood Marrow Transplant 7(Suppl):19S–22S

221. Cortez K et al (2002) Immune-globulin prophylaxis of respiratory syncytial virus infection in patients undergoing stem-cell transplantation. J Infect Dis 186(6):834–838

222. Robinson P et al (2007) Evidence-based guidelines on the use of intravenous immune globulin for hematologic and neurologic conditions. Transfus Med Rev 21(2 Suppl 1):S3–S8

223. Sullivan KM et al (1990) Immunomodulatory and antimicrobial efficacy of intravenous immunoglobulin in bone marrow transplantation. N Engl J Med 323(11):705–712

224. Winston DJ et al (1987) Intravenous immune globulin for prevention of cytomegalovirus infection and interstitial pneumonia after bone marrow transplantation. Ann Intern Med 106(1):12–18

225. Raanani P et al (2009) Immunoglobulin prophylaxis in hematopoietic stem cell transplantation: systematic review and meta-analysis. J Clin Oncol : Off J Am Soc Clin Oncol 27(5):770–781

226. Raanani P et al (2008) Immunoglobulin prophylaxis in hematological malignancies and hematopoietic stem cell transplantation. Cochrane Database Syst Rev 4:CD006501

227. Cordonnier C et al (2003) Should immunoglobulin therapy be used in allogeneic stem-cell transplantation? A randomized, double-blind, dose effect, placebo-controlled, multicenter trial. Ann Intern Med 139(1):8–18

228. Schmidt-Hieber M et al (2009) Prophylactic i.v. Igs in patients with a high risk for CMV after allo-SCT. Bone Marrow Transplant 44(3):185–192

229. Norlin AC et al (2008) Allogeneic stem cell transplantation: low immunoglobulin levels associated with decreased survival. Bone Marrow Transplant 41(3):267–273

230. Sneller MC et al (1993) NIH conference. New insights into common variable immunodeficiency. Ann Intern Med 118(9):720–730

231. Kerr JP et al (2003) The use of stimulated granulocyte transfusions to prevent recurrence of past severe infections after allogeneic stem cell transplantation. Br J Haematol 123(1):114–118

232. Oza A et al (2006) Granulocyte-colony-stimulating factor-mobilized prophylactic granulocyte transfusions given after allogeneic peripheral blood progenitor cell transplantation result in a modest reduction of febrile days and intravenous antibiotic usage. Transfusion 46(1):14–23

233. EMA (2006) E.M.A., Guideline on clinical evaluation of new vaccines. EMEA/CHMP/VWP/164653/2005

234. Dignani MC et al (2002) Valacyclovir prophylaxis for the prevention of Herpes simplex virus reactivation in recipients of progenitor cells transplantation. Bone Marrow Transplant 29(3):263–267

235. Kim DH et al (2008) Clinical efficacy of prophylactic strategy of long-term low-dose acyclovir for Varicella-Zoster virus infection after allogeneic peripheral blood stem cell transplantation. Clin Transplant 22(6):770–779

236. Erard V et al (2007) One-year acyclovir prophylaxis for preventing varicella-zoster virus disease after hematopoietic cell transplantation: no evidence of rebound varicella-zoster virus disease after drug discontinuation. Blood 110(8):3071–3077

237. Oshima K, et al. (2010) One-year low-dose valacyclovir as prophylaxis for varicella zoster virus disease after allogeneic hematopoietic stem cell transplantation. A prospective study of the Japan Hematology and Oncology Clinical Study Group. Transpl Infect Dis 12(5):421–427

238. Asano-Mori Y et al (2008) Long-term ultra-low-dose acyclovir against varicella-zoster virus reactivation after allogeneic hematopoietic stem cell transplantation. Am J Hematol 83(6):472–476

239. Einsele H et al (1995) Polymerase chain reaction monitoring reduces the incidence of cytomegalovirus disease and the duration and side effects of antiviral therapy after bone marrow transplantation. Blood 86(7):2815–2820

240. Reusser P et al (2002) Randomized multicenter trial of foscarnet versus ganciclovir for preemptive therapy of cytomegalovirus infection after allogeneic stem cell transplantation. Blood 99(4): 1159–1164

241. Einsele H et al (2006) Oral valganciclovir leads to higher exposure to ganciclovir than intravenous ganciclovir in patients following allogeneic stem cell transplantation. Blood 107(7):3002–3008

242. Ayala E et al (2006) Valganciclovir is safe and effective as preemptive therapy for CMV infection in allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant 37(9):851–856

243. Burns LJ et al (2002) Randomized clinical trial of ganciclovir vs acyclovir for prevention of cytomegalovirus antigenemia after allogeneic transplantation. Bone Marrow Transplant 30(12):945–951

244. Verdonck LF et al (1997) A risk-adapted approach with a short course of ganciclovir to prevent cytomegalovirus (CMV) pneumonia in CMV-seropositive recipients of allogeneic bone marrow transplants. Clin Infect Dis 24(5):901–907

245. Micklethwaite K et al (2007) Ex vivo expansion and prophylactic infusion of CMV-pp 65 peptide-specific cytotoxic T-lymphocytes following allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 13(6):707–714

246. Lau GK et al (2002) Preemptive use of lamivudine reduces hepatitis B exacerbation after allogeneic hematopoietic cell transplantation. Hepatology 36(3):702–709

247. Loomba R et al (2008) Systematic review: the effect of preventive lamivudine on hepatitis B reactivation during chemotherapy. Ann Intern Med 148(7):519–528

248. Chang TT et al (2006) A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med 354(10): 1001–1010

249. Tamori A et al (2014) Prospective long-term study of hepatitis B virus reactivation in patients with hematologic malignancy. J Gastroenterol Hepatol 29(9):1715–1721

250. Shang J et al (2016) A comparison of lamivudine vs entecavir for prophylaxis of hepatitis B virus reactivation in allogeneic hematopoietic stem cell transplantation recipients: a single-institutional experience. Bone Marrow Transplant 51(4):581–586

251. Koskinas JS et al (2014) The role of tenofovir in preventing and treating hepatitis B virus (HBV) reactivation in immunosuppressed patients. a real life experience from a tertiary center. Eur J Intern Med 25(8):768–771

252. Leong J et al (2014) Lamivudine resistance leading to de novo hepatitis B infection in recipients of hepatitis B core antibody positive liver allografts. Hepatol Res 44(12):1248–1252

253. Chiba T et al (2003) Successful clearance of hepatitis B virus after allogeneic stem cell transplantation: beneficial combination of adoptive immunity transfer and lamivudine. Eur J Haematol 71(3):220–223

254. Matsue K et al (2009) High risk of hepatitis B-virus reactivation after hematopoietic cell transplantation in hepatitis B core antibody-positive patients. Eur J Haematol 83(4):357–364

255. Foppa CU et al (1991) A retrospective study of primary and maintenance therapy of toxoplasmic encephalitis with oral clindamycin and pyrimethamine. Eur J Clin Microbiol Infect Dis 10(3):187–189

256. Katlama C (1991) Evaluation of the efficacy and safety of clindamycin plus pyrimethamine for induction and maintenance therapy of toxoplasmic encephalitis in AIDS. Eur J Clin Microbiol Infect Dis 10(3):189–191

257. Leport C et al (1989) An open study of the pyrimethamine-clindamycin combination in AIDS patients with brain toxoplasmosis. J Infect Dis 160(3):557–558

258. Cordonnier C et al (2009) Randomized study of early versus late immunization with pneumococcal conjugate vaccine after allogeneic stem cell transplantation. Clin Infect Dis 48(10):1392–1401

259. Seggewiss R, Einsele H (2010) Immune reconstitution after allogeneic transplantation and expanding options for immunomodulation: an update. Blood 115(19):3861–3868

260. Eisenberg RA et al (2013) Rituximab-treated patients have a poor response to influenza vaccination. J Clin Immunol 33(2):388–396

261. Bedognetti D et al (2011) Impaired response to influenza vaccine associated with persistent memory B cell depletion in non-Hodgkin's lymphoma patients treated with rituximab-containing regimens. J Immunol 186(10):6044–6055

262. Berglund A et al (2014) The response to vaccination against influenza A (H1N1) 2009, seasonal influenza and Streptococcus pneumoniae in adult outpatients with ongoing treatment for cancer with and without rituximab. Acta Oncol 53(9):1212–1220

263. Juergens C et al. (2014) Safety and immunogenicity of 13-valent pneumococcal conjugate vaccine formulations with and without aluminum phosphate and comparison of the formulation of choice with 23-valent pneumococcal polysaccharide vaccine in elderly adults: A randomized open-label trial. Hum Vaccin Immunother 10(5)

264. Hata A et al (2002) Use of an inactivated varicella vaccine in recipients of hematopoietic-cell transplants. N Engl J Med 347(1):26–34

265. Burrows SR et al (1997) Cross-reactive memory T cells for Epstein-Barr virus augment the alloresponse to common human leukocyte antigens: degenerate recognition of major histocompatibility complex-bound peptide by T cells and its role in alloreactivity. Eur J Immunol 27(7):1726–1736

266. Dhedin N et al (2014) Comparable humoral response after two doses of adjuvanted influenza A/H1N1pdm2009 vaccine or natural infection in allogeneic stem cell transplant recipients. Vaccine 32(5):585–591

267. Olkinuora H et al (2012) Immunity after (re) vaccination of paediatric patients following haematopoietic stem cell transplantation. Acta Paediatr 101(8):e373–e377

268. Hilgendorf I et al (2011) Vaccination of allogeneic haematopoietic stem cell transplant recipients: report from the international consensus conference on clinical practice in chronic GVHD. Vaccine 29(16):2825–2833

269. Pao M et al (2008) Response to pneumococcal (PNCRM7) and haemophilus influenzae conjugate vaccines (HIB) in pediatric and adult recipients of an allogeneic hematopoietic cell transplantation (alloHCT). Biol Blood Marrow Transplant 14(9):1022–1030

270. Cordonnier C et al (2010) Immune response to the 23-valent polysaccharide pneumococcal vaccine after the 7-valent conjugate vaccine in allogeneic stem cell transplant recipients: results from the EBMT IDWP01 trial. Vaccine 28(15):2730–2734

271. Avetisyan G et al (2008) Evaluation of immune responses to seasonal influenza vaccination in healthy volunteers and in patients after stem cell transplantation. Transplantation 86(2):257–263

272. Ljungman P, Avetisyan G (2008) Influenza vaccination in hematopoietic SCT recipients. Bone Marrow Transplant 42(10):637–641

273. Engelhard D et al (1993) Antibody response to a two-dose regimen of influenza vaccine in allogeneic T cell-depleted and autologous BMT recipients. Bone Marrow Transplant 11(1):1–5

274. Gueller S et al (2011) Enhanced immune response after a second dose of an AS03-adjuvanted H1N1 influenza A vaccine in patients after hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 17(10):1546–1550

275. de Lavallade H et al (2011) Repeated vaccination is required to optimize seroprotection against H1N1 in the immunocompromised host. Haematologica 96(2):307–314

276. Inaba H et al (2012) Longitudinal analysis of antibody response to immunization in paediatric survivors after allogeneic haematopoietic stem cell transplantation. Br J Haematol 156(1):109–117

277. Lambert LC (2014) Pertussis vaccine trials in the 1990s. J Infect Dis 209(Suppl 1):S4–S9

278. Edwards KM, Berbers GA (2014) Immune responses to pertussis vaccines and disease. J Infect Dis 209(Suppl 1):S10–S15

279. Parkkali T et al (1997) A randomized comparison between early and late vaccination with tetanus toxoid vaccine after allogeneic BMT. Bone Marrow Transplant 19(9):933–938

280. Ljungman P et al (1990) Response to tetanus toxoid immunization after allogeneic bone marrow transplantation. J Infect Dis 162(2):496–500

281. Li Volti S 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(2):225–227

282. Dengler TJ et al (1999) Vaccination against tick-borne encephalitis under therapeutic immunosuppression. Reduced efficacy in heart transplant recipients. Vaccine 17(7–8):867–874

283. Ljungman P, Duraj V, Magnius L (1991) Response to immunization against polio after allogeneic marrow transplantation. Bone Marrow Transplant 7(2):89–93

284. Parkkali T et al (1996) Loss of protective immunity to polio, diphtheria and Haemophilus influenzae type b after allogeneic bone marrow transplantation. APMIS 104(5):383–388

285. Engelhard D et al (1991) Immune response to polio vaccination in bone marrow transplant recipients. Bone Marrow Transplant 8(4):295–300

286. Parkkali T et al (1997) Randomized comparison of early and late vaccination with inactivated poliovirus vaccine after allogeneic BMT. Bone Marrow Transplant 20(8):663–668

287. Ljungman P et al (2004) Long-term immunity to poliovirus after vaccination of allogeneic stem cell transplant recipients. Bone Marrow Transplant 34(12):1067–1069

288. Parkkali T et al (2007) A randomized study on donor immunization with tetanus-diphtheria, Haemophilus influenzae type b and inactivated poliovirus vaccines to improve the recipient responses to the same vaccines after allogeneic bone marrow transplantation. Bone Marrow Transplant 39(3):179–188

289. Barra A et al (1992) Immunogenicity of Haemophilus influenzae type b conjugate vaccine in allogeneic bone marrow recipients. J Infect Dis 166(5):1021–1028

290. Guinan EC et al (1994) Polysaccharide conjugate vaccine responses in bone marrow transplant patients. Transplantation 57(5):677–684

291. Parkkali T et al (1996) A comparison of early and late vaccination with Haemophilus influenzae type b conjugate and pneumococcal polysaccharide vaccines after allogeneic BMT. Bone Marrow Transplant 18(5):961–967

292. Vance E et al (1998) Comparison of multiple immunization schedules for Haemophilus influenzae type b-conjugate and tetanus toxoid vaccines following bone marrow transplantation. Bone Marrow Transplant 22(8):735–741

293. van Wessel K et al (2011) Nontypeable Haemophilus influenzae invasive disease in The Netherlands: a retrospective surveillance study 2001–2008. Clin Infect Dis 53(1):e1–e7

294. Kalies H et al (2009) Invasive Haemophilus influenzae infections in Germany: impact of non-type b serotypes in the post-vaccine era. BMC Infect Dis 9:45

295. Patel SR et al (2007) Revaccination with measles, tetanus, poliovirus, Haemophilus influenzae type B, meningococcus C, and pneumococcus vaccines in children after hematopoietic stem cell transplantation. Clin Infect Dis 44(5):625–634

296. Jacobsson S et al (2008) Characteristics of Neisseria meningitidis isolates causing fatal disease. Scand J Infect Dis 40(9):734–744

297. Poolman JT et al (1986) Meningococcal serotypes and serogroup B disease in north-west Europe. Lancet 2(8506):555–558

298. Onozawa M et al (2008) HB vaccination in the prevention of viral reactivation in allogeneic hematopoietic stem cell transplantation recipients with previous HBV infection. Biol Blood Marrow Transplant 14(11):1226–1230

299. Jaffe D et al (2006) Immunogenicity of recombinant hepatitis B vaccine (rHBV) in recipients of unrelated or related allogeneic hematopoietic cell (HC) transplants. Blood 108(7):2470–2475

300. Idilman R et al (2003) Hepatitis B virus vaccination of recipients and donors of allogeneic peripheral blood stem cell transplantation. Clin Transplant 17(5):438–443

301. Ljungman P et al (1989) Efficacy and safety of vaccination of marrow transplant recipients with a live attenuated measles, mumps, and rubella vaccine. J Infect Dis 159(4):610–615

302. Spoulou V et al (2004) Long-term immunity to measles, mumps and rubella after MMR vaccination among children with bone marrow transplants. Bone Marrow Transplant 33(12):1187–1190

303. King SM et al (1996) Response to measles, mumps and rubella vaccine in paediatric bone marrow transplant recipients. Bone Marrow Transplant 17(4):633–636

304. Sauerbrei A et al (1997) Varicella vaccination in children after bone marrow transplantation. Bone Marrow Transplant 20(5):381–383

305. Issa NC et al (2014) Live attenuated varicella-zoster vaccine in hematopoietic stem cell transplantation recipients. Biol Blood Marrow Transplant 20(2):285–287

306. Kussmaul SC et al (2010) Safety of the live, attenuated varicella vaccine in pediatric recipients of hematopoietic SCTs. Bone Marrow Transplant 45(11):1602–1606

307. Aoki T et al (2016) Safety of live attenuated high-titer varicella-zoster virus vaccine in pediatric allogeneic hematopoietic stem cell transplantation recipients. Biol Blood Marrow Transplant 22(4):771–775

308. Cordonnier C et al (2015) 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 61(3):313–323

309. Begue PC et al (1998) Comparative reactogenicity and immunogenicity of booster doses of diphtheria-tetanus-acellular pertussis-inactivated poliovirus vaccine and diphtheria-tetanus-inactivated poliovirus vaccine in preadolescents. Pediatr Infect Dis J 17(9):804–809

310. Meerveld-Eggink A et al (2009) Antibody response to polysaccharide conjugate vaccines after nonmyeloablative allogeneic stem cell transplantation. Biol Blood Marrow Transplant 15(12):1523–1530

311. Townsend K et al. (2014) Evaluation and validation of a serum bactericidal antibody assay for Haemophilus influenzae type b and the threshold of protection. Vaccine 32(43):5650–5656

312. Pinson JB, Weart CW (1992) New considerations for Haemophilus influenzae type b vaccination. Clin Pharm 11(4):332–336

313. Centers for Disease, C. and Prevention (2011) Licensure of a meningococcal conjugate vaccine for children aged 2 through 10 years and updated booster dose guidance for adolescents and other persons at increased risk for meningococcal disease–Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 60(30):1018–1019

314. Toneatto D et al (2011) Early clinical experience with a candidate meningococcal B recombinant vaccine (rMenB) in healthy adults. Hum Vaccin 7(7):781–791

315. Mahler MB et al (2012) Safety and immunogenicity of the tetravalent protein-conjugated meningococcal vaccine (MCV4) in recipients of related and unrelated allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 18(1):145–149

316. Beran J, Xie F, Zent O (2014) Five year follow-up after a first booster vaccination against tick-borne encephalitis following different primary vaccination schedules demonstrates long-term antibody persistence and safety. Vaccine 32(34):4275–4280

317. McMahon BJ et al (2009) Antibody levels and protection after hepatitis B vaccine: results of a 22-year follow-up study and response to a booster dose. J Infect Dis 200(9):1390–1396

318. Tung J et al (2010) A randomized clinical trial of immunization with combined hepatitis A and B versus hepatitis B alone for hepatitis B seroprotection in hemodialysis patients. Am J Kidney Dis 56(4):713–719

319. Kim HN et al (2009) Hepatitis B vaccination in HIV-infected adults: current evidence, recommendations and practical considerations. Int J STD AIDS 20(9):595–600

320. Li Volti S et al (1997) Immune status and the immune response to hepatitis B virus vaccine in thalassemic patients after allogeneic bone marrow transplantation. Bone Marrow Transplant 19(2):157–160

321. Fahlgren K (1988) Two doses of MMR vaccine–sufficient to eradicate measles, mumps and rubella? Scand J Soc Med 16(3):129–135

322. American Academy of Pediatrics Committee on Infectious Diseases (1997) Immunization of adolescents: recommendations of the advisory committee on immunization practices, the american academy of pediatrics, the american academy of family physicians, and the american medical association. Pediatrics 99(3):479–488

323. Nader S et al (1995) Age-related differences in cell-mediated immunity to varicella-zoster virus among children and adults immunized with live attenuated varicella vaccine. J Infect Dis 171(1):13–17