



Onconeurology Symposium 2026

Basics of Stem Cell Transplantation:

What Transplanters Wished Nephrologists Knew

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Disclosure statement

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- Consulting Fees/Honoraria: Sanofi, Incyte, Syndax, CSL Behring, CareDx, GSK, Takeda, Medexus, Knight Therapeutics
- Consulting Fees/Equity: Cimeio, Oxford Immune Algorithmics, OrcaBio
- Stock/Funds: Allogene, Actinium, Cue, Northwest Biotherapeutics, Verastem
- DSMB: Incyte

What We Wished You Knew

- Transplant is quite simple, repetitive, algorithmic
 - Even I can still do it
 - There are many ‘recipes’ (conditioning, GVHD prevention) – most are associated with similar outcomes.
- Most of us are hyperaggressive. ‘No’ is generally not an acceptable answer
 - Might not be right often, but in those rare instances where we are, the rewards are huge
- We really, really, really don’t understand those black boxes you know so much about



Learning Objectives

- Understand the Basics of Transplantation Processes
- Recognize Potential Points of Renal Injury
- Understand Therapies and Their Impact on Transplant Patients

Indications for Hematopoietic Stem Cell Transplantation (HSCT)

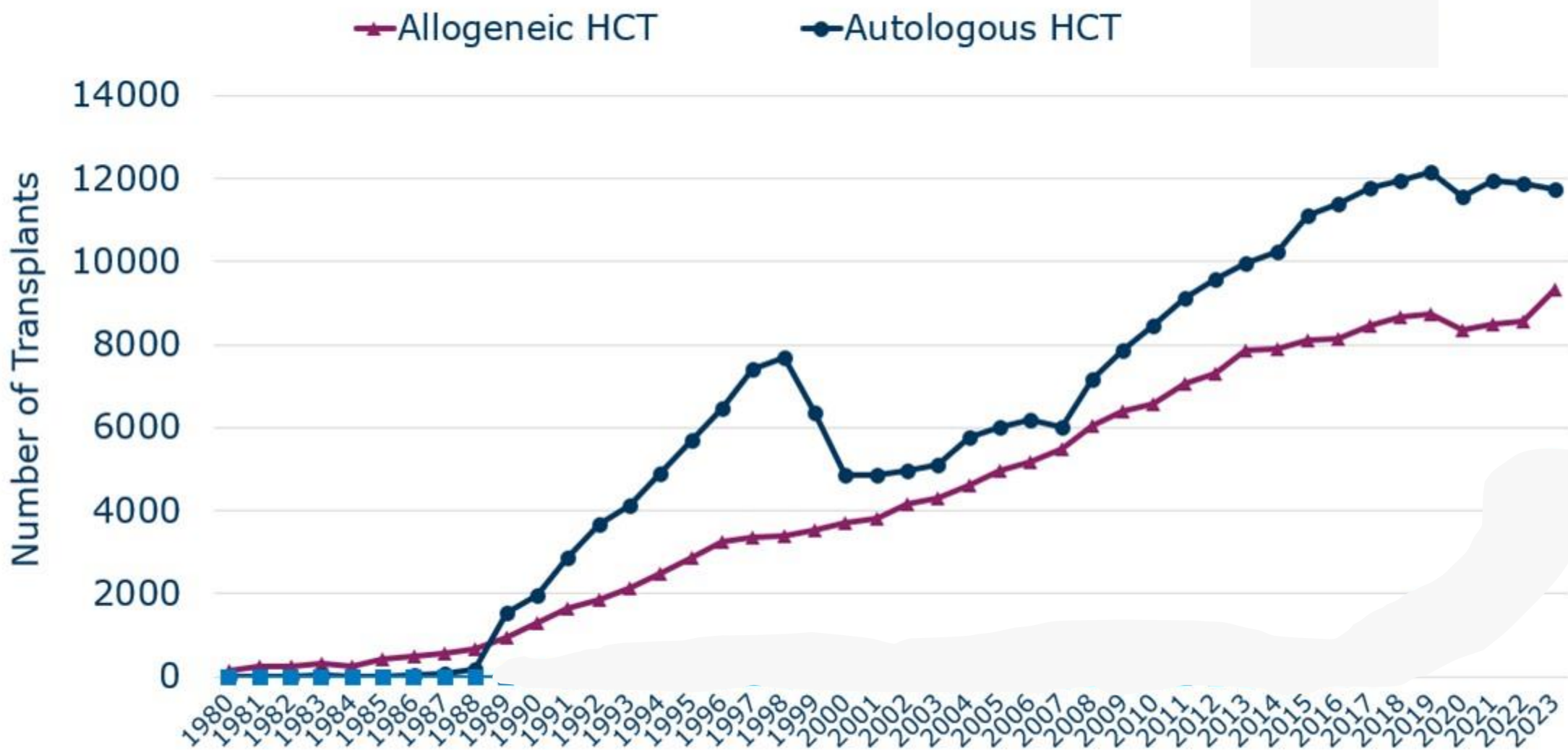
- Bone marrow failure
 - Congenital bone marrow failure
 - Acquired bone marrow failure: Aplastic anemia
- Immune deficiency
 - Replacement therapy for a large variety of genetic diseases
- Genetic metabolic diseases
 - Provides cells that will produce normal metabolic enzymes

Always Allogeneic

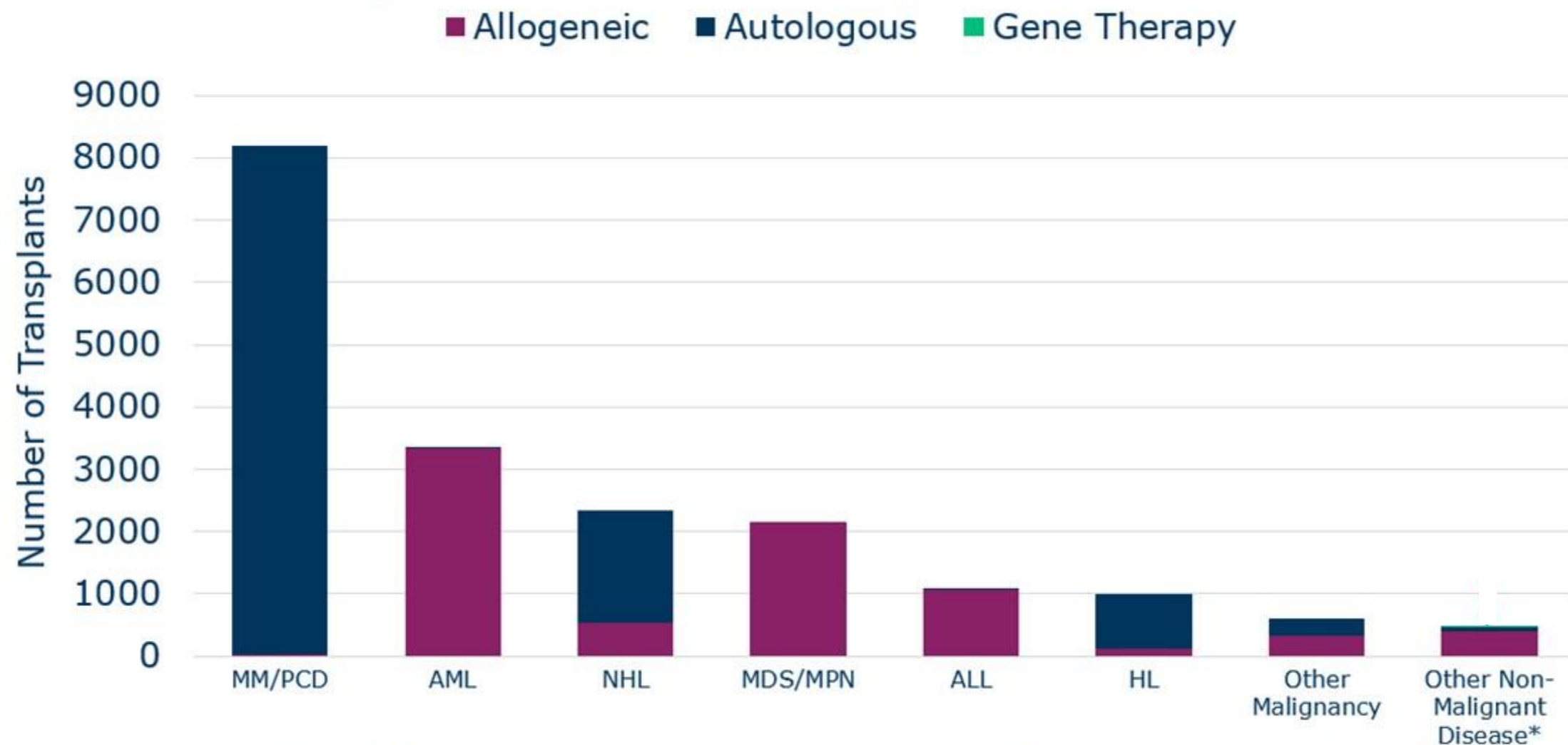
- Hematologic malignancies
 - Myeloid and Lymphoid Leukemias, Lymphomas, Myeloma
 - Allows the administration of high dose myeloablative chemotherapy

Usually Allogeneic, but sometimes Autologous

Number of 1st Cellular Therapies Reported to CIBMTR in the US



Number of HCTs by Indications in the US, 2023, Adult



*Includes 22 limited gene therapy events

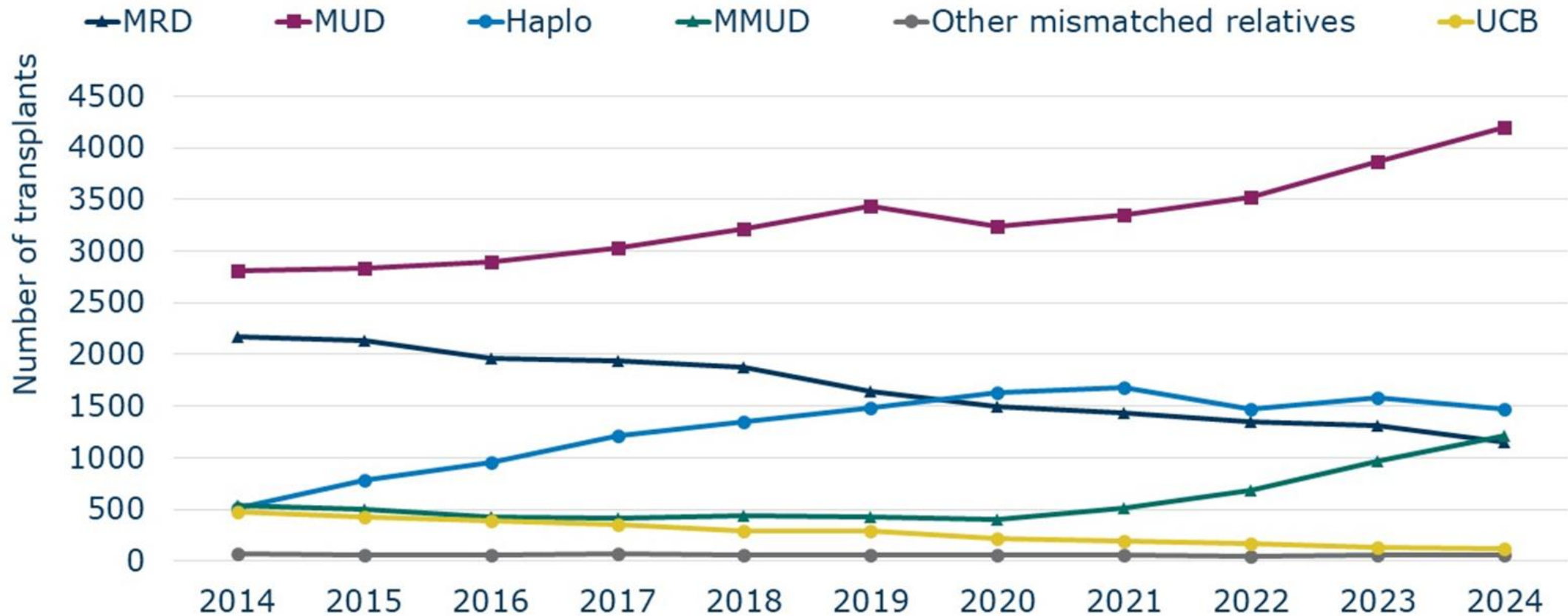
Abbreviations:

ALL, acute lymphoblastic leukemia;
AML, acute myeloid leukemia;
CLL, chronic lymphocytic leukemia;
HL, Hodgkin lymphoma;
MDS, myelodysplastic syndromes;

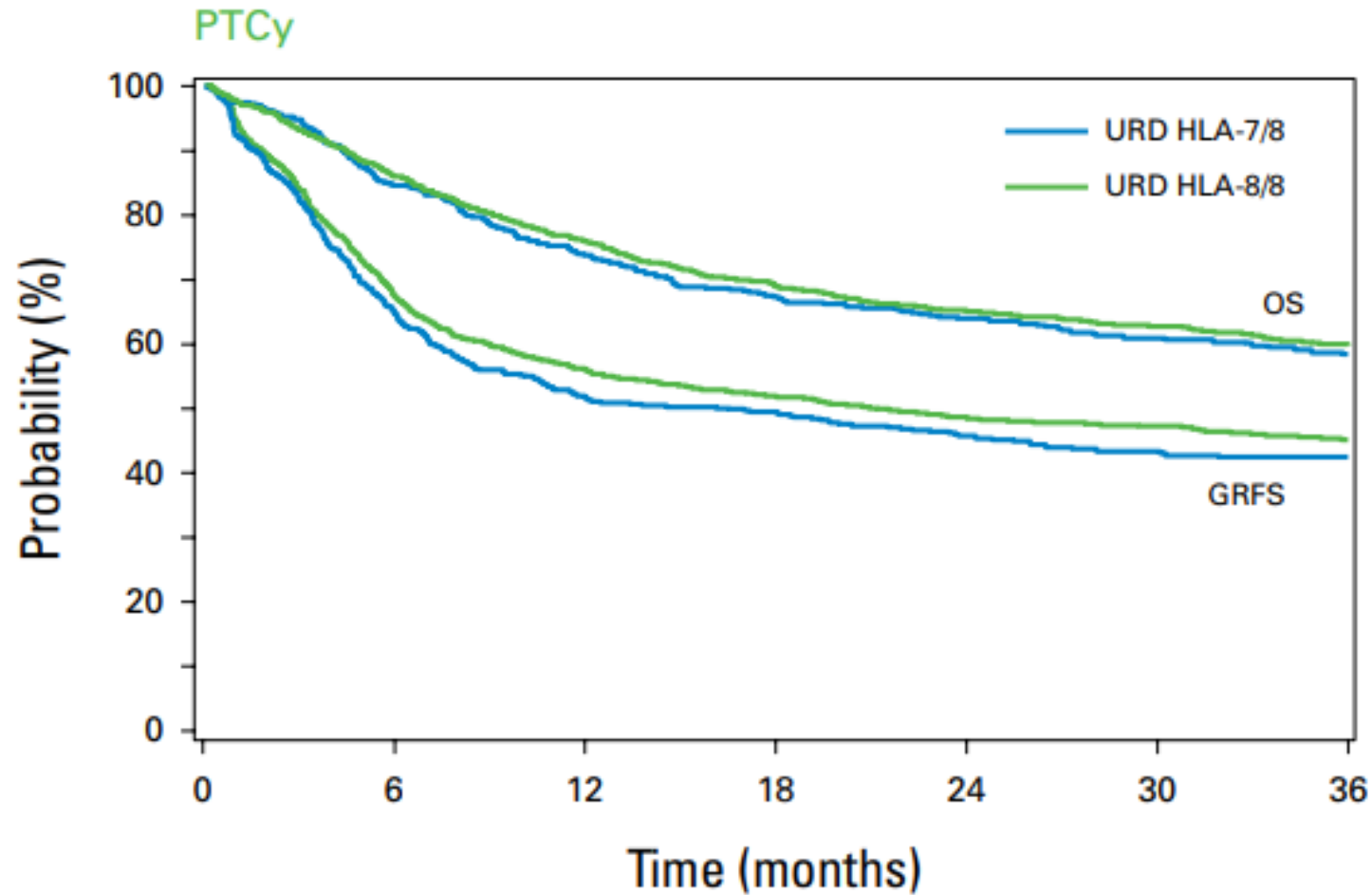
MM, multiple myeloma;
MPN, myeloproliferative neoplasms;
NHL, non-Hodgkin lymphoma;
PCD, plasma cell disorders.

Donor Sources and Selection

First alloHCTs in US, by donor type, 2014-2024, adults



Impact of HLA Mismatching and Donor Availability





How We Define Success

- Overall Survival ?
- Relapse-Free Survival ?
- GVHD Incidence ?
- GVHD-Free, Relapse-Free Survival ?

- Moving towards Win-ratio hierarchical outcomes

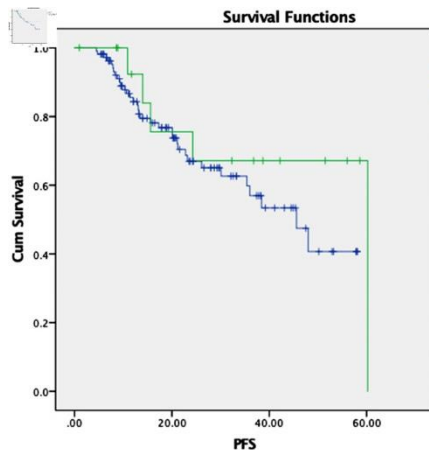


How We *Try* To Injure the Kidney

- Conditioning
- GVHD Prevention
- Endothelial Injury Syndromes and Acute GVHD
- Chronic GVHD

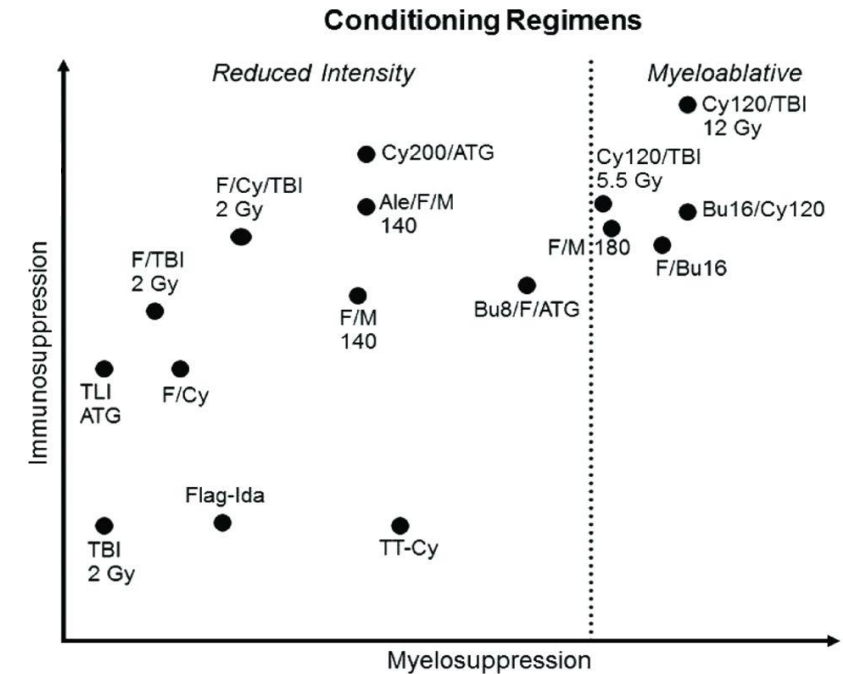
Conditioning Therapy and Renal Injury Syndromes

- Conditioning Therapy: Designed to make physical space in the marrow (myeloablation) and immunologic space to prevent graft rejection (most T cell active drugs – basis of reduced intensity conditioning)
- Most of our drugs are not inherently renally toxic
 - Some are metabolized by the kidney
 - Fludarabine requires dose modification in low-GFR states
 - <50 ml/min/m² 25-50% dose reduction
 - <30 ml/min/m² – not recommended for use
 - Some are entirely unimpacted by renal state
 - Melphalan is given with impunity in RRT patients – Myeloma

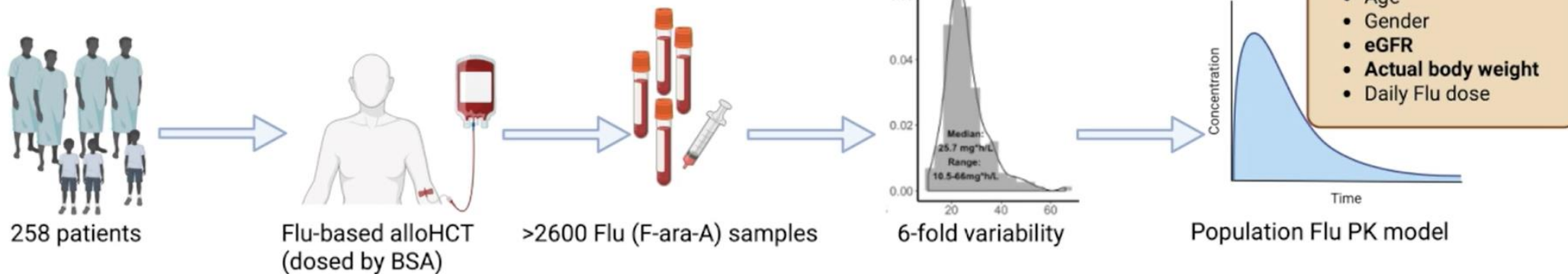


— CKD
— No CKD

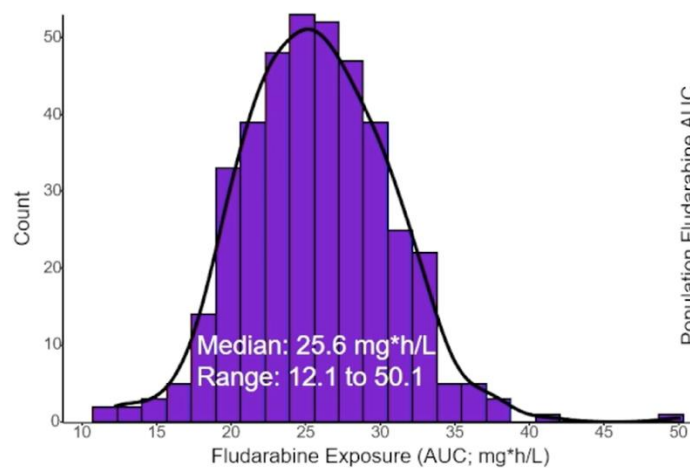
Ursu *et al*, J Hematol 2023



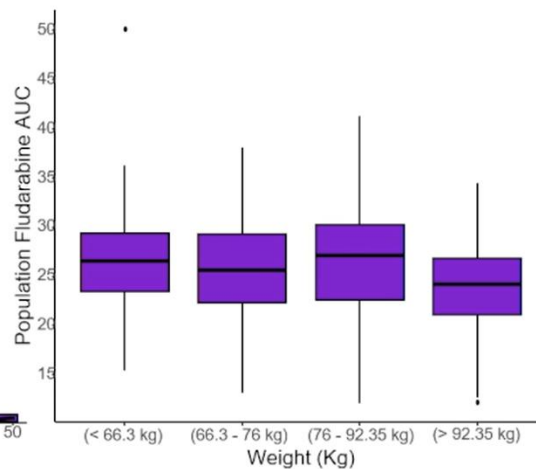
Fludarabine Pharmacokinetics



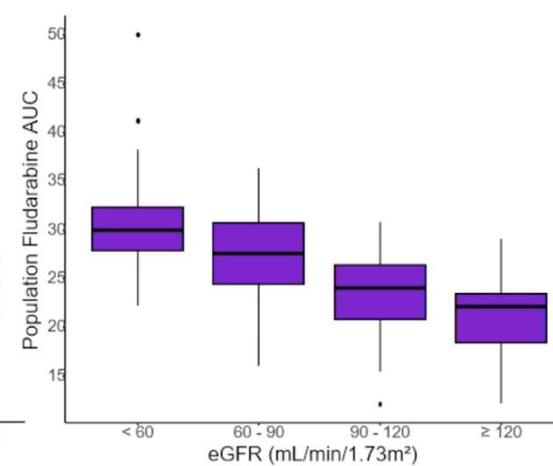
Flu exposure distribution



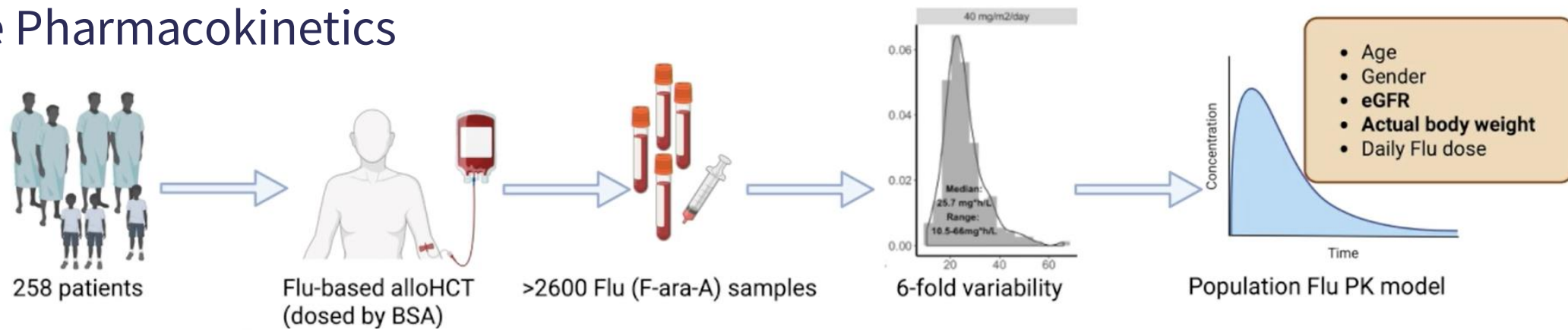
Flu exposure by weight



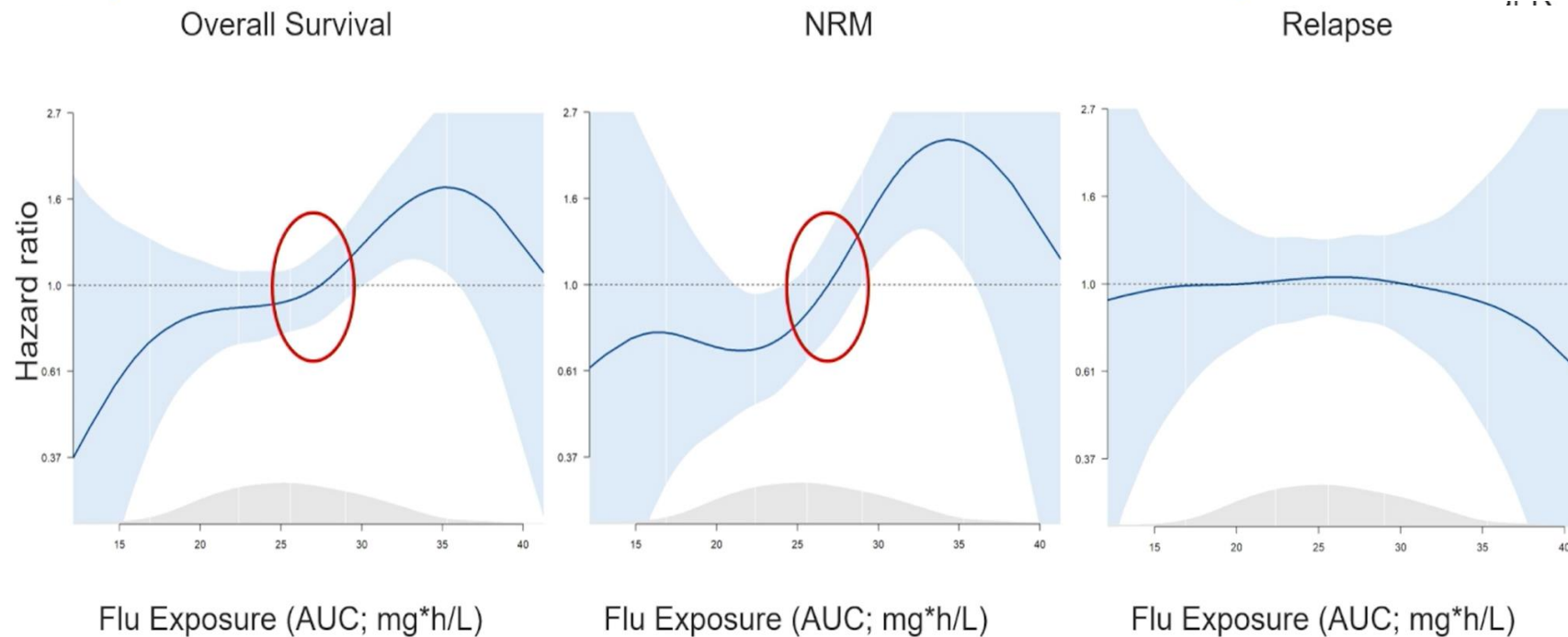
Flu exposure by eGFR



Fludarabine Pharmacokinetics

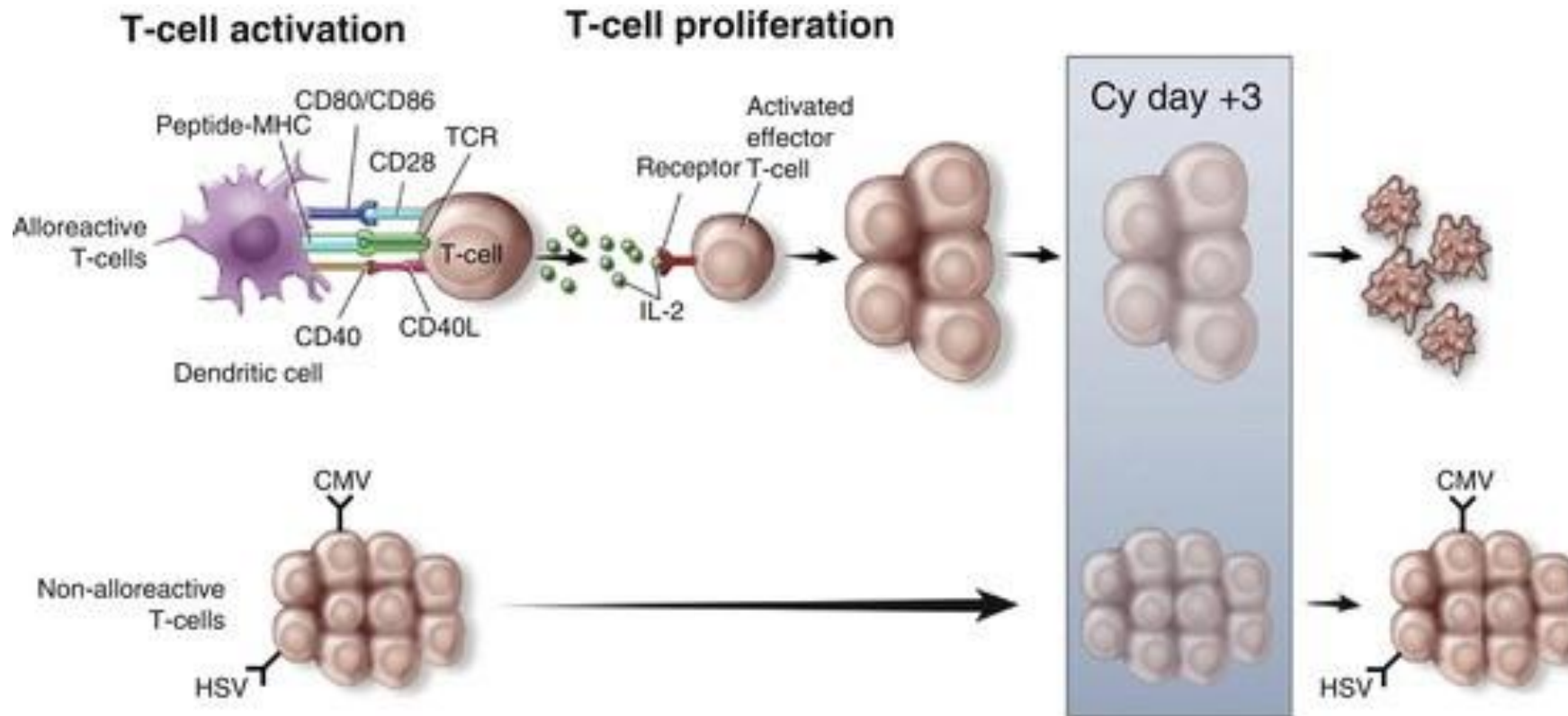


Population Flu PK Model Identified Two Distinct Exposure Groups



GVHD Prophylaxis

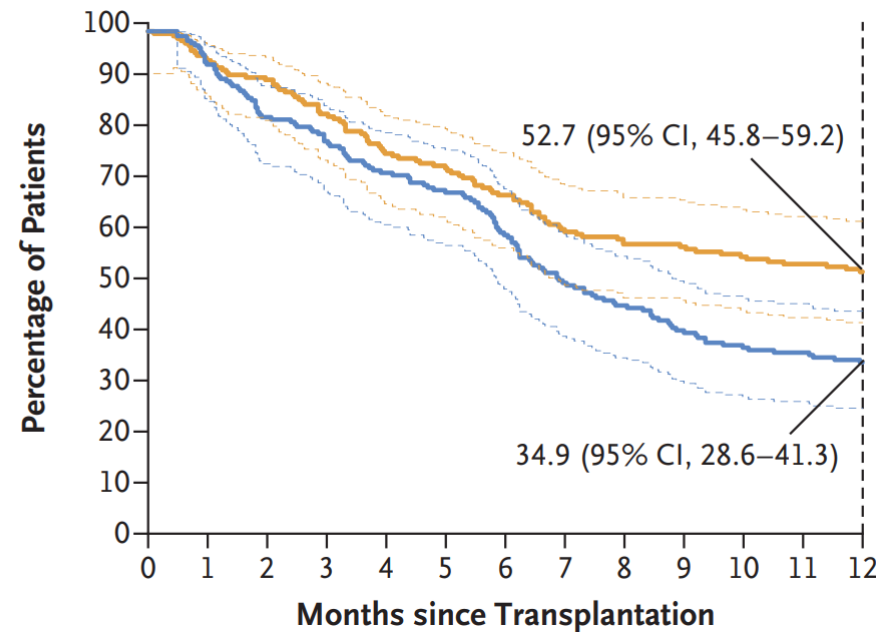
- Post-Transplantation Cyclophosphamide has become the standard - broadly



GVHD Prophylaxis

- Post-Transplantation Cyclophosphamide has become the standard - broadly

Adjusted GVHD-free, Relapse-free Survival



Bolanos-Meade *et al*, NEJM

***Hyponatremia from Cytoxan (SIADH-like) – over 50% in our patient population, resolves in 48-72h
Gomez-Hernando *et al*, BMT 2002

Tacrolimus

- Used ubiquitously
 - Started FOLLOWING transplant in PTCy
 - Started PRE transplant in all other regimens
- Replaced Cyclosporine nearly entirely in Adults
 - Few laggards, esp in Pedi
- Goal: 5-10 (or 5-15 ng/ml)
- Love/Hate relationship

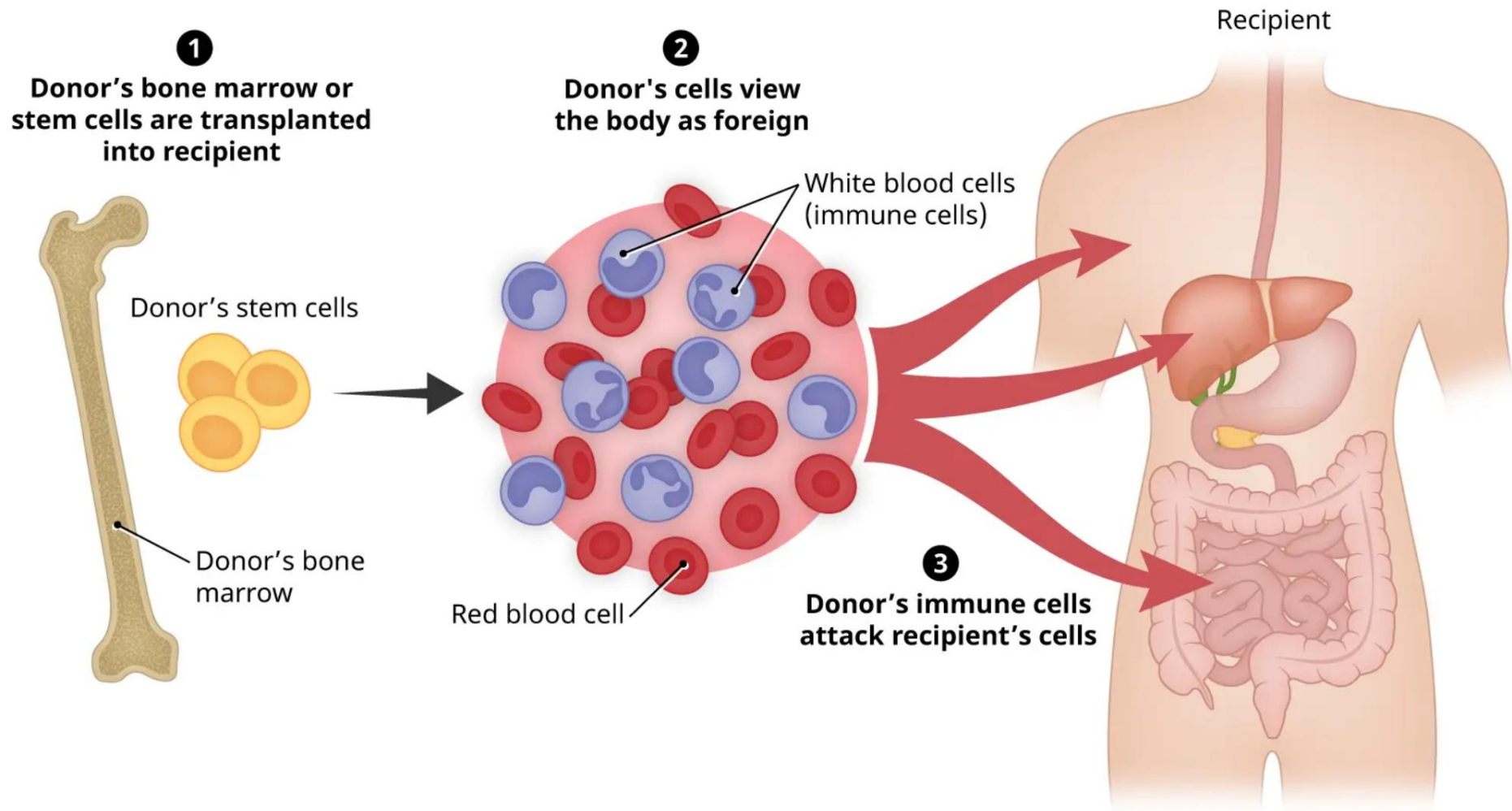
Multiple mechanisms of Renal Injury

Vasoconstriction

Promotion of TMA

Interaction with other agents (ie azoles)
(potentiating their toxicity)

Graft-vs.-Host Disease



Endothelial Syndromes: TMA and VOD

- Likely within the spectrum of GVHD
 - Occurs in autologous transplantation but at a lower frequency, suggesting an alloimmune effect against the endothelium

Thrombotic Microangiopathy

- TTP-like syndrome
- Generally related to Tacrolimus, but also late following transplant more related to Radiation
- Incidence much higher when Sirolimus given with Tacrolimus (sadly, Cutler *et al*, 2004)
- Treatment Pearls
 - Stop Tacrolimus (Sirolimus can actually stay)
 - Plasma exchange does not work
 - Some evidence to support use of eculizumab
 - Newly approved for use: Narsoplimab

Endothelial Syndromes: TMA and VOD

Veno-Occlusive Disease

- Primary damage to the hepatic sinusoidal endothelium
- Risk factors: Radiation, inotuzumab, gemtuzumab, liver disease
- Classic triad: Hyperbilirubinemia (direct), Weight gain (ascites), RUQ capsular pain
- Hepatic Doppler Ultrasound: Blunting of portal venous waveforms → Reversal of portal vein flow
 - Elastography might be more sensitive

→ Sudden increase in Tac levels, hepatorenal syndrome, thrombocytopenia

Therapy:

Defibrotide: Single strand oligonucleotides (pig intestinal mucosa), acting at Adenosine A₂ receptors (?)

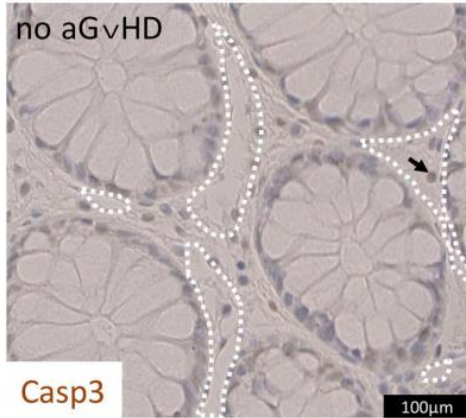
FDA-approved – The earlier it is started, the better the outcomes

Early recognition is CRITICAL

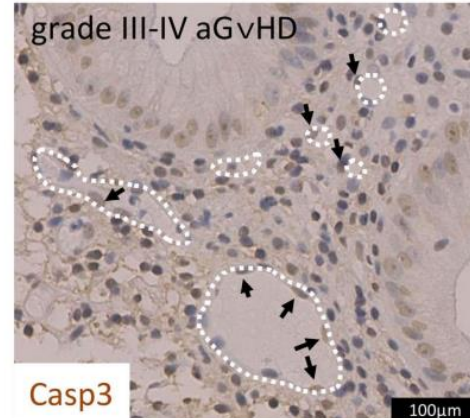
Acute GVHD as Endothelial Injury

Endothelial apoptosis in human biopsies

A

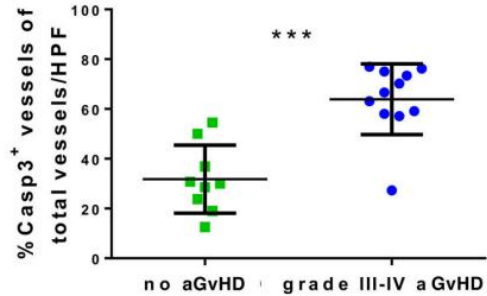


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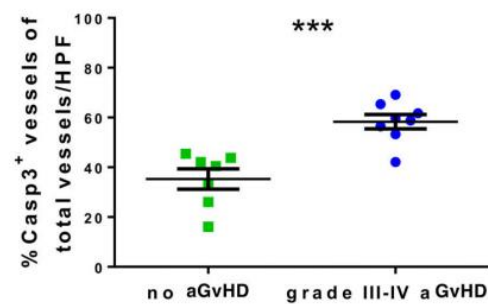
C

Duodenum

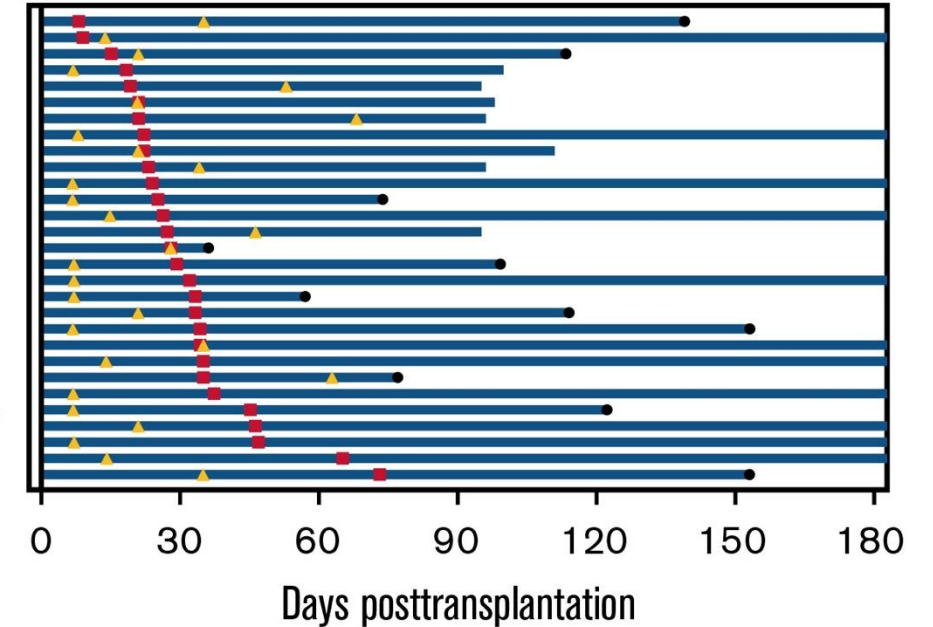


D

Colon

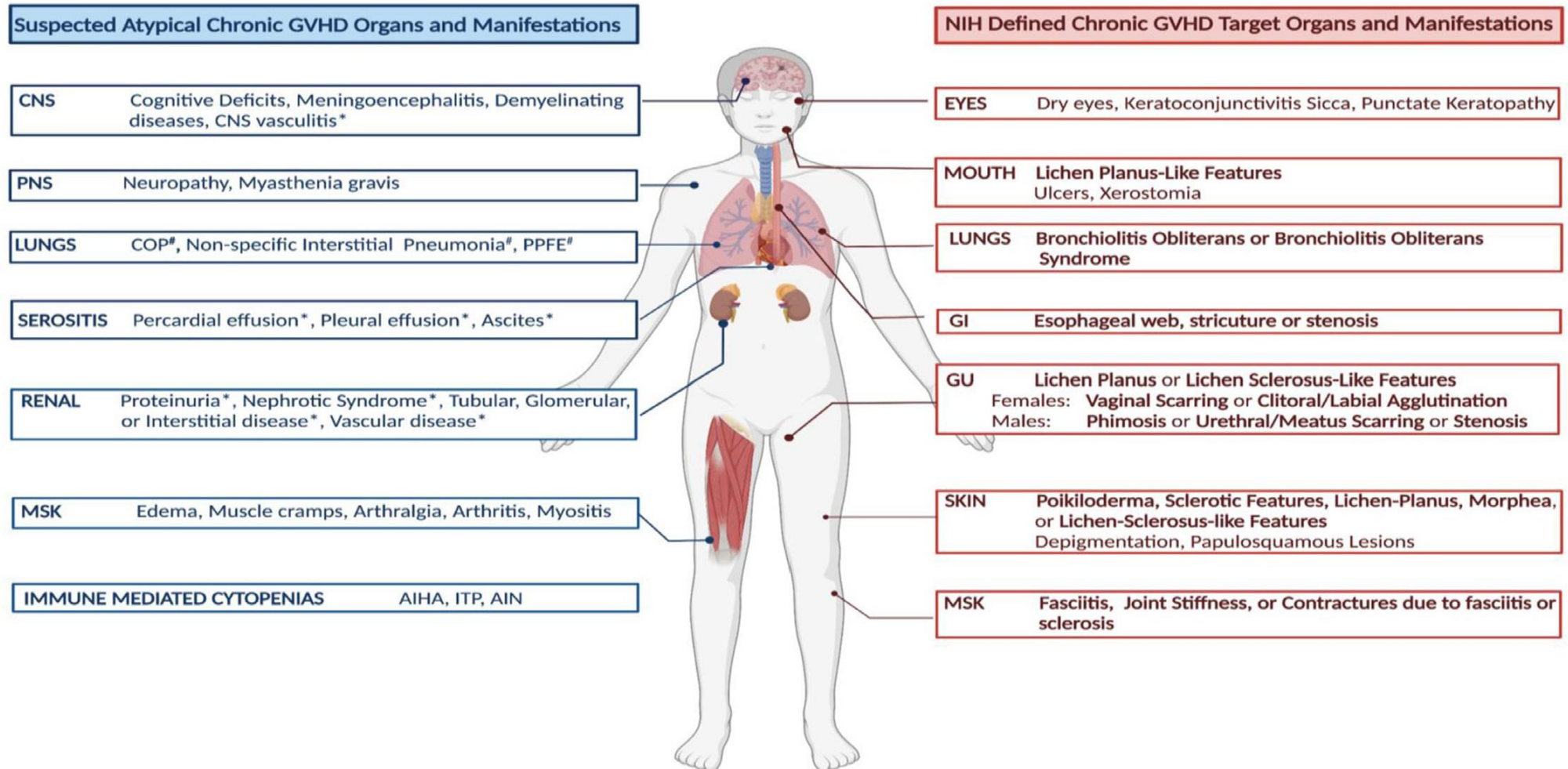


In patients with **maximum overall grade 3-4 acute GVHD**, yellow triangles show time to onset of severe TA-TMA and red squares show time to onset of GVHD



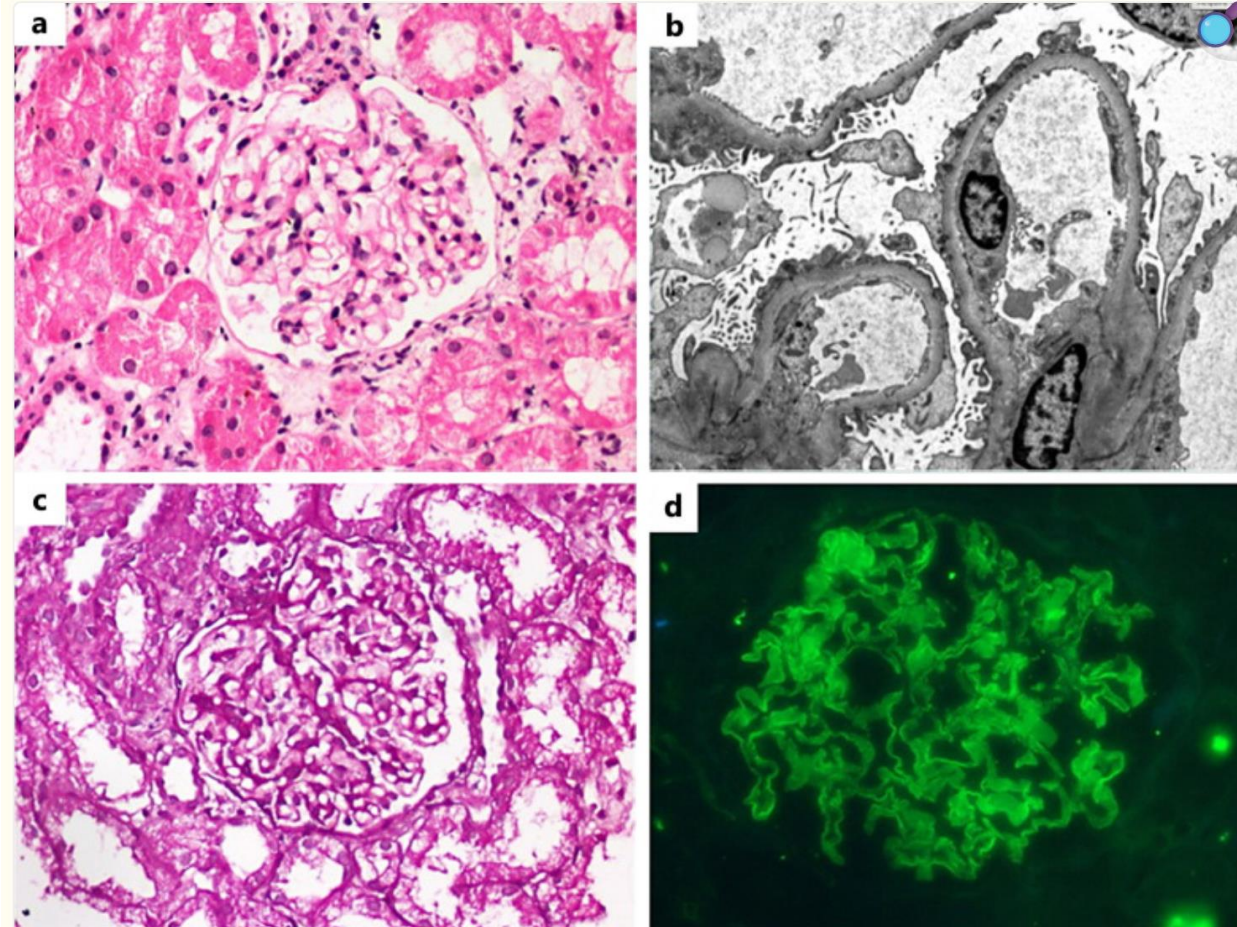
Chronic GVHD and the Kidney

- Officially, not a target organ of the allogeneic immune system. Untrue.



Renal Chronic GVHD

- Incidence: ~2% of all chronic GVHD (Doering *et al*, TCT 2023)
- 2 patterns of injury noted in renal biopsy specimens post-BMT
- Late renal disease – Nephrotic Syndrome-type
 - Membranous
 - MCD
 - Lupus-like
- TMA-like pattern exists
 - Whether this is a manifestation of cGVHD is less clear
 - Non-immune Rx responsive
- **Therapy**
 - Per histology in non-BMT patients
 - Heavy reliance on anti-B cell therapy



RRT in Critically Ill BMT Patients

AKI Treated with Kidney Replacement Therapy in Critically Ill Adult Allogeneic HSCT Recipients

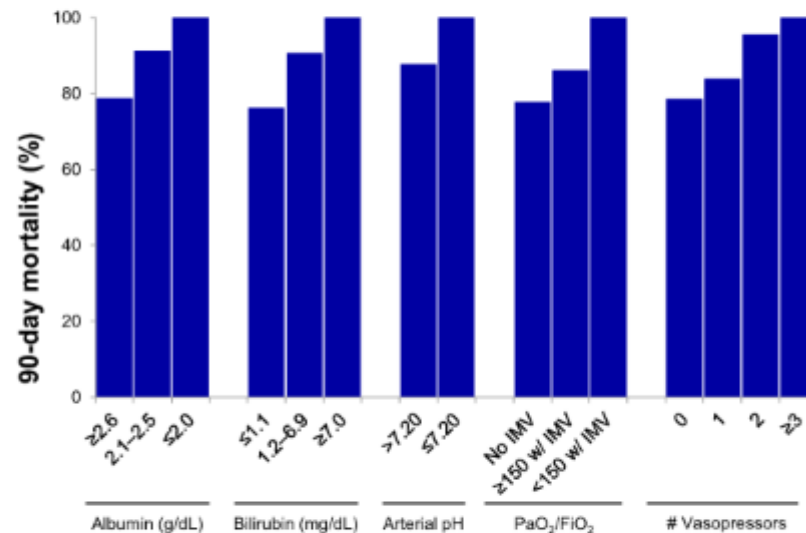
Multicenter cohort study of 3728 adult allo-HSCT recipients transplanted between 2011-2021

 **529** Admitted to ICU within 1-yr post transplant

 **21%** Developed AKI treated with kidney replacement therapy (AKI-KRT) in the ICU

 **87%** Died within 90 days of AKI-KRT

90-day mortality was 100% in multiple subgroups of patients with AKI-KRT



Abbreviations: AKI-KRT, acute kidney injury treated with kidney replacement therapy; IMV, invasive mechanical ventilation

MSKCC Series:

43% of RRT patients recovered renal function

DFCI Series:

25% of RRT patients recovered renal function

Conclusion

AKI treated with kidney replacement therapy is a common complication among allo-HSCT recipients admitted to the ICU and is associated with exceptionally high short-term mortality



Take Home Messages

- Many, many ways for us to damage the kidney
- The smart transplanters have a good relationship with their nephrologists
- Thank you for your collaboration!