Transplant Outcomes in Older Adults with MDS and AML

Celebrating a Second Chance at Life Survivorship Symposium

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Gabrielle Meyers, MD
Center for Hematologic Malignancies, Oregon Health & Science University

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Gabrielle Meyers, MD
Associate Professor of Medicine
Oregon Health and Sciences University
Knight Cancer Institute
Goals of this talk

- Present information regarding transplant for AML and MDS, including:
  - Outcomes with transplant compared to outcomes without transplant
  - Quality of life after transplant
  - Response rates to transplant
  - Treatment before and after transplant
- Discuss strategies to improve outcomes with transplant
  - Importance of exercise and nutrition
  - Treatments to help reduce risk of relapse

Key Points

- Most AML and MDS can only be cured with a stem cell transplant
- Allogeneic transplant in older adults is becoming much more common
- Studies show that age alone is not a barrier to a successful transplant
- Studies show a survival advantage for transplant in higher risk MDS and AML in older adults compared to not getting a transplant.
- How strong and fit you are prior to transplant effects how well you do
- Overall, transplant outcomes continue to improve, including in those over the age of 60.
Number of transplants for patients > age 65 is increasing

AML and MDS most common diseases for allogeneic transplant
Let’s start by talking about MDS, and transplant for MDS

Myelodysplastic Syndrome (MDS)

• MDS is primarily a disease of older adults
  Average age at diagnosis around 71 years old
• MDS is a bone marrow stem cell problem
• The bone marrow stem cells in MDS are “damaged” and dysfunctional, so that they don’t make blood cells like they are supposed to (“lazy”)
• MDS is associated with low blood cell counts
  • Patients frequently require blood transfusions
  • Patients are at increased risk of infections and bleeding
• MDS has a risk of developing into acute leukemia (AML in particular)
• While there are treatments to help make the MDS cells function better, the only way to potentially cure MDS is with a stem cell transplant from a donor
Not all MDS is the Same

• We think of MDS as being in 2 categories
  • LOWER RISK
  • HIGHER RISK
• The short term and long term treatment options vary between lower risk and higher risk MDS
• While all MDS can only be cured by transplant, lower risk MDS may not benefit from a transplant if it is done “too early”
• Let’s talk more about risk of MDS and how that helps us decide about transplant

Risk Assessment in MDS

• MDS scoring systems take into account features of the disease:
  • Need for blood transfusions
  • How low is the neutrophil count and platelet count?
  • What is the blast count in the bone marrow?
  • What, if any, chromosome changes are present?
  • What, if any, mutations in genes are present?
  • Is the MDS responding to treatment?
• For many patients with truly lower risk MDS, their expected life span is many years
• On the other side are patients with high-risk MDS - these patients have a high risk of transforming into leukemia or having another life-threatening complication of their disease
• Before deciding to pursue transplant, you have to balance the risks of the procedure with the risks of the disease
Considerations for Transplant in **Lower Risk MDS**

In this case, the risk of the transplant is HIGHER than the risk of the MDS. We wouldn’t want to transplant right now.

Considerations for Transplant in **Higher Risk MDS**

In this situation, the risk of the MDS is much higher than the risk of the transplant. This would be a situation where we would want to proceed to transplant.

Studies show that in this situation, **transplant leads to improved survival**.
Studies Comparing Transplant to NO Transplant in MDS

- Biggest and best trial was reported in December 2020.
- Randomized higher risk MDS patients to transplant or no transplant
  - Randomized based on whether they had a fully matched donor or not
- Average age both arms = 66, with ~60% of patients over age of 65. Highest age was 75
- The 3 year survival rate was 48% in transplant arm and 27% in no transplant arm - this difference was statistically significant
- No significant difference in quality of life
- Conclusion: all patients with higher risk MDS up to age 75 should be considered for transplant

Transplant vs. NO Transplant in MDS

A Multi-Center Biologic Assignment Trial Comparing Reduced Intensity Allogeneic Hematopoietic Cell Transplantation to Hypomethylating Therapy or Best Supportive Care in Patients Aged 50-75 with Advanced Myelodysplastic Syndrome. Blood and Marrow Transplant Clinical Trials Network Study 1102 ASH 2020 Abstract, Nakamura R et al.
Transplant for MDS - Key Points

• In higher risk MDS, transplant increases survival compared to non-transplant therapy
• Quality of life does not appear to be worse in those undergoing transplant, and may actually improve significantly for many patients
• Relapse can be a problem after transplant
• We will talk more about this after talking about transplant for AML
Transplant for Acute Myelogenous Leukemia (AML) - Key Points

• Transplant for AML is best performed when patients are in an excellent remission
  • Best if there is no evidence of minimal residual disease
• AML can be very difficult to get into a second remission
• Transplant for AML leads to longer survival rates compared to no transplant, and for many patients, the only chance for cure

AML in Older Adults

• AML is a disease of older adults; average age of diagnosis is 68
• Like MDS, there are features of the disease that impact the risk of the disease
• Unlike MDS, over 70% of older AML patients have higher risk disease
• Therefore, almost every patient over the age of 60 with AML could be considered for transplant if we just focused on their disease
• But, there are many factors beyond disease that impact that decision to consider transplant
What are the outcomes for patients with AML who are undergoing a transplant?

Survival after Unrelated Donor HCT for Acute Myelogenous Leukemia (AML), Age ≥18 Years, in the US, 2008-2018

CR=Complete Remission
You can see that response to treatment before transplant is a very important factor in outcomes
What about transplant outcomes in those over 70?

Our experience in patients the age of 70 and older
Dramatic improvement in survival in those getting
Transplant vs. NO transplant

What influences outcomes of transplant in patients with AML or MDS?

• Age alone is not a factor that influences outcome
  • Multiple studies show similar outcomes in those > or <60 years old
• Functional status and comorbidities are important factors in outcomes
• Disease relapse is a real issue after transplant
  • Use of post-transplant therapies is being studied to reduce risk of relapse
• Studies to optimize conditioning regimens, GVHD prevention and alternative donor options are showing great promise
But what about Quality of Life?

- Quality of life (QOL) after transplant, in general, is reported as good
  - Dip initially after transplant that then heads back to pre-transplant levels in 6-12 months.
- There are factors that are known to impact quality of life
- GVHD can lead to poorer QOL
- Functional status - how strong you are - impacts QOL
- Impact on ability to work and financial security can decrease QOL
- These factors are present in younger and older adults

How can we improve functional status?

- Exercise
  - In the cancer world there is a lot of research on “prehabilitation”
  - The idea is to build up the strength in your body before treatment
  - Higher strength/performance status leads to better QOL
  - Combination of activity as well as strengthening to counteract muscle loss
- Nutrition
  - Making sure adequate calories and adequate protein intake (goal protein intake 1.5-2 grams/kg of body weight to help gain muscle back)
- Optimizing your mood
  - Research has shown that mood and functional status are very connected; a structured prehab program was most beneficial for those with depression
  - Talk with your treatment team about how you are feeling
Disease Control Before and After Transplant

- Before transplant we want MDS with blasts <5% and AML in complete remission
  - Best to have NO minimal residual disease in AML
  - However, if we can’t get this level of disease control we can still do a transplant successfully
- Best treatments for AML include intensive chemotherapy
- Those over the age of 60 can tolerate intensive AML therapy; it’s important to treat patients with the best treatment
- With transplant we can give full dose chemotherapy vs. reduced intensity chemotherapy conditioning
  - Reduced intensity conditioning has lower complications from transplant
  - But with reduced dosing we see higher risk of relapse
- The choice of the regimen is optimized for each patient taking into account health problems and disease status

Disease Control After Transplant

- After transplant we have treatment options to help control disease without harming the graft vs. leukemia (or graft vs. MDS) activity
- Use of these agents (azacytidine, decitabine or targeted agents) after transplant in both MDS and AML has shown to be well-tolerated
- These treatments have also shown to reduce relapse risk
GVHD Prevention and Management

- GVHD is the biggest fear for many patients have when considering a transplant
- Lots of focus on trying to prevent GVHD and manage GVHD if it comes
- GVHD does reduce the risk of relapsed disease
- Worth asking about clinical trial options at your institution
  - Vedolizumab is an antibody being studied to prevent gut GVHD
  - Multiple trials looking at modification of the transplanted cells to reduced the chance of GVHD
Summary

- We can successfully transplant patients with MDS and AML over age 60
- The number of patients getting transplant in their 70’s continues to rise
- The best outcomes are seen when you have:
  - Good control of your disease
  - Good performance status prior to transplant
- It is important to continue to exercise and stay strong throughout the treatment - both before and after transplant
- Treatments are available after transplant to help prevent relapse
- Age alone is not a factor, but the health status and functional status are key markers of success