

Chronic Graft-Versus-Host Disease

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Etiology/Pathogenesis

- Chronic GVHD is a syndrome that mimics the autoimmune diseases
 - Multisystem fibro-inflammatory process – seen in 50-70% of allo-HCT patients
- Organ damage caused by allo-reactive T cells/B-cells/Macrophages
- Most frequent long-term complication after alloHCT
 - Decreased QoL and increased morbidity/mortality
 - Leading cause of late NRM
- Not simply an evolution from aGVHD
- Manifestations restricted to single organ or widespread

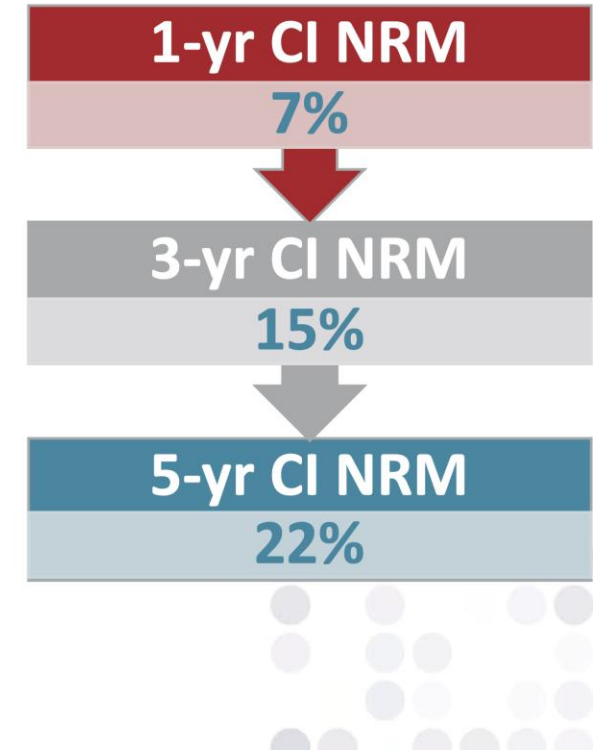
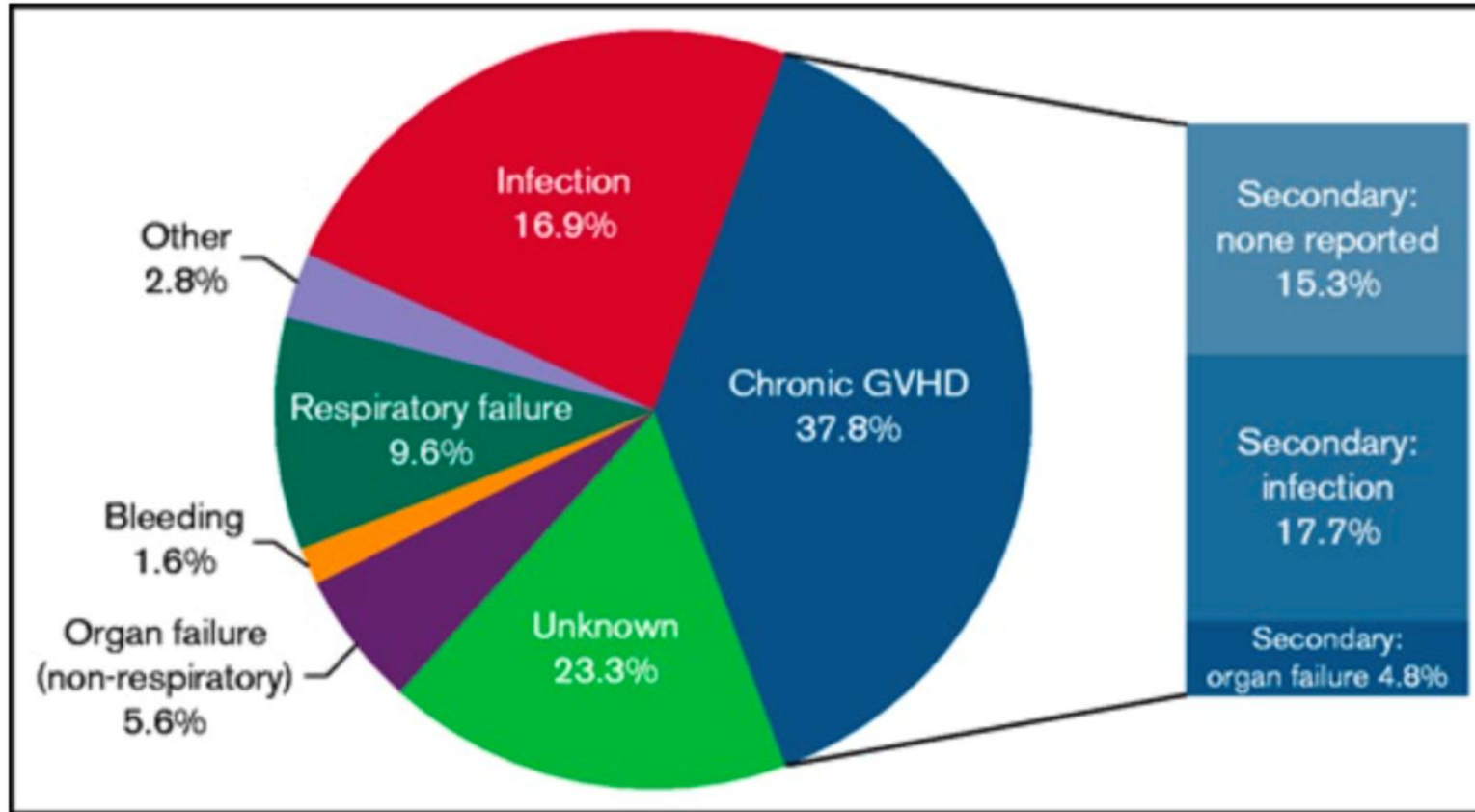
Arai S, Arora M, Wang T, et al. Biol Blood Marrow Transplant. 2015;21(2):266-274

Lee S. Blood. 2017;129(1):30-37

DeFilipp Z, Couriel DR, Lazaryan A, et al. Transplantation Cellular Ther. 2021;1-9

Bhatt VR, Wang T, Chen K, et al. Transplantation Cellular Ther. 2021;S2666-6367

NRM in Patients Diagnosed with CGVHD - from the cGVHD Consortium



Graft-versus-Host-Disease

Category	Time post-HCT or DLI	Presence of aGVHD features	Presence of cGVHD features
Acute GVHD			
Classic aGVHD ^A	≤ 100 days	Yes	No
Persistent, recurrent, or late-onset GVHD (no cGVHD diagnosis) ^B	>100 days		
Chronic GVHD			
Classic cGVHD (lack of aGVHD) ^C	No time frame	No	Yes
Overlap syndrome ^D	No time frame	Yes	
<p>A. Characterized by erythema, maculopapular rash, N/V/D, ileus, anorexia or cholestatic hepatitis occurring within 100 days of transplantation or DLI (without s/sx of cGVHD)</p> <p>B. Features of classic aGVHD without distinctive manifestations of cGVHD occurring beyond day 100 after HCT or DLI</p> <p>C. Classic cGVHD without features of aGVHD</p> <p>D. Presence of 1 or more aGVHD manifestation in patient with diagnosis of cGVHD</p> <p><input type="checkbox"/> aGVHD may be present at initial cGVHD diagnosis or develop after cGVHD diagnosis and may recur +/- resolution of prior cGVHD</p>			

Filipovich AH, Weisdorf D, Martin P, et al. Biol Blood Marrow Transplant. 2005;11:945-946
 Jagasia MH, Greinix HT, Arora M, et al. Biol Blood Marrow Transplant. 2015;21:389-401

Established Risk Factors/Predisposing Factors

- **Prior aGVHD**
 - Improvements in prevention/treatment of aGVHD have not prevented cGVHD
- **HLA disparity**
 - Incidence/severity ↑ with disparity
 - 33% MRD, 49% MMRD (haploidentical)
64% MUD
- **Stem cell source**
 - PBSCs(73%) > BM >UCB (50%)
 - Higher donor T-cell dose
 - No difference in aGVHD in MRD BM vs. PBSC
- **Sex mismatching**
 - Female donor → male recipient
- **Older age of donor/host**
- **Conditioning intensity**
 - MAC > RIC/NMA
- **Exposure to CPIs**
 - Pre- and post-HCT
- **Secondary insults**
 - DLI, weaning of IST
 - Infections, sun damage

Higman MA, et al. Br J Haem 2004;125:435-454

Jacobson DA. Bone Marrow Transplant. 2007;41:215-221

Arai S, Arora M, et al. Biol Blood Marrow Transplant 2015;21(2):266-274

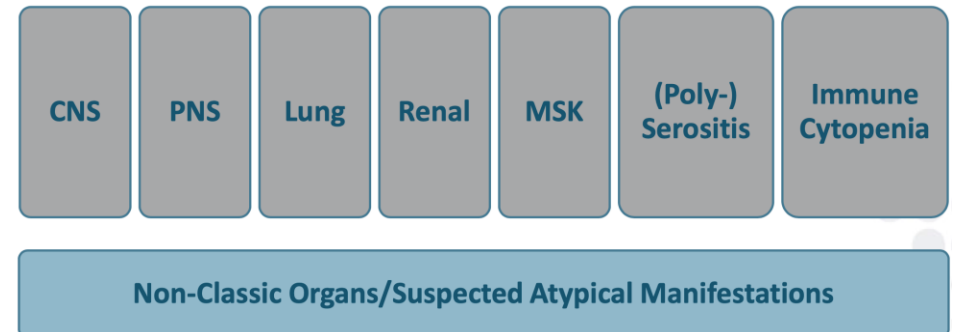
Wolff D, et al. Transplant Cellular Therapy 2021;27(10):817-835

Okoev G, Weisdorf DJ, et al. Bone Marrow Transplant 2021;56(6):1373-1380

Mehta RA, et al. Transplant Cellular Therapy 2021;27(12):1003

Clinical Presentation

- NIH "Classic" organ specific manifestations
 - Skin 65-80%
 - Mouth 48-72%
 - Liver 40-73%
 - Eye 18-47%
 - GIT 16-26%
 - Lung: 10-15%
 - Joints/fascia 2-12%
- Atypical features more recently recognized
 - Occur at taper of IST
 - +/- classic organ involvement
- Histopathologic findings ~ auto-immune disorders



Higman MA, et al. Br J Haem 2004;125:435-454

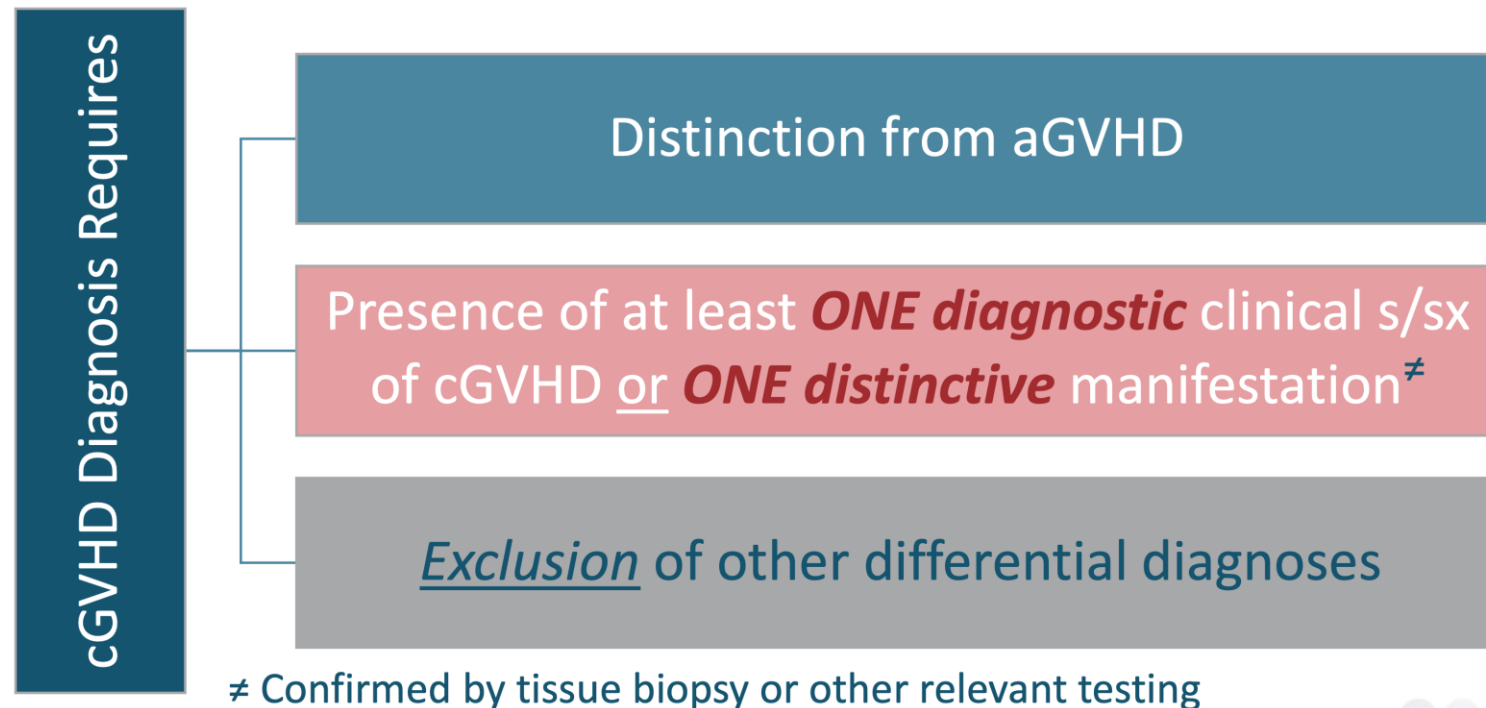
Shulman HM, et al. Biol Blood Marrow Transplant 2006;12:31-47

Cuvelier GDE, et al. Transplant Cell Ther 2022;28(8):426-445

Doering J, et al. Transplant Cell Ther 2023;29(12):772

Diagnosis and Clinical Manifestations

- Prior to 2005, cGVHD → s/sx of GVHD > Day+100
- 2014 NIH consensus guidelines



Filipovich AH, Weisdorf D, et al. Biol Blood Marrow Transplant 2005;11:845-956

Lee SJ and Flowers MED. Hematology. 2008:134-141

Shulman HM, et al. Biol Blood Marrow Transplant. 2006;12:31-47

Definitions of Clinical Features

Categories

- **Diagnostic:** s/SX that are established in the presence of cGVHD without the need for further testing or evidence of additional organ involvement
 - aGVHD cannot produce these patterns-sclerosis and lichen-planus-like changes are signature immune-fibrotic lesions
- **Distinctive:** s/sx that are not ordinarily found in aGVHD but are not sufficient to establish unequivocal diagnosis of cGVHD
 - Distinctive = “supportive chronicity”
- **Others features/unclassified manifestations:** non-specific, rare, and controversial s/sx that cannot be used to establish cGVHD diagnosis
- **Common features:** s/sx that may be found in both aGVHD and cGVHD

Clinical Manifestations

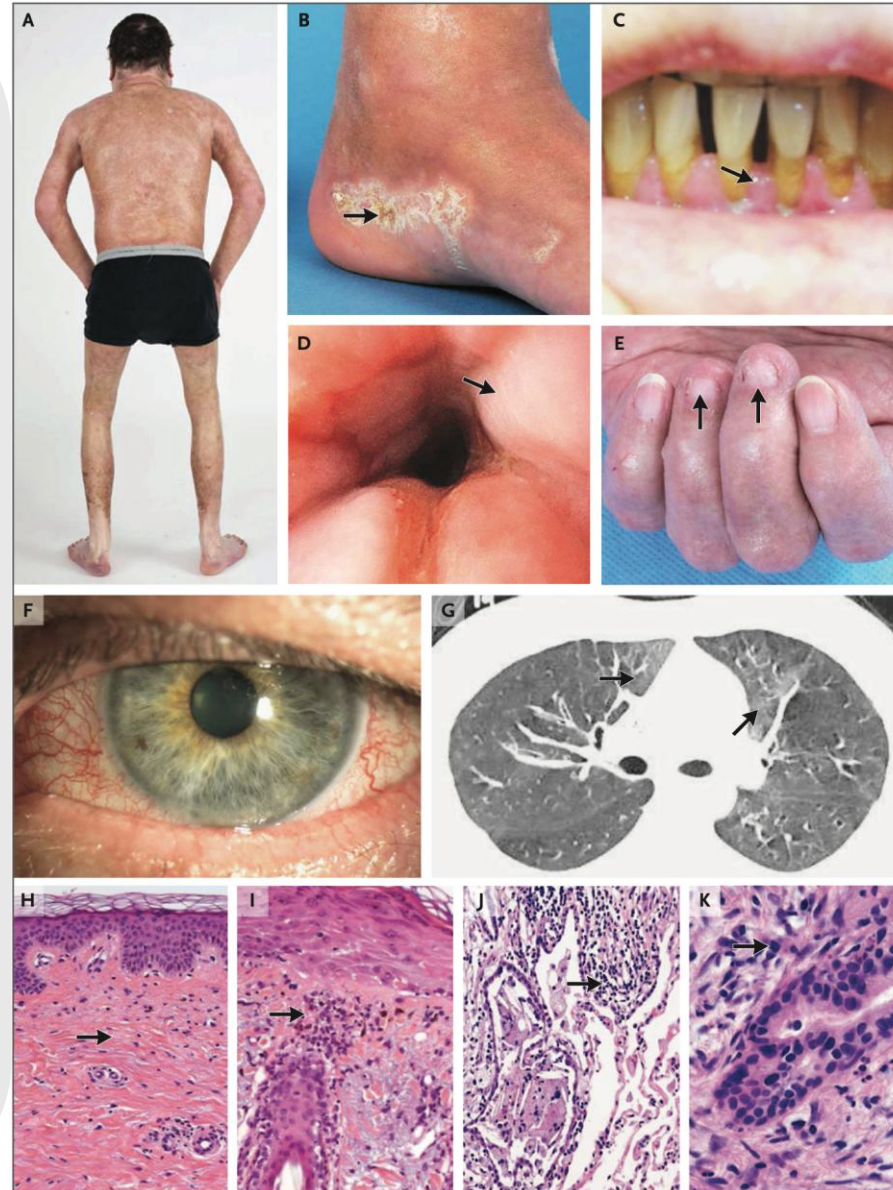
Skin

- Sclerotic/fibrotic features
 - Lichenoid/plaque-like
 - Dry papulosquamous lesions
- Poikiloderma
 - Dyspigmentation: hyper-/hypo-pigmentation
- Signs/Symptoms
 - Sweat impairment
 - Intolerance to temperature changes
 - Erythema, pruritus, rash

Eyes

- New onset dry, gritty or pain
- Keratoconjunctivitis sicca
- Photophobia
- Excessive tearing
- Periorbital hyperpigmentation
- Blepharitis

Physical function significantly impacted



Mouth

- Hyperkeratotic white lacy plaques
 - +/- ulcerations/erythema
- Lichen-type features
- Signs/Symptoms
 - Xerostomia/food sensitivity
 - Mucosal atrophy
 - Pseudomembranous ulcers
 - Gingivitis, erythema, pain

Lung

- Slow onset DoE +/- wheezing
- Bronchiolitis obliterans (BOS)
 - Diagnosed with PFTs and/or radiology (air trapping & bronchiectasis)
 - Obstructive process
- Chronic non-productive cough
- Reduced exercise tolerance

Physical function/mortality significantly impacted

NIH Clinical and Global Scoring System

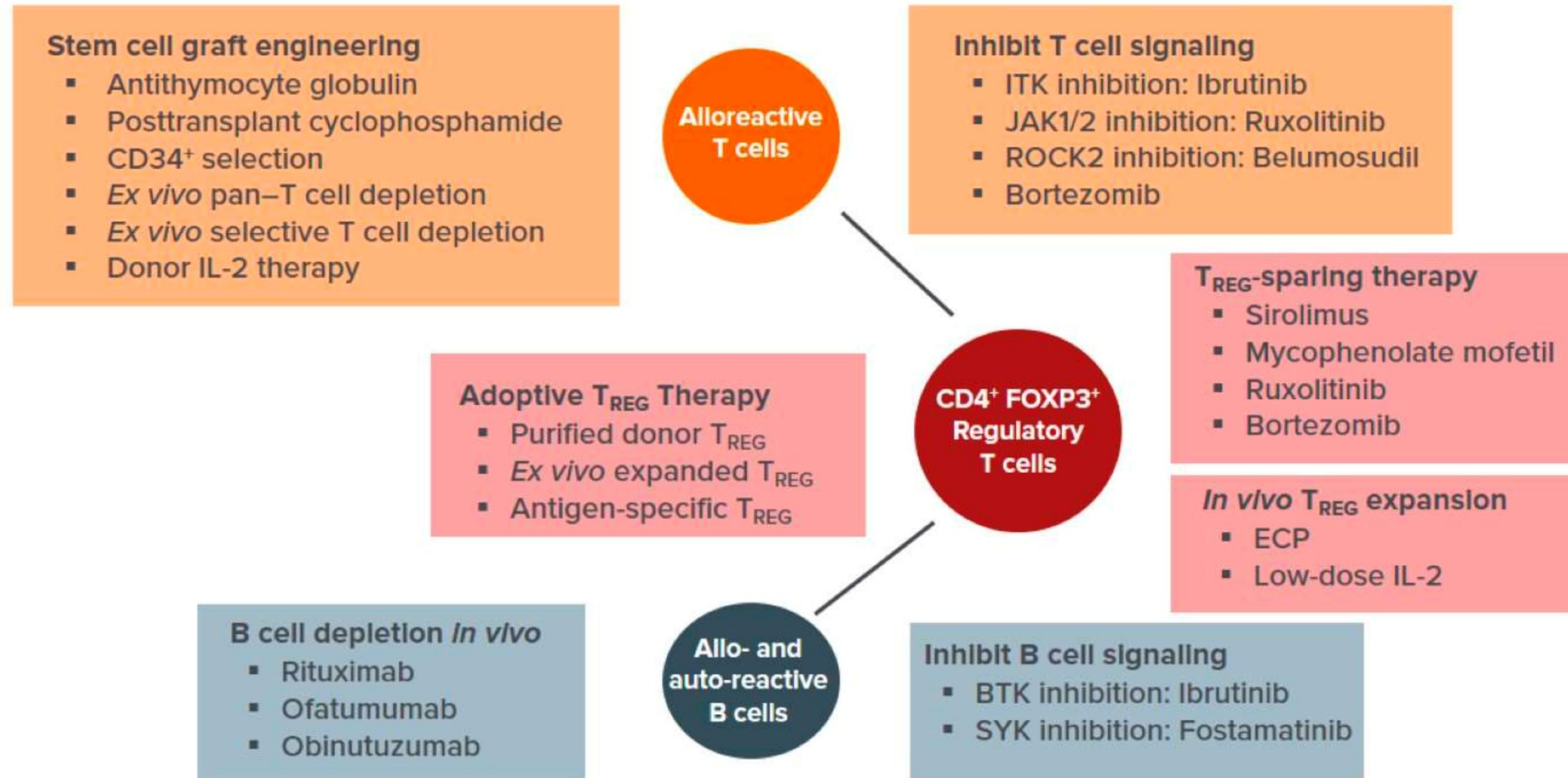
- Allows grading of each individual organ system
- 8 total “classic” sites: skin, mouth, eyes, GI, liver, lung, joint/fascia, genital tract
- Calculation of **global score** based on individual location scores
 - # of sites/organ involved + severity within affected sites
 - Effect of GVHD on PS (0-3)

NIH Clinical and Global Scoring System for cGVHD

Severity of cGVHD	Description
Mild cGVHD	<ul style="list-style-type: none"> • Involves only 1 or 2 organs/sites (EXCEPT lung) <ul style="list-style-type: none"> • No clinically significant functional impairment • <u>Max score of 1</u> in all affected organs/sites
Moderate cGVHD	<ul style="list-style-type: none"> • Involves at least 1 organ/site <ul style="list-style-type: none"> • With clinically significant but no major disability • <u>Max score of 2</u> in any affected organ/site <u>OR</u> • ≥ 3 organs/sites <ul style="list-style-type: none"> • With no clinically significant functional impairment • <u>Max score of 1</u> in all affected organs or sites <u>OR</u> • Lung score of 1
Severe cGVHD	<ul style="list-style-type: none"> • Major disability caused by cGVHD – <u>score of 3 in any organ or site.</u> • Lung score of ≥ 2 will also be considered severe cGVHD

• Skin: higher of 2 scores (BSA and skin features) used
 • Lung: FEV1 is used instead of clinical score

Mechanistic Interventions For Prevention or Treatment of cGVHD

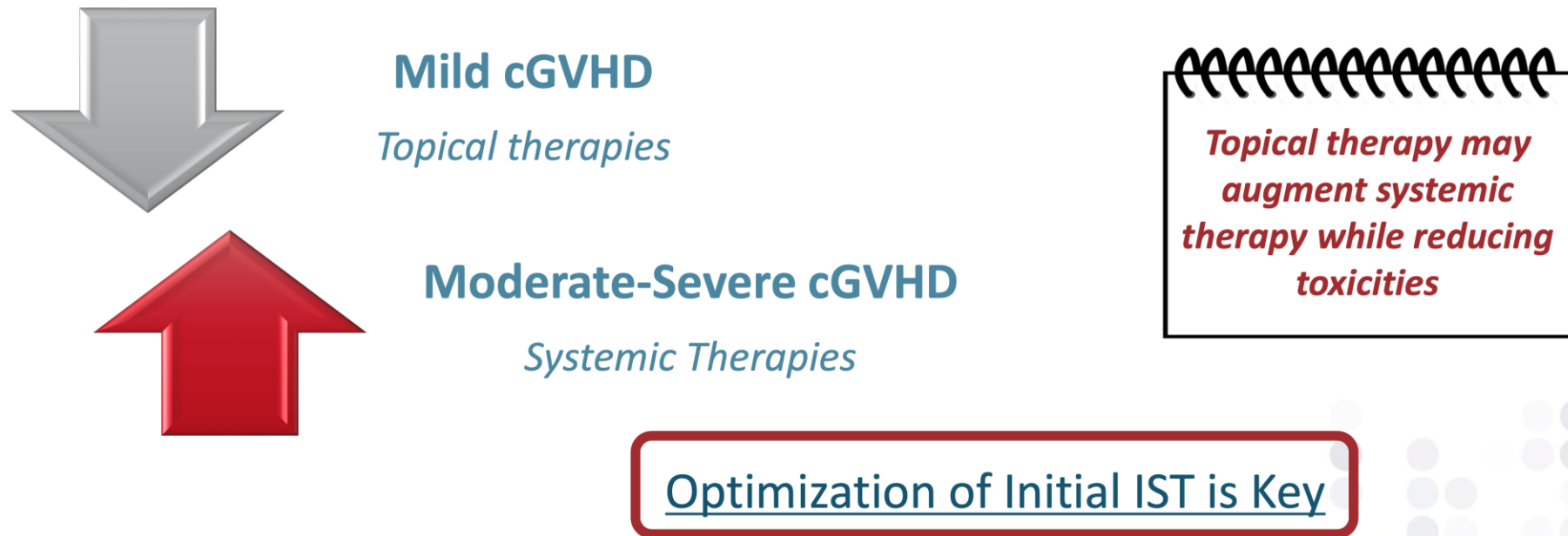


We Are Making PROGRESS in cGVHD Prevention

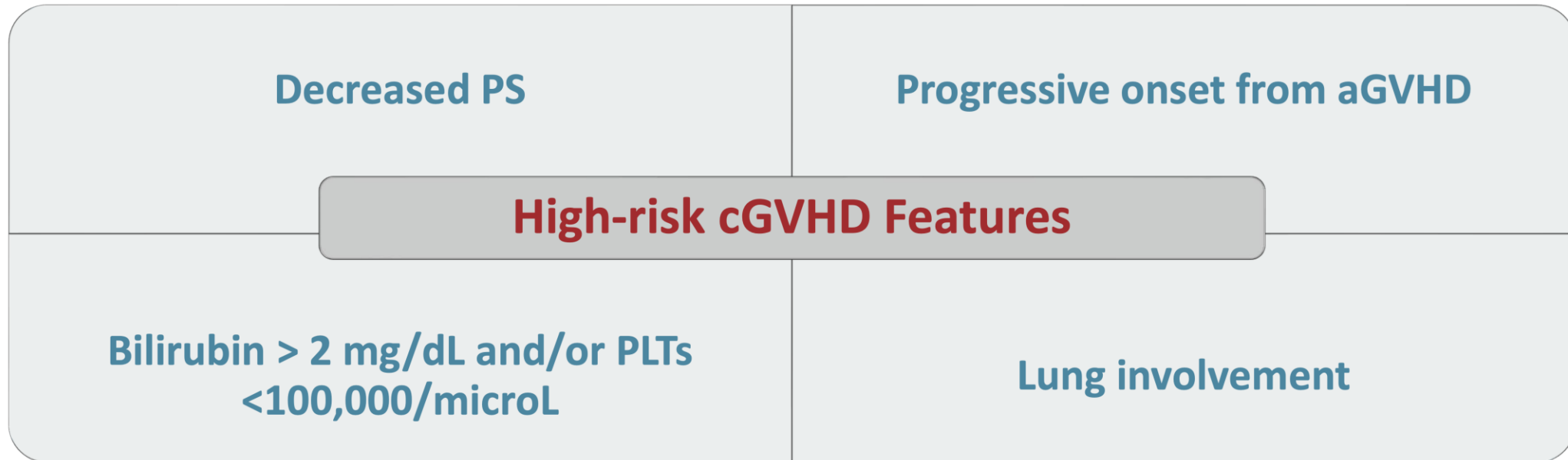
	Bolanos-Meade J, et al NEJM 2023	Curtis DJ, et al. NEJM 2025
Study Type	BMT CTN 1703 Phase III	ALLG BM12 CAST Phase III
Total patients	N=431(mean age: 64.3y; range: 18-75)	N=134 (mean age: 52.2y, range: 21-71)
Study Arms	Experimental: PTCy/Tac/MMF Control: Tac/MTX	Experimental: PTCy/CSA Control: CSA/MTX
Donor Type	MRD(6/6): 28%; MUD(8/8): 69%	MRD(6/6): 100%
Conditioning Intensity	100% RIC:	MAC: 44%; RIC: 56%
Graft Source	100% PBSC	100% PBSC
Primary Endpoint	1-yr GVHD-free, relapse-free survival [GRFS] (%): 52.7% (PTCY) vs. 34.9% (T/MTX)	1-year GVHD-free, relapse-free survival [GRFS] (%): 58% (PTCY) vs. 33% (CSA/MTX) 3-year GRFS: 49% (PTCY) vs. 14% (CSA/MTX) Median GRFS: 26.2 m (PTCy) vs. 6.4 m (CSA/MTX)
Other Results	Lower 1-year incidence of cGVHD with PTCy (21.9%) vs. T/MTX (35.1%)	Lower 1-year incidence of cGVHD with PTCy (14%) vs. CSA/MTX (24%)
	Higher immunosuppression-free survival with PTCy (50%) vs. T/MTX (39.7%)	Higher immunosuppression-free survival with PTCy (54%) vs. CSA/MTX (31%)
	Similar 1-year disease relapse, TRM, and OS	Similar 1-year disease relapse, TRM, and OS
	No difference in grade III/IV toxicities	No difference in grade III/IV toxicities

Initial cGVHD Treatment

- Goal: Relieve symptoms, control disease activity, while preventing additional damage/disability and increasing immune tolerance development
- Indications for treatment:



Systemic Treatment Considerations



Balancing Act: Graft failure vs. Infection vs. Relapse

Future goal: risk stratification strategies

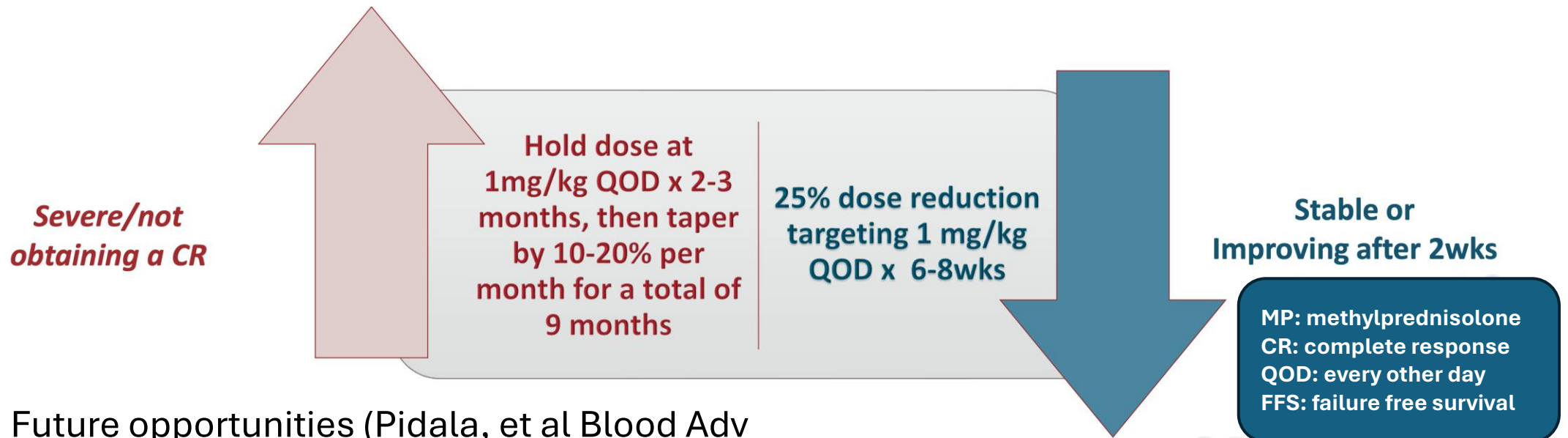
Dignan FL, et al. Br J Haematol. 2012;158:46-61

Wolff D, et al. Biol Blood Marrow Transplant. 2010;16:1611-1628

Williams KM, et al. Transplant Cellular Ther 2021;27(10):452-466

First Line Treatment of cGVHD

- Corticosteroids: 1st treatment since the 1980s with 33% initial response rate
 - Effect: lymphocytic effects and anti-inflammatory
 - Provide inconsistent benefits with FFS at 6-months=68% and 12-months=54%
 - Standard dosing: 0.5-1 mg/kg/day of MP (or equivalent) +/- 1 other agents; Tac or CSA



- Future opportunities (Pidala, et al Blood Adv 2021): Steroid-free/reduced steroids upfront

- Lee SJ and Flowers MED. Hematology 2008
- Dignan FL, et al. Br J Haematol 2012
- Wolff D, et al. Biol Blood Marrow Transplant 2010
- DeFilipp Z, et al. Transplantation Cellular Ther. 2021

Second Line Treatment of cGVHD

- What to do after steroids fail?
 - Intolerance due to toxicities
 - **Steroid refractory/dependent cGVHD**
 - Progression on prednisolone ≥ 1 mg/kg/day for 1-2 weeks
 - Stable disease on prednisolone ≥ 0.5 mg/kg/day for 4-8 weeks
 - Inability to taper prednisolone **below** 0.25 mg/kg/day (0.5 mg/kg QOD) with two unsuccessful attempts to taper at least 8 weeks apart
- Consider agents with adequate safety profile and activity
 - Second line treatment options needed for ~ 50%
- Goal of secondary therapy is steroid sparing
 - Assess response 8-12 weeks after initiation of new therapy
 - Sclerotic skin lesions response may take up to 6 months
 - Progression occurs after 4 weeks?
 - Discontinue most recent addition and start a new option
- No consensus for which 2nd/3rd or 4th line agents to begin first

Novel SD/SR-cGVHD Therapies

Ibrutinib

BTK/ITK inhibitor

Approved August 2017

Adults/children (\geq 1yo) after failure of \geq 1 prior LOT

Belumosudil

ROCK2 inhibitor

Approved July 2021

Adults/children (\geq 12yo) after failure of \geq 2 prior LOT

Ruxolitinib

JAK 1/2 inhibitor

Approved September 2021

Adults/children (\geq 12yo) after failure of \geq 1 prior LOT

Axatilimab

CSF-1R Inhibitor

Approved August 2024

Adults/children (weighing \geq 40kg) after failure of \geq 2 prior LOT

Miklos D, et al. Blood 2017
Cutler C, et al. Blood 2021
Zieser R, et al. NEJM 2021
Kitko CL, et al. J Clin Oncol 2022

ROCK-2: Rho-associated-coiled-coil containing protein kinase-2
CSF-1R: colony stimulating factor 1 receptor

Ibrutinib

- Rationale: Inhibits both B and T-cell signaling
- Suggested dosage: 140-420 mg PO daily (consider drug-drug-interactions)

Trial	Patient Population	ORR/FFS	Other End Points	Adverse Effects
Phase Ib/II Trial (Miklos, et al): (N= 42) ¹ 1-year follow-up (Waller, et al) ²	Steroid-dependent and/or SR-cGVHD (64% were steroid dependent, 17% SR)	ORR: 67% ¹ (21% CR/ 45% PR) ORR 69% ² (31% CR/38% PR)	Sustained response: 55% ≥ 44wks ² 75% reduced steroids → 28% D/C steroids ¹	<u>Grade 1–2</u> : fatigue (57%), diarrhea (36%), muscle spasms (29%), nausea (26%), bruising (24%) <u>Grade ≥ 3</u> : PNA, fatigue, diarrhea *AEs 71% (at 13.9mo) → 25% (at 26mo)
Retrospective, single-center review (Chin KK, et al): (N=53)	Moderate-severe cGVHD (62%) 4+ organs (36%)	2-yr FFS 9% *median FFS: 4.5mo 12% CR/PR, 64% SD	2-yr OS 76% No decrease in average steroids use (32% D/C)	Infection (lung, skin, enterocolitis); N=6 Bleeding/bruising, muscle aches

Miklos D, et al. Blood 2017

Waller EK, et al. Biol Blood Marrow Transplant 2019

Cutler C, et al. Biol Blood Marrow Transplant 2018

Chin KK, et al. Transplant Cell Ther 2021

***LOT: line of therapy**

***PNA: pneumonia**

Belumosidil (KD025)

- Rationale: ROCK2 inhibition modulates inflammatory response → inhibition of T-cell signaling
 - ↓ Th₁₇ and T_{fh} responses (STAT3)/ ↑ T_{regs} (STAT5)
- Suggested dosage 200 mg PO daily
 - Consider drug-drug-interactions: ↑ to 200mg PO BID with PPI or strong CYP3A4 inducer

Trial	Patient Population	ORR/FFS	Other End Points	Adverse Effects
Phase II, open-label, randomized, multi-center (ROCKstar) KD025-213 trial [NCT03640481]: (N=132)	Steroid-dependent and/or SR-cGVHD (67% severe) 52% ≥ 4 organs ~30% prior ibrutinib/ruxolitinib	200 mg QD: 74% (62%-84%) 200 mg BID: 77% (65%-87%) 1-yr FFS 56%	Median: Time to response= 5 weeks 44% on therapy for ≥ 1 year > 50% Response in mouth, joint/ fascia, upper/lower GI , responses in lung (26%) and liver (39%) 45% mean steroid reduction → 21% D/C steroids	Transaminitis (24%), nausea (31%), diarrhea (33%), fatigue (38%), URIs (27%) 54% grade ≥ 3 toxicities *Only 12% D/C due to toxicities
Pooled Analysis from KD025-208 and 213 ; (Lazaryan, et al): N=186 *70% severe cGHD, 52% ≥ 4 organs		1-yr FFS 54%, 2-yr FFS 38% *Median FFS 14mo	RF for tx failure: progressive onset, absence of steroids in upfront tx, ≥ 2 lines of therapy	10% D/C KD02 due to drug-related toxicities

Cutler C, et al. Blood 2021

Jagasia M, et al. Biol Blood Marrow Transplant 2019

Cutler C, et al. Blood 2020

Gonzalez R, et al. Transplant Cell Ther 2023

Ruxolitinib

- Rationale: Anti-inflammatory properties and promotion of tolerance
 - ↓ proliferation of effector T-cells (Th₁ , Th₁₇) → ↑ Treg development
 - ↓ proinflammatory cytokines
- Suggested dosage 5-10mg PO twice daily (must consider renal)

Trial	Patient Population	ORR	Other End Points	Adverse Effects
Multicenter survey (Zeiser, et al): N = 41	Moderate-severe cGVHD Median lines of 3 prior therapies	ORR: 85.4% (7.3% CR/78% PR) Median time to response 3 wks	Responses <u>not</u> restricted to any organ 24% of responders off IST 1-yr OS 92.7%	Cytopenias (17%), 7% grade ≥ 3, CMV reactivation (15%)
Multicenter, retrospective review (White, et al): N=115	60% severe, 38.3% Moderate Median 3 organs involved 84.2% received tx as ≥ 4 th line	6-mo ORR: 61.8% *Severe ORR 46.8% 1-yr ORR: 62.3%	63.8% tapered steroids < 0.1mg/kg/d at 1-yr 1-yr FFS 64.6% (RF: GVHD severity/HCT-CI ≥ 3) and OS 83.3%	NR
Multicenter, Phase II (Bhatt, et al): N=47	Use in sclerotic cGVHD (skin/joint/fascia) Median 3 prior lines	Ruxo 10mg BID for at least 6mo ORR: 49% PR in skin/joints, overall PR 47%, no CRs 1-yr FFS 77.1%	24% reduced steroids by >50% at 6mo NRM 2.2%, 1-yr OS 97.8%	Grade 3+ 40%

Zeiser R, et al. Leukemia 2015

Zeiser R, et al. Blood 2016

Zeiser R, et al. NEJM 2021

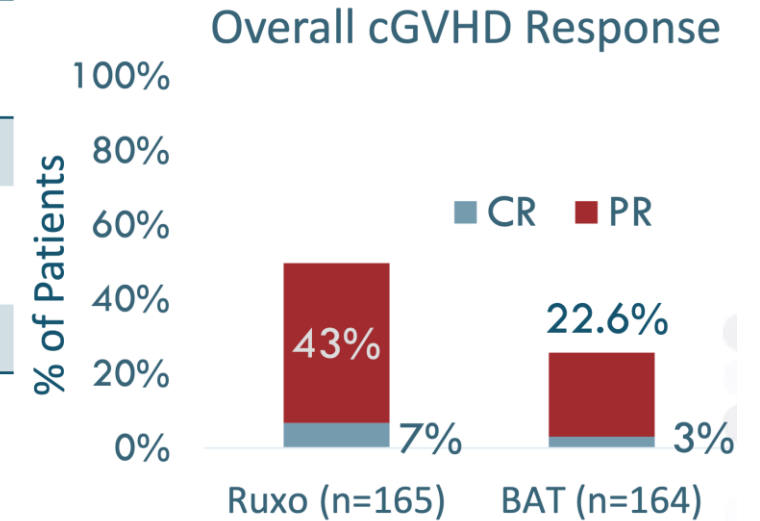
White J, et al ASH 2021

Bhatt VR, et al. J Clin Oncol. 2024

Zeiser R, et al J Clin Oncol 2025

REACH3

Study Design	Phase III randomized, open-label, prospective multicenter study: SR/dependent-cGVHD (N = 329)
cGVHD	Moderate-severe cGVHD (Stratified by cGVHD grade)
Tx Option	[Ruxo 10mg PO BID vs. BAT*] + steroids +/- CNI <i>*Optional crossover @ week 24</i>
Primary Endpoint	ORR @ 24 weeks (C7D1)
Follow-up at 24wks	Ruxo OR 2.99, p <0.0001 Best OR 76.4% Ruxo vs. 60.4% BAT <i>*37.2% crossover to Ruxo arm (ORR 50%)</i>
3-year final Analysis	Median FFS 38.4 (Ruxo) vs 5.7-mo; HR 0.361 <ul style="list-style-type: none"> 1-yr FFS probability 64 vs. 28.8% (BAT) Median OS not reached; DOR <u>not reached</u> vs. 6.4mo (BAT)
Post-Hoc Analysis	Early (<14 days) vs. late (>14-28) tx (Ruxo vs. BAT) <ul style="list-style-type: none"> ORR superior with Ruxo (early OR=2.83, Late/very late OR 3.10) PBR: median time to 1 st response 29 days (ruxo) vs. 50 days (BAT) <ul style="list-style-type: none"> Ruxo higher PBR at all time points



AE's: Anemia (33.9%) → 17.6% severe, thrombocytopenia (21%) → 15% severe CMV reactivation (5.5% vs. 8.2% BAT)

BAT: best alternative therapy

C: cycle

PBR: probability of being in response

Superior response for ruxolitinib vs. BAT in pts. With inadequate steroid response with similar grade ≥ 3 AE's (74.5% vs. 63.3%)

Axatilimab (SNDX-6352)

- Rationale: Humanized IgG4 mAb that binds to CSF-1R
 - Selective inhibition of CSF-1/CSF-1R on circulating monocytes blocks expansion and infiltration of macrophages → ↓ fibrosis
- Dose = 0.3mg/kg IV Q2wks

Trial	Patient Population	ORR	Other End Points	Adverse Effects
Phase I/II (Kitko CL, et al): N = 40 (n=17 phase I, n=23 phase II) Combine phase I dose escalation (0.15-3mg/kg IV Q2wks (n=11), 3mg/kg IV Q4wks (n=6)) and Phase II expansion (1mg/kg Q2wks (n=23))	Recurrent/refractory cGVHD after ≥ 2 LOT 65% ≥ 4 organs, 90% had sclerotic skin ~prior: ibrutinib (65%)/ruxo (53%)/bel (20%)	Best ORR by Cycle 7: 67% (n=40) vs. 82% (n=23) • Prior novel Tx: 50-65% response Median TTR: 4-wks 1-yr FFS (Phase II): 77%	<u>Joint/fascia</u> (61% PRs) >> <u>Lung</u> (31%~13% CR) >> Skin (14%) responses 52% responders dec steroids by 22% mean dose reduction	50% G3+ AE's Increased AST/ALT (38%/33%), CPK (35%), amylase/Lipase (~26%), fatigue (47%), periorbital edema (20%)
Phase II, open-label, randomized (1:1:1) multicenter trial (n=241) AGAVE-201 3 dose cohorts → 0.3 mg/kg IV Q2wks, 1 mg/kg IV Q2wks, 3 mg/kg IV Q4wks *Stratified: severity/prior ruxo, ibrutinib or bel	54% ≥ 4 organs, 80% had severe cGVHD ~prior exposure: ibrutinib (31%)/ruxo (74%)/bel (23%)	ORR 74% (0.3mg Q2W), 67% (1mg Q2W), 50% (0.3mg Q4W) Median DOR: not reached Sustained response ≥20wks: 50% (0.3mg Q2W), 49% (1mg Q2W), 38% (0.3mg Q4W)	0.3mg/kg Q2W Dosing Median FFS 17.3mo 1-yr FFS 64% Responses in fibrosis-organs: GI (~86%), <u>Joint/fascia (76%)</u> > <u>Mouth</u> (52), <u>lungs</u> (42%) >> skin (27%)	47% had G3+ AE's; 0.3mg Q2W 17.7% 0.3mg Q2W: Increased AST/ALT (~13%), CPK (11.4%), amylase/Lipase (~11.4%), fatigue (22.8%), periorbital edema (2.5%)

Kitko CL, et al. J Clin Oncol 2022, Wolff D, et al. Blood 2023, Wolff D, et al. NEJM 2024

Chronic GVHD (cGVHD)-Summary

- **What is cGVHD?**

- **cGVHD mimics the autoimmune/immunologic diseases**
- Classically occurs >100 days from HCT but can occur earlier
- Manifestation of both acute and chronic GVHD can present simultaneously
- **Leading cause of NRM**
- Risk factors for cGVHD
- **cGVHD effects** skin, mouth, liver, **eye**, GIT, **lungs, joints/fascia, and genitals**

- Therapeutic application

- **Treatment based on organ specific/severity** of cGVHD
- Consider topical +/- systemic therapy options
- Prevent over or under-treatment
- Provide **ancillary and supportive therapy** to avoid additional morbidities
- Consider your **patient and drug toxicities**
- **Create definitive monitoring plans to assess for cGVHD complications**

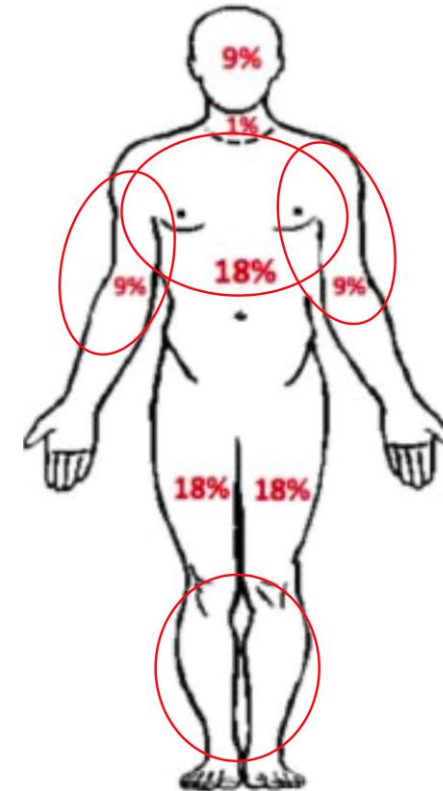
Question #1

- KT is a 50-year-old female currently day +298 status post matched sibling donor allograft for AML (IST: CSA/MTX). Her course was complicated on Day+150 with ocular GVHD and lower extremity scleroderma. During her clinic visit today, she reports new onset of diffuse erythematous rash on her back, chest, neck which has evolved since tapering ciclosporine 1-month ago.
- Current GVHD medications include ciclosporine eye drops, prednisolone 5 mg daily
- What classification of GVHD does she have?
 - A. Classic cGVHD
 - B. Persistent recurrent aGVHD
 - C. Classic acute GVHD
 - D. Overlap syndrome

Question #2

- ST is D+250 post matched sibling donor transplant for AML
 - Physical examination: (+) new extensive psoriatic changes in **upper arms, both lower legs, and trunk** that have worsened over the past month
 - Difficulty raising arms over his head
 - Minimal pinchable skin in affected areas
- Labs: S creat: 3.6 mg/dl (baseline: 2mg/dl post-HCT), LFTS: WNL, Platelets: 75K/micL, weight: 98 kg
- Current medications: amlodipine 10 mg/d, acyclovir & Septran prophylaxis, tacrolimus 0.5mg/d (on taper)
- He reports being sunburnt on a trip to Goa
- **Overall findings are consistent with diagnosis of cGVHD**
- **How much BSA is involved and what grade is it?**

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
SKIN†				
SCORE % BSA <input type="text"/>				
<i>GVHD features to be scored by BSA:</i>	<input type="checkbox"/> No BSA involved	<input type="checkbox"/> 1-18% BSA	<input type="checkbox"/> 19-50% BSA	<input checked="" type="checkbox"/> >50% BSA
Check all that apply:				
<input type="checkbox"/> Maculopapular rash/erythema				
<input type="checkbox"/> Lichen planus-like features				
<input checked="" type="checkbox"/> Sclerotic features				
<input type="checkbox"/> Papulosquamous lesions or ichthyosis				
<input type="checkbox"/> Keratosis pilaris-like GVHD				
SKIN FEATURES SCORE:	<input type="checkbox"/> No sclerotic features		<input type="checkbox"/> Superficial sclerotic features "not hidebound" (able to pinch)	Check all that apply:
				<input type="checkbox"/> Deep sclerotic features
				<input checked="" type="checkbox"/> "Hidebound" (unable to pinch)
				<input checked="" type="checkbox"/> Impaired mobility
				<input type="checkbox"/> Ulceration
<i>Other skin GVHD features (NOT scored by BSA)</i>				
Check all that apply:				
<input type="checkbox"/> Hyperpigmentation				
<input type="checkbox"/> Hypopigmentation				
<input type="checkbox"/> Poikiloderma				
<input type="checkbox"/> Severe or generalized pruritus				
<input type="checkbox"/> Hair involvement				
<input type="checkbox"/> Nail involvement				
<input type="checkbox"/> Abnormality present but explained entirely by non-GVHD documented cause (specify):				



- **ST was started on prednisolone 1 mg/kg (100 mg/d). Returns to clinic after 4 weeks of prednisolone**
 - He is currently on 45 mg of prednisolone (on slow taper) and azole prophylaxis
 - Overall skin manifestations and ROM are improving however cutaneous involvement remains at a partial response (>50% but less than complete organ response)
- **At this time what additional therapies should be offered?**
- **A) Ruxolitinib B) Ibrutinib C) Belumosudil D) Axatilimab**