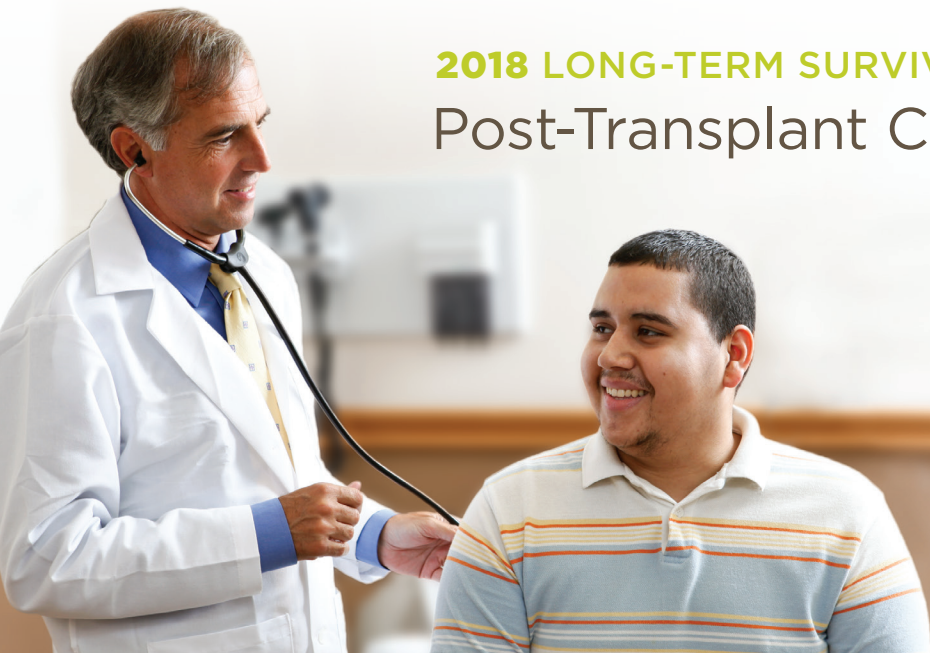




2018 LONG-TERM SURVIVAL GUIDELINES

Post-Transplant Care Recommendations



SCREENING • IMMUNIZATION • GVHD



[BeTheMatchClinical.org](https://www.BetheMatchClinical.org)

Recommended post-transplant care

After your patient leaves the transplant center and returns to your care, your support is critical to his or her long-term recovery and survival. This three-part guide contains post-transplant care guidelines developed in partnership with leading transplant organizations and based on peer-reviewed publications.

Part I: Long-term screening

Includes a list of recommended post-transplant screening and preventive practices.

Consult this section at a patient's six-month, one-year and annual appointments.

Patient-friendly version available at BeTheMatchClinical.org/guidelines.

Part II: Vaccinations

Provides a recommended vaccination schedule.

Consult this prior to a patient's six-month appointment and as needed at future appointments.

Part III: Screening for chronic GVHD

Identifies clinical manifestations and symptoms of chronic graft-versus-host disease (GVHD) and includes photo atlas.

Consult this section when chronic GVHD is suspected or to review the full range of chronic GVHD manifestations.



IN THE APP

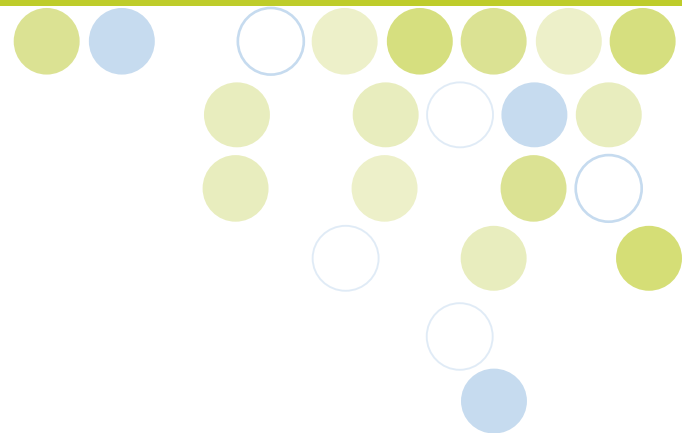
Create and email custom checklists of tests and procedures

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PART I: LONG-TERM SCREENING







Part I: Long-term screening

Recognizing complications early, while there are more therapeutic options and while treatments are more effective, is critical to the well-being of transplant recipients.

Complications from hematopoietic cell transplantation (HCT) can develop long after a patient leaves a transplant center and returns to a primary physician. Use these guidelines to deliver the specialized care transplant patients need to prevent late complications and to reduce morbidity.

These long-term screening guidelines are based on ***Recommended Screening and Preventive Practices***, developed by experts from seven international transplant professional societies.¹

1. Majhail NS, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation; Center for International Blood and Marrow Transplant Research (CIBMTR), American Society for Blood and Marrow Transplantation (ASBMT), European Group for Blood and Marrow Transplantation (EBMT), Asia-Pacific Blood and Marrow Transplantation Group (APBMT), Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ), East Mediterranean Blood and Marrow Transplantation Group (EMBMT) and Sociedade Brasileira de Transplante de Medula Ossea (SBTMO). Co-published in *Biol Blood Marrow Transplant*, 2012; 18(3): 348-371; *Bone Marrow Transplant*, 2012 47(3): 337-341; and *Hematol Oncol Stem Cell Ther*, 2012; 5(1): 1-30.

Use the following chart to:

- Become aware of the specialized care transplant recipients need
- Plan for tests and treatments
- Trigger discussions with patients on proper self-care



Patient version

We offer a version of these long-term screening guidelines using patient-friendly language. Your patients can use this version to understand and prepare for their 6-month and annual follow-up care appointments.

Available through the Transplant Guidelines mobile app, online and in print.

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IN THE APP

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Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Immune system	Complications: - Infections Tests: - CMV antigen or PCR testing in patients at high risk for CMV reactivation - Radiologic studies (e.g., chest X-ray, CT scan) - Immunoglobulin levels, T-cell subset tests	All HCT recipients			
		Pneumocystis pneumonia (PCP) prophylaxis for initial 6 months after HCT	✓		
		Immunizations post-transplant according to published guidelines (see Part II: Vaccinations)	✓	✓	✓
		Administration of antibiotics for endocarditis prophylaxis according to American Heart Association guidelines Visit http://circ.ahajournals.org/content/116/15/1736.full.pdf	✓	✓	✓
		Additional measures for special populations*			
		Antimicrobial prophylaxis targeting encapsulated organisms for the duration of immunosuppressive therapy	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids
		Antimicrobial prophylaxis targeting PCP for the duration of immunosuppressive therapy	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids
		Screening for CMV in patients at high risk for CMV reactivation	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids

Key:

✓ = recommended preventative measures

+ = Assessment recommended for patients with pre-existing conditions, if clinically indicated, if abnormal testing in a previous time period, or with new signs/symptoms

*Special populations = GVHD (patients with GVHD), Steroids (patients with ongoing significant corticosteroid exposure), Pediatric (pediatric patients), TBI (patients who have received total body irradiation)

Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Ocular	Complications: • Cataracts • Microvascular retinopathy • Sicca syndrome Tests: • Ophthalmologic exam	All HCT recipients			
		Routine ocular clinical symptom evaluation; prompt ophthalmologic examination in patients with visual symptoms	✓	✓	✓
		Ophthalmologic examination with measurement of visual acuity and fundus examination		✓	+
		Additional measures for special populations*			
		Routine clinical evaluation, and if indicated, ophthalmologic examination more frequently	✓ GVHD	✓ GVHD	✓ GVHD
Oral	Complications: • Sicca syndrome • Caries • Periodontal disease • Oral cancer Tests: • Dental assessment	All HCT recipients			
		Clinical oral assessment with particular attention to intra-oral malignancy evaluation	✓	✓	✓
		Check for history of xerostomia and high-risk habits and provide education about preventive oral health practices	✓	✓	✓
		Dental assessment. Perform a thorough oral, head and neck and dental exam		✓	✓
		Additional measures for special populations*			
		Assessment of teeth development		✓ Pediatric	✓ Pediatric
		Consider more frequent oral and dental assessments with particular attention to intra-oral malignancy evaluation	✓ GVHD	✓ GVHD	✓ GVHD

Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Respiratory	Complications: • Idiopathic pneumonia syndrome • Bronchiolitis obliterans syndrome • Cryptogenic organizing pneumonia • Sino-pulmonary infections Tests: • Pulmonary function testing (PFT) • Radiologic studies (e.g., chest X-ray, CT scan)	All HCT recipients			
		Routine clinical pulmonary evaluation	✓	✓	✓
		Assessment of tobacco use and counseling against smoking	✓	✓	✓
		PFT and focused radiologic assessment as clinically indicated for patients with symptoms or signs of lung compromise	✓	✓	✓
		Additional measures for special populations*			
		Some experts recommend earlier and more frequent clinical evaluation and PFTs	✓ GVHD	✓ GVHD	✓ GVHD

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Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Cardiac and vascular	Complications: • Cardiomyopathy • Congestive heart failure • Arrhythmias • Coronary artery disease • Valvular anomaly • Cerebrovascular disease • Peripheral arterial disease Tests: • Cumulative dose of anthracyclines • Echocardiogram with ventricular function, ECG in patients at risk and in symptomatic patients • Fasting blood sugar • Fasting lipid profile (including HDL-C, LDL-C and triglycerides)	All HCT recipients			
		Routine clinical assessment of cardiovascular risk factors		✓	✓
		Education and counseling on “heart healthy” lifestyle (regular exercise, healthy weight, no smoking, dietary counseling) Visit uspreventiveservicestaskforce.org	✓	✓	✓
		Early treatment of cardiovascular risk factors such as diabetes, hypertension and dyslipidemia	✓	✓	✓
		Administration of antibiotics for endocarditis prophylaxis according to American Heart Association guidelines Visit http://circ.ahajournals.org/content/116/15/1736.full.pdf	✓	✓	✓

Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Liver	Complications: • GVHD • Hepatitis B • Hepatitis C • Iron overload Tests: • Liver function testing (LFT) • Polymerase Chain Reaction (PCR) for hepatitis B or C • Liver biopsy • Serum ferritin • Imaging for iron overload (MRI or SQUID)	All HCT recipients			
		LFTs; may be performed more frequently as clinically indicated	✓	✓	✓
		Monitor viral load by PCR for patients with known hepatitis B or C, with liver and infectious disease specialist consultation. Consider liver biopsy at 8-10 years after HCT to assess cirrhosis in patients with chronic HCV infection	+	+	+
		Serum ferritin for patients who have received RBC transfusions; consider liver biopsy or imaging study for abnormal results based on magnitude of elevation and clinical context; subsequent monitoring is suggested for patients with elevated LFTs, continued RBC transfusions, or presence of HCV infection		+	+
Renal and genitourinary	Complications: • Chronic kidney disease (CKD) • Bladder dysfunction • Urinary tract infections Tests: • Urine protein • Serum creatinine • BUN	All HCT recipients			
		Blood pressure assessment with aggressive hypertension management	✓	✓	✓
		Assess renal function with serum creatinine, BUN and urine protein. Further workup (kidney biopsy or renal ultrasound) for renal dysfunction as clinically indicated	✓	✓	✓
		Avoid nephrotoxins and consider early referral to a nephrologist for evaluation and treatment in patients with progressive CKD	✓	✓	✓

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Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Muscle and connective tissue	Complications: • Myopathy • Fasciitis/scleroderma • Polymyositis Tests: • Evaluate ability to stand from a sitting position • Clinical evaluation of joint range of motion	All HCT recipients			
		Physical activity counseling. Follow general population guidelines for physical activity	✓	✓	✓
		Additional measures for special populations*			
		Frequent clinical evaluation for myopathy by manual muscle tests or by assessing ability to go from sitting to standing position	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids
		Evaluate joint range of motion to detect sclerotic changes. Patients should also be instructed to perform self-assessment of range of motion	✓ GVHD	✓ GVHD	✓ GVHD
Mucocutaneous	Complications: • Cutaneous sclerosis • Genital GVHD Tests: • Skin exam • Pelvic exam	All HCT recipients			
		Counsel patients to perform routine self-exam of skin and avoid excessive exposure to sunlight without adequate protection	✓	✓	✓
		Annual gynecologic exam in women		✓	✓
		Additional measures for special populations*			
		Consider more frequent gynecologic evaluation based on clinical symptoms	✓ GVHD ✓ TBI	✓ GVHD ✓ TBI	✓ GVHD ✓ TBI

Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Skeletal	Complications: • Osteopenia/osteoporosis • Avascular necrosis Tests: • Dual photon densitometry • MRI	All HCT recipients			
		Dual photon densitometry for adult women, all allogeneic HCT recipients and patients who are at high risk for bone loss (e.g., prolonged corticosteroid exposure); subsequent testing determined by defects or to assess response to therapy		✓	+
		Counseling about physical activity, vitamin D and calcium supplementation to prevent loss of bone density	✓	✓	✓
		Additional measures for special populations*			
		Consider dual photon densitometry at an earlier date in patients with prolonged corticosteroid or calcineurin inhibitor exposure	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	+ GVHD + Steroids
Nervous system	Complications: • Leukoencephalopathy • Neuropsychological and cognitive deficits • Late infections • Calcineurin neurotoxicity • Peripheral neuropathy Tests: • MRI • Neuropsychological testing	All HCT recipients			
		Clinical evaluation for symptoms and signs of neurologic dysfunction. Diagnostic testing (e.g., radiographs, nerve conduction studies) for those with symptoms or signs	+	✓	✓
		Evaluate for changes in cognitive function, which may be subtle in adults	+	✓	✓
		Additional measures for special populations*			
		Assessment for cognitive development milestones		✓ Pediatric	✓ Pediatric

Key:

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*Special populations = GVHD (patients with GVHD), Steroids (patients with ongoing significant corticosteroid exposure), Pediatric (pediatric patients), TBI (patients who have received total body irradiation)

Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Endocrine	Complications: • Hypothyroidism • Hypoadrenalism • Hypogonadism • Growth retardation Tests: • Thyroid function tests • FSH, LH, testosterone • Growth velocity in children	All HCT recipients			
		Thyroid function testing — additional testing if relevant symptoms develop		✓	✓
		Clinical and endocrinologic gonadal assessment for post-pubertal women, subsequent follow-up based on menopausal status		✓	+
		Gonadal function in men, including FSH, LH, and testosterone, should be assessed as warranted by symptoms		+	+
		Additional measures for special populations*			
		Clinical and endocrinologic gonadal assessment for pre-pubertal boys and girls within 1 year of transplant, with further follow-up as determined in consultation with a pediatric endocrinologist	✓ Pediatric	✓ Pediatric	✓ Pediatric
		Monitor growth velocity in children; assessment of thyroid, and growth hormone function if clinically indicated		✓ Pediatric	✓ Pediatric
		Consider stress doses of corticosteroids during acute illness for patients who have received chronic corticosteroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids
		Slow terminal tapering of corticosteroids for those with prolonged exposure	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids	✓ GVHD ✓ Steroids

Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Second cancers	Complications: • Solid tumors • Hematologic malignancies • Post-transplant lymphoproliferative disorder (PTLD) Tests: • Mammogram • Screening for colon cancer (e.g., colonoscopy, sigmoidoscopy, fecal occult blood testing) • Pap smear	All HCT recipients			
		Counsel patients about risks of secondary malignancies and encourage them to perform self-exam (e.g., skin, testicles/genitalia) and counsel to avoid high-risk behaviors (e.g., smoking)		✓	✓
		Screen for second cancers — follow general population recommendations for cancer screening		✓	✓
		Additional measures for special populations*			
		Clinical and dental evaluation with particular attention toward oral and pharyngeal cancer	✓ GVHD	✓ GVHD	✓ GVHD
		Screening mammography in women starting at age 25 or 8 years after radiation exposure, whichever occurs later but no later than age 40	✓ Women with exposure to TBI/chest irradiation		

Key:

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Tissues/Organs	Complications and Tests	Preventive Measures	Recommended Timing		
			6 mo.	12 mo.	Annually
Psychosocial and sexual	Complications: - Depression - Anxiety - Fatigue - Sexual dysfunction Tests: - Psychological evaluation	All HCT recipients			
		Clinical assessment throughout recovery period, with mental health professional counseling recommended for those with recognized symptoms	✓	✓	✓
		Regularly assess level of spousal/caregiver psychological adjustment and family functioning. Encourage robust support networks	✓	✓	✓
		Query adults about sexual function	✓	✓	✓
Fertility	Complications: - Infertility Tests: - FSH, LH levels	All HCT recipients			
		Consider referral to appropriate specialists for patients who are contemplating a pregnancy or are having difficulty conceiving		+	+
		Sexual function assessment. Counsel sexually active patients in the reproductive age group about birth control post-HCT	✓	✓	✓
General health		All HCT recipients			
		Recommended screening as per general population: hypertension, hypercholesterolemia, diabetes, depression, sexually transmitted diseases, osteoporosis (in women), cancer screening. For details visit uspreventiveservicestaskforce.org	✓	✓	✓

Key:

✓ = recommended preventive measures

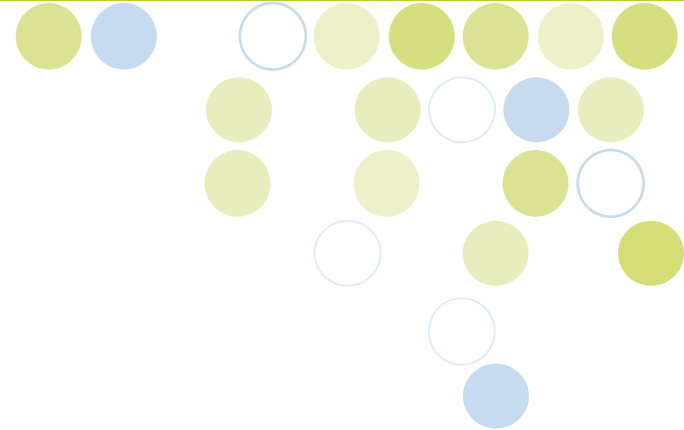
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PART II: VACCINATIONS



Part II: Vaccinations





Part II: Vaccinations

Routine administration of vaccinations is vital for prevention of infectious complications in transplant recipients.

Transplant recipients may remain immunocompromised far beyond 2 years post-transplant, especially individuals with chronic GVHD. Therefore, patients should be routinely revaccinated after transplant until they regain immune competence.

This vaccination schedule¹ is based on international consensus guidelines^{2,3} for preventing infectious complications among all transplant recipients and is recommended for both autologous and allogeneic HCT recipients.

1. Majhail NS, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation; Center for International Blood and Marrow Transplant Research (CIBMTR), American Society for Blood and Marrow Transplantation (ASBMT), European Group for Blood and Marrow Transplantation (EBMT), Asia-Pacific Blood and Marrow Transplantation Group (APBMT), Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ), East Mediterranean Blood and Marrow Transplantation Group (EMBT) and Sociedade Brasileira de Transplante de Medula Ossea (SBTMO). Co-published in *Biol Blood Marrow Transplant*, 2012; 18(3): 348-371; *Bone Marrow Transplant*, 2012 47(3): 337-341; and *Hematol Oncol Stem Cell Ther*, 2012; 5(1): 1-30.
2. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009; 15: 1143-1238.
3. Ljungman P, Cordonnier C, Einsele H, et al. Vaccination of hematopoietic cell transplant recipients. *Bone Marrow Transplant*. 2009; 44: 521-526.

Use the chart on the following page to:

- Become aware of the vaccinations transplant recipients need
- Plan for administration of vaccines

This information is also accessible
through the *Transplant Guidelines* app.
Visit [BeTheMatchClinical.org/guidelines](https://www.bethematchclinical.org/guidelines)

Vaccine	Recommended for use after HCT	Time post-HCT to initiate vaccine	No. of doses ^a
Pneumococcal conjugate (PCV)	Yes	3-6 months	3-4 ^b
Tetanus, diphtheria, acellular pertussis ^c	Yes	6-12 months	3 ^d
<i>Haemophilus influenzae</i> conjugate	Yes	6-12 months	3
Meningococcal conjugate	Follow country recommendations for general population	6-12 months	1
Inactivated polio	Yes	6-12 months	3
Recombinant hepatitis B	Follow country recommendations for general population	6-12 months	3
Inactivated influenza	Yearly	4-6 months	1-2 ^e
Measles-mumps-rubella (live) ^{f,g}	Measles: All children and seronegative adults	24 months	1-2 ^h

See references on previous page for vaccinations considered optional or not recommended for HCT recipients and for vaccinations for family, close contacts and health care workers.

^a A uniform specific interval between doses cannot be recommended, as various intervals have been used in studies. As a general guideline, a minimum of 1 month between doses may be reasonable.

^b Following the primary series of three PCV doses, a dose of the 23-valent polysaccharide pneumococcal vaccine (PPSV23) to broaden the immune response might be given. For patients with chronic GVHD who are likely to respond poorly to PPSV23, a fourth dose of the PCV should be considered instead of PPSV23.

^c DTaP (diphtheria tetanus pertussis vaccine) is preferred, however, if only Tdap (tetanus toxoid-reduced diphtheria-toxoid reduced acellular pertussis vaccine) is available (for example, because DTaP is not licensed for adults), administer Tdap. Acellular pertussis vaccine is preferred, but the whole-cell pertussis vaccine should be used if it is the only pertussis vaccine available.

^d See references on previous page for consideration of an additional dose(s) of Tdap for older children and adults.

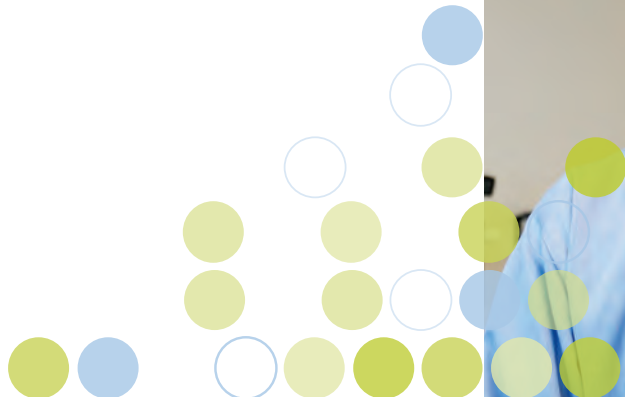
^e For children <9 years of age, two doses are recommended yearly between transplant and 9 years of age.

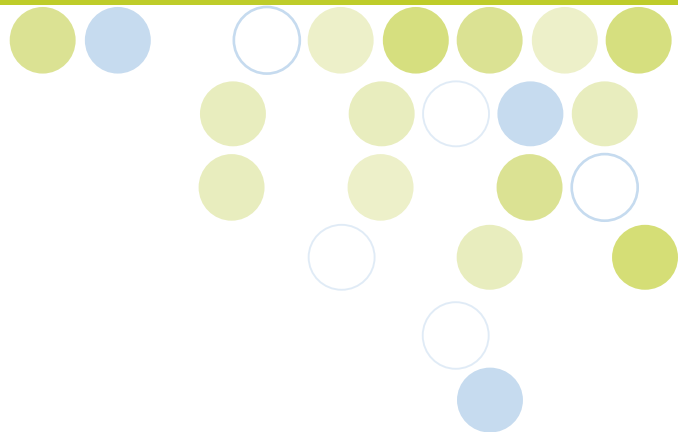
^f Measles, mumps and rubella vaccines are usually given together as a combination vaccine. In females with pregnancy potential, vaccination with rubella vaccine either as a single or a combination vaccine is indicated.

^g Not recommended <24 months post-HCT, in patients with active GVHD, and in patients on immune suppression.

^h In children, two doses are favored.

PART III: SCREENING FOR CHRONIC GVHD







Part III: Screening for chronic GVHD

Early detection of chronic graft-versus-host disease (GVHD) can help prevent irreversible organ damage and increase the quality of life of your transplant recipient.

Chronic GVHD, an immune response of the donor-derived T cells against recipient tissues, occurs in approximately 30–70% of patients receiving an allogeneic transplant. This is a serious, potentially life-threatening post-transplant complication. Uncontrolled chronic GVHD is associated with increased non-relapse mortality, significant morbidity and lower health-related quality of life. However, with ongoing surveillance, judicious management and multidisciplinary care, most cases of chronic GVHD resolve within 5 years and the median duration of treatment is 2–3 years.

GVHD that is characterized by red rash, diarrhea, and elevated liver tests, and that usually starts before

day 100, is called *acute* GVHD. When people develop GVHD symptoms in their mouth, eyes, skin or other organs, it is called *chronic* GVHD. When symptoms appear, the treatment recommendation is: ***Collaborate with the transplant center to confirm the diagnosis and develop a treatment plan.***

The following guidelines are based on published diagnostic criteria from the National Institutes of Health (NIH) Consensus Development Project on Chronic GVHD^{1,2,3} (see references on page 22).

Use the following chart to:

- Identify clinical manifestations that are potential early indicators of chronic GVHD
- Trigger prompt clinical action if GVHD is suspected

If GVHD is suspected, it is recommended that you ***collaborate with the patient's transplant center to confirm the diagnosis and to develop a treatment plan.*** Your early detection and actions to manage chronic GVHD can help minimize permanent damage and improve the quality of life of your transplant recipient.

Important care principles

- Early detection and definitive diagnosis are essential for successful treatment
- Definitive diagnosis of chronic GVHD requires excluding other diagnoses such as infection, drug effects, malignancies and residual post-inflammatory damage and scarring
- Involvement of a multidisciplinary team is essential
- Both topical and/or systemic treatment may be appropriate
- Infection prophylaxis and prompt and effective management of infections are crucial; infection is a leading cause of death in chronic GVHD
- Long-term follow-up is required to monitor for late sequelae



IN THE APP

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Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Skin (continued from previous page)	Patient-reported symptoms and signs • Itching • Dry skin • Limited mobility • Rash • Sores • Changes in skin coloring or texture • Edema Clinical examination • Complete visual examination of the skin with particular attention to pigmentary changes, rashes, textural changes, tightness, areas of thickening or skin breakdown, ulcers or erosions • Palpation for areas of sclerosis or fasciitis Diagnostic testing • Skin biopsy	Sweat impairment**	May manifest as heat intolerance due to loss of sweat glands	
		Ichthyosis**	Rough, thick and scaly skin	
		Hypopigmentation**	Diminished pigmentation of the skin	8
		Hyperpigmentation**	Darkening of the skin due to pigment deposition	4, 7, 8
		Keratosis pilaris**	Pale to erythematous perifollicular papules with spiny keratotic plugs within the follicular openings	3
		Maculopapular rash***	Raised and flat small, red lesions	12
		Erythema***	Abnormal redness of the skin	
		Pruritus***	Localized or generalized itching	
		Erosion ³	Localized skin lesion characterized by complete or partial loss of only the epidermis	11
		Ulcer ³	Localized skin lesion in which the whole of the epidermis and at least part of the dermis has been lost. May extend into the subcutaneous fat	

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Nails	Patient-reported symptoms and signs • Brittle nails • Increased ridging in nails • Splitting nails • Nail loss Clinical examination • Visual inspection of nails Diagnostic testing None	Dystrophy*	Longitudinal ridging, splitting or brittleness	13
		Onycholysis*	Loosening of a nail from the nail bed beginning at the free edge and proceeding to the root	
		Nail loss*	Usually symmetric; affects most nails	
		Pterygium unguis*	Forward growth of the cuticle over the nail	
Scalp/body hair	Patient-reported symptoms and signs • Premature gray or thinning hair • Itchy scalp • Hair loss Clinical examination • Visual inspection of scalp hair/body hair for changes in hair distribution, consistency and color Diagnostic testing None	New onset of scarring or non-scarring scalp alopecia*	After initial recovery following chemotherapy or radiotherapy	14
		Loss of body hair*		
		Scaling*	An eruption composed of papules and scales	
		Thinning scalp hair**	Typically patchy, coarse or dull (not explained by endocrine or other causes)	
		Premature gray hair**		

* Distinctive but insufficient alone to establish an unequivocal diagnosis of chronic GVHD without further testing or additional organ involvement.

** Rare, controversial, or non-specific features of chronic GVHD.

*** Common in both acute and chronic GVHD.

³ See references on page 22.

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Eyes	Patient-reported symptoms and signs • Dry, burning, gritty eyes • Itching • Orbital pain • Difficulty opening eyes in the morning • Sensitivity to light and wind • Excessive tearing • Diminished visual acuity and/or blurring Clinical examination • Visual inspection of the conjunctivae and sclerae • Ophthalmologic exam Diagnostic testing • Schirmer's tear test • Slit-lamp examination	New onset dry, gritty or painful eyes*	New ocular sicca documented by low Schirmer's test values with a mean value of both eyes ≤ 5 mm of wetting at 5 minutes, but note that Schirmer's test values are not useful for follow-up of ocular GVHD due to poor correlation with symptom change	
		Cicatricial conjunctivitis*	Fibrous tissue scarring and inflammation	
		Keratoconjunctivitis sicca (KCS)*	Inflammation of cornea and conjunctivae, with dryness, grittiness and/or orbital pain. Slit lamp exam with mean Schirmer's test values of 6 to 10 mm, not due to other causes	22, 23
		Confluent areas of punctate keratopathy*	Closely spaced, non-inflamed pinpoint defects indicating loss of corneal epithelium, and observed with fluorescein staining	
		Photophobia**	Increased sensitivity to light	
		Periorbital hyperpigmentation**	Excess pigmentation in the tissues surrounding or lining the orbit of the eye	
		Blepharitis**	Erythema and edema of the eyelids and telangiectasia of lid margin	24

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Mouth	Patient-reported symptoms and signs • Dryness • Chapped lips • Ulcers • Swelling, redness, pain and/or bleeding of gums • Sensitivity to spicy foods, toothpaste or soda pop • Pain Clinical examination • Visual inspection of the entire mouth Diagnostic testing • Oral biopsy	Lichen planus-like changes	Hyperkeratotic white lines and lacy-appearing lesions on the buccal mucosa and tongue, palate or lips	16
		Xerostomia*	Abnormal dryness of the mouth	
		Mucocele*	Vesicle-like or raised masses due to minor salivary gland inflammation and damage	17
		Mucosal atrophy*	Thinning of mucosal tissue	19
		Pseudomembranes*	Loosely adherent fibrinous exudate on the surface of a mucous membrane	20
		Ulcers*	Open sore inside mouth caused by a break in mucous membrane or epithelium on lips or surrounding mouth	20, 21
		Erythema***	Severity of erythema or “redness” can vary from mild to severe	17, 18, 19, 20
		Gingivitis***	Mucosal fiber damage causes smooth/inflamed gingival surface, in contrast to the dimpled or stippled appearance of normal gingivae. Entire width of the attached gingivae will be erythematous	
		Mucositis***	Inflammation of mucous membrane	
		Pain***		

* Distinctive but insufficient alone to establish an unequivocal diagnosis of chronic GVHD without further testing or additional organ involvement.

** Rare, controversial, or non-specific features of chronic GVHD.

*** Common in both acute and chronic GVHD.

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Lungs	Patient-reported symptoms and signs • Difficulty breathing • Wheezing • Shortness of breath at rest and/or with exertion • Dry cough Clinical examination • Chest auscultation • Pulse oximetry Diagnostic testing • Pulmonary function testing (PFT) • Expiratory CT • Lung biopsy	Bronchiolitis obliterans diagnosed using PFT	Obstructive lung defect. May include dyspnea on exertion, cough, or wheezing	
		Air trapping and bronchiectasis on chest CT*	Evidence of air trapping on expiratory CT, small airway thickening	
		Cryptogenic organizing pneumonia**	Inflammation of the bronchioles and surrounding tissue in the lungs	

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Muscles, fascia, joints	Patient-reported symptoms and signs • Muscle cramps • Muscle pain • Muscle weakness • Joint stiffness • Restricted range of motion • Tightened muscles, tendons and fascia • Contractures Clinical examination • Palpation for areas of thickening, tightening, shortening of muscles or fascia; muscle tenderness • Evaluate range of motion • Muscle strength testing • Inspection for signs of edema or peau d'orange skin changes • Visual inspection for grooving, ridging Diagnostic testing • Creatinine kinase • Aldolase • Electromyography	Fasciitis	Stiffness, restricted range of motion	9
		Joint stiffness or contractures (secondary to fasciitis or sclerosis)	Groove sign, dimpling	
		Myositis or polymyositis*	Muscle tenderness and elevated muscle enzymes. Evaluate with electromyography and measurement of creatinine phosphokinase and aldolase. Muscle/sural nerve biopsies should be considered in the absence of other manifestations of GVHD to rule out other causes of myositis	
		Edema**	Present in extremities, with or without erythema and peau d'orange skin	15
		Muscle cramps**	May be present with increased muscle enzymes	
		Arthralgia or arthritis**	Uncommon, occasionally associated with the presence of autoantibodies	

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** Rare, controversial, or non-specific features of chronic GVHD.

*** Common in both acute and chronic GVHD.

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
GI tract	Patient-reported symptoms and signs • Anorexia • Nausea • Vomiting • Abdominal pain • Diarrhea • Bloating • Cramping • Weight loss • Painful swallowing • Difficulty swallowing dry foods/pills Clinical examination • Examination of mouth and hypopharynx Diagnostic testing • Endoscopy • Barium contrast radiograph • Swallowing study • Stool test for fecal fat • Biopsy • Amylase • Lipase	Esophageal web	Smooth, circumferential ring of squamous mucosa; documented by endoscopy or barium contrast radiograph	
		Upper esophageal strictures or stenosis	Narrowing of the upper to mid third of the esophagus; documented by endoscopy or barium contrast radiograph	
		Pancreatic exocrine insufficiency**	Pancreatic atrophy and exocrine insufficiency leading to inability to properly digest food due to a lack of digestive enzymes; often improves with enzyme supplementation	
		Anorexia***		
		Nausea***		
		Vomiting***		
		Diarrhea***		
		Weight loss***		
		Failure to thrive (infants and children)***		

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Liver	Patient-reported symptoms and signs • Jaundice • Malaise • Itching • Fatigue Clinical examination • Assess for hepatomegaly and right upper quadrant abdominal tenderness Diagnostic testing • Total and direct bilirubin • Alkaline phosphatase • ALT: Alanine aminotransferase • AST: Aspartate aminotransferase • GGT: Gamma glutamyl transpeptidase • 5'-NT: 5' Nucleotidase • Liver biopsy may be needed in the absence of GVHD in another organ	Hepatitis***	Rise in serum alanine aminotransferase, > 2x upper limit of normal, with or without jaundice	
		Progressive cholestatic features***	The flow of bile from the liver is blocked; total bilirubin, alkaline phosphatase > 2x upper limit of normal; elevated gamma-glutamyl transpeptidase, followed by jaundice	

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*** Common in both acute and chronic GVHD.

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Genitalia	Patient-reported symptoms and signs • Itching • Painful intercourse • Dryness • Painful urination • Burning Clinical examination • Visual inspection of genitalia • Pelvic exam Diagnostic testing • Biopsy	Lichen planus-like features	Erythematous/violaceous tissue changes	
		Lichen sclerosus-like features	White, atrophic papules that may coalesce into plaques	
		Females: Vaginal scarring or clitoral/labial agglutination	A narrowing of the vagina, often with accompanying tissue changes such as dryness, loss of elasticity and resilience, adhesion and scar tissue	
		Males: Phimosis or urethral/meatus scarring or stenosis		
		Fissures*	A break or slit in tissue typically appearing at the junction of skin and mucous membrane	
		Erosions*	Localized destruction or loss of the epidermis	
		Ulcers*	Localized destruction or loss below the epidermis	

Organ/Sites	Evaluation	Clinical Manifestation	Description of Clinical Manifestation	Photo Atlas
Hematopoietic/ immune	Patient-reported symptoms and signs None	Thrombocytopenia**	Persistent decrease in the number of blood platelets; <100,000/ μ L	
	Clinical examination None	Eosinophilia**	Abnormal increase in the number of eosinophils; >500/ μ L	
	Diagnostic testing • Complete blood count and differential • Test for presence of autoantibodies • Quantitative immunoglobulin levels	Lymphopenia**	Reduction in the number of lymphocytes; <500/ μ L	
		Hypo- or hyper-gammaglobulinemia**	Deficiency or excess of gamma globulins in the peripheral blood	
		Autoantibodies**	Autoimmune hemolytic anemia (AIHA). Idiopathic thrombocytopenic purpura (ITP). Autoantibodies may develop, including antinuclear antibody, anti-centromere antibody, anti-mitochondrial antibody, anti-ENA screen, anti-double stranded DNA antibody, anticardiolipin antibody	
Other	For these manifestations, chronic GVHD is often a diagnosis of exclusion	Raynaud's phenomenon**	Disruption of blood flow to digits and skin	
		Pericardial or pleural effusions** Ascites** Peripheral neuropathy** Nephrotic syndrome** Myasthenia gravis** Cardiac conduction abnormality or cardiomyopathy**	Although these manifestations cannot be used to establish a diagnosis of chronic GVHD, a wide range of organ system manifestations including neurologic complications, nephrotic syndrome and cardiac abnormalities have been described in association with cGVHD and may represent cGVHD manifestations. If after careful differential diagnosis no alternative etiologic factor is identified, it may be concluded that these manifestations represent chronic GVHD disease activity.	

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** Rare, controversial, or non-specific features of chronic GVHD.

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Chronic GVHD Photo Atlas

This photo atlas contains pictorial representations of various clinical manifestations of chronic GVHD. Refer to the information in the preceding chart for a full description of all manifestations.



1. Poikiloderma

Hypo- and hyper-pigmentary changes with erythema and atrophy.

See Chart page 3



2. Morphea-like

Localized patchy area(s) of moveable smooth or shiny skin with a leather-like waxy or hardened consistency. Note the fibrotic, hypopigmented area in the center of the plaque with a slightly hyperpigmented border.

See Chart page 3



3. Keratosis pilaris

Skin-colored to erythematous perifollicular papules with spiny keratotic plugs within the follicular openings.

See Chart page 4



4. Lichen planus-like

Hyperpigmented/purple papules which may coalesce into annular (ring-like) small plaques. These lesions closely resemble the dermatologic disease lichen planus.

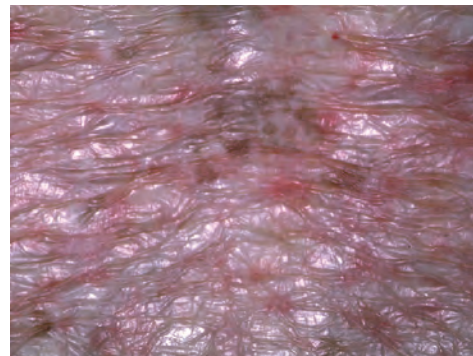
See Chart page 3, 4



5. Lichen planus-like

Discrete to coalescent gray to white moveable papules or plaques.

See Chart page 3



6. Lichen sclerosus-like

Close-up showing wrinkled texture and shiny appearance. Lesions tend to be grouped in discrete patches.

See Chart page 3



7. Hyperpigmentation

Excess pigmentation in the skin; may manifest in a widespread reticulated pattern.

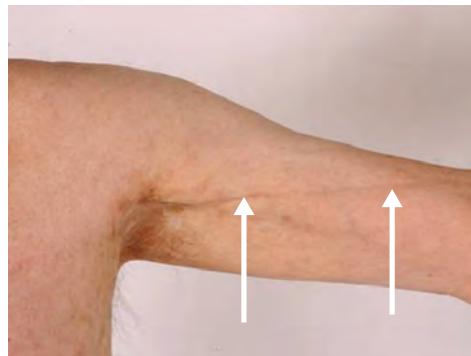
See Chart page 4



8. Hypopigmentation, hyperpigmentation, depigmentation, sclerosis

Diminished (hypo-) or excess (hyper-) pigmentation in the skin. Sclerotic tissue is hard and fibrous, with a decreased ability to pinch. Superficial sclerosis is moveable upon palpation, while deep sclerosis is hidebound and fixed.

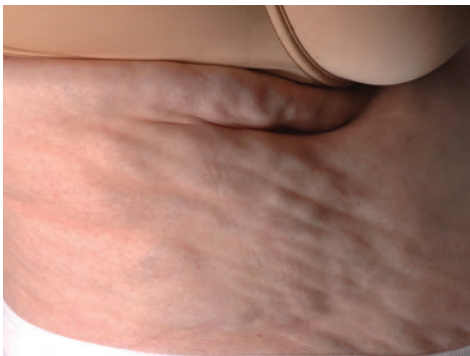
See Chart page 3, 4



9. Sclerosis, fasciitis

Subcutaneous sclerosis/fasciitis can be detected by a "groove sign" seen here.

See Chart page 3, 9



10. Sclerosis

Subcutaneous sclerosis can be manifested by rippling, dimpling of the skin and a resultant cellulite-like appearance.

See Chart page 3



11. Erosion

Localized tissue destruction characterized by complete or partial loss of only the epidermis.

See Chart page 4



12. Maculopapular

Raised and flat small, red lesions.

See Chart page 4



13. Nail dystrophy

Longitudinal ridging, splitting, or brittle features of nails. Note periungual erythema.

See Chart page 5



14. Alopecia

Patchy alopecia is shown. May also include loss of body hair (after initial recovery of hair growth following chemotherapy or radiotherapy).

See Chart page 5



15. Edema

Edema in the extremities can be bilateral or unilateral (shown). May be present with erythema and peau d'orange skin. Edema may be associated as prodromal symptom to subcutaneous sclerosis and fasciitis.

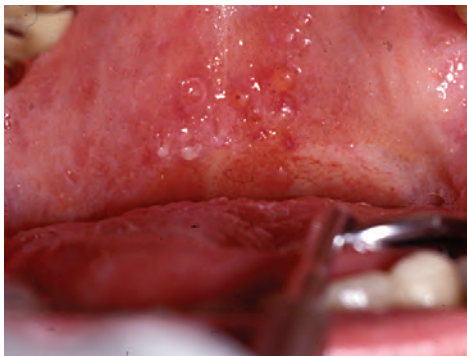
See Chart page 9



16. Lichen planus

Lichenoid changes extending from the labial mucosa to the lip. Cheilosis (surface scaling and fissures in the corners of the mouth) is also present.

See Chart page 7



17. Mucocoeles

Numerous vesicle-like mucocoeles are seen along the center of the soft palate. Patchy white lichenoid hyperkeratosis and interspersed moderate erythematous changes are also evident across soft palate.

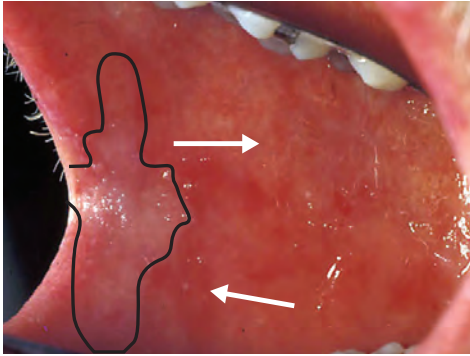
See Chart page 7



18. Erythema

Chapping and erythema of the vermilion lip. Erythema of labial mucosa.

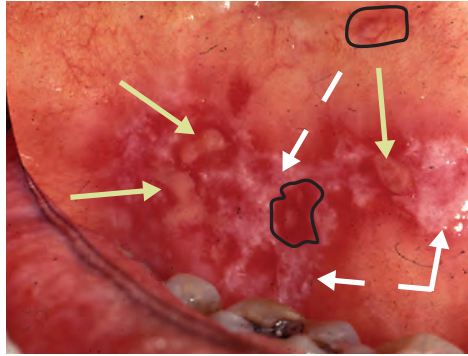
See Chart page 7



19. Erythema, hyperkeratinization

Patchy erythema (arrows) and sheet-like hyperkeratinization (black outline). Also note atrophy of buccal mucosal tissues.

See Chart page 7



20. Erythema, ulcerations, hyperkeratinization

Mixed pseudomembranous fibrin exudate (light green arrows). Lichenoid hyperkeratotic changes (white arrows) involving the buccal mucosa. Erythema (black outline) surrounding pseudomembranous ulcerations.

See Chart page 7



21. Ulcerations

White patchy pseudomembranous ulcerations.
See Chart page 7



22. Keratoconjunctivitis sicca

Inadequate tear production (measured by Schirmer's test) and conjunctival erythema. Also note scleral injection and chemosis (conjunctival edema).

See Chart page 6



23. Keratoconjunctivitis sicca

Note scleral injection and conjunctival erythema.

See Chart page 6



24. Blepharitis

Thickened, edematous and erythematous eyelid margins. Also note plugging of meibomian gland orifices (along the eyelid margin) and significant conjunctival hyperemia/injection.

See Chart page 6

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References:

¹Jagasia MH, Greinix HT, Arora M, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Response Criteria Working Group Report. *Biol Blood Marrow Transplant*. 2015; 21(3): 389-401.

²Lee SJ, Wolff D, Kitko C, et al. Measuring therapeutic response in chronic graft-versus-host disease. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: IV. The 2014 Response Criteria Working Group Report. *Biol Blood Marrow Transplant*. 2015; 21(6): 984-999.

³These guidelines have been developed by the National Marrow Donor Program® (NMDP)/Be The Match® in consultation with Sandra A. Mitchell, CRNP, MScN, AOCN; National Institutes of Health Clinical Center; and Steven Z. Pavletic, M.D.; National Cancer Institute, National Institutes of Health, Bethesda, Md. The information in this document does not represent the official position of the NIH or the U.S. Government.

Additional review from:

Dennis L. Confer, M.D., NMDP/Be The Match, Minneapolis, Minn.

Linda J. Burns, M.D., NMDP/Be The Match, Minneapolis, Minn.

Madan Jagasia, M.D., Vanderbilt University Medical Center, Nashville, Tenn.

Stephanie J. Lee, M.D., Fred Hutchinson Cancer Research Center, Seattle, Wash.

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