The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Conditioning Intensity in Patients Aged > 50 Years Undergoing Allogeneic Hematopoietic Cell Transplantation for Myelodysplastic Syndrom: A Study on Behalf of the Chronic Malignances Working Party of the EBMT

Noureddine Henoun Loukili [1], Luuk Gras Sr., MD PhD [2], Linda Koster [3], Didier Blaise, MD PhD [4], Tobias Gedde-Dahl, MD [5], Johan Maertens, MD PhD [6], Regis Peffault De Latour [7,8,9,10,11,12,13,14,15], Henrik Sengeloev [16], Stephan Mielke, MD [17], Patrice Chevallier, MD [18], Jakob R. Passweg, MDMS [19], Jenny Louise Byrne, MD PhD [20], Urpu Salmenniemi, MD PhD [21], Anne Sirvent, MD [22], Denis Guyotat, MD [23], Simona Sica [24], Liesbeth C. de Wreede, PhD [25], Francesco Onida, MD [26], Christoph Scheid [27], Carmelo Gurnari, MD [28,29], Joanna Drozd-Sokolowska, MDPhD [30], Kavita Raj, MDPhD [31], Marie Robin, MD [32], Donal P McLornan, MDPhD [31], Ibrahim Yakoub-Agha, MDPhD [33]

[1] CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000, Lille, France
[2] EBMT Statistical Unit, Leiden, Netherlands
[3] EBMT Leiden Study Unit, Leiden, Netherlands
[4] Institut Paoli Calmettes, Marseille, FRA
[5] Oslo University Hospital, Oslo, NOR
[6] Department of Hematology, University Hospitals Leuven, Leuven, Belgium
[7] French Référence Center for Aplastic Anemia and Paroxysmal Nocturnal Hemoglobinuria, Paris, France
[8] BMT Unit, Assistance Publique Hôpitaux de Paris, Université Paris Cité, Paris, France
[9] Hematology and Transplantation Unit, Hôpital Saint Louis, AP-HP, Paris, France
[10] Saint-Louis Hospital, Paris, France
[11] Hôpital Saint-Louis, Paris, France
[12] Hopital St. Louis, Department of Hematology - BMT, Paris, France
[13] Hôpital Saint-Louis, Hematology Department, AP-HP, Paris, France
[14] Hôpital Saint-Louis, Paris, France
[15] French Reference Center for Aplastic Anemia and Paroxysmal Nocturnal Hemoglobinuria, Paris, France
[16] Rigshospitalet, Copenhagen, Denmark
[17] Department of Cellular Therapy and Allogeneic Stem Cell Transplantation, Karolinska Institute & University Hospital, Stockholm, Sweden
[18] CHU De NANTES, Nantes Cedex 1, France
[19] Department of Hematology University Hospital of Basel, Basel, Switzerland
[20] Nottingham University, Nottingham, GBR
[21] Turku University Hospital, Turku, FIN
[22] CHU Montpellier, Montpellier, France
[23] Institut de Cancerologie Lucien Neuwirth, CHU Saint Etienne, Saint Etienne, FRA
[24] Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Rome, Italy
[25] Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, Netherlands
[26] Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico - University of, Milan, Italy
[27] University of Cologne, Cologne, Germany
[28] Department of Translational Hematology and Oncology Research, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH
[29] Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy
[30] Central Clinical Hospital, The Medical University of Warsaw, Warsaw, Poland
[31] University College London Hospitals NHS Trust, London, United Kingdom
[32] Hopital Saint-Louis, Paris, France
[33] CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000, LILLE, FRA

Introduction

Myelodysplastic syndromes (MDS) affect mainly older individuals, with a median age > 70 years. Reduced intensity conditioning (RIC) is usually used for MDS patients undergoing allo-HCT to balance the toxicity of myeloablative conditioning (MAC), particularly in the more elderly or those with multiple comorbidities. In addition, the clinicians subjective opinion/ experience remains a major guide in choosing the intensity of conditioning. The majority of studies comparing RIC and MAC reported a higher cumulative incidence (CI) of relapse (RP) and lower non-relapse mortality (NRM) in the RIC groups. However, the impact of conditioning intensity on outcome after allo-HCT remains controversial. To gain more insight into the impact of conditioning on outcomes following allo-HCT for MDS, we evaluated RIC *versus* MAC in MDS patients aged > 50 years in a large EBMT cohort.

Patients and methods

This was a registry-based retrospective multicenter study that included MDS patients above 50 years, who received a first allo-HCT following RIC or MAC conditioning between 2014 - 2018 and had data on IPSS-R at allo-HCT and RIC/MAC conditioning available. Data collected included disease features, patient, donor and transplantation characteristics. Patients with *ex vivo* T-cell depletion were excluded. Variables with missing values ≤35% were handled with multiple imputation. OS, DFS, RP and NRM were compared using the Log-rank and Gray's test for CI, and (cause-specific) Cox proportional hazard models for multivariable analyses (MVA). A conditional logistic regression after propensity score matching (PSM) was also performed for potential risk confounders.

Results

Among the 1393 included patients (from 121 centres), 922 (66%) were men and the median age at allo-HCT was 62.8 (IQR:58.2-66.9) years. The majority of patients (n=884; 64.3%) had RAEB. The IPSS-R was recorded as very low/low (n=598, 43%), intermediate (n=352, 25%) and high/very high (n=443, 32%). Cytogenetic risk score was very good/good (n=932, 66.9%), intermediate (n=250, 17.9%) and poor/very poor (n=211, 15.1%). Karnofsky index was ≥ 90 in 916 pts (69.3%) and HCT-CI ≥ 3 in 292 pts (27.3%). Disease status at transplant was recorded as complete remission (n=486, 34.9%), untreated/stable disease (n=544, 39.0%), and progressive disease (n=310, 22.3%). Donor was HLA-matched (related/unrelated) (n=989, 71.1%), unrelated HLA-mismatched (n=286, 20.5%) or familial HLA haplo-identical donor (n=153, 10.9%). Source of SC was BM (n=112, 8.0%) and PB (n=1255, 90.0%). A RIC regimen was used in 1053 (75.5%) patients. *In vivo* T-cell depletion with anti-thymocyte globulin (ATG) was used in 941 pts (67.5%).

Median time of follow up was 27.9 months (IQR: 26.4-30.6). Median rate of OS in RIC *vs* MAC group was 54.2(95% CI: 33.5-NA) *vs* 46.2(95% CI: 32.6-69.4), p=0.84; median rate of DFS was 28.4(95% CI: 19.4-58) *vs* 28.0 (95% CI: 22.5-39.1), respectively, p=0.64. Cumulative incidence rate of RP and NRM for RIC *vs* MAC regimen at 36 months were 31.2% *vs* 29.7% and 29.9% *vs* 30.4%, respectively (Figure 1). Both in univariable and MVA we did not observe a significant (> 0.05) association between the conditioning regimen on the outcomes. Similar results were obtained using PSM to control potential confounders (such as age, source of SC, stage of disease, HCT-CI, cytogentic risk score, neutrophile and platelet counts and sAML) and conditional logistic regression analysis (Table1).

Conclusion

To our knowledge, this is the largest retrospective cohort study that highlights a lack of association between RIC/MAC regimen and outcomes in MDS patients undergoing allo-HCT. Our results are in line with the recent published systematic review and metanalysis where evidence for using a one conditioning regimen over another remains weak [1,2].

1) Rashidi et al. Biology of Blood and Marrow Transplantation. 2020; 26:138-141.
2) Akbar et al. Blood.2020; 136:40-41.

Figure 1: Kaplan-Meier curves of Overall Survival (OS), Disease Free Survival (DFS) and Cumulative incidence of Relapse and NRM depending on RIC *vs* MAC conditioning

a. Kaplan-Meier curves of Overall Survival (OS)

b. Kaplan-Meier curves of Disease Free-Survival (DFS)

c. Cumulative incidence of Relapse events

d. Cumulative incidence of NRM events
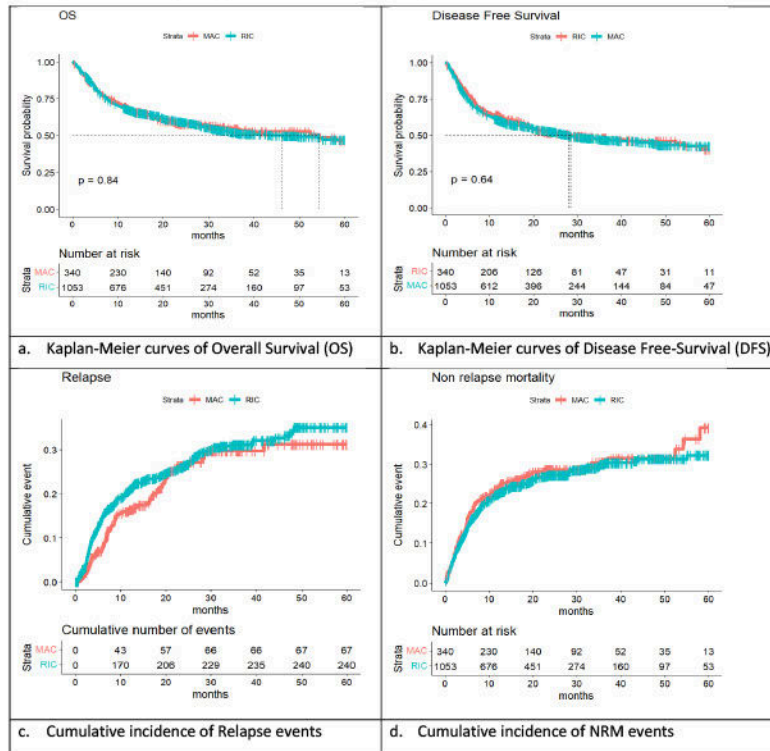
Table 1: Impact of the intensity of conditioning (RIC vs MAC) on patients' outcomes.

	Full cohort : UVA HR [CI95%], p-value	Full cohort : MVA HR [CI95%], p-value	PSM analysis : UVA HR [CI95%], p-value	PSM analysis : MVA HR [CI95%], p-value
OS	1.02 (0.84-1.23), p=0.84	1.15 (0.86-1.55), p = 0.32	1.15 (0.86-1.55), p = 0.32	1.27 (0.85-1.92), p=0.24
DFS	1.04 (0.95-1.24), p= 0.63	1.03 (0.85-1.26), p= 0.75	1.20 (0.89-1.61), p = 0.22	1.21 (0.82-1.80), p=0.34
NRM	0.97 (0.82-1.15), p = 0.80	0.91 (0.76 -1.09), p=0.29	0.83 (0.61-1.12), p = 0.22	0.91 (0.64-129), p=0.59
Relapse	1.19 (0.86-1.56), p=0.20	1.18 (0.88-1.60), p=0.27	1.33 (0.92-1.91), p=0.12	1.11 (0.68-1.80), p=0.68

UVA : univariate analysis, MVA : multivariate analysis, PSM : propensity score matching

Figure 1

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