Memorial Sloan Kettering Cancer Center

PEDIATRIC
STEM CELL AND CELLULAR THERAPY PROGRAM

Created Date: 2019	**Acute Graft Versus Host Disease (AGvHD) Guidelines**	

1. **PURPOSE**
   The purpose of this guideline is to educate regarding early recognition and treatment of hematopoietic stem cell transplant (HCT) patients with suspected Acute Graft-Versus-Host Disease (aGvHD) as well as to standardize the management of patients with aGvHD.
2. **SCOPE**
   This guideline focuses on recognition and treatment of skin, GI and hepatic aGvHD.
3. **GUIDANCE**
   1. **OVERVIEW**
      aGvHD is a common complication of allogeneic HCT that classically presents in the early post-transplantation period. It is thought to be primarily a T-cell mediated disease that occurs when the immune cells transplanted from a donor graft recognize the host as foreign, thereby initiating an immune reaction that causes disease in the transplant recipient. The classic target organs are skin, gastrointestinal tract (AKA “gut”, “GI”) and liver.

      Patients should receive education about aGvHD, including that it may be untreatable and can therefore be life-threatening. Patients and parents should also be aware that acute GVHD is a major risk factor for subsequently developing chronic GvHD. Explain precautions for immunosuppressant medications and sunlight sensitivity.

      All patients undergoing allogeneic transplant require some form of prophylaxis for GvHD (See separate GvHD prophylaxis guidelines). Prophylaxis of GvHD can be done in several ways:
      a. Use of combinational immunosuppressive agents to suppress the capacity of donor T-cells to proliferate and function
      b. ex-vivo or in-vivo T-cell depletion
   2. **RISK FACTORS**
      In addition to unrelated transplantation and HLA mismatch:
      a. Inflamed/compromised bowel (e.g. pre-transplant infection or autoimmune enteropathy),
      b. Infectious enteritis may delay reduction of immunosuppression due to higher risk of aGvHD
      c. Engraftment syndrome requiring systemic therapy increases risk for moderate to severe GVHD

      Patients who develop Grade 2-4 acute GvHD in the absence of CD4 reconstitution (CD4 ≥50 x 10^6/L) have inferior overall survival and increased non-relapse mortality and should be considered for more aggressive management.

3. **SCREENING**

   Patients are evaluated for the presence of signs or symptoms of GvHD at each encounter. Features of GvHD and Staging and Grading (see below) should be captured in weekly GvHD assessment notes until Day +100 post HCT and in consensus notes at Day+100, 180 and 365.

   Patients with diarrhea should have volumes and consistency quantified to the extent possible. Use Bristol Stool Chart (see appendix II) for clinical stool classification. Half (50%) of the total volume will be estimated to be stool volume in instances where volumes of mixed stool and urine are recorded. If unable to quantify stool volume, each episode of diarrhea (in adults or patients >50kg) will be estimated to be a volume of 200 mL or 3 mL/kg for children < 50 Kg. If there is a more accurate estimate of volume based on some stools being measurable, that volume can be used and documented in the GvHD assessment note.

4. **DIAGNOSIS**
   1. GvHD is a clinical diagnosis. The presence of GVHD symptoms without an alternative etiology and/or patient treated for GvHD regardless of biopsy result will be classified as GvHD. Biopsy can support the clinical diagnosis and is preferred – particularly of the gastrointestinal tract – but is not mandatory. Negative GvHD diagnosis requires confirmation of an alternative diagnosis, unequivocally negative laboratory/pathologic evidence and/or disappearance of symptoms in the absence of GvHD treatment.
   2. Prior to initiation of systemic steroids patients should have blood drawn for GvHD biomarkers including **Reg3a** (order: Regenerating Islet-Derived 3-alpha), **HGF** (order: Hepatocyte Growth Factor), **ST2**, **Elafin**.
      1. Calculation and Interpretation of the MAP (MAGIC Algorithm Probability)
         MAP = -11.63 + 1.844*(log ST2) + 0.577*(log Reg3a)
         MAP < 0.141 vs 0.141 – 0.290 vs > 0.290 at baseline predicts NRM
   3. Prior to initiation of systemic steroids patients should have blood drawn for immune reconstitution if not performed within 10 days for standard of care monitoring.
   4. Histologic grade does not correlate with clinical grade or severity.

5. **DIFFERENTIAL DIAGNOSIS**

   Broadly the differential diagnosis in each organ includes infection, toxicity and drug reactions. Evaluation to assess the etiology can include risk assessment, biomarkers, biopsies, and therapeutic trials, but ultimately GvHD is frequently a clinical diagnosis.
   1. **Skin:**

      Drug reaction, infectious causes (bacterial, viral, yeast / fungi). Consideration should be made for early biopsy. Medical photography should be employed to document rash at baseline.

      Skin Biopsy: Perform when unclear about diagnosis and starting systemic therapy if possible. A 4mm punch biopsy should be obtained at the site with most confluent or pronounced rash. Should also be assessed for evaluation by confocal microscopy.
   2. **Gastrointestinal and Hepatic GVHD**
      1. **GI considerations**

         Stool should be sent for fecal occult blood, calprotectin, Clostridium difficile PCR, GI PCR panel and adenovirus PCR. Biopsy confirmation of gut GVHD is preferred whenever safe and feasible. Upper endoscopy for patients with upper GI symptoms, and upper endoscopy and flexible sigmoidoscopy/ colonoscopy or rectal biopsy for patients with lower GI symptoms. (B.

Thomson et al, BMT 2006). For patients with symptoms/signs concerning for isolated upper GI GVHD, a biopsy should be obtained for evaluation before initiation of treatment in the absence of a clear contraindication for endoscopy.

2. **Liver considerations**
   Isolated hepatic GvHD is a rare presentation and biopsy is recommended when isolated liver GvHD is suspected. Patients with GvHD with concomitant hepatic abnormalities should be assessed for the possibility of hepatic GvHD as well as other causes of cholestasis as well as infectious causes of hepatitis and medication related injury. A complete hepatic panel including GGTP, fractionated bilirubin and lipase should be evaluated. An abdominal USG or HIDA scan for evaluation of biliary disease and/or SOS

Upper-gut GVHD	**Lower-gut GVHD**	**Liver GVHD**		
		Early jaundice	**Cholestatic**	**Hepatitis**
Nauseating medications	Residual effects of conditioning therapy (<day 20): depending on regimen	Cholangitis	Cholangitis lenta (infection-related jaundice from IL-6, TNF-α)	virai infection (HBV, HCV)
Residual effects of conditioning therapy (<day 20)	Viral infection (CMV > adenovirus > astrovirus, norovirus, rotavirus)	Parenteral feeding	Biliary obstruction (sludge, stones, tumor)	Other viral infections (adenovirus > herpesviruses)
Herpesvirus infections	Bacterial infection (Clostridium difficile > Clostridium septicum)	Drug-induced liver inury http://www.dilin.org/	Drug induced liver injury	Drug induced liver injury
Helicobacter pylori infection	Parasitic infection (Giardia lamblia,	(Residual effects of) SOS (if < 30 days)		Hypoxic hepatitis (SOS, respiratory

with ulcers	cryptosporidium)			failure, shock)
Increased intracranial pressure	Medication effects (Mg++, MMF, brincidofovir (if used >2wks), anticholinergics, μ-agonist opioids)			

(requires doppler) should be performed. PCRs for viral hepatitis should be sent.

Confidence Levels				
	Pathologic evidence	**Clinician assessment**	**Treatment for acute GVHD**	**Comments**
Confirmed	Unequivocal pathologic evidence of GVHD	GVHD is the etiology for symptoms	Not applicable	GVHD is clearly present even if other etiologies may co-exist simultaneously
Probable	Not required	GVHD most likely etiology for symptoms (as evidenced by treatment being provided)	Yes	GVHD is most likely present but other etiologies may also explain the symptoms and there insufficient evidence to make a confirmed diagnosis
Possible	Not required	GVHD in differential diagnosis (but no treatment is being provided)	No	GVHD may be present, but other etiologies are favored to the degree that GVHD treatment is not initiated

Negative	Unequivocal evidence of a diagnosis other than GVHD (e.g., drug rash)	GVHD is not considered as an explanation for the symptoms	No **and** the symptoms resolve without GVHD treatment	A "negative" biopsy (e.g., normal skin) is not unequivocal evidence of a diagnosis other than GVHD

6. **Stagi g**

In patients that develop aGvHD, individual organs are assigned a stage and then these are combined to assign an overall grade of aGvHD. There are several staging/grading systems. For purposes of reporting to the CIBMTR we use the Przepiorka system. For clinical trials and clinical care, we will use the MAGIC criteria (AC Harris et al, Biol Blood Marrow Transplant 2016) unless otherwise specified by a trial protocol. **Downgrading for competing etiologies is not recommended, and the decision to downgrade based on other explanations for an individual organ system disorder should be documented in the GvHD assessment note.**

1. **Staging**
    1. Skin Use "Rule of Nines" to determine extent of rash. (Appendix V).
    2. Liver Use serum total bilirubin
    3. Upper GI Use presence of nausea/vomiting/anorexia. Upper GI GVHD should not be considered a possible etiology when nausea lasts fewer than 3 days, patients experience fewer than 2 vomiting episodes per day, or anorexia is not accompanied by weight loss.
    4. Lower GI Use volume of diarrhea or presence of Stage 4 signs/symptoms. At onset, the highest one-day volume of stool in the preceding three days should be used instead. For subsequent staging, use stool volume based upon stool volume using (in the order of preference): (1) average of 3 consecutive days, (2) average of 2 consecutive days, (3) volume on the day of assessment.

Biopsy Results and Confidence Levels					
Pathology Results	Target Organ Confidence Level			Other Symptomatic Organ Confidence Level(s)	
	Treated as GVHD	Not treated but GVHD in differential diagnosis	Not treated and GVHD not in differential diagnosis	Treated as GVHD (including systemic GVHD therapy)	Not treated but GVHD in differential diagnosis
Positive	**Confirmed**			**Probable**	
Equivocal	Probable	**Possible**		**Probable**	**Possible**
Non-Diagnostic	**Probable**	**Possible**	**Negative**	**Probable**	**Possible**

Non-GVHD Etiology	**Probable**	**Negative**	**Probable**	**Possible**

GVHD confirmed in a biopsied target organ raises the confidence level from possible to probable for other target organs where GVHD is suspected, even in the absence of treatment.

	Skin (active erythema only)	**Liver (Total Bilirubin)**	**Upper GI**	**Lower GI (stool output/day)***
0	No rash	<2 mg/dL	No or intermittent nausea, vomiting or anorexia	Adult (≥50kg): <500 mL/day or <3 episodes/day Child (50kg): <10 ml/kg/day or <4 episodes/day
1	Maculaopapular Rash <25% of BSA	2-3 mg/dL	Persistent nausea, vomiting or anorexia	Adult: 500–999 ml/day or 3-4 episodes/day Child: 10 -19.9 ml/kg/day or 4-6 episodes/day
2	Maculopapular Rash 25-50% of BSA	3.1-6.0 mg/dL		Adult: 1000-1500 ml/day or 5-7 episodes/day Child: 20 – 30 ml/kg/day or 7-10 episodes/day
3	Generalized rash or erythroderma (>50% of BSA)	6.1-15 mg/dL		Adult: >1500 ml/day or >7 episodes/day Child: > 30 ml/kg/day or >10 episodes/day
4	Generalized erythroderma (>50% BSA) with bullae and/or desquamation >5% BSA	>15 mg/dL		Severe abdominal pain with or without ileus, or grossly bloody stool (regardless of stool volume).

* If stool volume is not quantified each episode of diarrhea should be assigned an estimated volume.
>50kg adults 200mL
<50kg ~ 3mL/kg or if better estimate is available based on some stools being measured

2. Grading
Use highest grade based on organ staging.

Organ	Stage	Przepiorka Grade*	MAGIC Criteria
Skin	1	1	1
	2	1	1
	3	2	2
	4	4	4
Upper GI	1	2	2
GI (lower)	1	2	2
	2	3	3
	3	3	3
	4	3	4
Liver	1	2	2
	2	3	3
	3	3	3
	4	4	4

*Used for CIBMTR reporting

7. NEWLY DIAGNOSED GvHD
    1. See section 3.4 for baseline labs including immune monitoring and biomarkers.
    2. BMT GvHD Order set:
       Please note that the “BMT GvHD Order set” includes consultations, medications and supportive care, but does not include handling of biopsy specimens.
    3. Newly Diagnosed aGvHD:
       Patients who have a new aGvHD diagnosis should be evaluated for enrollment on study:
       17-468 Pilot Study for the Collection and Evaluation of Biomarkers for the Prognostication of Transplant-Related Mortality and Graft-versus-Host Disease Risk after Allogeneic Stem Cell Transplantation
8. TREATMENT
    1. In the event of strong clinical suspicion, treatment should not be delayed while awaiting tissue diagnosis as a longer interval between onset of symptoms and start of treatment can negatively impact outcome.

• ****Always evaluate availability/eligibility for clinical trials** (See Appendix IIIA)** • In the absence of available/eligible clinic trial, treatment is as follows (also see Appendix IIIB):	
• Optimize prophylactic CNI – Cyclosporine 250-350 or Tacrolimus 8-12	
• Isolated skin Grade 1-2	Topical steroids
• Isolated skin Grade ≥3 or Overall Grade ≥2	Systemic steroids

• Most patients start systemic steroids at	2 mg/kg methylprednisolone or equivalent (e.g. 2.5 mg/kg prednisone)
• Consider basing dose on adjusted weight if weight is >125% over ideal body weight.	
• See Appendix VI for all steroid taper schedules	

2. If patient is not eligible for a clinical trial the general approach for 1st line treatment:
3. Treatment of Isolated skin aGVHD:
    1. Stage I: If patient has little or no discomfort, consider observation
    2. Patients with skin-only disease (Stage 1-2)
       Can receive a trial of topical steroids at the discretion of the treating attending prior to initiation of systemic treatment. Corticosteroid ointment (Corticosteroid potency class 3 for affected areas of body/hands/feet/scalp and class 5-6 for face/neck/folds) twice daily, until rash is gone.
    3. Isolated skin Stage ≥3:
       Methylprednisolone 2 mg/kg/day or equivalent (PO/IV) divided in 2 doses. For stage 3 isolated skin and/or stage 1 upper GI GVHD requiring systemic steroids due to progression on topical therapy, consider starting methylprednisolone 1 mg/kg/day (or equivalent).
    4. See below and Appendix IV for skin GvHD topical treatments

Treatment of skin aGvHD

Skin Stage	Treatment	Comment
Stage 1-2	Topical corticosteroids	Select agent based on BSA and area affected
Stage 3	Methylprednisolone/equivalent 1-2 mg/kg + high potency topical corticosteroids + optimize/start CNI (see trough levels above)	Can receive a trial of topical steroids or use concurrently. If widespread and patient has no history of +ANA or photosensitivity, consider narrowband ultraviolet B (NBUVB) phototherapy 3 times/week.
Stage 4	Methylprednisolone/equivalent 2 mg/kg + high potency topical corticosteroids + optimize/start CNI (see trough levels above)	Consult dermatology and wound team. Burn sheets should be placed on mattress/pillow; Clinitron bed to offload and promote wound healing. Cleanse with warm normal saline.

		Apply thin film of Mupirocin or non-adherent dressing (Adaptic, Kerralite cool with border or RadiaDres hydrogel sheets, Mepilex transfer Ag) on open areas. For generalized bullae/denudation, apply Silverlon Elastic Burn Wrap. Secure with Kerlix or Surgilast tubing then Exu-Dry Vest

4. **Treatment of Upper and Lower Gastrointestinal aGVHD**
    1. Isolated Upper GI GvHD
       Trial of budesonide
       Beclomethasone is preferred for upper GI GvHD but difficult to obtain.
       Budesonide enteric capsules deliver topical steroids to the upper GI tract if patients are on acid reducing medications (a PPI).
       EGD for documentation should be obtained when upper GI GVHD is suspected in the absence of a clear contraindication (Frairia et al. Blood 2014)
    2. Lower GI GvHD
       First line therapy is corticosteroids – need to consider possible malabsorption and initiate w/ IV dosing
       Prednisone PO or methylprednisolone IV +/- budesonide
    3. Supportive Care for GI GvHD
        1. Nutrition consult.
        2. Diet as tolerated. In patients with diarrhea, a diet low in fat, lactose, fiber, and caffeine is recommended (low residue diet).
           See Appendix II for BRATT diet
        3. “Modified BRATT diet: Phase I”
           Recommended for patients with Stages 2-4 GI GvHD. Like traditional BRATT diet (See Appendix II): Includes banana, apple sauce, diluted apple juice, white rice/bread/pasta/cereal products (< 3g fiber per serving), de-caffeinated tea, non-dairy milk, skinless potato, egg whites, soy nut butter, broth, and Pedialyte.
        4. “Modified BRATT diet: Phase II”
           Recommended for patients with Stage 1-2 GvHD especially w/o rapid response to steroids. Further liberalized: Includes above foods plus non-dairy cheese, plain yogurt, yucca/plantains, oatmeal (NOT steel-cut or high-fiber), canned soft fruit, pulp-free fruit juice, crackers/pretzels, lean poultry and fish, Gatorade, chicken soup.
        5. Total parenteral nutrition (TPN):
           Recommended for patients with ≥ Grade 3 GI GvHD.

6. Perianal skin care:
   Sitz bath and NDX cream (nystatin, zinc oxide).
7. Gastrointestinal blood loss:
   1) Keep platelets >50
   2) Tranexamic acid IV or PO (is acceptable on M9: max 4 x 500mg). IV needs PICU/ICU admission. Note: hemorrhagic cystitis is (relative) contraindication.
   3) Octreotide 25-50 microg per hour as continuous infusion
   4) In life-threatening bleeding – rFVIIa (NovoSeven) 90 mcg/Kg once (measure clotting factors if not-life threatening)

Treatment of GI aGvHD

GI Stage	Treatment	Supportive care
Isolated upper	Budesonide <20 kg 3mg 20 kg–50 kg 6mg >50 kg 9mg IF severe or non-responsive: Methylprednisolone/equivalent 1-2 mg/kg/day + optimize / start CNI (see trough levels above)	Antiemetics as needed Metoclopramide for impaired GI motility Olanzapine for anorexia
Lower Stage I	Methylprednisolone/equivalent 2 mg/kg/day + optimize / start CNI (see trough levels above)	
Lower Stage II-IV	Methylprednisolone* (or IV equivalent) 2 mg/kg + optimize / start CNI (see trough levels above)	Antidiarrheals (lomotil, loperamide, tincture of opium) as needed. Octreotide 100 to 500 mcg IV q8 hrs if bloody diarrhea > 500ml after 24 hrs of maximizing antidiarrheals** Manage GI bleeding as above (3.8.4.3.7)

**IV corticosteroids formulation is preferred in patients with high volume diarrhea*

**Discontinue Octreotide as soon as diarrhea has resolved, but re-assess every 4-7 days, or if no response at 4 to 7 days of continuing Octreotide.

5. Treatment of hepatic aGvHD
    1. Discontinue all concomitant hepatotoxins
    2. First line therapy of stage 1-4 hepatic aGVHD
       methylprednisolone at 2mg/kg/day (or equivalent)
    3. Supportive care:
       Ursodiol, spironolactone as indicated for fluid overload, intravenous albumin as indicated for hypoalbuminemia, vitamin K 10 mg IV weekly
       Consider discontinuation of TPN or cycling to 20 hours as soon as possible.
       Fat soluble vitamin monitoring and replacement as needed (ADEK).

9. **RESPONSE**

After initiation:

Evaluate response to treatment AND either taper immune suppression or intensify it.

Patients with clinical response have superior NRM

Patients with a baseline CD4+ T cell of >50/uL have superior NRM (de Koning et al 2020)

Patients with improvement in biomarkers (MAP) have superior NRM (Srinagesh et al, 2019)

Repeat biomarkers (REG3a and ST2) at 7, 14 and 28 days to calculate the MAP

Calculation and Interpretation of the MAP

-11.63 + 1.844*(log ST2) + 0.577*(log Reg3a)

MAP > vs < 0.290 at 1 and 4 weeks after initiation of treatment predicts different NRM

RESPONSE DEFINITIONS

Response definition	Criteria
Complete Response (CR)	Resolution of all aGVHD symptomatology in all GVHD target organs with no additional intervening GVHD therapy.
Very good partial response (VGPR)	Skin with no rash or erythematous rash involving <25% of body surface area without bullae (residual hyperpigmentation does not count). Total serum bilirubin <2 mg/dL. Tolerating food or enteral feeding, predominantly formed stools, no more than occasional nausea or vomiting.
Partial response (PR)	Improvement in aGVHD in all initial GVHD target organs without complete resolution and without worsening or new involvement of any other GVHD target organs

Mixed response (MR)	Improvement in one or more GVHD target organs with deterioration in another organ manifesting symptoms of aGVHD or development of symptoms of aGVHD in a new organ.
Progression	worsening of GVHD in at least one organ without any improvement in others
No response (NR)/stable	Absence of any improvement in aGVHD. Subjects receiving secondary therapy (including need to re-escalate corticosteroid dose to 2mg/kg/day MP or equivalent.

1. **Steroid refractory aGvHD** (progression within 3 days or no response within 7 days).
   Across approaches studies suggest that up to 50% of pediatric patients with severe aGvHD will be refractory to steroids.
   1. Failure **is defined as** *(MacMillan et al, Blood 2010)* any of
      1. Incomplete response (refractory) after 14 days.
      2. Progression (worsening stage or new involvement in at least one organ +/- improvement in other organs) after 3 days of 2mg/kg/day MP/ equivalent.
      3. No change (refractory=same grade or progression) after 7 days.
   2. Patients who flare after initial control (going up by one grade at least):
      May receive 2mg/kg/day steroid pulse x 3 days.
      Patients with repeated flares unable to taper steroids ("steroid dependent") should be considered for second line therapy (particularly if steroids dose continues to be >1mg/kg/day).
   3. First Line Treatment of steroid refractory or steroid dependent aGvHD
      Always first review suitability/eligibility for open clinical trials.
      1. In the absence of protocol, patients 12 years and older, should be started on Ruxolitinib (1st line) unless there is a contraindication (see table below)

Drug	Site of Involvement	Dose	Comments
Ruxolitinib	ALL	**<12 y/o Dosing:** <25 kg: 2.5mg BID >25 kg: 5mg BID >50kg 10mg BID Increase every 1-2 weeks to maximum of 10mg BID	Hematologic toxicity may require dosage modification. Monitor for serious infections; these should be resolved prior to treatment initiation. Platelets >20 and ANC >1prior to initiation; Monitor for cytopenias,

		If tolerating (blood counts) **≥12 y/o:** 10 mg BID *dose adjustment for azoles: start at half initial dose, double if tolerated after 2 weeks.	dose reduce or hold treatment for platelets <20, ANC <1 not responsive to GCSF Consider rule out pneumatosis with Abdominal XR prior to initiation.

2. Though not FDA approved in patients <12 years of age, every effort should be made to appropriately dose ruxolitinib for these patients.
3. If not on CNI, start CSA or TAC
4. Consider section 3.9.1.4 If protocol therapy is not available, patient is unable to tolerate, obtain, or gain control with ruxolitinib,

4. Second-Line Treatment and beyond of steroid refractory or steroid dependent aGvHD:
   Screen for open protocols. Link to BMT Pediatric Project Portfolio. If not eligible for trials consider the following agents:
5. **Details for Second/Third -line Treatment Options**

Drug	**Site of Involvement**	**Dose**	**Comments**
Mesenchymal stromal cells (MSCs)	All	1-2M/kg according protocol	Currently not available outside if SPU
Extracorporeal Photopheresis (ECP)	All	Weeks 1-8: 2- 3 times/week Follow taper per ECP guidelines	Requires large bore catheter or MediPort (Vortex) Apheresis consult (Order in CIS)
Infliximab	Gastrointestinal	10 mg/kg weekly median of 4 doses	CMV monitoring twice weekly Consider obtaining BD glucan/ galactomannan
Alpha-1 AntiTrypsin	All	60mg/kg/dose twice weekly x 8 doses	Responses typically after ~ 5 doses.
Pentostatin	Liver, Gastro	1.5 mg/m^2 IV daily x3, may	

	intestinal	repeat in 2 weeks	
HCG (Pregnyl)	All	2000 units uhCG/m^2 subQ q48 hours for up to 7 weeks	
Vedolizumab	Gastrointestinal	300 mg IV at weeks 0, 2 and 6 weeks then every 8 weeks. Consider 150mg dose in smaller patients (i.e. <40kg)	

2. **Transitioning from IV to oral CNIs and corticosteroids** (Immunosuppressant guidelines)
    1. When the patient can tolerate PO medications, CSA or TAC may be fully switched to oral.
    2. In patients receiving simultaneous IV CNI and IV corticosteroids- switch CNI from IV to PO first and ensure adequate levels (therefore GI absorption) before switching IV steroid to PO.
    3. CsA and Tacrolimus IV to PO conversion: Oral **CSA** dose is 2-**3x** the IV dose at the time of conversion.
    4. MP to prednisone conversion: Prednisone PO dose will be 25% higher than MP. See conversion table in appendix for examples or use an online steroid conversion tool such as https://globalrph.com/medcalcs/corticosteroid-converter-based-on-anti-inflammatory-potency/. Convert from MP IV to prednisone PO equivalent as one step in any taper.

    Supportive care

    Infection prevention- Infections are the major non-relapse cause of death in patients receiving therapy for severe aGVHD (≥ Grade II). Therefore, systemic infection prophylaxis is recommended (see links below).

    Patients who develop Grade 2-4 acute GvHD in the absence of CD4 reconstitution (CD4 ≥50 x 10^6/L) have inferior overall survival and increased non-relapse mortality and should be considered for more aggressive management.
3. Antimicrobial prophylaxis and coverage (see links)
    1. Bacterial Prophylaxis and Treatment
    2. Fungal and Parasitic Prophylaxis and Treatment (w/ mold-active -azole)
    3. Adjust CNI/sirolimus if -azole is used
    4. Consider other drug-drug interactions with -azoles in consultation with pharmacy and drug appendix
    5. Viral Prophylaxis and Treatment
4. Monitor IgG levels and replete per guidelines. There is no evidence supporting the routine use of IVIG in patients receiving immunosuppression in the absence of severe hypogammaglobulinemia.
5. Hygiene measures
6. Consults (see table below)

SUPPORTIVE CARE

Consults	
Dermatology Nutrition consult Dental Rehabilitation medicine Multidisciplinary GvHD Clinic	Early consultation is encouraged. Patients without rapid response to steroids, with need for second line therapy, or who remain on ≥1mg/kg/day of prednisone should be seen in GvHD clinic at least every 3 months and have regular assessments for multiorgan involvement and/or toxicity.
Laboratory/other testing	
IgG level	IVIG repletion if controversial, but recommend checking level q4 weeks and replete if clinically indicated (recurrent infections) or hypogammaglobulinemia
Immune function	At diagnosis of GvHD
GvHD biomarkers	At diagnosis At 7 and 14 days after start of systemic steroids Consider on protocol or on a case by case basis (ST2, elafin, hepatocyte growth factor, soluble regenerating islet-derived 3-α)
Pulmonary	PFTs at diagnosis or 100 days post HCT and every 3 months Patients with PFTs c/w GvHD should be monitored monthly Patients unable to perform PFTs should have imaging (CT) q6mo Patients w/ CT c/w GvHD should be considered for q3mo imaging
Encourage weight bearing and aerobic exercises	For 30 min 3-5 x/week
Bone health	See bone health in cGVHD guidelines

10. RELATED MATERIALS/ DOCUMENTATION:
    1. **Evaluation of organ status**
       In each clinical encounter (by exam+/- laboratory testing)
    2. **Acute GvHD assessment forms**
       Must be completed weekly for all HCT recipients from day +7 until day +100
        1. *Outpatient assessment*
           To be completed by clinic APP or fellow
        2. *Inpatient assessment*
           To be completed by inpatient attending or APP
    3. **If aGvHD symptoms remain active after day +100:**
       At least monthly GvHD documentation using the late acute/chronic form is encouraged until resolution of symptoms.

4. **Acute GvHD signs and/or symptoms will be captured:**
   All skin, upper GI, lower GI, and liver symptoms active within the prior 7 days of the date of assessment will be captured on this document (regardless if the symptoms are attributable to GvHD).
5. **Acute GvHD grading will be reviewed:**
   By a transplant clinician panel to reach a consensus of acute GvHD diagnosis, onset and maximum grade. The consensus data will be captured on a GvHD specific electronic document.
6. **Patients will be censored if any of the following events develop:**
   Primary graft failure, secondary graft failure requiring stem cell transplant rescue, received unplanned donor lymphocyte infusion, malignant disease relapse, second allogeneic stem cell transplantation, and if the patient is lost to follow up.

4. **RELATED MATERIALS**
   1. Appendices
      1. Bristol Stool Chart
      2. BRATT diets
      3. GvHD Treatment Algorithm
      4. Skin Direct Therapy
      5. Rule of 9s
      6. Acute GvHD Grading/Staging conversions
      7. Taper Schedules
      8. IV/PO steroid conversions
5. **DOCUMENTATION**
   1. Non applicable
6. **REFERENCES**

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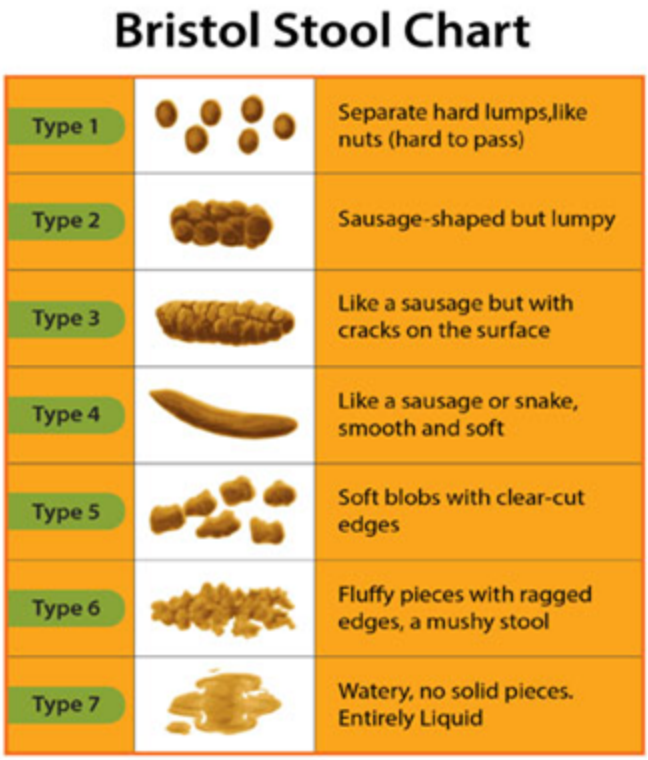
7. CONTENT EXPERTS

Author(s)	Reviewer(s)	Revision Date	Changes

Maria Cancio, MD JJ Boelens, MD, PhD Susan Prockop, MD Andrew Harris, MD	Andrew Harris, MD	10/05/2022	• Added review for availability/eligibility for clinical trials at GVHD onset
Andrew Harris, Jaap Jan Boelens	Harris/Boelens	10/17/24	Some patch work, TXA oral allowed on M9,

Appendix I: Bristol Stool Scale

The Bristol stool scale or Bristol stool chart is a medical aid designed to classify the form of human feces into seven categories.



Type 1	**Separate hard lumps, like nuts (hard to pass).**
Type 2	**Sausage-shaped, but lumpy.**
Type 3	**Like a sausage but with cracks on its surface.**
Type 4	**Like a sausage or snake, smooth and soft.**
Type 5	**Soft blobs with clear cut edges (passed easily).**
Type 6	**Fluffy pieces with ragged edges, a mushy stool.**
Type 7	**Watery, no solid pieces. Entirely liquid.**

Appendix II. BRATT Phase I and II Diets

BRATT PHASE I DIET

PURPOSE:

The Modified BRATT PHASE I Diet is designed to promote weight maintenance and optimal nutrition status for incidents of severe diarrhea in the pediatric and adult populations, especially for patients with Graft Versus Host Disease (GVHD).

INDICATIONS FOR USE:

Modified BRATT PHASE I is used in patients with acute diarrhea who are continuing to receive aggressive Oral Rehydration Therapy (ORT), whose nausea and vomiting have not appropriately resolved, and whom the medical team have prescribed intermittent bowel rest.

DESCRIPTION:

Foods that encourage water re-absorption and increased fecal bulk are included such as: bananas, rice, apples, and toast.

DISCUSSION:

At MSKCC we face a multi-faceted challenge as both our pediatric and adult population often experience frequent treatment and frequent infection related diarrhea. These include complications like prolonged antibiotic use, diarrhea associated with antineoplastic therapies, or deterioration of the gut mucosa by additional treatment side effects as seen in GVHD among Allogenic Bone Marrow Transplant patients. The goal of the BRATT PHASE I Diet is to promote weight maintenance and optimal nutrition status in patients with diarrhea. Early nutrition intervention is crucial for the prevention of overt nutrient deficit and associated malnutrition. Resuming a normal healthy diet including ORT early during incidents of diarrhea is superior to the practice of “resting the gut,” by the provision of only clear liquids and diluted milks in this population.

BRATT I

FOOD GROUPS	ALLOWED	NOT ALLOWED
Milk and Dairy Products	Rice milk Lactaid Soy milk Almond milk	Milk (whole, low-fat, and skim) Half-and-half Cream Sour cream Regular ice cream Yogurt
Vegetables	Skinless baked, boiled, or mashed potatoes	All other except those mentioned in the “allowed” category
Fruit and Juices	Banana Applesauce Diluted apple juice	All other except those mentioned in the “allowed” category

Breads and Grains	Breads and products made with white flour Dry toast Rice Krispies, Rice Chex Cream of Rice White pasta White rice Rice porridge	Whole wheat or whole grain breads, rolls, crackers, or pasta Brown or wild rice Barley, oats, and other whole grains Cereals made form whole grain or bran Breads or cereals made with seeds or nuts
Meats and Meat Substitutes	Boiled, scrambled, or poached egg whites Eggbeater or egg white omelet Creamy nut butters (1 tablespoon/day)	Cooked meats, fish, and soy products Fried meat, poultry, or fish Luncheon meats, such as bologna or salami Sausage and bacon Hot dogs Fatty meats Egg yolks Nuts Chunky nut butters
Fat	Use Sparingly: Butter Olive oil	All other except those mentioned in the “allowed” category
Beverages	Pedialyte Decaffeinated Hot Tea Diluted Gatorade	Beverages with caffeine or sorbitol
Soups	Vegetable or Chicken Broth	All others not listed in “Allowed” category
Miscellaneous	Sweeteners in moderation (sugar, Equal, Sweet-N-Low, Splenda) Lemon Juice Jell-O Jelly	All other except those mentioned in the “allowed” category

BRATT PHASE II DIET

PURPOSE:

The Modified BRATT PHASE II Diet is designed to promote weight maintenance and optimal nutrition status for incidents of severe diarrhea in the adult and pediatric population, especially for patients with Graft Versus Host Disease (GVHD).

INDICATIONS FOR USE:

Modified BRATT PHASE II will be recommended for use by patients who have been successfully rehydrated, who's nausea and vomiting have been controlled, and whose volume of emesis, stool output and formation has progressed to a scale that is medically improved as determined by the primary medical team members.

DESCRIPTION:

Foods that encourage water re-absorption and increased fecal bulk are included such as: bananas, rice, apples, and toast. This diet is also expanded to include a wide range of foods as tolerated by the patient.

DISCUSSION:

At MSKCC we face a multi-faceted challenge as both our pediatric and adult population often experience frequent treatment and frequent infection related diarrhea. These include complications like prolonged antibiotic use, diarrhea associated with antineoplastic therapies, or deterioration of the gut mucosa by additional treatment side effects as seen in (GVHD) among Allogenic Bone Marrow Transplant patients. The goal of the BRATT PHASE II Diet is to promote weight maintenance and optimal nutrition status in patients with diarrhea. Early nutrition intervention is crucial for the prevention of overt nutrient deficit and associated malnutrition. Resuming a normal healthy diet including Oral Rehydration Therapy (ORT) early during incidents of diarrhea is superior to the practice of "resting the gut," by the provision of only clear liquids and diluted milks in this population.

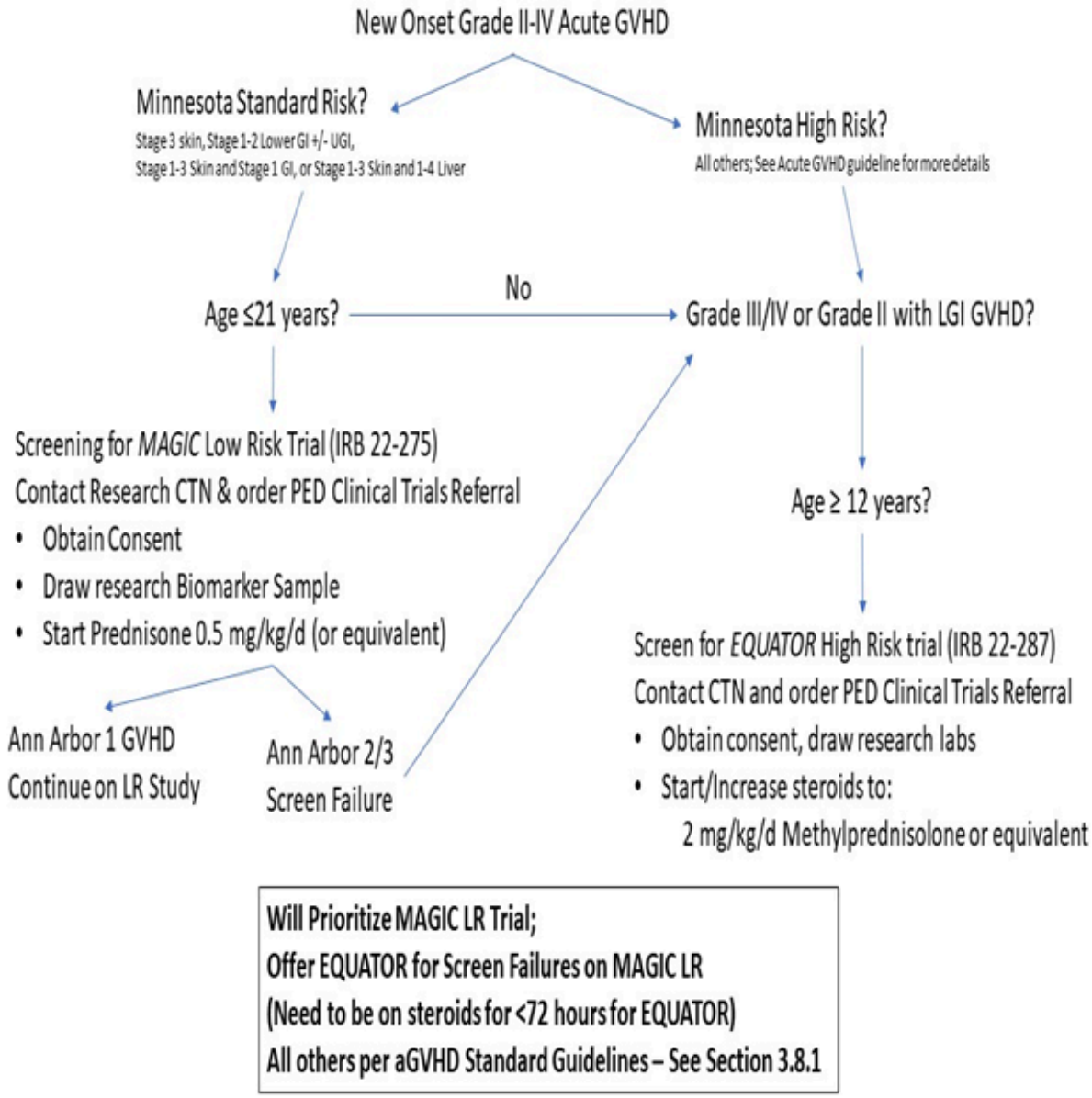
Other links:
https://www.mskcc.org/experience/patient-support/nutrition-cancer/diet-plans-cancer/
https://health.ucdavis.edu/cancer/specialties/stem-cell-transplant/pdf/nutrition-GI-GVHD.pdf

BRATT II

FOOD GROUPS	ALLOWED	NOT ALLOWED
Milk and Dairy Products	Rice milk Lactaid Soy milk Almond milk Soy Cheese Plain Yogurt	Milk (whole, low-fat, and skim) Half-and-half Cream sour cream Regular ice cream Yogurt with berries, dried fruit, or nuts
Vegetables	Skinless baked, roasted, boiled, or mashed white and sweet potatoes Yucca Plantains Canned or very well-cooked vegetables without seeds, stems or skin (i.e.: green beans, squash, carrots, asparagus)	Raw vegetables Fried vegetables Beets Broccoli Brussels sprouts Cabbage Cauliflower Collard, mustard, and turnip greens Corn, Peas Potato skins
Fruit and Juices	Banana Applesauce Baked, peeled apples Canned soft fruit Melon (cantaloupe, honeydew, watermelon up to 1 cup/day) Diluted fruit juice (except prune) without pulp	All raw fruits except banana Dried fruits, including prunes and raisins Fruit juice with pulp Fruits in heavy syrup
Breads and Grains	Breads and products made with white flour (including flour tortillas, English muffins, bagels) Saltine, graham, and rice crackers White noodles and pasta Couscous Soft pretzel Cereal with less than 3 grams of fiber (i.e.: Rice Krispies, Rice Chex, Corn Flakes) Cream of Rice Oatmeal (not steel cut) White rice Rice porridge	Whole wheat or whole grain breads, rolls, crackers, or pasta Brown or wild rice Barley, oats, or other whole grains Cereals made form whole grain or bran Breads or cereals made with seeds or nuts Popcorn

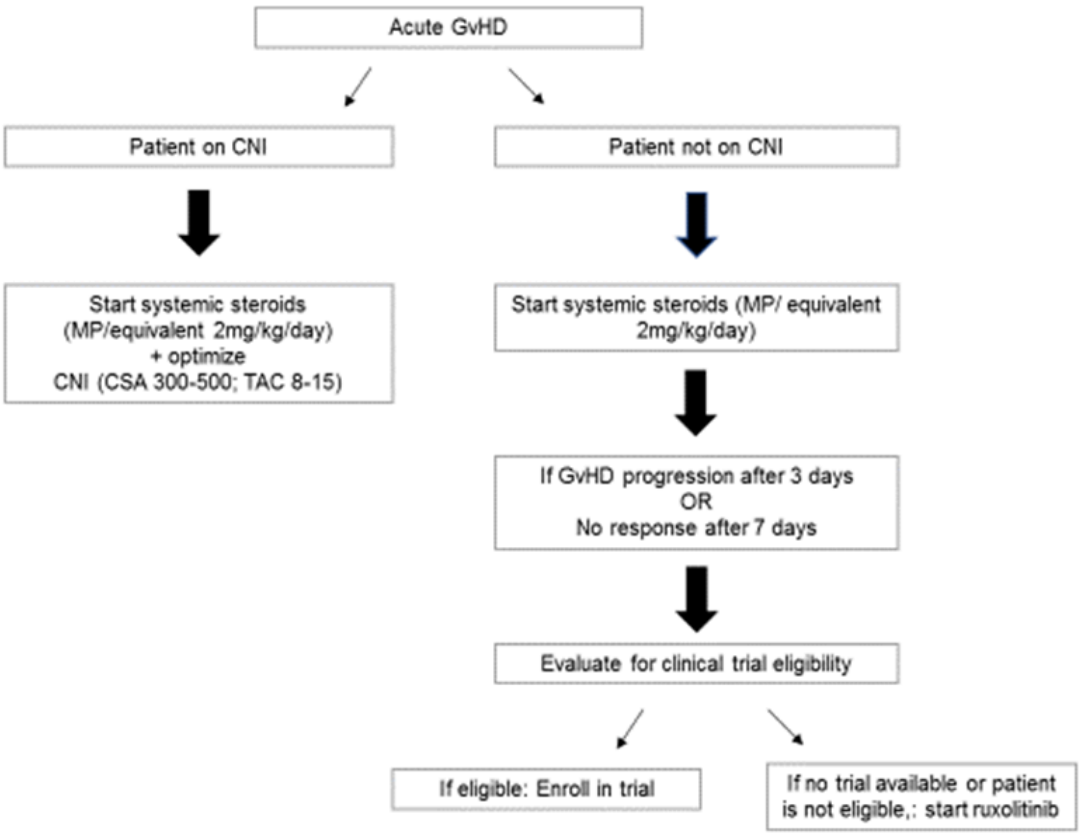
FOOD GROUPS	ALLOWED	NOT ALLOWED
Meats and Meat Substitutes	Grilled, Roasted, or Baked Chicken Roasted, sliced turkey Flaky fish Boiled, scrambled, or poached eggs, egg whites, or egg beaters (up to 2 whole eggs/day) Tofu Creamy nut butters	Fried meat, poultry, or fish Luncheon meats, such as bologna salami Sausage and bacon Hot dogs Fatty meat Nuts Chucky nut butters
Fat	Use sparingly: Vegetable or Olive Oil Butter Margarine Low-fat Mayonnaise	Anything not mentioned in “Allowed” category
Beverages	Pedialyte Decaffeinated coffee and Tea Gatorade Crystal Lite Caffeine-free regular or diet soda in moderation (Ginger ale, 7-Up, Sprite, cola) Seltzer water Smoothies made with any of the “Allowed” foods	Anything not mentioned in “Allowed” category
Soups	Vegetable, Beef or Chicken Broth Dairy-free potato or squash soup Chicken Noodle or Chicken Rice Rice Porridge	Anything not mentioned in “Allowed” category
Miscellaneous	Sorbets, popsicles, fruit ices Angel food cake Sweeteners in moderation (sugar, Equal, Sweet-N-Low, Splenda) Lemon Juice Regular or Sugar Free Jelly	Foods sweetened with artificial sweeteners sorbitol or xylitol Honey Foods and beverages with caffeine or sorbitol

APPENDIX IIIA: Current Trials of 1st Line Therapy for Acute GVHD



Will Prioritize MAGIC LR Trial;
Offer EQUATOR for Screen Failures on MAGIC LR
(Need to be on steroids for <72 hours for EQUATOR)
All others per aGVHD Standard Guidelines – See Section 3.8.1

Appendix IIIB: Algorithm for treatment of aGvHD



Appendix IV: Skin directed treatments for aGvHD

Topical corticosteroids

Drug/Potency	Strength	Formulation
Mild (Low potency; Class 6-7)		
Hydrocortisone	2.5%	Cream/ointment
Alclometasone+	0.05%	Cream
Moderate (Intermediate potency; Class 3-4)		
Triamcinolone	0.1%	Cream/ointment/spray
Strong (High and Super High potency; Class 1-2) *		
Triamcinolone	0.5%	Cream/ointment
Clobetasol+	0.05%	Cream/ointment/foam/spray+

***** Restricted use of moderate/strong potency steroids on the face and genital area. Caution with use of strong potency steroids in infants.

+ Insurance restrictions may apply for alclometasone and clobetasol foam/spray.

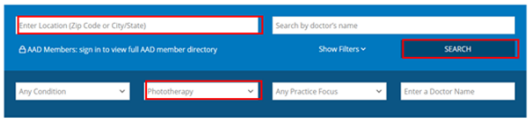
Skin GVHD Management: Skin directed therapies

Cutaneous aGVHD Body Site	Initial (BID use)	Refractory (BID use)
Scalp	Triamcinolone 0.1% cream* or spray	Clobetasol 0.05% Spray**
Face, neck, genitalia, axilla	Hydrocortisone 2.5% cream	Alclometasone cream +/- tacrolimus 0.1% ointment
Trunk, extremities (localized)	Triamcinolone 0.1% cream or ointment*	Clobetasol 0.05% Spray**
Trunk, extremities (generalized)	Clobetasol 0.05% Spray BID**, OR Triamcinolone 0.5% cream or ointment*	Clobetasol 0.05% Spray** + NBUVB Phototherapy 2-3x/wk
Hands, feet	Clobetasol cream/ointment/foam**	Clobetasol** + tacrolimus 0.1% ointment under occlusion with cotton/nitrile gloves or saran wrap

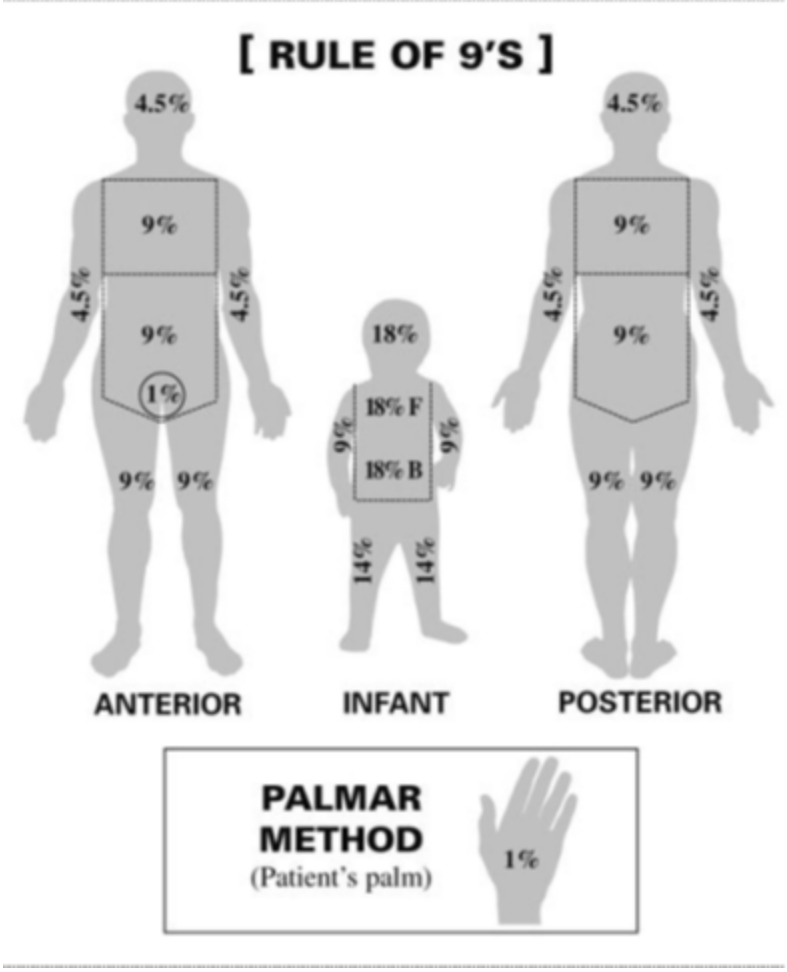
*available in 454g/ 1-lb jar

**use max of 30 days without dermatology involvement

Narrowband Ultraviolet B (NBUVB) Phototherapy: Skin-directed steroid-sparing therapy; anti-proliferative and cutaneous immunosuppressive effects	
Indication	Widespread body involvement (>25% BSA) not on systemic steroids; Steroid-dependent or refractory cutaneous aGVHD
Treatment course	Length of treatment approximately 2months; 2-3x/week. If erythema observed, treatment should be withheld until erythema resolved, then dose reduced by 20%. NBUVB can be discontinued if: Clinically clear of rash Systemic steroid tapered off and rash had cleared or reached a plateau At the discretion of the treatment team (worsening rash, hospitalization, development of significant aGvHD in other organ(s), or development of chronic GvHD, in some cases).
Contraindications	History of photosensitivity disorder (i.e., xeroderma pigmentosum, lupus erythematosus, dermatomyositis, porphyria, Fanconi anemia) History of melanoma History of multiple non-melanoma skin cancer (including skin-cancer predisposing syndromes such as Lynch or Gorlin syndromes)
Caution	History of photosensitivity +ANA Current use of photosensitizing medications (e.g., tetracyclines, voriconazole, sulfonamides, quinolones; thiazide diuretics, amiodarone)
Screening	Ask about history of photosensitivity (if yes, consider checking ANA); avoid in patients on voriconazole If on photosensitizing medications, may need lower dose NBUVB therapy
Phototherapy Facility	May be referred to Cornell Dermatology (646) 962-3376; or to a local facility https://find-a-derm.aad.org; Enter patient zip code AND under ‘Show Filters’, select ‘Phototherapy’)

	
Protection	Eyes protected using small UV-opaque goggles Face, if not involved, covered with a pillow case Male genitalia protected using a jockstrap During a course of treatment exposure to sunlight should be limited and the use of sunscreen encouraged
Anticipated Adverse effects	NBUVB Short-term (within 24 hours) potential side effects are erythema (~20%), pruritus (10%), burning, tenderness, stinging, blistering, tanning, and xerosis. Erythema related to NB-UVB has its onset at 2 to 6 hours after radiation, peaks at 12 to 24 hours, and resolves largely in 48 hours
Pruritus	
Anti-pruritic agents	Ice packs PRN Pramoxine 1% or Sarna and Hydrocortisone 1%(Pramosone) Q day/BID Doxepin 5% cream TID to max area <10% BSA Hydroxyzine 25 mg PO QHS PRN, diphenhydramine 25 to 50 mg PO QHS PRN, gabapentin 300mg PO TID, pregabalin 50mg PO QHS (can increase to BID); aprepitant 3-day dose pack (125mg/80mg/80mg); doxepin 10-25mg PO QHS; or mirtazapine 7.5-15mg PO QHS.
Moisturizers	
Moisturizers	Apply 20-30 min after topical steroids, and 2-3 x/day Use Petrolatum ointment (Aquaphor ointment, Vaseline ointment, generic), Cetaphil cream
Cleansing	
Use Dove or Cetaphil gentle cleanser daily to hands, feet, underarms, groin and just water is adequate to all other areas	

Appendix V; Rule of Nines



Appendix VI: aGrade/Staging Conversion Table:

Stage (Skin/Gi/Liver)	IBMTR Grade*	Przepiorka Grade**	Magic Criteria***
1 Skin	A	I	I
2 skin	B	I	I
3 skin	C	II	II
4 skin	D	IV	IV
Upper GI	B	II	II
1 GI	B	II	II
2 GI	B	III	III
3 GI	C	III	III
4 GI	D	III	IV
1 Liver	B	II	III
2 Liver	B	III	III
3 Liver	C	III	III
4 Liver	D	IV	IV

* IBMTR Grading; No longer in widespread use clinically or for research. Ref: Rawlings et al. Br J Haematol 1997 Junl97(4)855-64.

**Przepiorka (also referred to as the Keystone or Modified Glucksburg criteria; For use for CIBMTR data submission. Ref: Przepiorka et al, Bone Marrow Transplant 1995 Jun; 15(6):825-8.

*** MAGIC Criteria; For clinical use and MAGIC participation/trials. Ref: Harris et al., Biol Blood Marrow Transplant 2016 Jan; 22(1):4-10

Reference: Schoemans et al. Bone Marrow Tranpslantation 2018 Nov; 53(11):1401-1415

Appendix VI: Recommended steroid tapers

Responders

Taper 1

Recommended taper for rapid steroid responders (Minnesota Standard Risk*)		
Dose		**Length of therapy**
Prednisone or Methylprednisolone 2 mg/kg/day		days 1-3
Prednisone or Methylprednisolone 1 mg/kg/day**		days 4-7**
For patients on or converting to PO:	**For patients continuing on IV**	
Prednisone 1mg/kg/day	**Methylprednisolone** 0.8 mg/kg/day	week 2
Prednisone 0.5 mg/kg/day	Methylprednisolone 0.5 mg/kg/day	week 3
Prednisone 0.25 mg/kg/day	Methylprednisolone 0.25 mg/kg/day	week 4
Prednisone 0.2 mg/kg/day	Methylprednisolone 0.2 mg/kg/day	week 5
Prednisone 0.1 mg/kg/day	Methylprednisolone 0.1 mg/kg/day	week 6
Discontinue	Discontinue	Discontinue

Standard Risk: One organ involvement: Stage 1-3 skin, Stage 1-2 GI; Two-organ involvement: Stage 1-3 skin plus Stage 1 GI **or stage 1-4 liver*
***If the starting dose is 1 mg/kg/day, keep same dose for a minimum of 7 days*

Taper 2

Recommended steroid taper for patients with initial diagnosis of Minnesota High Risk* and rapid response to steroids of Minnesota Standard Risk*		
Dose		**Length of therapy**
Prednisone or Methylprednisolone 2 mg/kg/day		week 1
For patients on or converting to PO:	**For patients continuing on IV**	
Prednisone 1.5 mg/kg/day	**Methylprednisolone** 1.5 mg/kg/day	week 2
Prednisone 1 mg/kg/day	Methylprednisolone 1 mg/kg/day	week 3
Prednisone 0.5 mg/kg/day	Methylprednisolone 0.5 mg/kg/day	weeks 4
Taper by 0.1 mg/kg/day weekly	Taper by 0.1 mg/kg/day weekly	weeks 5-10

Standard Risk: One organ involvement: Stage 1-3 skin, Stage 1-2 GI; Two-organ involvement: Stage 1-3 skin plus Stage 1 GI **or stage 1-4 liver; High risk: One organ involvement: Stage 4 skin, Stage 1-4 liver, Stage 3-4 GI; 2 Organ involvement: Stage 1-3 skin plus stage 2-4 GI; GI plus Liver involvement (any staging); 3 organ involvement: Any staging (1-4) in all 3 organs.*

Taper 3

Recommended steroid taper for standard steroid responders with Minnesota High Risk*		
Dose		**Length of therapy**
Methylprednisolone 2 mg/kg/day		week 1
Methylprednisolone 1.75 mg/kg/day		week 2
Methylprednisolone 1.5 mg/kg/day		week 3
Methylprednisolone 1.25 mg/kg/day		week 4
Methylprednisolone 1 mg/kg/day		week 5
For patients converting to PO:	**For patients continuing on IV**	
Prednisone 1.2 mg/kg/day	**Methylprednisolone** 1 mg/kg/day	week 6
Prednisone 1 mg/kg/day	Methylprednisolone 0.75 mg/kg/day	week 7
Prednisone 0.75 mg/kg/day	Methylprednisolone 0.5 mg/kg/day	week 8
Prednisone 0.5 mg/kg/day	Methylprednisolone 0.5 mg/kg/day	week 9
0.5 mg/kg/day alternating with 0.4 mg/kg/day	0.6 mg/kg/day alternating with 0.5 mg/kg/day	week 10
0.5 mg/kg/day alternating with 0.3 mg/kg/day	0.6 mg/kg/day alternating with 0.375 mg/kg/day	week 11
0.5 mg/kg/day alternating with 0.2 mg/kg/day	0.6 mg/kg/day alternating with 0.25 mg/kg/day	week 12
0.5 mg/kg/day alternating with 0.1 mg/kg/day	0.6 mg/kg/day alternating with 0.125 mg/kg/day	week 13
0.5 mg/kg/day every other day	0.6 mg/kg/day every other day	week 14
Taper OFF	Taper OFF	weeks 15-17

*High risk: Stage 4 skin, Stage 1-4 liver **without** stage 1-3 skin or GI involvement, Stage 1-3 skin plus stage 2+ GI; Stage 3-4 GI, All GVHD affecting skin, liver *and* GI (3 organ involvement; any staging).

Reference: MacMillan et al. Biol Blood Marrow Transplant 2015 Apr; 21(4):761-767

Non-responders and flare management

Taper 4

Recommended steroid taper in patients who progress or who are non-responders:	
Dose	**Length of therapy**
Methylprednisolone 2 mg/kg/day	week 1
Methylprednisolone 1.5 mg/kg/day	week 2
Methylprednisolone 1 mg/kg/day	week 3
***Optional**:* Prednisone 1.2mg/kg/day	HOLD

*If adequate absorption of steroid can be ensured

Taper 5

Recommended steroid taper in patients who have aGvHD flare during taper	
Dose	**Length of therapy**
2 mg/kg/day*, in 2 divided doses	3 days
Most recently tolerated steroid dose	2 weeks
Taper by 10%** q2 weeks until 0.5 mg/kg/day	every 2 weeks
0.5 mg/kg/day	2 weeks
Taper to 0.5 mg/kg every other day***	over 4 weeks
Taper OFF	over 2 weeks

***2 mg/kg/day either PO prednisone or IV methylprednisolone**
****Taper % from baseline dose (most recently tolerated dose)**
***** follow weeks 10-14 from Taper 3 above**

Appendix VIII: IV/PO Steroid Conversion

Methylprednisolone – Prednisone conversion	
Methylprednisolone (IV)	**Prednisone (PO)**
2 mg/kg/day	2.5 mg/kg/day
1.75 mg/kg/day	2.2 mg/kg/day
1.5 mg/kg/day	1.9 mg/kg/day
1.25 mg/kg/day	1.6 mg/kg/day
1 mg/kg/day	1.2 mg/kg/day
0.75 mg/kg/day	0.9 mg/kg/day
0.5 mg/kg/day	0.6 mg/kg/day