5 Minute JournalClub

CIBMTR Analysis of HCT in Older Patients with AML or MDS

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CME INFORMATION

OVERVIEW OF ACTIVITY

Acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS) account for approximately 20 percent of all hematologic cancer and related hemopathies diagnosed on an annual basis. Emerging and continuing clinical research has resulted in an increased understanding of the heterogeneous nature of these diseases and in the availability of novel treatment strategies and options. In order to offer optimal patient care — including the option of clinical trial participation — the practicing medical oncologist must be well informed of the rapidly evolving data sets in AML and MDS. To bridge the gap between research and patient care, this CME activity will deliver a serial review of recent key presentations and publications and expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for AML and MDS.

LEARNING OBJECTIVE

- Consider the CIBMTR study results on reduced-intensity or nonmyeloablative HCT when evaluating treatment options for elderly patients with AML or MDS.

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FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

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5 MinuteJournalClub

Inside this issue: Four interesting AML nuggets:

1. **A Phase II study** evaluating clofarabine in 112 older patients (median age 71) with AML and one or more adverse prognostic factors. Treatment was "well tolerated" and resulted in 38% CRs.

2. **A Phase II study** of the hypomethylating agent decitabine in 55 older patients (median age 74) with AML. Morphologic CR was observed in 24%; febrile neutropenia was observed in 24%.

3. **A literature review** suggesting that assays for NPM1mut and FLT3 ITDneg could be the new ER and HER2 of AML. (Ok, maybe that is an overstatement, but these are highly prognostic and predictive.)

4. **A retrospective analysis** demonstrating roughly similar results with allogeneic hematopoietic stem cell transplant in patients with AML over and under age 65.

Editor's comment: Who should treat patients with AML?

Mike Schwartz, a Memorial-trained medical oncologist practicing in Miami Beach, is one of several dozen "master clinicians" across the country who have assisted us with our CME programs. Mike's most recent contribution was helping us plan an upcoming **Satellite Symposium** that we will host in New Orleans on Friday night, December 4, preceding the ASH annual meeting.

Dr Schwartz will join four other community-based physicians as they present challenging cases of AML, MDS, CML, and myeloma from their practices to our all-star faculty. In addition to discussing these carefully selected patients, we will also reveal the results of our recent **national Patterns of Care survey** of US-based oncologists, specifically focusing on the management of the cases being presented at the meeting.

One interesting survey question that we will discuss live is "Do you treat some or most patients with AML or do you generally refer them to a tertiary center?" To my mild surprise, more than two thirds of the survey respondents generally manage these patients themselves, and that includes Mike, who will present a 59-year-old woman recently diagnosed with AML.

Our prior surveys have documented that oncologists in practice see about as many cases of breast cancer a year as breast cancer investigators, but AML is a complicated disease that occurs at less than one tenth the frequency.

Of course there is more than science required in these intense situations, as evidenced by Mike's patient, an Asian woman, who asked if she could take traditional therapeutic herbs during chemo (Mike said "No," as did 79 percent of the oncologists surveyed).

Certainly physicians who offer patients a local means to receive treatment for a very scary disease must do their best to keep up with the gradual but definite progress in AML. In New Orleans, we'll see what our faculty has to say about Mike's patient and whether they think she, like many others, can be effectively managed in the community. From my standpoint, this woman is fortunate to be receiving care from one of the many, many extraordinary clinicians working outside of academic medicine.

Next up on 5-Minute Journal Club: The final four papers highlighted in our series along with results from our Patterns of Care study documenting oncologists' management of MDS.

Neil Love, MD
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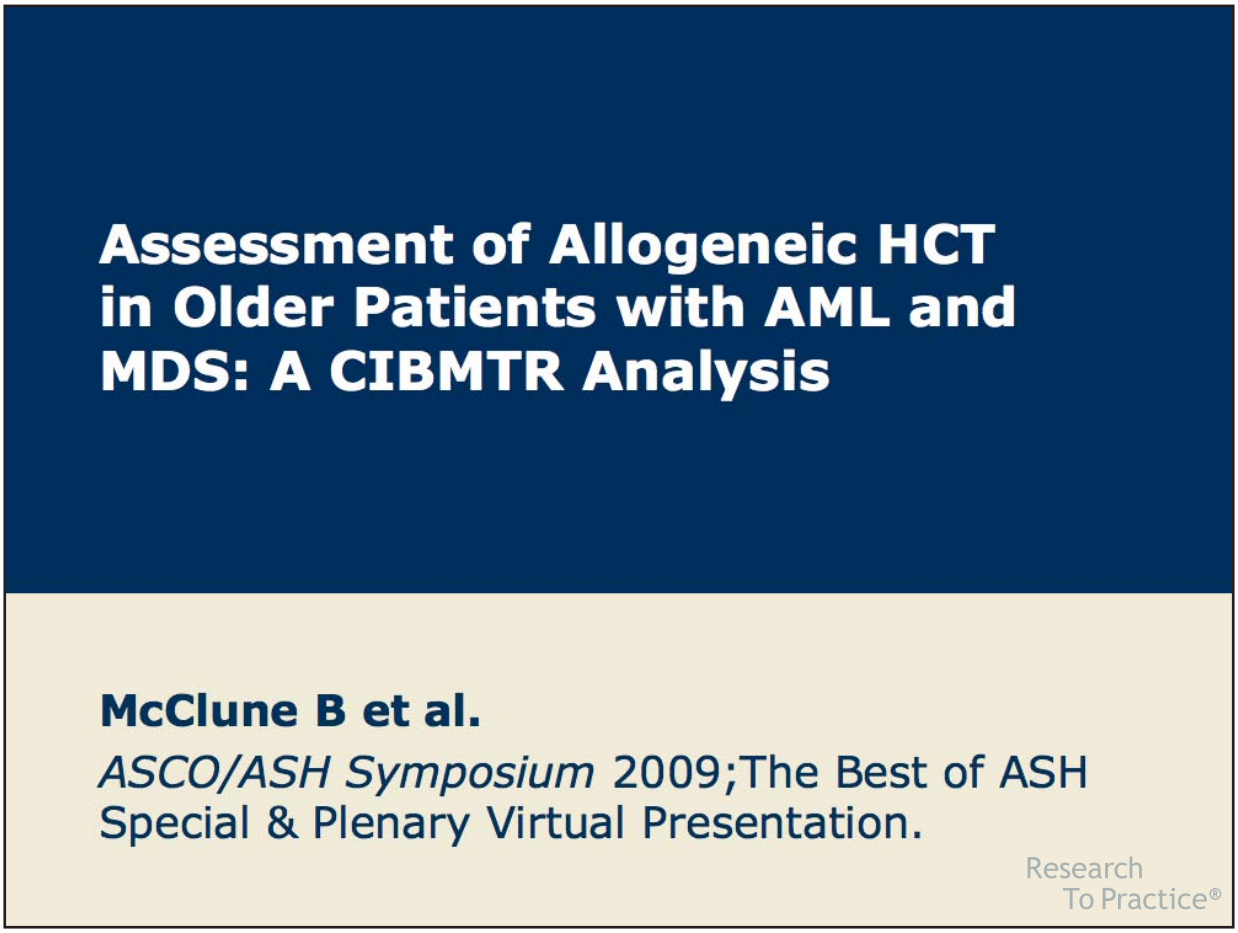
CIBMTR Analysis of HCT in Older Patients with AML or MDS

Presentation discussed in this issue:

McClune B et al. **Assessment of allogeneic HCT in older patients with AML and MDS: A CIBMTR analysis.** The Best of ASH Special and Plenary Virtual Presentation. ASCO/ASH Symposium 2009. **Abstract**

Slides from a presentation at ASCO 2009 and transcribed comments from a recent interview with Gail J Roboz, MD (11/20/09) below



Introduction

- Median age at diagnosis of acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) is > 65 years.
- Five-year overall survival for patients with AML who are ≥ 60 years old is 6.6% (*Blood* 2006;108:63).
- The outcome with standard chemotherapy is worse in older patients, but allogeneic hematopoetic stem cell transplantation (HCT) can be curative.
- **Current study objectives:**
  - Determine the impact of age on outcomes for older patients with AML and MDS undergoing transplantation

Source: McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

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Methods

- Study population: patients referred to the Center for International Blood & Marrow Transplant Research (CIBMTR) between 1995 and 2005 undergoing non-myeloablative HCT
- ≥ 40 years old with MDS (n=535) or AML (n=545) in 1st complete remission
- **Reduced intensity or non-myeloablative HCT**
- Matched related donor or unrelated donor
- Primary endpoints: overall survival, leukemia-free survival, treatment-related mortality (TRM), relapse, engraftment, acute and chronic GVHD (aGVHD/cGVHD)
- Retrospective data review including multivariate modeling with age in all models
  - Four age groups were analyzed: 40-54; 55-59; 60-64; ≥65 yrs

Source: McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

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Outcomes of Nonmyeloablative HCT in Patients with AML (n=545)

Endpoint	Range across all age groups	*P*-value* (multivariate analysis)
Overall survival at 2 years	34% - 50%	0.06
Leukemia-free survival at 2 years	31% - 43%	0.15
Treatment-related mortality at 1 yr	18% - 35%	0.66
Relapse at 2 yrs	29% - 37%	0.87
Neutrophil recovery at 28 days	>80%	0.14
Acute GVHD	31% - 36%	0.96
Chronic GVHD	41% - 53%	0.30

* *P*-values apply to differences in the particular endpoints based only on age.

Source: McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

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Outcomes of Nonmyeloablative HCT in Patients with MDS (n=535)

Endpoint	Range across all age groups	*P*-value* (multivariate analysis)
Overall survival at 2 years	35 - 45%	0.37
Leukemia-free survival at 2 years	32% - 39%	0.68
Treatment-related mortality at 1 yr	18% - 35%	0.66
Relapse at 2 yrs	29% - 37%	0.87
Neutrophil recovery at 28 days	>80%	0.25
Acute GVHD	31% - 36%	0.89
Chronic GVHD	37% - 45%	0.79

* *P*-values apply to differences in the particular endpoints based only on age.

Source: McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

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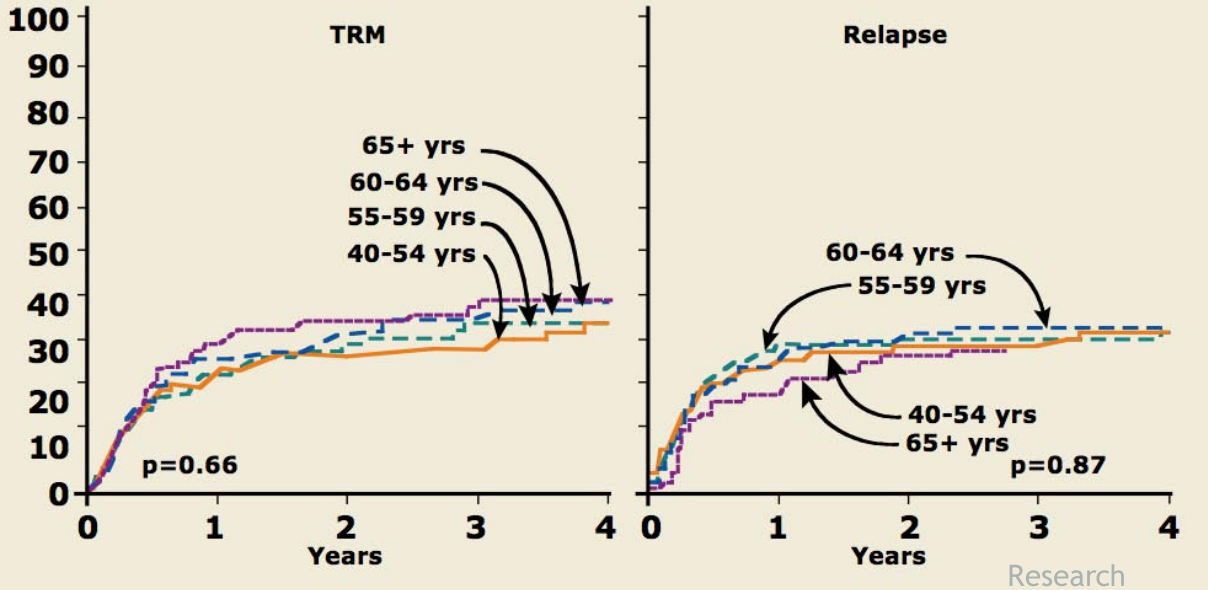
TRM and relapse of patients 40+ years receiving nonmyeloablative allogeneic HSCT for AML and MDS, 1995-2005, by age



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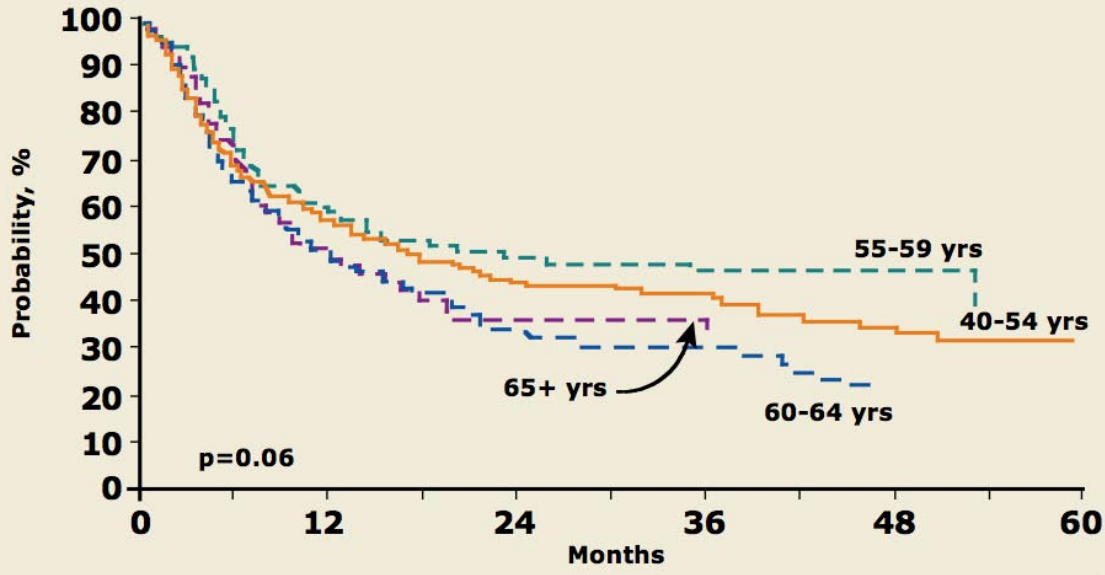
Source: With permission from McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

Overall survival of patients 40+ years receiving nonmyeloablative allogeneic HSCT for AML in CR1, 1995-2005, by age



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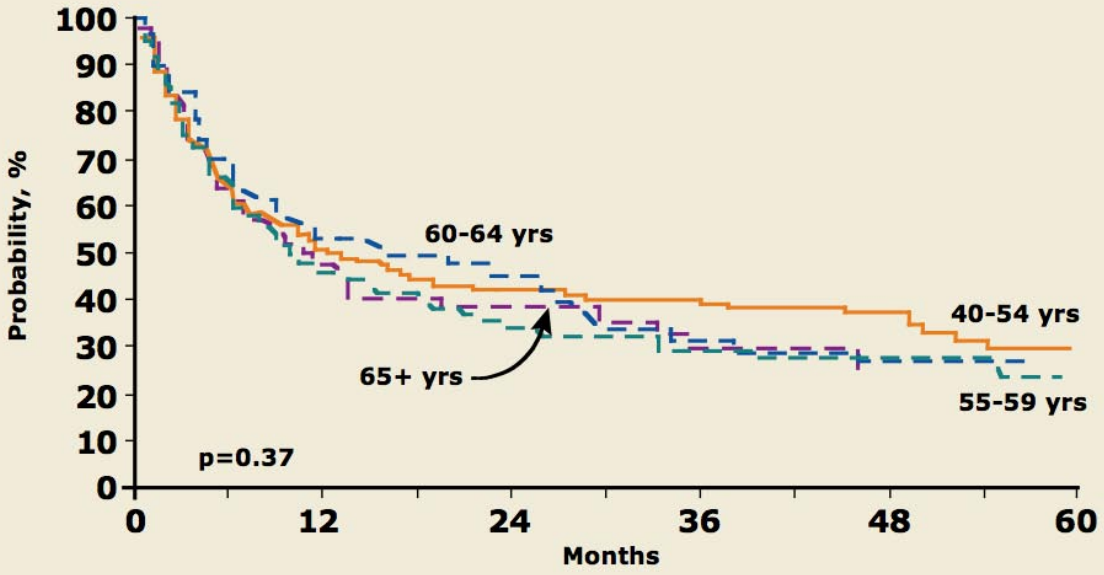
Overall survival of patients 40+ years receiving nonmyeloablative allogeneic HSCT for MDS, 1995-2005, by age



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Source: With permission from McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

Summary and Conclusions

- Multivariate analysis demonstrated equivalence in outcomes of non-myeloablative HCT in older versus younger patients:
  - Treatment related mortality (18% - 35%)
  - Two-year relapse (29% - 37%)
  - Acute GVHD (31% - 36%)
  - Chronic GVHD (MDS, 37% - 45%; AML, 41% - 53%)
  - Comparable two-year leukemia-free survival (MDS, 32% - 39%; AML, 31% - 43%)
- Age is not a contraindication to non-myeloablative allogeneic HCT

Source: McClune B et al. ASCO/ASH Symposium 2009, Best of ASH

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DR ROBOZ: The study by McClune is very important. Physicians make an assumption that there will be an age effect in transplant. The general reaction to transplant in older patients is one of horror — even reduced-intensity transplant.

This is an important paper because it demonstrates the feasibility of transplant in older patients and that once patients get through transplant, their survival at three years is not necessarily age related. Even though this is not a randomized study, historical data suggest that the numbers reported here are higher than expected with current chemotherapy, which argues that perhaps we should be attempting to get more patients to transplant.

DR LOVE: What's the age of the oldest patient you've sent for transplant?

DR ROBOZ: Seventy. The oldest patient described in this paper was 78 years old. At Cornell we haven't set an absolute upper age limit for transplant. I would probably be scowled at if I send a patient over 80, but it's not impossible to consider.

Dr Roboz is Associate Professor of Medicine and Director of the Leukemia Program at Weill Medical College of Cornell University at NewYork-Presbyterian Hospital in New York, New York.