Transplant and CAR T-cell Therapy for Older Adults: Finding the Balance between Benefit and Risk

Celebrating a Second Chance at Life Survivorship Symposium

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Transplantation and Cell Therapy in Older Adults

Modern Maturity Meets Modern Medicine

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National Cancer Institute-Designated Comprehensive Cancer Center

Disclosures

- I have no financial or other disclosures that are relevant to this presentation

Objectives/Agenda

- Why does age matter when considering transplant or cell therapy?
- Health issues (comorbidities) and other factors that affect risks for the older adult
- Assessments and interventions we can use to reduce risks
- How do outcomes compare with those of younger patients?

Why Is This Topic Important?

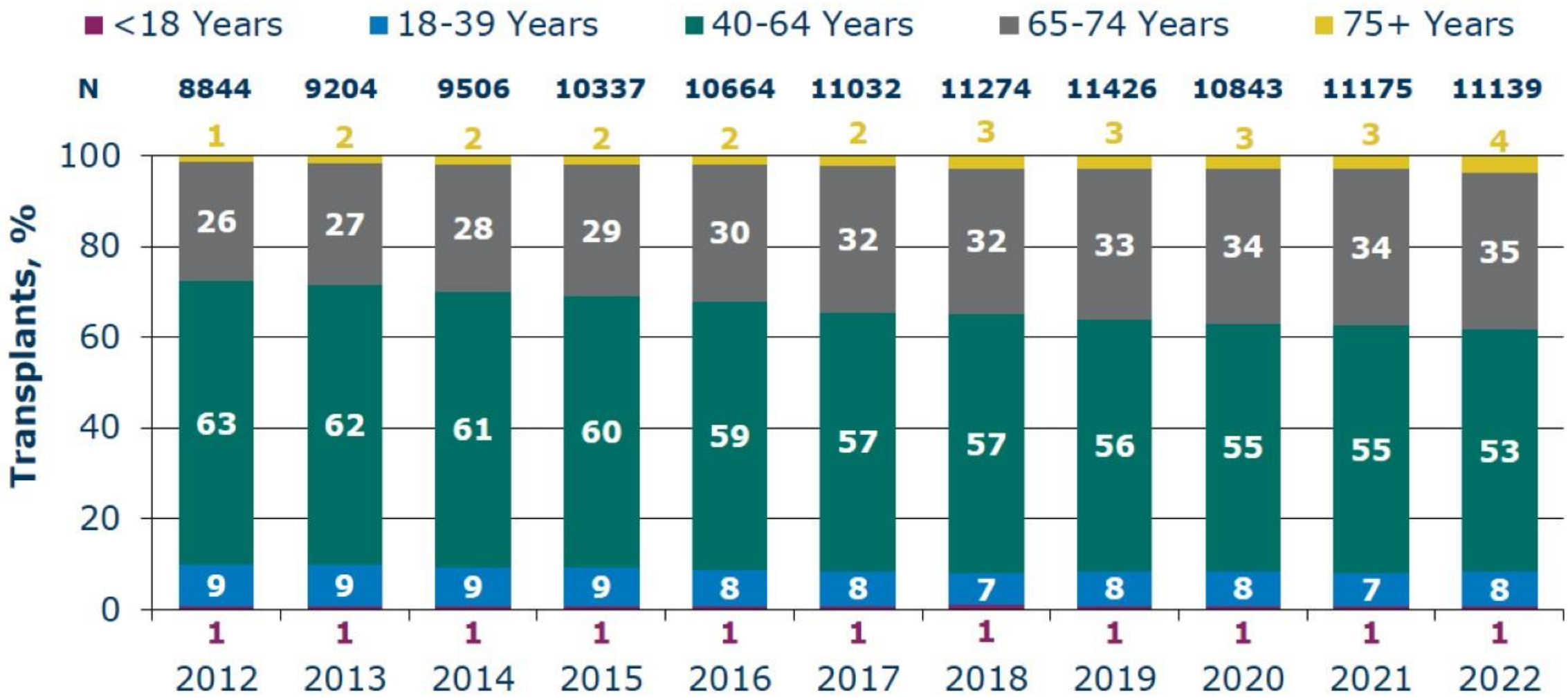
Median Age at Diagnosis for the Six Major Types of Blood Cancers, 2016-2020, as of January 1, 2020

Type	Median Age at Diagnosis (in years)
All blood cancers	68
Leukemia	67
Non-Hodgkin Lymphoma	68
Hodgkin Lymphoma	39
Myeloma	69
Myelodysplastic Syndromes (MDS)	77
Myeloproliferative Neoplasms (MPNs)	66

Table 3. SEER 22, 2016-2020, Age Distribution Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER Research Plus Limited-Field Data, 22 Registries, Nov 2022 Sub (2000-2020) - Linked To County Attributes - Total U.S., 1969-2021 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2023, based on the November 2022 submission.

Leukemia and Lymphoma Society, Facts and Statistics Overview (2024)

Recipient Age of Autologous HCTs in the US



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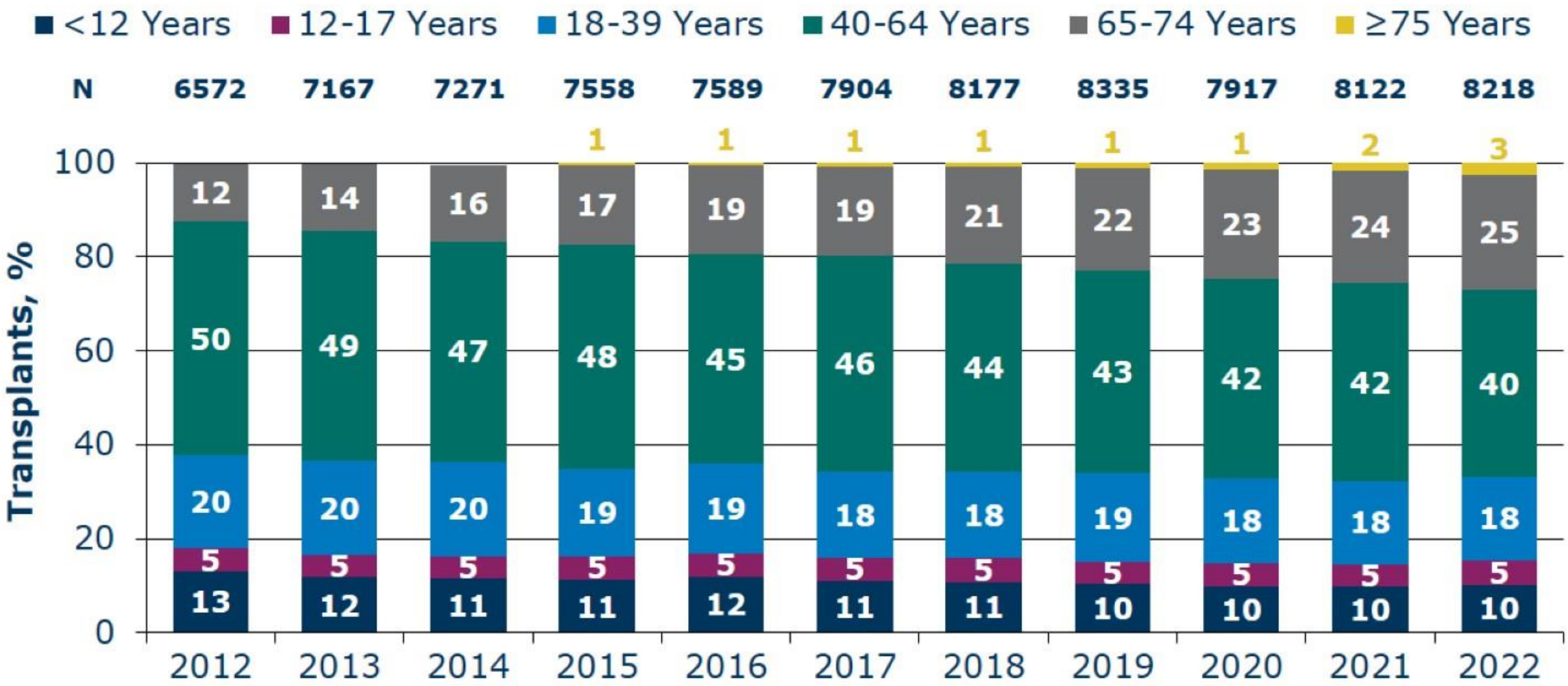
Recipient Age of Allogeneic HCTs in the US



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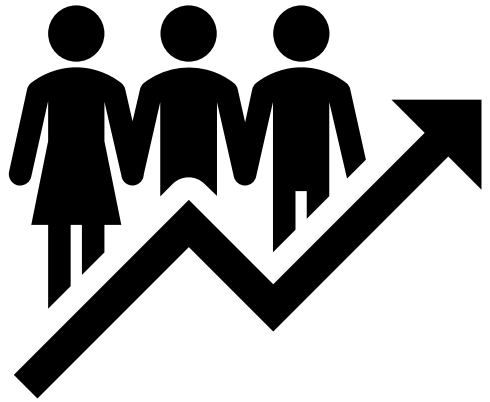
What Has Changed?

- Better supportive care for patients undergoing transplant
- Better treatments for infections
- Better immune suppressive meds
- Use of reduced-intensity chemotherapy conditioning regimens for allogeneic transplantation
- New and evolving types of adoptive cell therapy
- Advances in cardiovascular medicine
- Advances in the treatment of solid tumors



Let's Start With Facts

- Stem cell transplantation and adoptive cell therapy are generally our most powerful treatments for most blood cancers and marrow/ immune failure syndromes
- For many disease situations, transplant or CAR T-cell therapy offers the best (and sometimes the only) potentially curative option e.g.
  - Myelodysplastic syndrome (MDS)
  - Myeloproliferative disorders
  - High-risk or relapsed acute leukemias
  - High-risk and relapsed lymphomas

Transplant and Cell Therapy are Stress Tests

- Infections and “sepsis” syndrome
- Chemotherapy and medication toxicities
- Cytokine release syndrome and neurotoxicity (CAR–T)
- GVHD (allogeneic transplant)
- Effects of management of complications
  - Especially steroids and other immune suppressive medications
- Effects of prolonged hospital stay

Resilience

The capacity to withstand or to recover quickly from difficulties.
(Oxford Dictionary)

Resilience and Risk

How Do We Assess People as Potential Candidates for Cell Therapy?

- Comorbidity assessment
- Frailty/fitness assessment
  - How do we measure it?
- Can we make a treatment plan with a reasonable likelihood of success?
  - Can we justify the risks?

HCT Comorbidity Index

Comorbidity	Definitions of comorbidities included in the new HCT-CI	HCT-CI weighted scores
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias	1
Cardiac‡	Coronary artery disease,§ congestive heart failure, myocardial infarction, or EF ≤ 50%	1
Inflammatory bowel disease	Crohn disease or ulcerative colitis	1
Diabetes	Requiring treatment with insulin or oral hypoglycemics but not diet alone	1
Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	1
Psychiatric disturbance†	Depression or anxiety requiring psychiatric consult or treatment	1
Hepatic, mild‡	Chronic hepatitis, bilirubin > ULN to 1.5 × ULN, or AST/ALT > ULN to 2.5 × ULN	1
Obesity†	Patients with a body mass index > 35 kg/m^2	1
Infection†	Requiring continuation of antimicrobial treatment after day 0	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, or polymyalgia rheumatica	2
Peptic ulcer	Requiring treatment	2
Moderate/severe renal‡	Serum creatinine > 2 mg/dL, on dialysis, or prior renal transplantation	2
Moderate pulmonary‡	DLco and/or FEV_1 66%-80% or dyspnea on slight activity	2
Prior solid tumor‡	Treated at any time point in the patient's past history, excluding nonmelanoma skin cancer	3
Heart valve disease	Except mitral valve prolapse	3
Severe pulmonary‡	DLco and/or FEV_1 ≤ 65% or dyspnea at rest or requiring oxygen	3
Moderate/severe hepatic‡	Liver cirrhosis, bilirubin > 1.5 × ULN, or AST/ALT > 2.5 × ULN	3

Sorror et al. Blood 106: 2912 (2005)

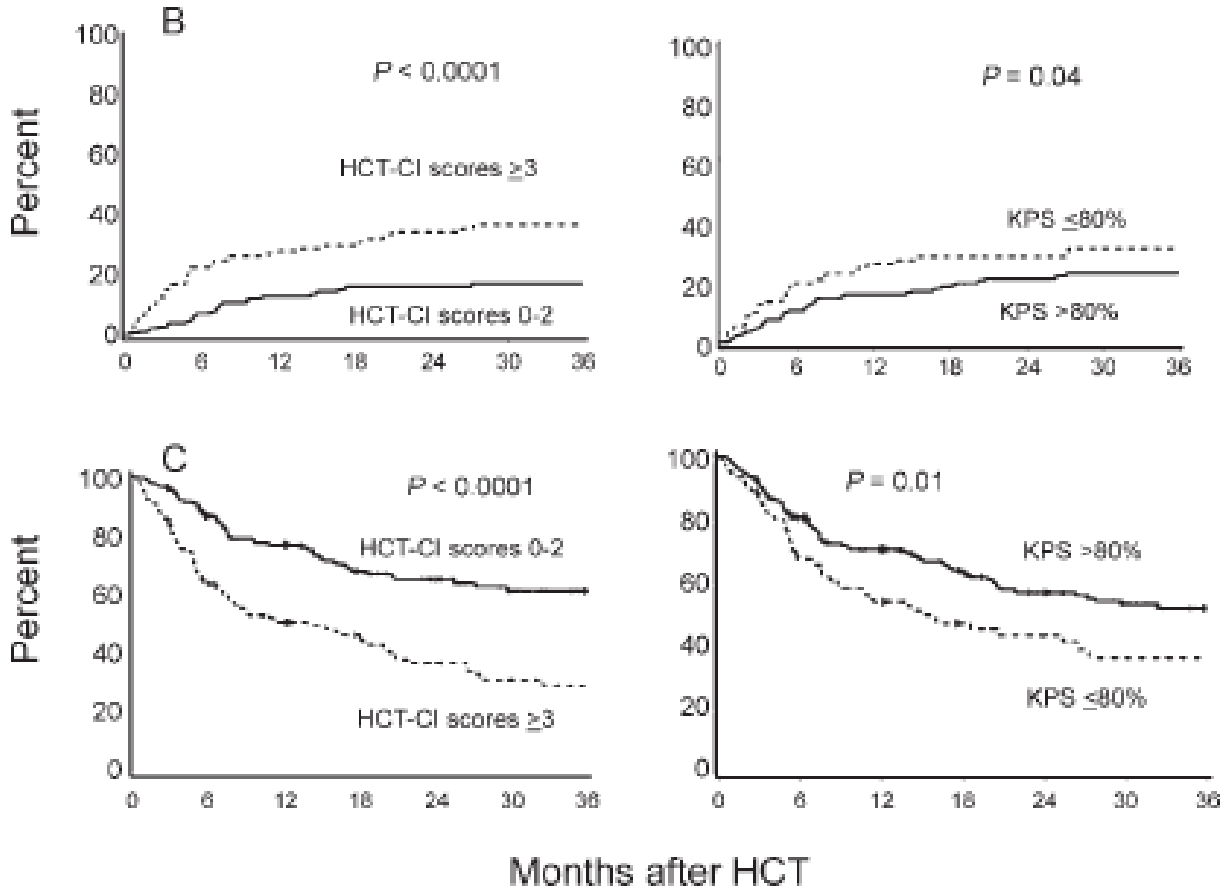
KARNOFSKY PERFORMANCE STATUS SCALE DEFINITIONS RATING (%) CRITERIA

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disable; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

HCT-Comorbidity Index and Karnofsky Performance Status Predict Non-Relapse Mortality and Survival after Allogeneic Stem Cell Transplant

Non-relapse mortality

Survival



M.L. Sorror et al. Cancer, 2008

Measuring Fitness and Frailty

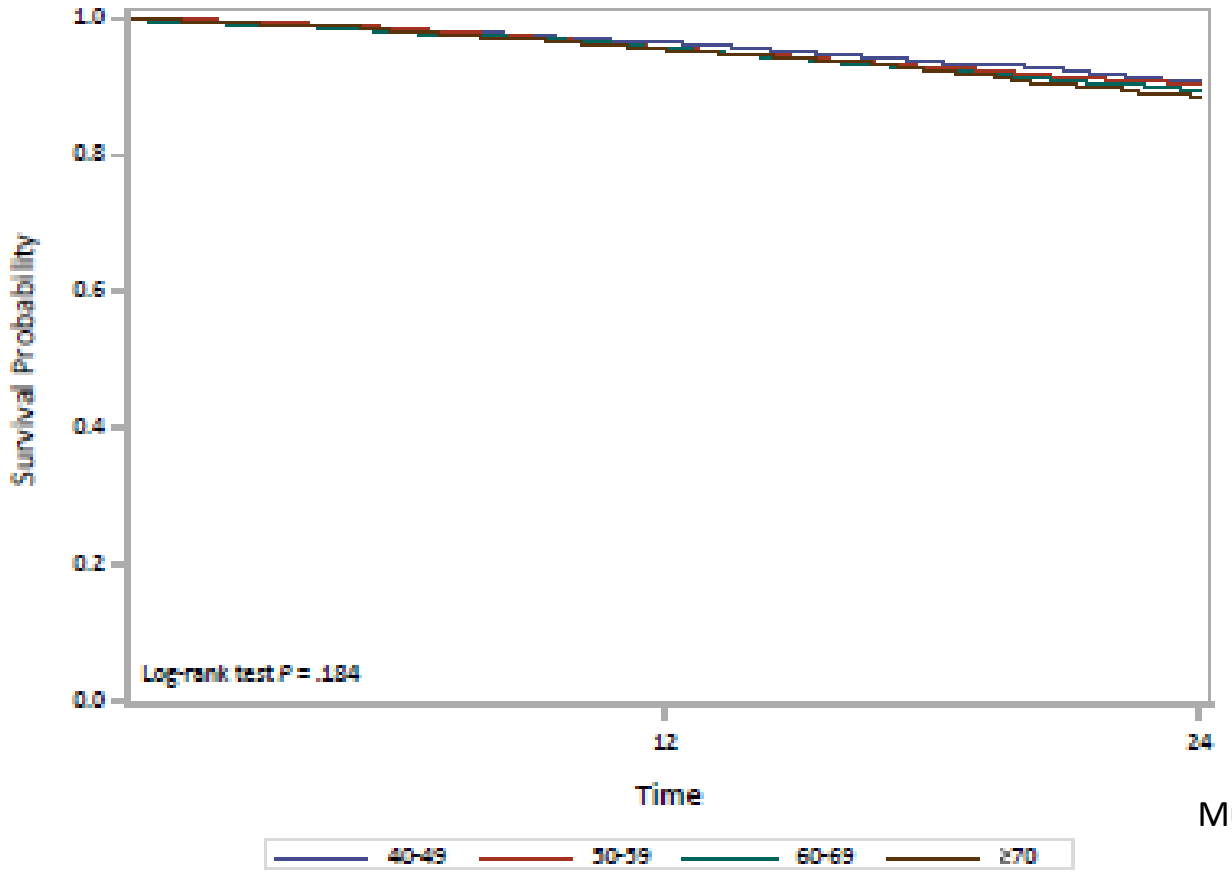
- Mobility
  - “Up and Go” test, 3-minute walk test
- Instrumental Activities of Daily Living (IADL) assessment
  - e.g. using a phone, shopping, cooking, managing medicine, managing bills, driving, etc
- Cognitive and mental health assessment
  - Do we need a formal geriatric assessment?
- Nutritional assessment

Other Things to Think About…

- The age and fitness of the proposed caregiver matters
- Tolerance of treatments leading up to cell therapy informs us about resilience
- Understanding your own goals is essential
- Ask for realistic expectations of short- and long-term outcomes

How Do Older Patients Do with These Therapies in the Real World?

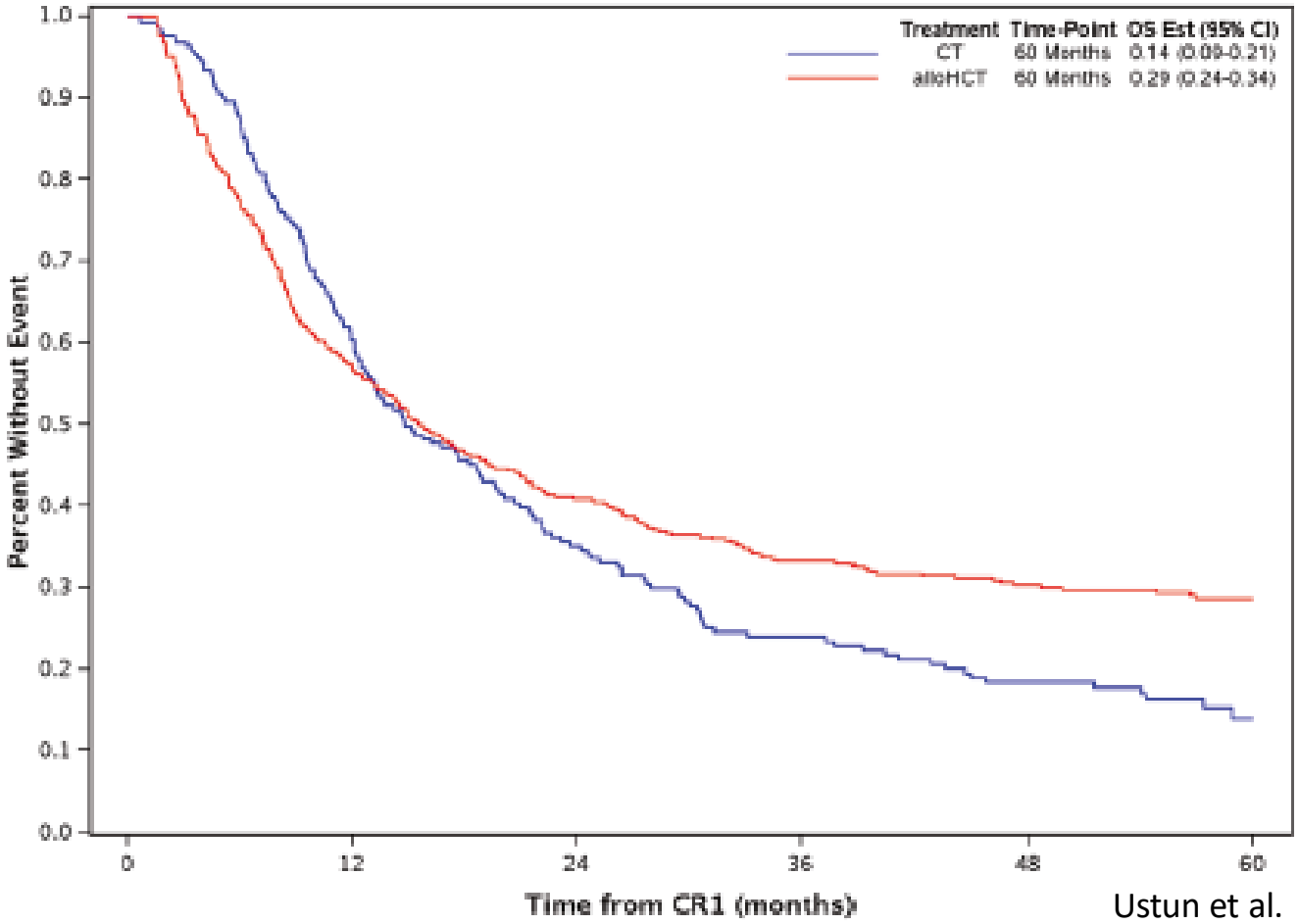
Age No Bar: A CIBMTR Analysis of Elderly Patients Undergoing Autologous Hematopoietic Cell Transplantation for Multiple Myeloma



Munshi et al. Cancer 2020; 126:5077-5087

Allogeneic stem transplant versus chemotherapy alone in older patients with acute myeloid leukemia

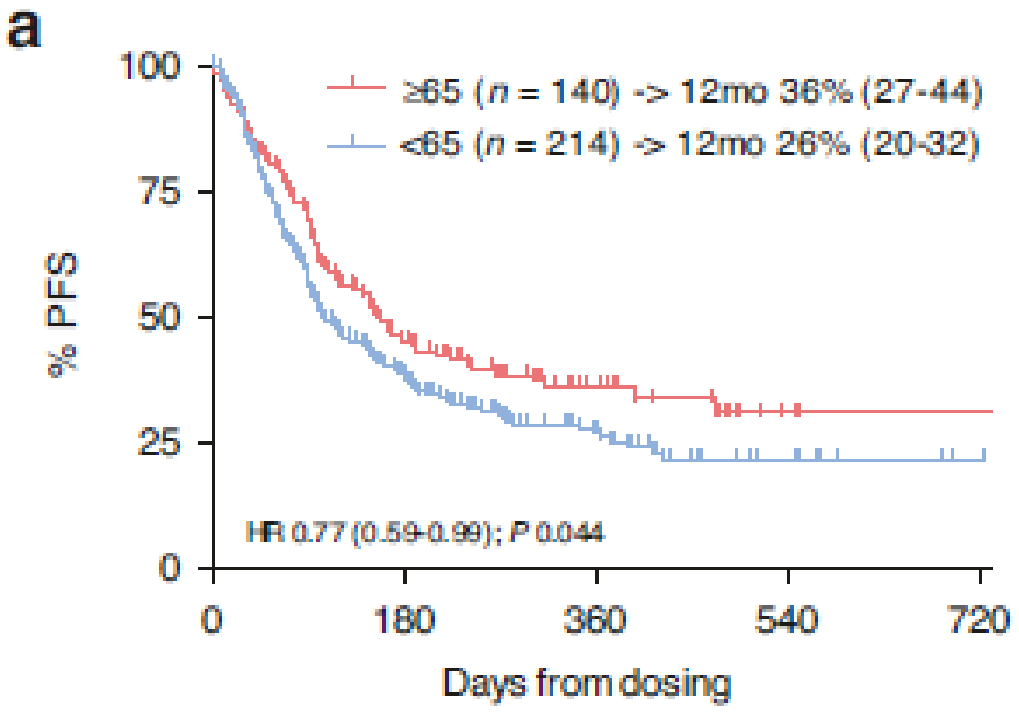
- Registry data on transplant
- Cooperative group study data on chemotherapy



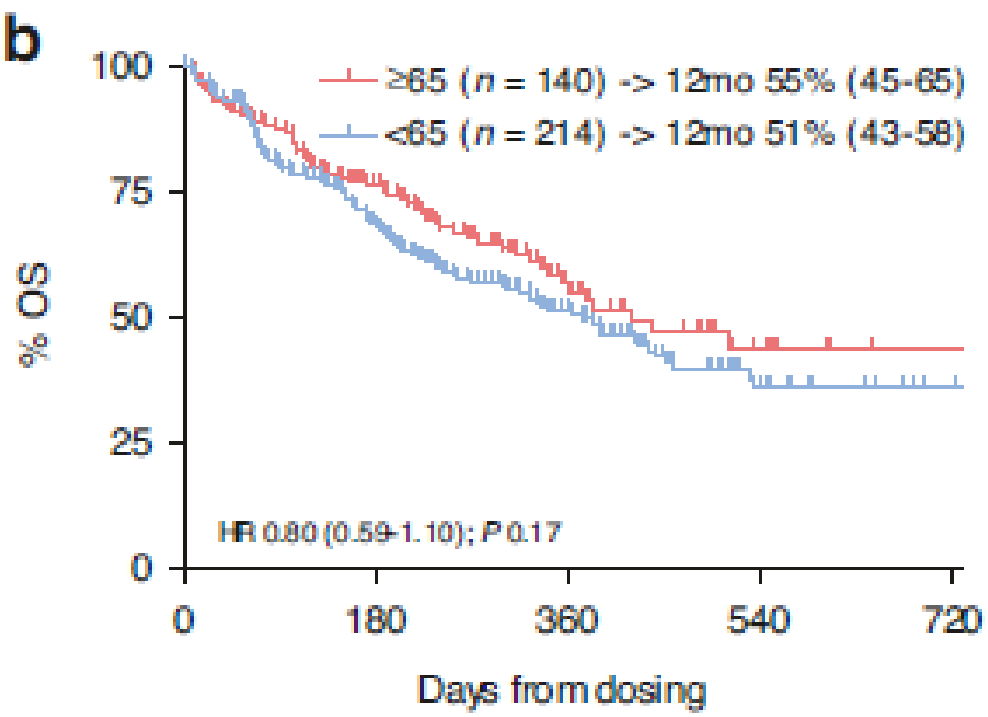
Ustun et al. Leukemia (2019) 33: 2599-2609

Impact of Age on Outcomes of CAR-T cell Therapies for Large B-cell Lymphoma: the GLA/DRST Experience

Progression-free Survival

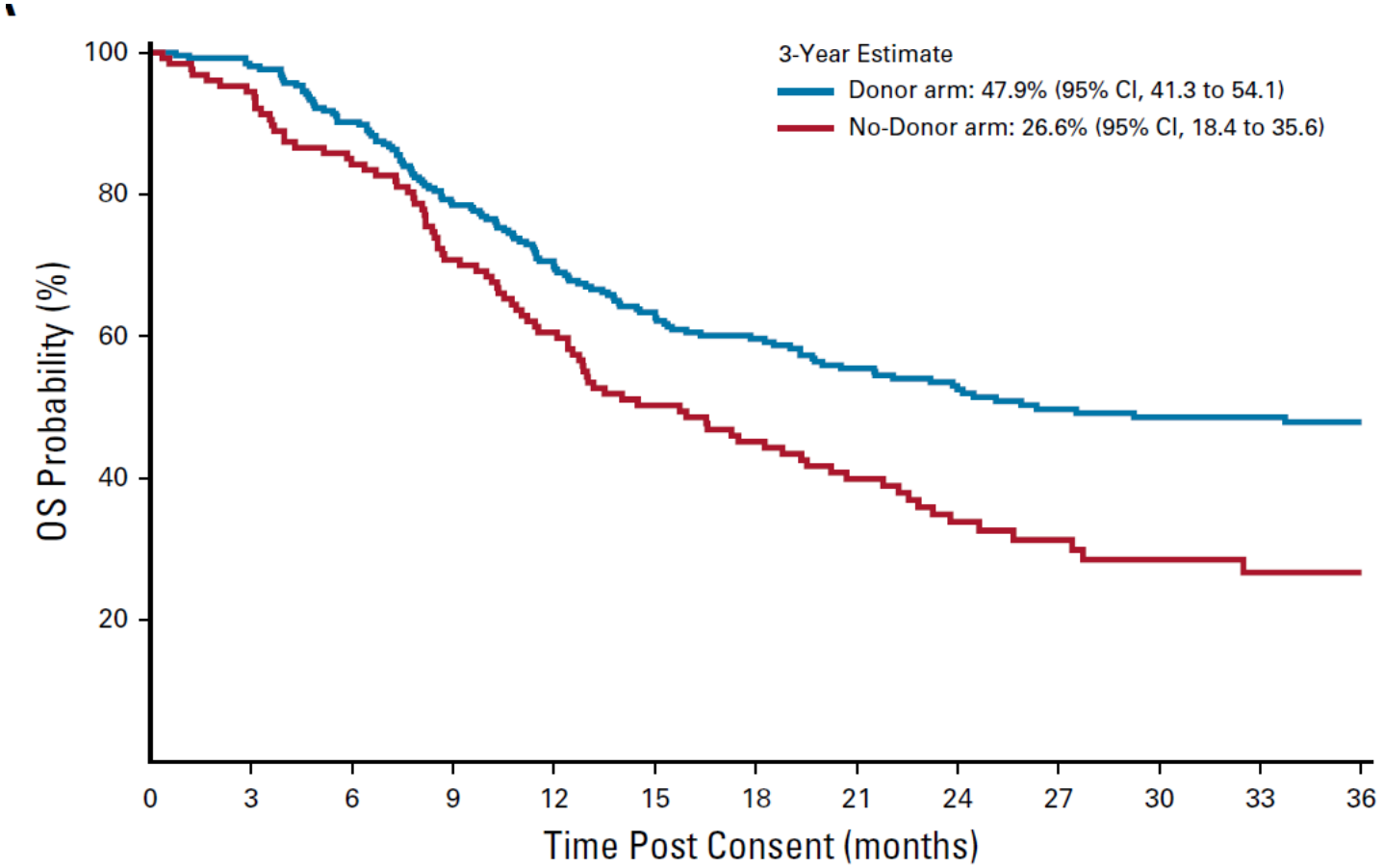


Overall Survival



Dreger et al. Bone Marrow Transplantation, 2023

Patient-Reported Outcomes after Reduced-Intensity Allogeneic Transplant Indicate as Good or Better Quality of Life Among Patients Receiving a Transplant



J Clin Oncol 39:3328-339

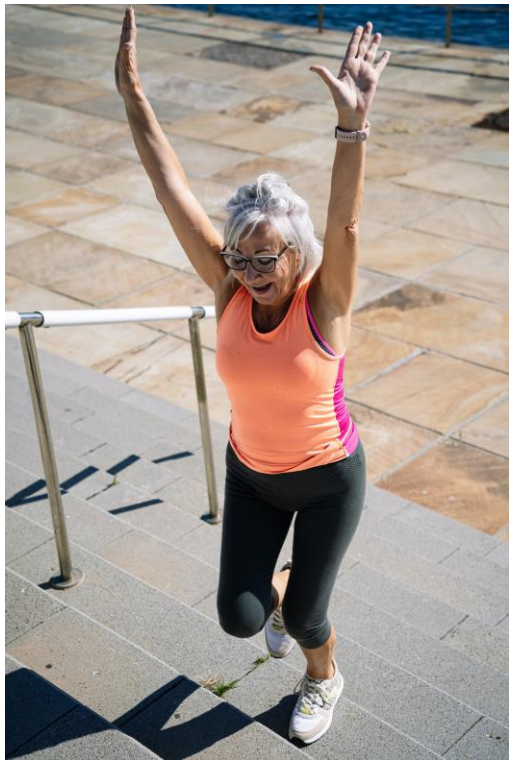
What Can We Do to Improve Outcomes?

- Optimize management of known medical conditions before we start the process
- Targeted evaluations by specialists
  - Geriatrics, cardiology, nutrition, infectious disease, etc
- Careful evaluation and assistance from a social worker
  - Support system, transportation, lodging, etc
- Full disclosure…

What Can You Do to Improve Outcomes?

Maximize your physical status before the start of intensive therapy, and fight not to lose ground during treatment

- "Prehab"— physical therapy and occupational therapy prior to treatment (if there is time)
- Keep activity going IN the hospital and after discharge



What Can You Do to Improve Outcomes?

- Optimize your support team of caregivers
  - Engage multiple family members and friends
  - Designate someone to be the “organizer” and information keeper
- Expect that setbacks and changes of plan may occur
  - Be adaptable

Conclusions

- Age is just a number…
  - Comorbidities, functional status, mobility, and support inform the risk-benefit equation
- The question is not who should get a transplant or cell therapy, but who shouldn’t
  - Transparent communication is essential
  - Shared decision-making is key
- The critical assessment and decision-making must be made just prior to the proposed treatment

Questions?

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Let Us Know How We Can Help You

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