The Impact of Risk-adapted Treatment Strategy on Outcome of Patients with Acute Myeloid Leukemia aged ≥ 60 years after allogeneic Stem Cell Transplant

Riwa SAKR¹, Sylvain PILORGE¹, Stephane DE BOTTON^{1,2,3}, Claude CHAHINE¹, Tereza COMAN¹, Marcel ADLER¹, Jean-Baptiste MICOL¹, Florence PASQUIER¹, Christophe WILLEKENS^{1,2}, Alina DANU¹, Julien LAZAROVICI¹, David GHEZ¹, Eric SOLARY^{1,2,3}, Vincent RIBRAG^{2,4}, Jean-Henri BOURHIS¹, Cristina CASTILLA-LLORENTE¹.

¹ Department of Hematology, Gustave Roussy Cancer Center- 114 rue Edouard Vaillant - 94805 Villejuif – France, ² Gustave Roussy Cancer Center, INSERM U1170- Villejuif- F-94805- France, ³ Faculty of Medicine, Université Paris- Sud-Le Kremlin- Bicêtre-France.

Background

-Acute myeloid leukemia (AML) is a common disease in elderly. It has a bad prognosis mainly due to poor disease characteristics as well as to low treatment tolerance resulting from the pre-existing age-related comorbidities^{1,2,3}.

-Treatment is still challenging. Most patients are considered ineligible for intensive chemotherapy for fear of increased treatment-related mortality^{4,5}.

-Reduced intensity conditioning (RIC) allogeneic stem cell transplantation (allo-HCT) is an effective treatment but presumed morbidity & mortality reduced its use in older patients^{6,7}.

-However, McClune *et al.* observed that transplantation toxicity, relapse & survival in older patients were similar to younger adults⁸.

-Strong evidence considers pre-treatment risk assessment based on the patient's characteristics, disease characteristics and disease status as necessary to select the subgroup of older patients that will benefit from allo-HCT and to offer a good estimates of the risk of relapse, NRM and survival^{4,6}.

Objectives

-To determine overall survival (OS; time to death irrespective of the cause), Relapse-free survival (RFS; survival without death or relapse), non-relapse mortality (NRM; time to death without evidence of disease relapse) and cumulative incidence of relapse (RI; time to relapse).

-To evaluate, after stratifying patients according to the risk-adapted treatment model, the NRM rate, relapse rate and survival rate according to the HCT-CI comorbidity score.

Table 1. Baseline Characteristics (N=47)

Median age at HCT, yr., range	64 (61-72)
60-65 years, no (%)	27 (57%)
≥ 65 years, no (%)	20 (43%)
Gender, no (%)	
Male	31 (66%)
Female	16 (34%)
Disease status, no (%)	
Complete remission (CR1)	29 (62%)
Complete remission (>CR1)	14 (30%)
Partial response	4 (8%)
HCT-CI, no (%)	
0-2	39 (83%)
≥ 3	8 (17%)
Donor, no (%)	
Related	17 (36%)
Matched unrelated 10/10	14 (30%)
Mismatched unrelated 9/10	9 (19%)
Umbilical cord	3 (6%)
Haplo-identical	4 (9%)
Conditioning regimen, no (%)	
Fludarabine/busulfan	38 (82%)
Cyclophosphamide/FTBI	1 (2%)
Haplo-identical Baltimore	4 (8%)
Others	4 (8%)

Materials & Methods

-From January 2010 to March 2016, we retrospectively analyzed patients aged 60 years or older, receiving RIC allo-SCT for AML at Gustave Roussy cancer center.

-Time of transplant defined the time of origin. Data analysis were censored at the last follow-up.

-Patients were classified according to the risk-adapted model described by *Sorror et al.*⁴ integrating information about patient's and HCT risk factors (Karnofski performance status, geriatric assessment, inflammatory biomarkers, donor type & HCT-CI comorbidity score) and about AML risk factors (cytogenetics & molecular abnormalities, MRD status and WBC count).

-Accordingly, 3 main categories were determined: patients with favorable, intermediate and unfavorable risk.

Figure 1: Overall Survival

Figure 2: Relapse-Free Survival

Figure 3: Cumulative incidence of relapse

Figure 4: Cumulative incidence of non-relapse-mortality

Results

Figure 5: According to the risk-adapted model the NRM rate, relapse rate and survival rate for the a) intermediate and b) unfavorable risk group.

Summary

Our study shows a low transplant-related toxicity with promising long-term outcome in patients aged 60 years or more. The observed RFS and OS especially in the unfavorable risk AML patients compares favorably with the results obtained with chemotherapy alone and suggest this population benefits from allogeneic HCT regardless of the HCT-CI comorbidity score. However, longer follow-up and further randomized trials are still needed.

References

- 1- Yates JW. Comorbidity considerations in geriatric oncology research. *CA Cancer J Clin.* 2001; 51:329–336.
- 2- Thein M, William B, Ershier W, Jemal A, Yates JW, Baer M. Outcome of Older Patients with Acute Myeloid Leukemia: An analysis of SEER Data over Three Decades. *Cancer.* 2013 August 1; 119(15). doi:10.1002/cncr.28129.
- 3- Appelbaum FR, et al. Age and acute myeloid leukemia. *Blood.* 2006; 107:3481–3485.
- 4- Sorror M and Estey E. Allogeneic hematopoietic cell transplantation for acute myeloid leukemia in older adults. *Hematology, ASH Education Book.* December 5, 2014 vol. 2014 no. 1 21-33. doi: 10.1182/asheducation-2014.1.21.
- 5- Juliusson G, et al. Attitude towards remission induction for elderly patients with acute myeloid leukemia influences survival. *Leukemia.* 2006; 20(1):42-47.
- 6- Oran B and Weisdorf DJ. Survival for older patients with acute myeloid leukemia: a population-based study. *Haematologica.* 2012; 97(12).
- 7- Estey E, et al. Prospective feasibility analysis of reduced- intensity conditioning (RIC) regimens for hematopoietic stem cell transplantation (HSCT) in elderly patients with acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome. *Blood.* 2007;109(4):1395-400.
- 8- McClune B, et al. Effect of Age on Outcome of Reduced-Intensity Hematopoietic Cell Transplantation for Older Patients with Acute Myeloid Leukemia in First Complete Remission or with Myelodysplastic Syndrome. *J Clin Oncol.* 2010;28:1878-87.