Transplant and CAR T-cell Therapy for Older Adults

Celebrating a Second Chance at Life
Survivorship Symposium

April 29 – May 5, 2023

Richard Lin, MD, PhD
Memorial Sloan Kettering Cancer Center

Financial Conflict of Interest

• Consultancy: Kite, A Gilead Company
• Independent Adjudication Committee: Priothera Ltd.
Learning Objectives

- Age limit for HCT or CAR T-cell therapy as a treatment option
- Health issues (co-morbidities) that may preclude an older adult from undergoing these treatment
- Outcomes after HCT and CAR T-cell therapy for older adults as compared to less intensive therapies
- Outcomes after an allogeneic or autologous HCT and CAR T-cell therapy in older adults as compared to younger adults
- Strategies some transplant and CAR T-cell programs are using to attend to the needs of older adults

Presentation Overview

- The aging patient: scope of the problem
- Older patient outcomes
- Geriatrics principles of care
- Geriatric assessment (GA) in Transplantation and Cellular Therapy (TCT)
- GA-guided management in TCT
- Barriers and challenges
# The Aging Patient with a Blood Cancer

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Median Age of Onset</th>
<th>Incidence per Year</th>
<th>Role of Hematopoietic Stem Cell Transplant (HCT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myeloid leukemia (AML)</td>
<td>63</td>
<td>10,500</td>
<td>Allogeneic HCT as consolidation of high risk CR1 patients or as salvage therapy for patients with advanced disease</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia (ALL)</td>
<td>12</td>
<td>6,950</td>
<td>Allogeneic HCT as consolidation of high risk CR1 patients or as salvage therapy for patients with advanced disease</td>
</tr>
<tr>
<td>Myelodysplastic syndromes (MDS)</td>
<td>70</td>
<td>16,000 estimate</td>
<td>Allogeneic HCT only curative therapy</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia (CLL)</td>
<td>70</td>
<td>16,000</td>
<td>Allogeneic HCT only curative therapy</td>
</tr>
<tr>
<td>Chronic myeloid leukemia (CML)</td>
<td>64</td>
<td>6,000</td>
<td>Allogeneic HCT as salvage therapy for patients who have failed tyrosine kinase inhibitors</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma (NHL)</td>
<td>66</td>
<td>72,000</td>
<td>Autologous HCT as consolidation of chemo-sensitive relapse of diffuse large B-cell lymphoma and follicular lymphoma. Consolidation of high-risk CR1 patients (mantle cell lymphoma, double hit lymphoma, high IPI scores). Allogeneic HCT as salvage for patients who relapse after autologous HCT.</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>73</td>
<td>18,000</td>
<td>Autologous HCT as consolidation of an initial remission considered standard of care. Allogeneic HCT as salvage for patients who relapse after autologous HCT.</td>
</tr>
</tbody>
</table>

---

**Trends in Autologous HCT in the US by Recipient Age**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18 Years</td>
<td>11</td>
<td>14</td>
<td>15</td>
<td>16</td>
<td>16</td>
<td>18</td>
<td>18</td>
<td>19</td>
<td>20</td>
<td>21</td>
<td>22</td>
<td>24</td>
<td>26</td>
<td>28</td>
<td>30</td>
<td>31</td>
<td>32</td>
<td>35</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>18-39 Years</td>
<td>68</td>
<td>66</td>
<td>67</td>
<td>67</td>
<td>66</td>
<td>65</td>
<td>66</td>
<td>65</td>
<td>66</td>
<td>63</td>
<td>62</td>
<td>61</td>
<td>60</td>
<td>59</td>
<td>57</td>
<td>57</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-64 Years</td>
<td>19</td>
<td>19</td>
<td>17</td>
<td>16</td>
<td>14</td>
<td>14</td>
<td>15</td>
<td>13</td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>65+ Years</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^Transplants for NHL, HD, MM
Challenges in Older Cancer Patients

- Comorbidities
- Functional Impairment
- Cognitive Impairment
- Impaired mobility
- Malnutrition & sarcopenia (muscle loss)
- Polypharmacy PIM
- Frailty phenotype

- Access barriers
- Higher risk disease
- Increased regimen Toxicities
- Geriatric survivorship
- Geriatric syndromes (falls, sun-downing, incontinence, etc.)
- Older caregiver, social support
- End-of-Life care

Donor Transplant Compared to Chemotherapy in AML Patients Aged 60-75 years

<table>
<thead>
<tr>
<th>Time Point (years)</th>
<th>CT</th>
<th>AlluCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>60.3% (53.9%-67.5%)</td>
<td>56.8% (51.9%-62.5%)</td>
</tr>
<tr>
<td>2</td>
<td>55.1% (50.9%-62.5%)</td>
<td>40.8% (36.7%-46.1%)</td>
</tr>
<tr>
<td>3</td>
<td>33.5% (18.6%-50.3%)</td>
<td>38.8% (26.9%-54.8%)</td>
</tr>
<tr>
<td>5</td>
<td>13.8% (9.0%-20.7%)</td>
<td>28.6% (24.4%-33.0%)</td>
</tr>
</tbody>
</table>

Utsun et al. 2019 Leukemia Transplant
Donor vs No-donor Biologic Assignment Trials for Older Patients with MDS

Nakamura R et al. 2021 JCO; Kroger N et al. 2021 JCO

Transplant
Chemotherapy

Transplant
Chemotherapy

From: Comparison of Patient Age Groups in Transplantation for Myelodysplastic Syndrome: The Medicare Coverage With Evidence Development Study

CAR T-cell Therapy in Older Lymphoma Patients

ZUMA-1 Study

- Median DOR (95% CI)
  - Age >65 y: 12.0 months (2.4-NE)
  - Age <65 y: 8.1 months (2.1-NE)

MSK Study

Challenges in Older Cancer Patients

- Comorbidities
- Functional Impairment
- Cognitive Impairment
- Impaired mobility
- Malnutrition & sarcopenia (muscle loss)
- Polypharmacy PIM
- Frailty phenotype
- Access barriers
- Higher risk disease
- Increased regimen Toxicities
- Geriatric survivorship
- Geriatric syndromes (falls, sun-downing, incontinence, etc.)
- Older caregiver, social support
- End-of-Life care
Geriatrics Principles of Care: Life Expectancy

- Fit/robust
- Average/vulnerable
- Frail/sick

Geriatrics Principles of Care: Multidisciplinary Management

- Atypical disease presentation with many causes likely
- Quality of life/Independence preference
- Cognition impairment and other geriatric syndromes
- Complex medication management:
  - start low and go slow, active deprescribe
Geriatric Principles of Care: Frailty and Resilience

<table>
<thead>
<tr>
<th>“Frailty” Constructs</th>
<th>Examples</th>
<th>Frailty and Resilience from the Perspective of a Complex Structure (Golden Gate Bridge)</th>
<th>Potential Strengths</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Phenotypic Frailty (defined state)</td>
<td>Fried CHS Study Seropenic Obesity</td>
<td></td>
<td>Capture existence of a clinically defined and measurable phenotypic state</td>
</tr>
<tr>
<td>B. Stochastic Frailty (accumulation of deficits)</td>
<td>Rockwood FI Index (e.g. Fickin, Fall)</td>
<td>Perform prognosis</td>
<td>Define cross-cutting risk factors</td>
</tr>
<tr>
<td>C. Resilience (Measure of homeostasis in face of stressor)</td>
<td>Orthostasis Vaccine Responses Recovery from infection, surgery, anesthesia, dehydration, bedrest, chemotherapy, trauma or BM transplant</td>
<td>Measure treatment effects when more frailty interventions are studied</td>
<td>Identify “hidden” vulnerability</td>
</tr>
</tbody>
</table>

Geriatric Assessment in TCT Biological versus Chronologic Age

![Diagram showing the relationship between Comorbidities, Functional Status, Cognition, Social Support, Polypharmacy, Nutrition, and Mental Health.](Slide courtesy: R. Olin UCSF)
Functional Status: ADL and IADL

**Katz Activities of Daily Living (ADL)**
- Bathing
- Dressing
- Toileting
- Transferring
- Continence
- Feeding

**Lawton Instrumental Activities of Daily Living (IADL)**
- Using the telephone
- Shopping
- Food preparation
- Housekeeping
- Laundry
- Using transportation
- Managing medications
- Handling money

**“Next level” performance status**

Timed Up and Go (TUG) Test

- Can be done in the clinic
- Easy assessment without a watch into 3 categories:
  - <10 secs (fit)
  - 10-20 secs (vulnerable)
  - >20 secs (frail)
- Can be followed overtime
The MiniCog Test

- Can be done in the clinic (3 minutes)
- Easy assessment to establish the need for more in-depth evaluation: 3 points or less on a total of 5 points (3 points for recall, 2 points for clock)
- Not sensitive to follow overtime

![MiniCog Test Diagram](image)

**FIGURE 2.** Interpretation of the Mini-Cog test, which requires the patient to recall three words and draw an analog clock.

---

Prognostically Important Geriatric Deficits in Donor Transplantation

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Function</th>
<th>Mobility</th>
<th>Cognition</th>
<th>Medication</th>
<th>Frailty scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRM +</td>
<td>NRM +</td>
<td>OS +</td>
<td>OS +</td>
<td>OS +</td>
<td>OS +</td>
</tr>
<tr>
<td>NRM +</td>
<td>OS +</td>
<td>PFS +</td>
<td>OS +</td>
<td>NRM +</td>
<td>NRM +</td>
</tr>
<tr>
<td>NRM +</td>
<td>NRM +</td>
<td>NRM +</td>
<td>NRM +</td>
<td>OS + PFS +</td>
<td>Toxicities + OS +</td>
</tr>
<tr>
<td>NRM +</td>
<td>OS +</td>
<td>PFS +</td>
<td></td>
<td>NRM +</td>
<td>OS +</td>
</tr>
</tbody>
</table>

**OS:** Overall survival  
**PFS:** Relapse-free survival  
**NRM:** Death without relapse
Geriatric Assessment in Patients Receiving CAR T

- **ADL**: Activities of daily living
- **IADL**: Instrumental activities of daily living
- **CIRS-G**: Comorbidities in older patients

Geriatric Impairments and CAR T Survival

**Overall Survival from CAR**

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>No Cognitive Impairment</th>
<th>Cognitive Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24  21  19  11  5  4  3  0  0</td>
<td>15  8  6  3  3  1  1  0</td>
</tr>
</tbody>
</table>

Log rank $p = 0.035$
Comprehensive Geriatric Assessment (CGA) Guided Managements

- **Comorbidities:**
  - Referral to geriatrics or appropriate specialty
  - Optimize disease management

- **Social Support:**
  - Referral to social worker
  - Financial assessment
  - Caregiver respite

- **Mental Health:**
  - Referral to psychologist or counselor
  - Support groups

- **Physical or functional limitations:**
  - Physical/Occupational Therapy
  - Exercise program
  - Falls precautions

- **Cognitive dysfunction:**
  - Caregiver involvement
  - Written instructions or reminders
  - Delirium precautions

- **Polypharmacy:**
  - Review of potentially inappropriate medications (Beers' criteria)
  - De-prescribing if possible

- **Nutritional deficits:**
  - Referral to nutritionist
  - Appetite stimulants

---

Multi-disciplinary Clinic for Older Patients Undergoing a Transplant with Donor Cells

- **Multidisciplinary Assessments & Optimizations**
  - Patient Surveys
  - Function & Cognition

- **Clinical Assessment/Optimizations**
  - Transplant MD + APP
  - PT/OT
  - Geriatric Oncology
  - Nutrition
  - Infectious Disease
  - Social Work
  - Team Meeting

- **Transplant Outcomes**
  - Inpatient Deaths
  - Nursing Home Admissions
  - Non-Relapse Mortality
  - Survival
GA-Guided Multi-disciplinary Clinic for Older Patients Prior to Donor Transplant

Impact of Post-Transplant Geriatric Syndromes
### Why Geriatric Assessment is Not Used at Some Transplant Centers

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertainty about which assessment tools to use</td>
<td>59%</td>
</tr>
<tr>
<td>Lack of training, knowledge, understanding or experience about geriatric assessment</td>
<td>53%</td>
</tr>
<tr>
<td>Lack of clinical support staff</td>
<td>45%</td>
</tr>
<tr>
<td>Not aware of available assessment tools</td>
<td>41%</td>
</tr>
<tr>
<td>Lack of time</td>
<td>38%</td>
</tr>
<tr>
<td>Lack of available resources for referrals</td>
<td>41%</td>
</tr>
<tr>
<td>Limited evidence to support geriatric assessment</td>
<td>34%</td>
</tr>
<tr>
<td>Limited or available space to conduct the assessment</td>
<td>28%</td>
</tr>
<tr>
<td>No or limited provider reimbursement</td>
<td>26%</td>
</tr>
</tbody>
</table>

---

### Quality of Life Following Transplant with Donor Cells

- **Risk Factors**
  - Age
  - Co-morbidity
  - Conditioning
  - Support
  - GVHD

- **Health Related Quality of Life**
  - Physical
  - Fatigue
  - Sleep
  - Psychological
  - Sexual Function
  - Social/Role

- **Timeline**
  - HSCT
  - Recovery
  - Reintegration
Similar Quality of life in MDS patients aged 50–75 with or without transplant with donor cells

Challenges in Older Cancer Patients

- Comorbidities
- Functional Impairment
- Cognitive Impairment
- Impaired mobility
- Malnutrition & sarcopenia (muscle loss)
- Polypharmacy PIM
- Frailty phenotype

- Access barriers
- Higher risk disease
- Increased regimen Toxicities
- Geriatric survivorship
- Geriatric syndromes (falls, sun-downing, incontinence, etc.)
- Older caregiver, social support
- End-of-Life care
Resilience and Stressors for Older Adults in Transplantation and Cellular Therapy

Lin and Artz, 2021 ASH Hematology Education Program
QUESTIONS?

Richard Lin, MD
Memorial Sloan Kettering Cancer Center
Email: linr@mskcc.org

LET US KNOW HOW WE CAN HELP YOU

Visit our website: bmtinfonet.org
Email us: help@bmtinfonet.org
Give us call: 888-597-7674