THE ROLE OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN TREATING BLOOD CANCER

DERIVED FROM THE LIVE ACTIVITY WHICH OCCURRED ON MARCH 23, 2023

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FACULTY

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- **Krishna Komanduri, MD**: Consultant for: Aegle Therapeutics, Avacta Life Sciences, Cargo Therapeutics, CRISPR, Incyte, Iovace, Genentech/Roche, Janssen, Novartis, OptumHealth
- **Corinne Shamehdi, MPAS, PA-C**: None
- **Lesley Hoerst, BSN, RN:** None
- **Lauren Berger, MPH:** None
- **Camille Dyer, MS, PA-C, AACC, DFAAPA:** None

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EDUCATIONAL OBJECTIVES

After completing this CE activity, the participant should be better able to:

- Describe the goals and types of hematopoietic cell transplantation used in the treatment of blood cancers, including autologous, allogeneic, and reduced-intensity allogeneic stem-cell transplantation
- Describe the indications for hematopoietic stem cell transplant
- Explain the process of pre-transplant evaluation, mobilization, cell collection, and cell infusion in patients with blood cancer
- Explain the short and long-term follow up requirements
- Identify resources for patient education and support

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Hematopoietic Stem Cell Transplantation and CAR-T Therapies for Blood Cancers

Krishna Komanduri, MD
Corinne Shamehdi, PA-C

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Alfred Velpeau Describes Leukemia in 1825

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1825-1950: ~1000 Publications About Leukemia

1960s
Combination chemotherapy + stem cell transplants

1825
First description of acute leukemia

1950-2000: ~175,000 publications about leukemia

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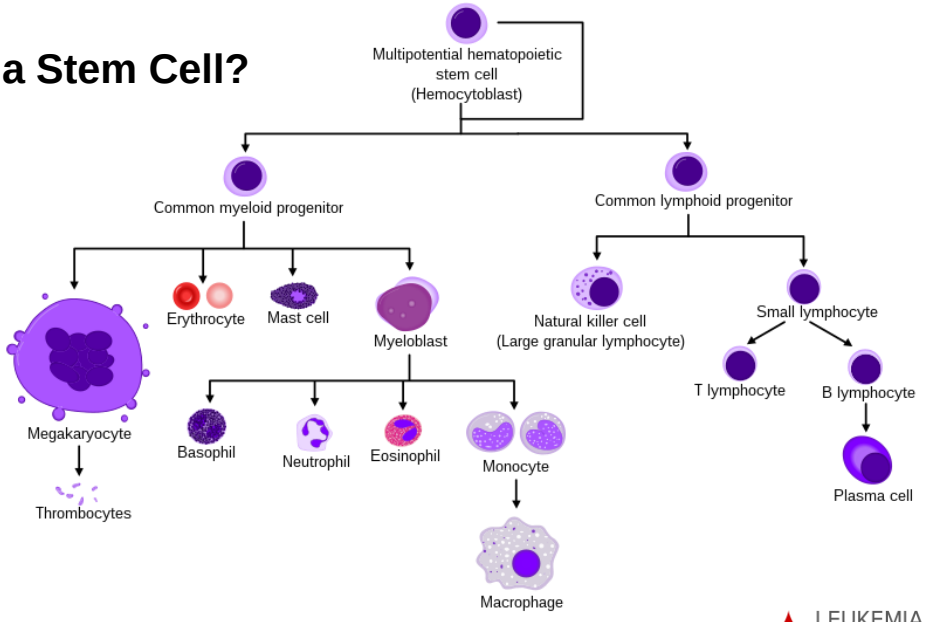
What is a Stem Cell?



A. Rad and Mikael Häggström, M.D. Simplified hematopoeisis. July 21 2009. https://commons.wikimedia.org/w/index.php? curid=7351905. Wikimedia Commons. Accessed March 17 2023.

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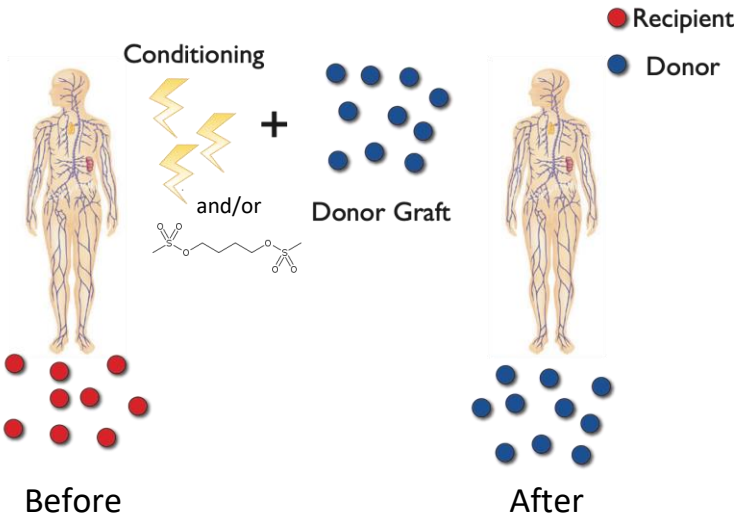
Concept of Myeloablative Stem Cell Transplant



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Categories of Stem Cell Transplants

- Autologous or “auto” uses patient’s own cells
- Allogeneic or “allo” uses cells from a donor, who may be a family member
- Haploidentical or “haplo” uses cells from a half-matched family member, usually a parent or child (but occasionally a sibling or grandchild)
- Unrelated donors may be matched “MUD” or mismatched “MMUD”
- Syngeneic = stem cells from a monozygotic identical twin (uncommon)

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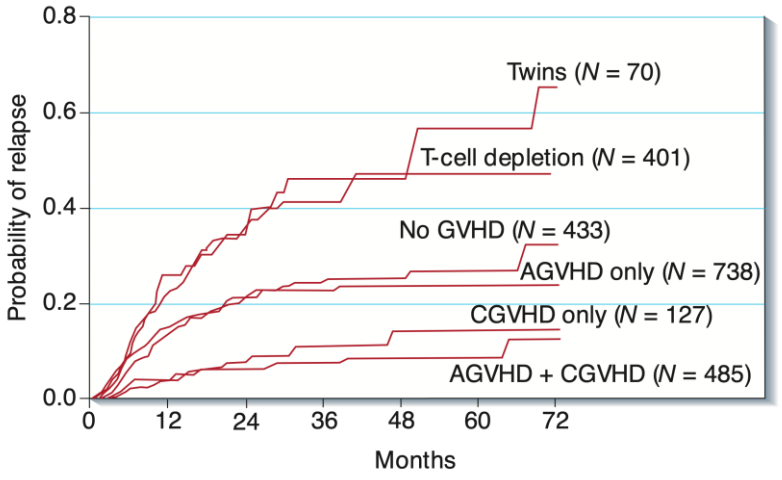
T Cell Depletion is Associated with Increased alloSCT Relapse



Appelbaum FR. Nature 411: 385-389 (2001). original, Horowitz M, Blood (1990)

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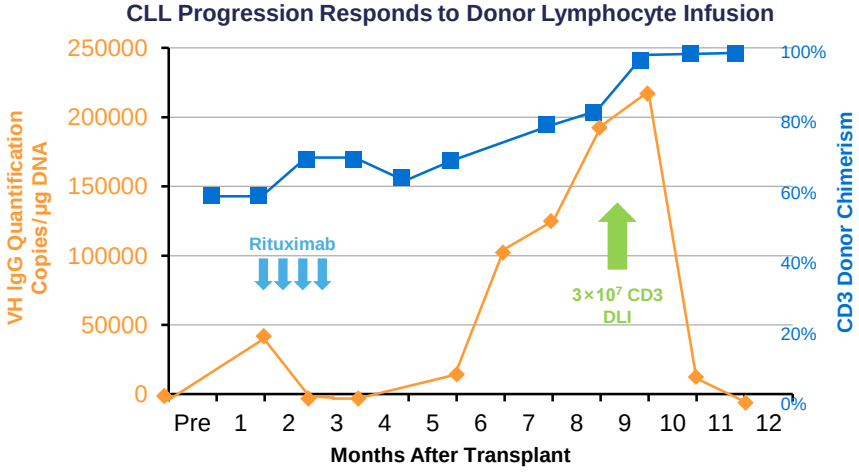
Efficacy of Donor Lymphocyte Infusions Provides Rationale for T-Cell Therapy



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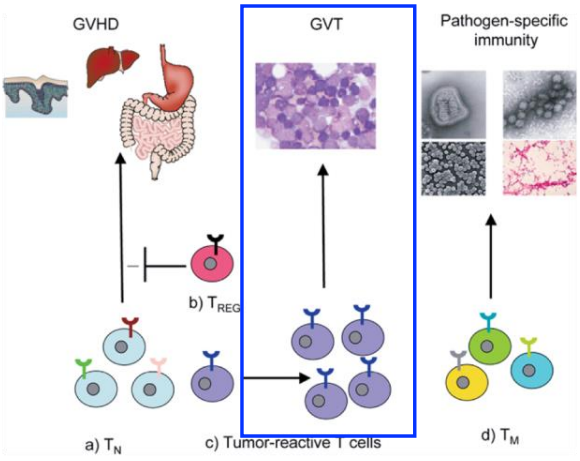
T cells in Donor Transplant Grafts Eliminate Residual Cancer



Riddell & Appelbaum, Graft v. Host Disease, PLOS Medicine, 2007

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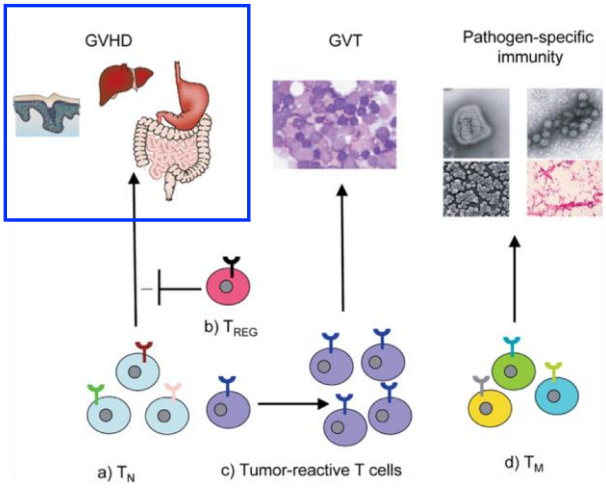
…but can attack healthy tissues in the patient



Riddell & Appelbaum, Graft v. Host Disease, PLOS Medicine, 2007

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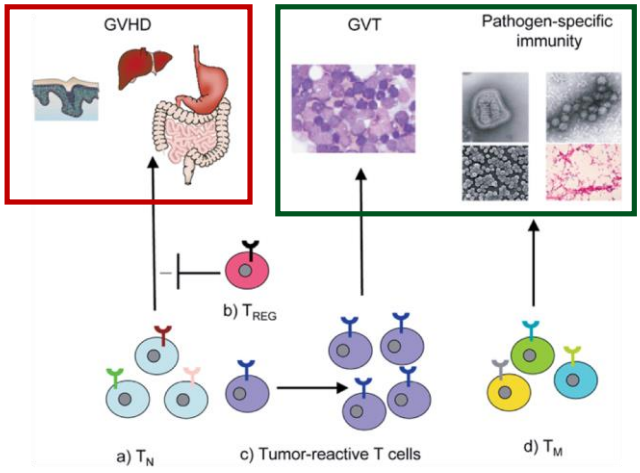
Improving Immune Outcomes of Stem Cell Transplants

Can we selectively inhibit these...



without impairing these?

Riddell & Appelbaum, Graft v. Host Disease, PLOS Medicine, 2007

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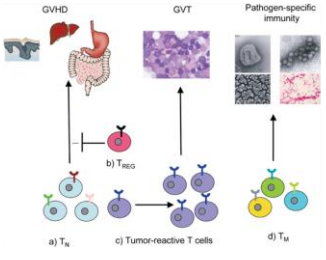
1960s

Combination chemotherapy + stem cell transplants

1825

First description of acute leukemia



1990s

T cells critical for transplant cures—dramatic increase in success

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Pre-Transplant Conditioning

- Chemotherapy, immunotherapy, and/or radiation therapy prior to transplant that prepares the patient for HSCT
  - ❑ Autologous conditioning
    - High doses of chemotherapy that kill malignant cells
    - Requires stem cell rescue
  - ❑ Allogeneic conditioning regimens
    - Eradicate malignant cells
    - Immunosuppress the recipient to prevent rejection

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Conditioning Regimen Intensity

Categorized into 3 groups based on level of intensity:

Myeloablative (MA)
- Cause irreversible (or near irreversible) pancytopenia
- Stem cell rescue is required to restore marrow function and prevent aplasia-related death

Non-myeloablative (NMA)
- Produces moderate-to-minimal cytopenia

Reduced Intensity Conditioning (RIC)
- Intermediate: likely ablative but much less intensive than standard MA regimens

Saad A, Loren A, Bolaños-Meade J, et al. NCCN Guidelines® Insights: Hematopoietic Cell Transplantation, Version 3.2022: Featured Updates to the NCCN Guidelines. *J Natl Compr Canc Netw*. 2023;21(2):108-115. doi:10.6004/jnccn.2023.0007

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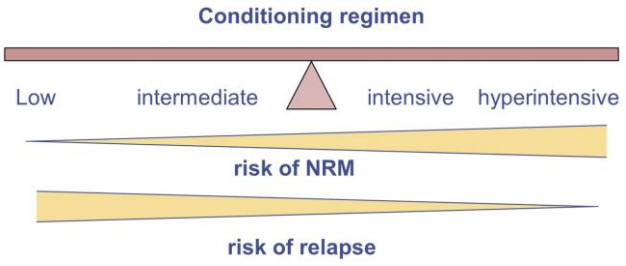
Conditioning: Goals and Principles

- Provide tumor cytoreduction and eradicate any remaining tumor cells
- Provide adequate immune suppression to overcome host rejection of the donor graft (alloSCT)
- Avoid therapies with overlapping toxicity profiles



1. Gagelmann N, Kröger N. Dose intensity for conditioning in allogeneic hematopoietic cell transplantation: can we recommend "when and for whom" in 2021?. Haematologica 2021;106(7):1794-1804; https://doi.org/10.3324/haematol.2020.268839.

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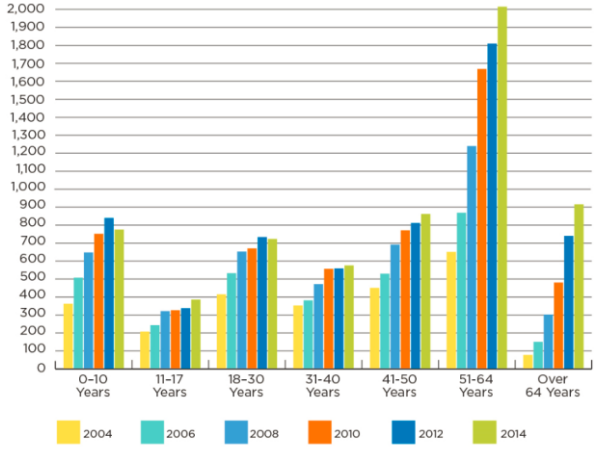
Reduced-Intensity Conditioning Facilitates a Dramatic Expansion of Transplantation in Older Adults (2004-2014)



Source: National Marrow Donor Program/Be The Match FY 2014

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Goals of Hematopoietic Stem Cell Transplants

- Restores normal hematopoiesis in BM failure syndromes
- Replaces disease marrow with healthy marrow
- Serves as a “rescue” following marrow-ablative treatments
- Serves as a means of correct congenital immunodeficiency disorders or other genetic diseases
  - Replaces a missing or abnormal hematopoietic or lymphoid component
- Establishes a graft-vs-leukemia (tumor) effect (alloSCT)

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Allogeneic Stem Cell Transplantation: Evolution and Limits

- Since the 1980s, alloSCT has evolved from ablation to immunotherapy
- The use of *less intensive* conditioning expanded eligibility from <55 to 75 (or older)
- Peripheral blood HCT and improved supportive care have substantially decreased non-relapse mortality (from ~30-40% to 5-10% in the first 100 days after alloHCT)
- Typical results for AML: 5-10% 100-day and 30% one-year mortality (~50:50 NRM:relapse)
- GVHD is still a major problem, in *acute* (10-30% severe) and *chronic* (20-70%) forms
- Immunosuppression has modestly improved in 50 years and is largely non-selective
- *Only three GVHD therapies (JAK1/2 inhibition for acute; ITK/BTK and ROCK2 inhibition for chronic) approved in 50 years*

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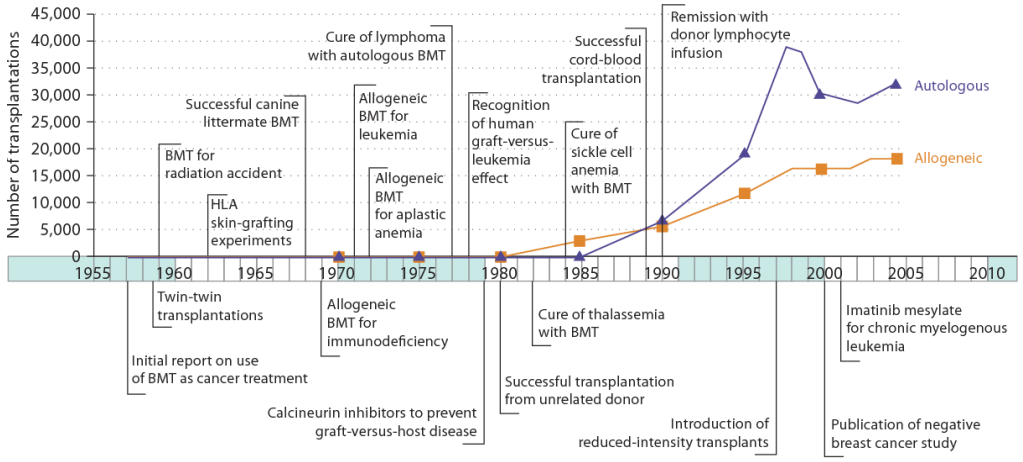
The First Half Century of Stem Cell Transplant History



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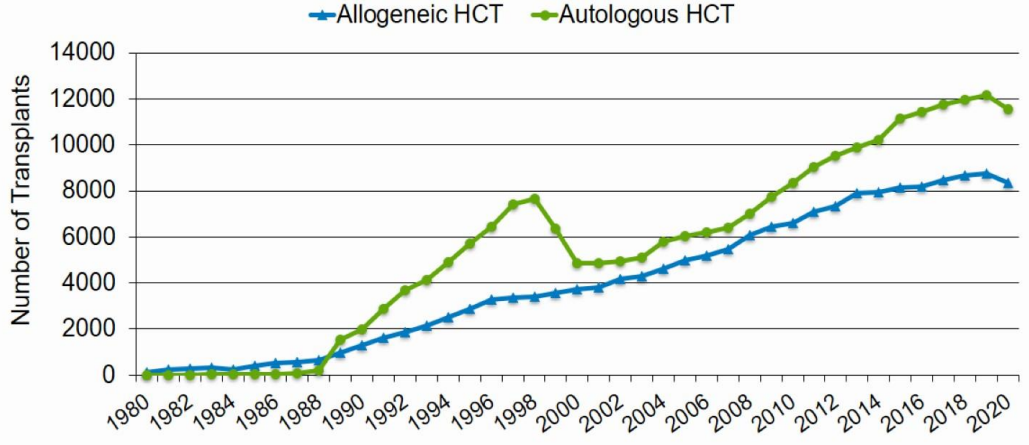
Number of HCTs in the US Reported to CIBMTR by Transplant Type



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Indications for Autologous Transplantation

Non-Hodgkin's lymphoma	Hodgkin's lymphoma	Myeloma
• Follicular: poor response or initial remission duration <12 months, transformation to DLBCL • DLBCL or high grade lymphomas: at first or subsequent relapse, CR1 for high and high-intermediate IPI risk, refractory disease • Mantle cell: after initiation of therapy • Other high risk lymphomas: after initiation of therapy	• Primary induction failure or relapse • CR2 and beyond	• All patients after initiation of therapy • At first progression

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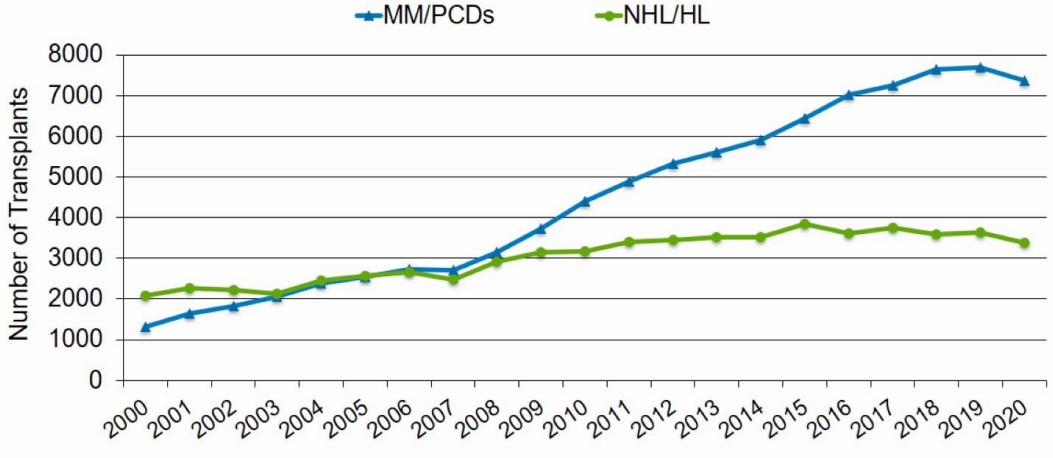
Number of Autologous HCTs in the US by Selected Disease



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Abbreviations – MM: Multiple myeloma; PCDs: Plasma cell disorders; NHL: Non-Hodgkin lymphoma; HL: Hodgkin lymphoma

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Indications for Allogeneic Transplantation

AML	MDS	CML
• CR1 – except favorable risk • Antecedent hematological disease • Treatment related leukemia • Primary induction failure or relapse • Presence of minimal residual disease after initial or subsequent therapy • CR2 and beyond	• Any intermediate or high IPSS score • Any MDS with poor prognostic features (i.e., treatment related, refractory cytopenias, adverse cytogenetics)	• Inadequate hematologic or cytogenetic response after multiple tyrosine kinase inhibitors (TKI) • Intolerance to TKIs • Accelerated phase • Blast crisis

ALL	CLL
• CR1 • Primary induction failure or relapse • Presence of minimal residual disease after initial or subsequent therapy • CR2 and beyond	• High-risk cytogenetics or molecular features (deletion 17p or 11q) • Fludarabine resistant • Richter's transformation • Poor initial response or short initial remission (recurrence within 12 mo)

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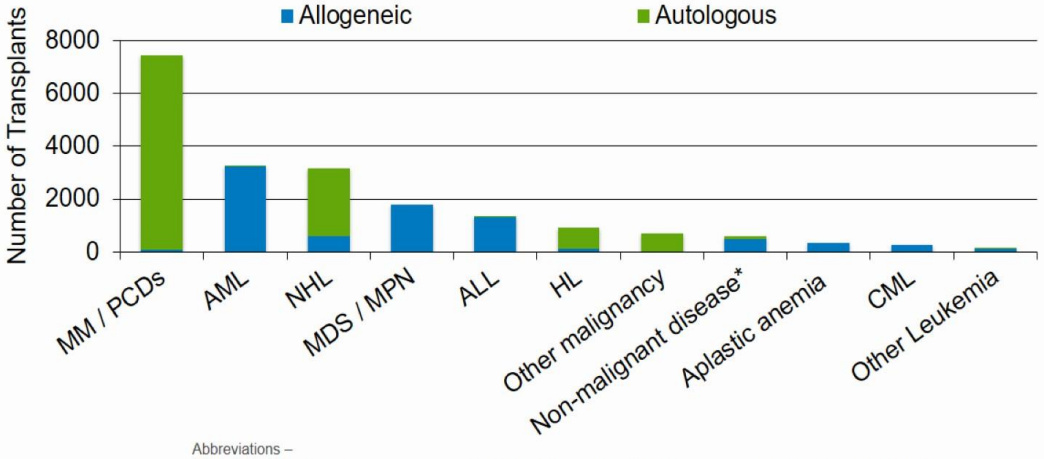
Number of HCTs by Indications in the US, 2020



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Abbreviations –
MM: Multiple myeloma;
PCDs: Plasma cell disorders;
AML: Acute myelogenous leukemia;
NHL: Non-Hodgkin lymphoma;
MDS: Myelodysplastic syndromes;
MPN: Myeloproliferative neoplasms;
ALL: Acute lymphoblastic leukemia;
HL: Hodgkin lymphoma;
CML: Chronic myeloid leukemia
*excludes Aplastic anemia

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Transplant Eligibility

- Clinical Factors
  - Health and performance status
  - Disease status, chemosensitivity
  - Identification of psychosocial issues that would interfere
- Donor Factors
  - Stem cell source
  - Related vs Unrelated
- Other
  - Psychosocial evaluation, caregiver support
- Transplant center requirements
  - Access

NMDP: Be The Match (n.d.). *Patient Eligibility for HCT*. Bethematch.org. Retrieved March 10, 2023, from https://bethematchclinical.org/transplant-indications-and-outcomes/eligibility/

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Phases of Transplant

Pre-Transplant

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Bone Marrow Harvest

- Bone Marrow Harvest
  - General anesthesia/surgical procedure
  - Multiple aspirations of posterior iliac crest
  - Equivalent of 50-100 bone marrow biopsies
- Collection goal
  - 10-20 mL/kg recipient weight = total nucleated cell (TNC) 2-4 x 108 /kg
  - Volume 1500 mL
- Limited by health of the donor
- Low complication rate
  - < 0.3% serious adverse events
- Recovery in a few days

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Confer DL, et al. Thomas' Hematopoeitic Cell Transplantation: Stem Cell Transplantation. Vol 1 Fifth Edition, Wiley-Blackwell, 2016. p423-430.

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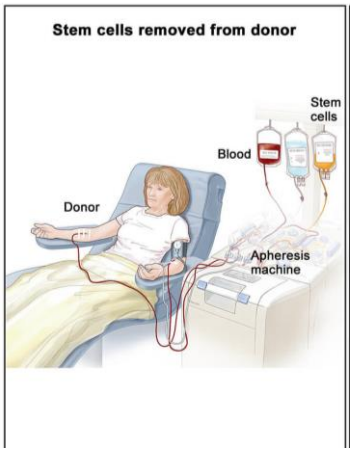
Peripheral Blood CD34+ Stem Cell Collection

- Requires cells to be "mobilized" prior to collection
  - CD34+ cell - Circulating cells in the blood stream with a surface antigen transmembrane glycoprotein that is present on immature hematopoietic cells (as well as endothelial and stromal cells)
  - Agents
    - Filgrastim, sargramostim, plerixafor
    - Chemotherapy (use in autologous donations only)
- Procedure is similar to a session of dialysis
  - Cells are collected via an apheresis catheter
  - CD34+ cell count by flow cytometry
    - Auto HSCT goal: 2-5 x 10e6 /kg (adult)
    - Allo HSCT goal: 4-6 x 10e6 /kg (adult)
    - Up to 10 x 106 /kg depending on number of planned HSCTs
- May require several collections
- Risks are minimal: anemia, thrombocytopenia, hypocalcemia, hypotension, thrombosis



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Confer DL, et al. Thomas' Hematopoeitic Cell Transplantation: Stem Cell Transplantation. Vol 1 Fifth Edition, Wiley-Blackwell, 2016. p423-430.
Duong HK, et al. Peripheral Blood Progenitor Cell Mobilization for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation. Biology of Blood and Marrow Transplantation, Volume 20, Issue 9, 1262 - 1273

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Umbilical Cord Blood

- Majority donated through anonymous public banks, less often via direct family member
- Most common in pediatric HCT
- Collection
  - Cord blood is collected at time of placenta delivery from umbilical cord vein
  - Cell dose 2.5 to 3 x10e7 TNC /kg
- Advantages: less stringent HLA matching, lower incidence of cGVHD
- Disadvantages: delayed engraftment, graft failure, higher rate of infectious complications, higher costs
- ADVANCES: double cord blood HCT, ex vivo expansion techniques

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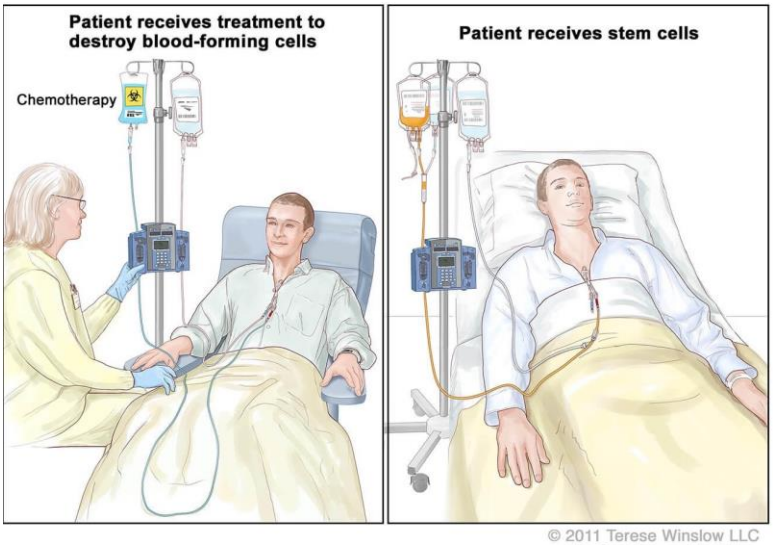

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Day 0 (Stem Cell Infusion)

- Stem cells may be infused fresh within a few hours of collection
- May be frozen using DMSO
  - Complications
    - Garlic smell/taste
    - Facial flushing
    - Tickling sensation
    - Rare: bradycardia, abdominal pain, encephalopathy, seizures, renal failure
      - Prevention: divide large volume infusions over 2 days and infuse cells slowly
    - Pre-medication to prevent reactions
- ABO mismatched
  - Watch for hemolytic reactions

Tormey CA, et al. Hematopoietic Stem Cell Transplantation: A Handbook for Clinicians. 2009;151-62.

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Common Complications of HCT

- Nausea, Vomiting, Diarrhea
- Mucositis and Pain
- Cytopenias
- Infection
- Graft vs Host Disease (acute and chronic)*
- Organ Injury/Toxicity
  - Veno-occlusive Disease (VOD)/ Sinusoidal Obstruction Syndrome (SOS)
  - Brochiolitis Obliterans (usually a late manifestation of cGVHD)
  - Thrombotic Microangiopathy (TMA, usually related to GVHD prevention)
- Graft failure
- Relapse

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General Supportive Care: Nausea and Vomiting

Management

- Medication options for breakthrough N/V (goal is to add one agent at a time from a different drug class to the existing N/V regimen)

Dexamethasone 4mg IV Q8-12h requires Attending approval (corticosteroid)

Diphenhydramine 25mg IV Q8h (histamine type 1 antagonist)

Dronabinol 5-10mg PO Q6-8h (cannabinoid)

Haloperidol 1-2 mg IV/PO Q6h (dopamine antagonist)

Lorazepam 0.5-2mg IV Q6h (benzodiazepine)

Metoclopramide 20mg IV Q6h (dopamine antagonist)

Olanzapine 2.5-5mg PO orally-disintegrating tab Q12h (atypical antipsychotic)

Ondansetron 8mg IV Q8h (serotonin antagonist)

Prochlorperazine 10mg IV Q6h (phenothiazine)

Scopolamine patch 1.5mg transdermal Q72h for movement related N/V (anticholingeric)

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General Supportive Care: Diarrhea

Management options:

– Manage any infectious causes as appropriate

– Medications for non-infectious diarrhea

1st line: Loperamide (Imodium®) 4 mg PO x 1 dose, then 2 mg PO Q4h for every unformed stool (max 16 mg/day)

2nd line: Add diphenoxylate/atropine (Lomotil®, 2.5mg/0.025mg) 2 tabs PO Q6h or 5 mL PO Q6h (max 20 mg diphenoxylate/day)

3rd line options:

- Octreotide*

- Opium tincture* *Discontinue within 24 hrs after the resolution to avoid the development of ileus

– Assess patient every 12-24 hrs

Ippoliti C, et al. J Clin Oncol. 1997;15(11):3350-4.
Benson A.B, et al. J Clin Oncol 1004;22:2918-2926.
Zidan J, et al. Annals of Oncology 2001;12:227-229.
Richardson G, et al. J Oncol Pharm Practice 2007;13:181–198.
Kornblau S, et al. Journal of Pain and Symptom Management 2000;19(2):118-129.

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What is Graft-Versus-Host Disease?

GVHD is a systemic disorder that occurs when the graft's immune cells recognize the host as foreign and attack the recipient's body cells.

"Graft" refers to donor-derived cells and "host" refers to the tissues of the recipient

Justiz Vaillant AA, Modi P, Mohammadi O. Graft Versus Host Disease. [Updated 2022 Oct 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538235/

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Graft versus Host Disease (GVHD)

- Major complication among all patients receiving allogeneic HSCT
  - ~30–50% of patients, with 14–36% developing severe aGVHD
  - 30-70% will have some chronic GVHD
- Most common cause of NRM after allogenic HSCT
  - Only 25–30% of patients with grade III aGVHD and 1–2% of patients with grade IV aGVHD surviving long term (>2 years)
- Increases health care cost and length of stay
- Significant driver of decreased quality of life (especially cGVHD)

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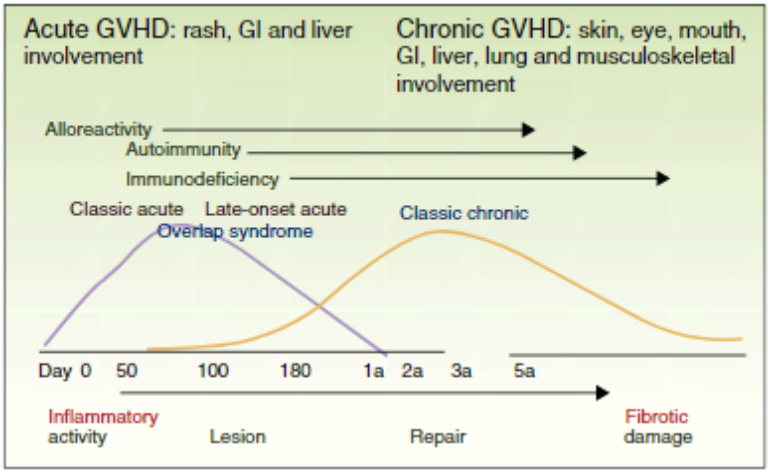
Typical Kinetics of Acute and Chronic GVHD



Ballester-Sanchez, R, Navarro-Mira M, Sanz-Caballer J, et all. Review of Cutaneous Graft-vs-Hose Disease. Actas Dermosifiliogr. 2016; 107 (3): 183-193.
Adatped from http://ccr/cancer.gov/resources/gvhd/about.asp.

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Manifestations of Acute GVHD

Skin

- Itchy, painful sunburn-like rash
- Often found on the palms of hands or the soles of feet

GI

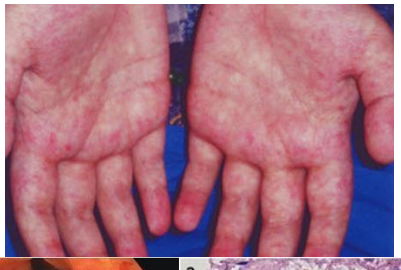
- Upper (anorexia, nausea/vomiting)
- Lower (diarrhea, abdominal pain)

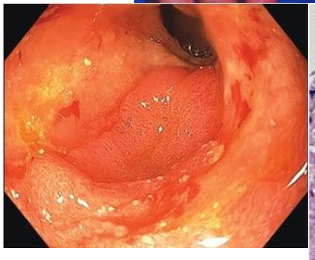
Liver

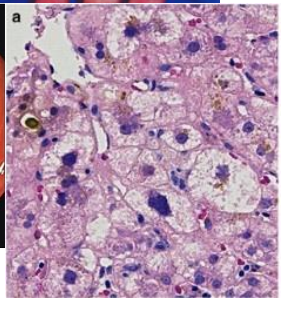
- Hyperbilirubinemia, jaundice

Immune System

- Lower blood counts and increased risk of infections







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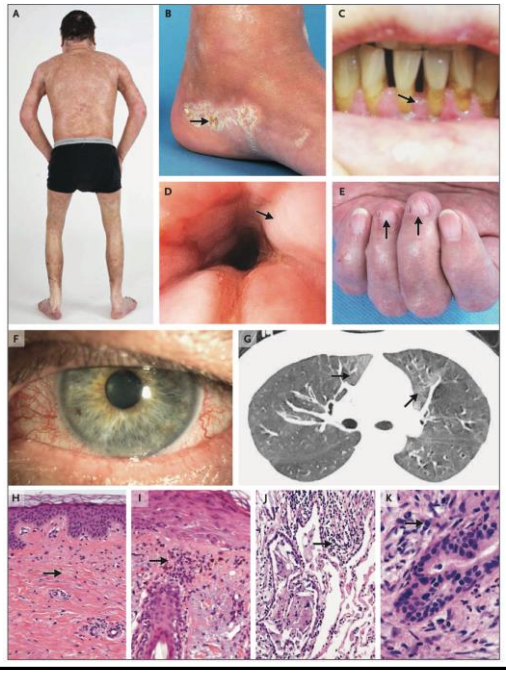
Manifestations of Chronic GVHD

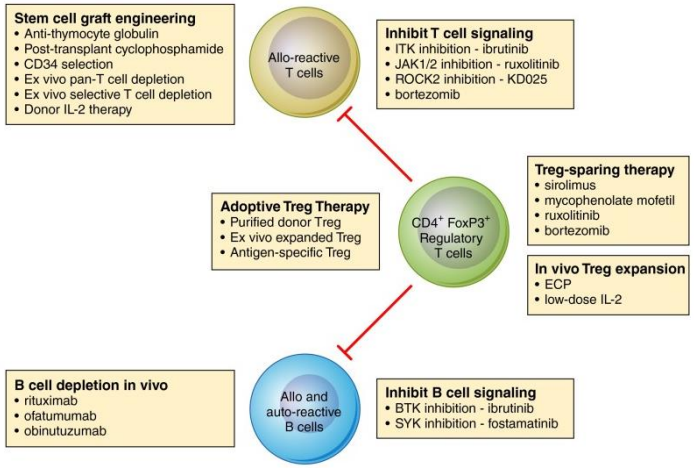
#1 Skin
#2 Liver
#3 Oral
#4 Ocular
#5 GI
#6 Immune
#7 Musculoskeletal
#8 GU
#9 Pulmonary



Zeiser R, Blazer BR. Pathophysiology of Chronic Graft-versus-Host Disease and Therapeutic Targets. Dec 28, 2017. N Engl J Med 2017; 377: 2565-2579.

43

Approaches (Most Experimental) to Prevent and/or Treat GVHD



Mechanistic approaches for the prevention and treatment of chronic GVHD. Cutler CS, Koreth J, Ritz J. ***Blood***. 2017

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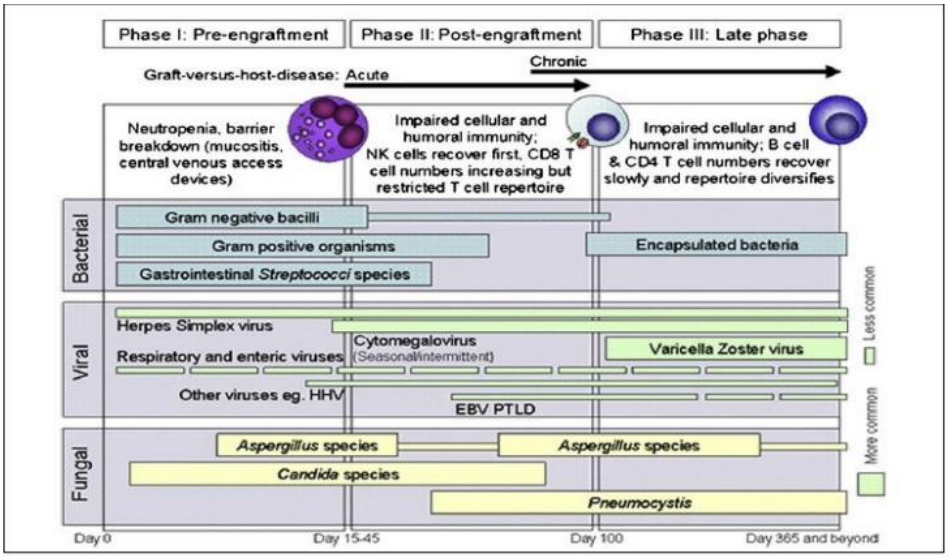
Infection Risk by Transplant Phase



Tomblyn M, Chiller T, Einsele H, et al. Biol Blood Marrow Transplant 2009;15:1143-1238.

45

Primary Causes of Mortality

Autologous SCT

- Early mortality now rare (<1-2% at most centers)
- Primary cause of mortality is relapse (some non-relapse mortality, most often due to infections)

Allogeneic SCT

- Nonrelapse mortality more common—increased with comorbidities, advanced disease, more intensive conditioning
- GVHD mortality is often related to infections and happens with degree of mismatch (though improving significantly over time)

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Phases of Care and Typical Care Requirements

Inpatient hospitalization

- Beginning of conditioning to resolution of acute toxicity after engraftment

Early ambulatory phase (~d+30 for auto, ~d+100 for allo)

- Visits typically 1-3x/week depending on complications

First year after SCT (beyond ~d+30 for auto, ~d+100 for allo)

- Visit frequencies typically decline to monthly depending on active issues
- Care typically transitions to primary oncology team away from cellular therapy center (with coordination between both teams)
- Communication and clear patient understanding critical

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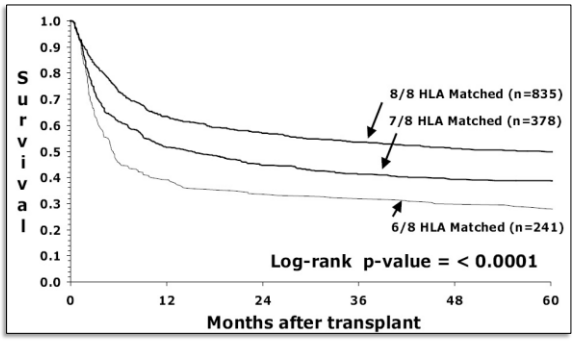
The HLA Barrier: Need for an HLA-matched donor

High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation

Stephanie J. Lee,[1] John Klein,[2] Michael Haagenson,[3] Lee Ann Baxter-Lowe,[4] Dennis L. Confer,[5] Mary Eapen,[2] Marcelo Fernandez-Viña,[6] Neal Flomenberg,[7] Mary Horowitz,[2] Carolyn K. Hurley,[8] Harriet Noreen,[9] Machteld Oudshoorn,[10] Effie Petersdorf,[1] Michelle Setterholm,[5] Stephen Spellman,[5] Daniel Weisdorf,[11] Thomas M. Williams,[12] and Claudio Anasetti[13]

[1]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA; [2]Center for International Blood and Marrow Transplant Research, Medical College of Wisconsin, Milwaukee; [3]Center for International Blood and Marrow Transplant Research, Minneapolis, MN; [4]Department of Surgery, University of California, San Francisco; [5]National Marrow Donor Program, Minneapolis, MN; [6]M. D. Anderson Cancer Center, Houston, TX; [7]Thomas Jefferson University Hospital, Philadelphia, PA; [8]Department of Oncology, Georgetown University Medical Center, Washington, DC; [9]Immunology/Histocompatibility Laboratory, University of Minnesota Medical Center, Fairview; [10]Eurpodonor Foundation, Leiden, the Netherlands; [11]Blood and Marrow Transplantation (BMT) Program, University of Minnesota, Minneapolis; [12]Department of Pathology, University of New Mexico, Albuquerque; and [13]H. Lee Moffitt Cancer Center, Tampa, FL.



- **Historically, mismatched URD transplants associated with worse survival**
- **Roughly 10% decrease in survival for each HLA mismatch**

BE THE MATCH® Operated by the National Marrow Donor Program®

Lee et al, Blood 2007;110:4576

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However, a Fully Matched Registry Donor is Not Available for Every Patient

29%
Black or African American

47%
Asian or Pacific Islander

48%
Hispanic or Latino

60%
American Indian and Alaska Native

79%
White

NATIONAL MARROW DONOR PROGRAM® BE THE MATCH®

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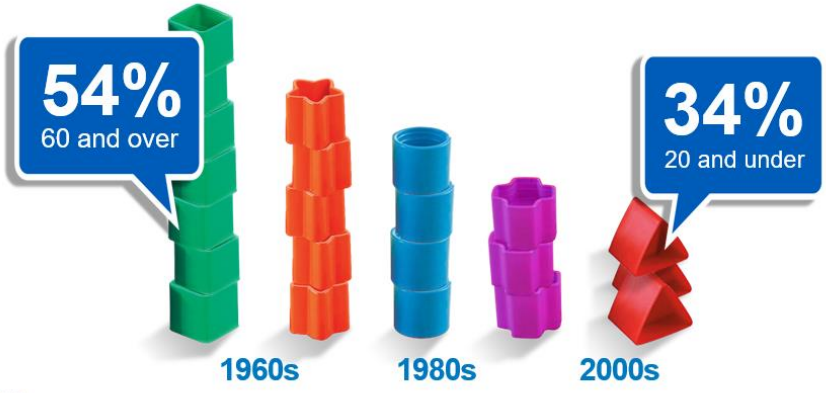
And, it's getting MORE DIFFICULT to match over time



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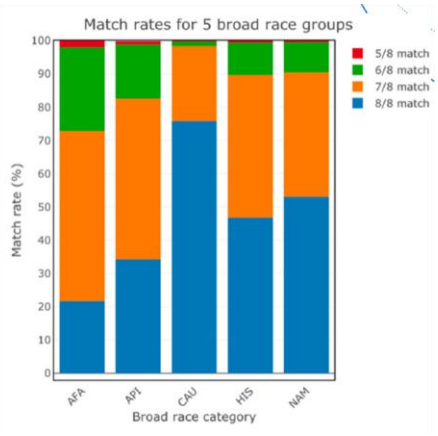
Mismatched grafts close the disparity gap

- Registry modeling from BTM Bioinformatics
- Successful 7/8 transplants increase donor availability to **72% for AFA pts**
- Successful 6-7/8 transplants increase donor availability to **97% for AFA pts**

AFA = African American
API = Asian Pacific
CAU = Caucasian
HIS = Hispanic/Latino
NAM = Native American



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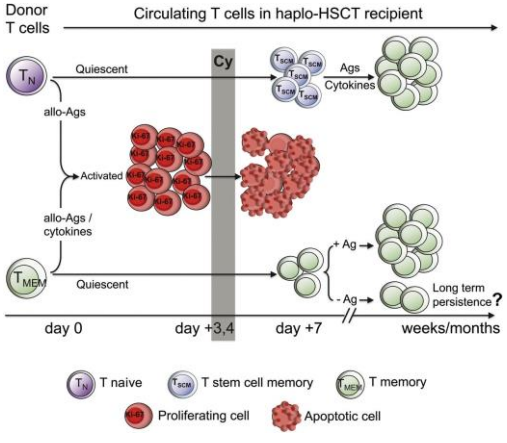
Post-transplant cyclophosphamide (PTCy) enhances GvHD prevention in the haploidentical setting



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Blood 2015;125:2855

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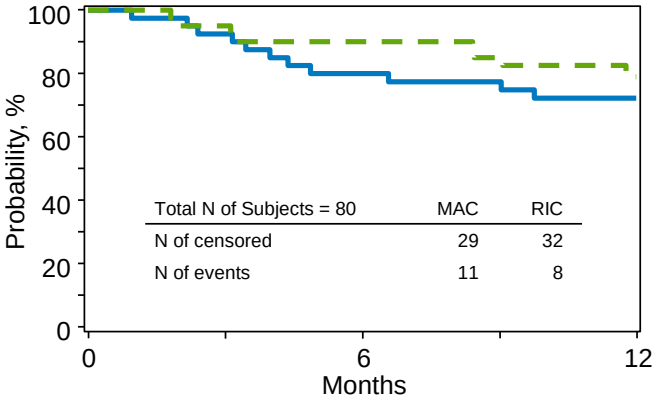
15-MMUD Study
Primary Endpoint: Overall Survival
72% MAC and 79% RIC



original reports

National Marrow Donor Program–Sponsored Multicenter, Phase II Trial of HLA-Mismatched Unrelated Donor Bone Marrow Transplantation Using Post-Transplant Cyclophosphamide

Bronwen E. Shaw, MD, PhD[1]; Antonio Martin Jimenez-Jimenez, MD, MS[2]; Linda J. Burns, MD[3]; Brent R. Logan, PhD[4]; Farhad Khimani, MD[5]; Brian C. Shaffer, MD[6]; Nirav N. Shah, MD[7]; Alisha Mussetter, BS[8]; Xiao-Ying Tang, MPH[4]; John M. McCarty, MD[7]; Asif Alavi, MD[9]; Nosha Farhadfar, MD[9]; Katarzyna Jamieson, MD[10]; Nancy M. Hardy, MD[11]; Hannah Choe, MD[12]; Richard F. Ambinder, MD, PhD[13]; Claudio Anasetti, MD[5]; Miguel-Angel Perales, MD[2]; Stephen R. Spellman, MBS[8]; Alan Howard, PhD[8]; Krishna V. Komanduri, MD[2]; Leo Luznik, MD[13]; Maxim Norkin, MD, PhD[14]; Joseph A. Pidala, MD, PhD[5]; Voravit Ratanatharathorn, MD[6]; Dennis L. Confer, MD[8]; Steven M. Devine, MD[8]; Mary M. Horowitz, MD, MS[4]; and Javier Bolaños-Meade, MD[13]

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CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

NATIONAL MARROW DONOR PROGRAM® BE THE MATCH®

ACCESS: A Multi-Center, Phase II Trial of HLA-Mismatched Unrelated Donor Hematopoietic Cell Transplantation with Post-Transplantation Cyclophosphamide for Patients with Hematologic Malignancies

Resource for Clinical Investigation in Blood and Marrow Transplantation (RCI BMT)

Version 1.0
January 28, 2021

NMDP Protocol Chair
Steven Devine, MD[1]

CIBMTR Protocol Officers
Bronwen Shaw[2] (adult)
Larisa Broglie[2] (pediatric)

Stratum 1	• Adult subjects undergoing HCT with a PBSC graft source and receiving a myeloablative conditioning (MAC) regimen and PTCy-based GVHD prophylaxis
Stratum 2	• Adult subjects undergoing HCT with a PBSC graft source and receiving a non-myeloablative (NMA) or reduced-intensity conditioning (RIC) regimen and PTCy-based GVHD prophylaxis
Stratum 3	• Pediatric and young adult subjects undergoing HCT from a BM graft source and receiving a MAC regimen and PTCy-based GVHD prophylaxis

Primary endpoint is 1 year OS in each adult cohort

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Trends in Stem Cell Transplantation

- AutoSCT remains most common type, 65% of all HSCTs
- Decrease in autoSCT for lymphoma and myeloma
  - New therapies (BTKIs, antibodies, immunotoxins, CAR-T cell)
- Increased use of alloSCT
  - Increased use of haplo donors
  - Increase in unrelated donors including mismatched unrelated donors
  - Major trend is increase in post-transplant cyclophosphamide
- *Everyone now has a suitable transplant donor!*

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CAR-T THERAPIES: PRESENT AND FUTURE

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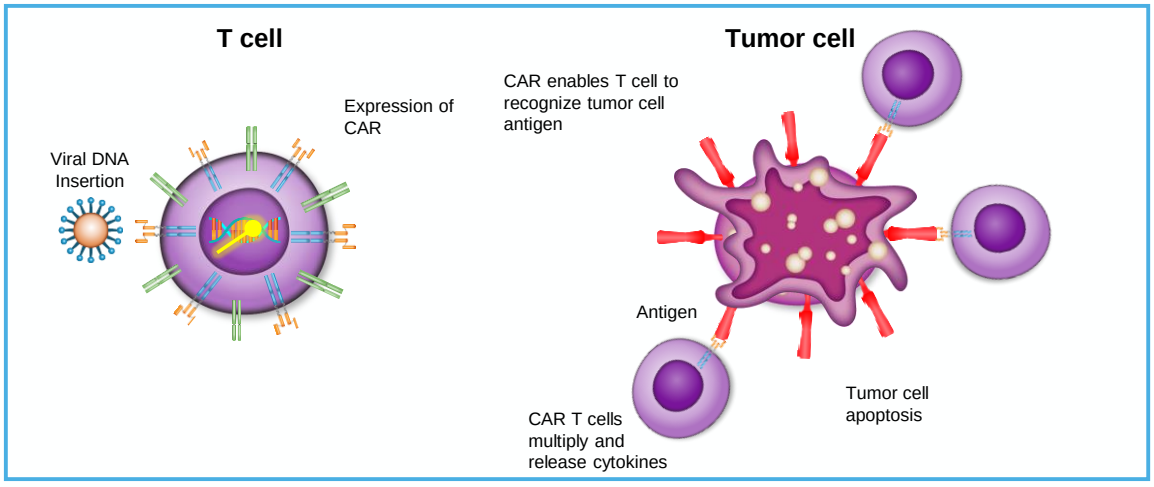
CAR T Cells: Mechanism of Action



CAR T WORKING GROUP

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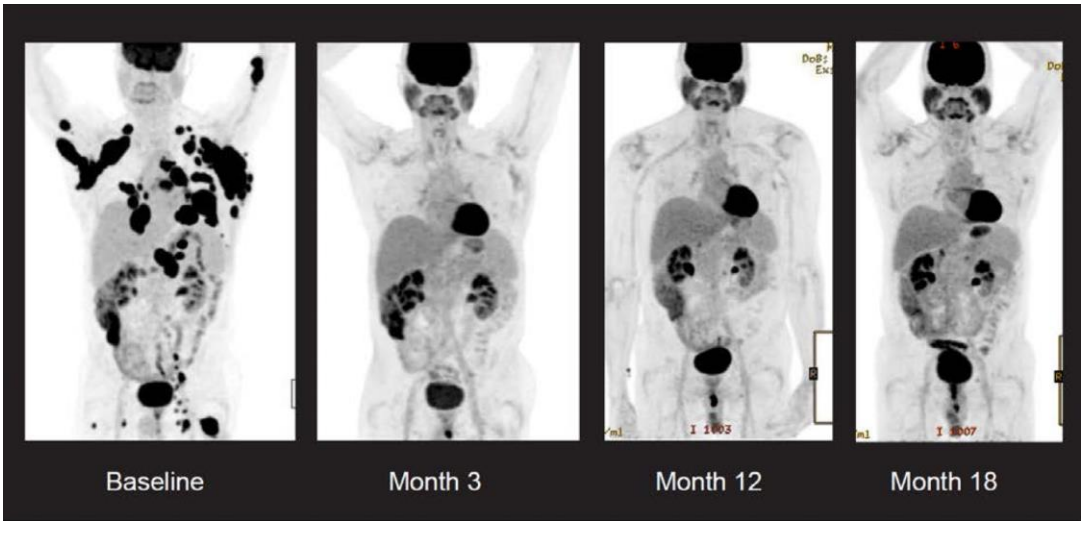
Refractory Lymphoma Remission After CAR-T therapy



Neelapu, et al., NEJM December 2017

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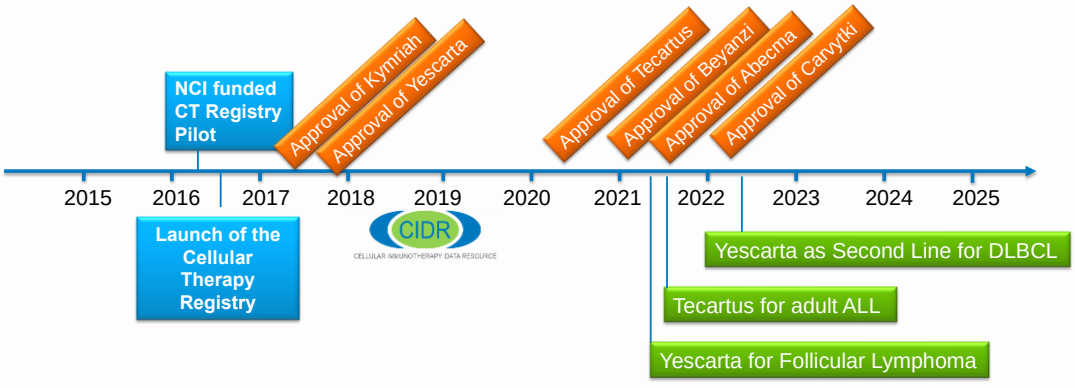
The Development of the Registry Parallel to the Expansion of the Field of Cellular Immunotherapy



CELEBRATING 50 YEARS 1972-2022 CIBMTR CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

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CIDR CELLULAR IMMUNOTHERAPY DATA RESOURCE

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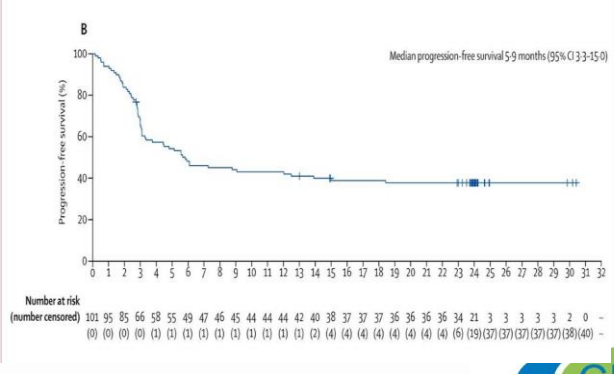
CD19 CAR-T therapy for Lymphoma is Curative

Progression-free Survival



Jacobson C. et al ASCO 2021, Locke F et al Lancet Oncology 2019

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CIDR CELLULAR IMMUNOTHERAPY DATA RESOURCE

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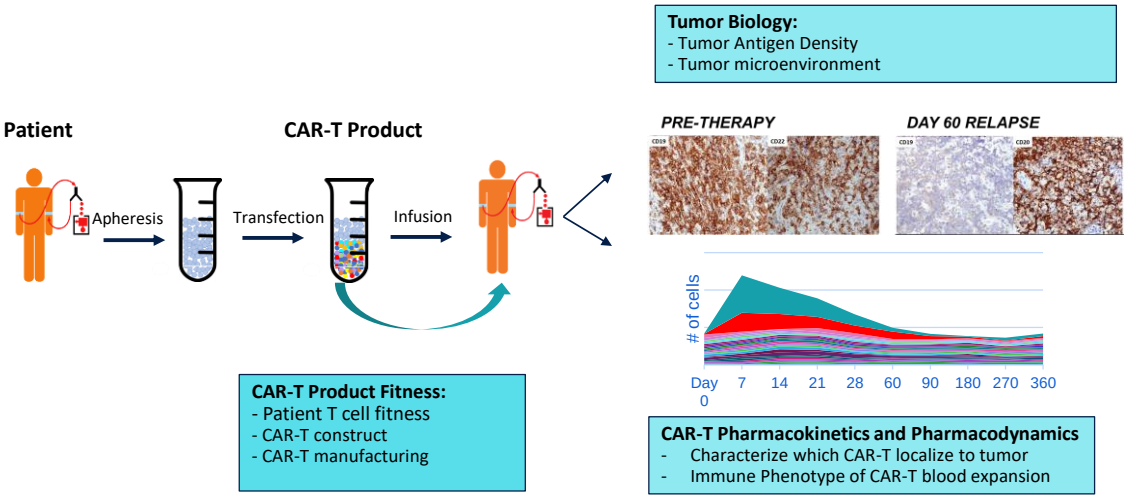
Optimizing CAR-T therapy: Model by Spiegel and Miklos



from Spiegel and Komanduri, *Blood Feb 17, 2022*

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ARE THERE ACCESS/EQUITY BARRIERS TO CELLULAR THERAPIES?

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What Do We Know About Access and Equity?

- All CAR-T therapies, in aggregate, are underutilized
- High cost, tertiary/quaternary therapies tend to maximize historical barriers to access (racial, socioeconomic, logistical)
- Early data suggest that African American patients are less likely to receive CAR-T therapy, and may have lower ORR, CR rates
- Unique access issues exist for pediatric patients, for whom fewer options exist
- Cost and complexity of access and care compound historic barriers
- Similar (sadly) to what was historically seen with stem cell transplants, also commonly underutilized

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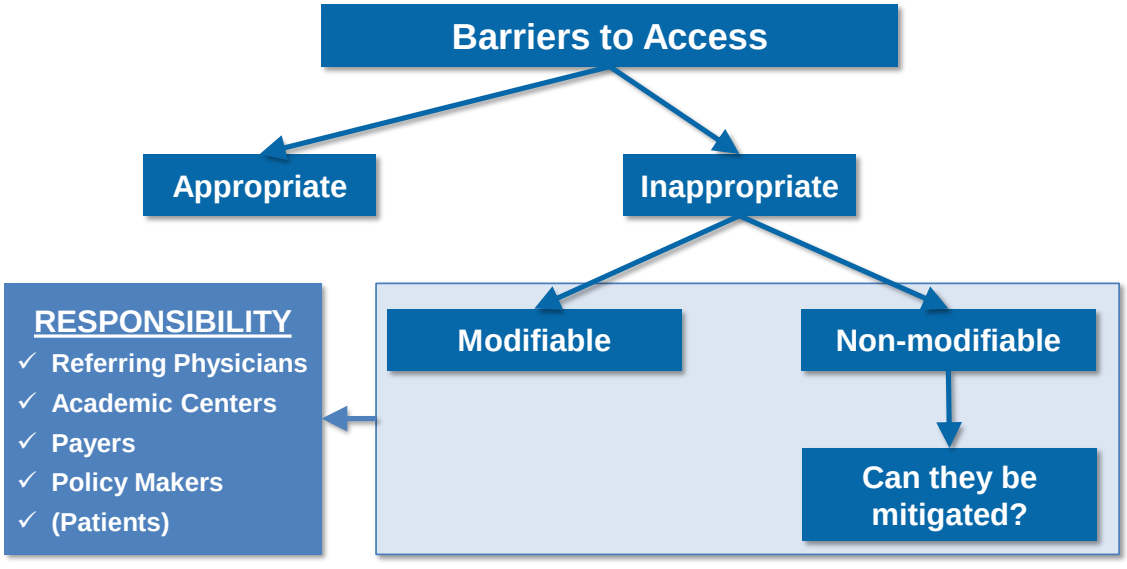

Modified from original by Navneet Majhail, Sarah Cannon.

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Cellular Therapy is a (highly rewarding)Team Sport

Cellular therapy is a highly complex specialty requiring a specialized multi-disciplinary team

- Attending Physicians
- Advanced Practice Providers (PAs and NPs)
- Pharmacists (often with PharmD and subspecialty oncology training)
- Nurses
- Nutrition (RD)
- Physical Therapy
- Social Work/Case management
- Specialty Consult Services (Infectious Disease, GI, Pulmonary, etc.)

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Cellular Therapy Nursing

Nurses play a vital role in the daily assessment and delivery of care of cell therapy patients

Supportive care

- Fatigue
- Shortness of breath
- Fever/infection
- Bleeding
- Fluid status (hypovolemia, diarrhea, fluid overload)
- Nutrition
- Pain management
- GVHD assessment
- Education

Fauer AJ, Choi SW, Friese CR. The Roles of Nurses in Hematopoietic Cell Transplantation for the Treatment of Leukemia in Older Adults. *Semin Oncol Nurs*. 2019;35(6):150960. doi:10.1016/j.soncn.2019.150960

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BMT Clinical Social Worker

- Core members of the BMT team
- Complete pre-transplant psychosocial evaluation, high risk screening for psychosocial factors that may negatively impact transplant outcomes
- Establish a therapeutic relationship and engage in problem solving and planning to develop caregiver and relocation plans
- Experts in providing psychosocial care
- Facilitate family meetings and bridge communication with the care team
- Contribute to optimizing patient outcomes and quality of life

NMDP/Be The Match Social Work Workforce Group (2017, June 1). *BMT Clinical Social Worker Role Description*. Bethematch.org. Retrieved March 10, 2023, from https://6c6ddacb61138d707862-923017c27b47b1cc7d06cb4f734aecf6.ssl.cf2.rackcdn.com/astct_13bdad0e972cbcdfa7413cc08f0ef243.pdf

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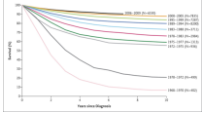
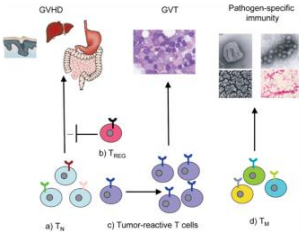
No effective therapies → *Chemotherapy era* → *Stem Cell Transplant era (Combinations of chemotherapy, immunotherapy)* → *Targeted agents, better stem cell transplants and more broadly effective immunotherapies*

1825
First description of acute leukemia

1960s
Combination chemotherapy + stem cell transplants





1990s
T cells critical for transplant cures—dramatic increase in success

2017
Approval of engineered T cell therapies

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Resources

- LLS – The Leukemia & Lymphoma Society www.LLS.org
- FACT – Foundation for the Accreditation of Cellular Therapy (FACT) www.factwebsite.org
- ASTCT – American Society of Transplant and Cellular Therapy www.astct.org
- CIBMTR – Center for International Blood & Marrow Transplant Research (CIBMTR) www.cibmtr.org
- ASH – American Society of Hematology www.hematology.org
- NCCN – National Comprehansive Cancer Network www.nccn.org
- National Marrow Donor Program (NMDP) www.bethematch.org
- Or…transplant professionals near or far!

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FREE LLS RESOURCES FOR HEALTHCARE PROVIDERS

- ❑ CME & CE courses: www.LLS.org/CE
- ❑ Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- ❑ Videos for HCPs: www.LLS.org/HCPvideos
- ❑ Podcast series for HCPs: www.LLS.org/HCPpodcast

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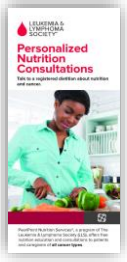
FREE LLS RESOURCES FOR PATIENTS

- **Information Specialists** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC).

- **Clinical Trial Nurse Navigators** – RNs provide a personalized service for patients seeking treatment in a clinical trial, sift through the information and provide information to bring back to their HC team (CTSC).
  - www.LLS.org/CTSC

- **Registered Dieticians** – (LLS) provides PearlPoint Nutrition Services® to patients/caregivers of all cancer types, free nutrition education and one-on-one consultations by phone or email.
  - www.LLS.org/nutrition

- **Reach out** **Monday–Friday, 9 am to 9 pm ET**
  - Phone: (800) 955-4572
  - Live chat: www.LLS.org/IRC
  - Email: infocenter@LLS.org
  - HCP Patient Referral Form: www.LLS.org/HCPreferral



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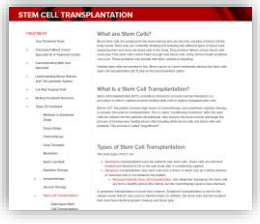
FREE LLS RESOURCES FOR PATIENTS

- **Webcasts, Videos, Podcasts, booklets**:
  - www.LLS.org/Webcasts
  - www.LLS.org/EducationVideos
  - www.LLS.org/Podcast
  - www.LLS.org/Booklets



- **www.lls.org/treatment/types-treatment/stem-cell-transplantation**

- **Support Resources**
  - Financial Assistance: www.LLS.org/Finances
    - Urgent Need
    - Patient Aid
    - Travel Assistance
  - Other Support: www.LLS.org/Support
    - LLS Regions
    - Online Weekly Chats Facilitated by Oncology SW
    - LLS Community Social Media Platform
    - First Connection Peer to Peer Program

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FREE LLS RESOURCES FOR YOUR PATIENTS

BOOKLETS AND FACT SHEETS

English – www.LLS.org/Booklets
Spanish – www.LLS.org/Materials

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Questions?

Ask a question by web:

- Click “Ask a question”
- Type your question
- Click “Submit”

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CLOSING

This activity is developed through a collaboration between
The Leukemia & Lymphoma Society and
The AAPA African Heritage PA Caucus.

The African Heritage PA Caucus is an international unified vehicle of mentorship, giving rise to professional leaders charged with the continued empowerment of PHYSICIAN ASSOCIATES of African Heritage and the populations they serve.

- Visit https://ahcaapa.mypanetwork.com/ for further information

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THANK YOU

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