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DR. MARIO TIRIBELLI (Orcid ID : 0000-0001-9449-2621)

DR. ALESSANDRA SPEROTTO (Orcid ID : 0000-0002-2762-4695)

PROF. DANIELA DAMIANI (Orcid ID : 0000-0002-1663-4468)

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Haploidentical transplant after failure of a first allogeneic transplant: a long and winding road

Mario Tiribelli[†], Alessandra Sperotto[†], Francesca Patriarca, Daniela Damiani, Renato Fanin

Division of Hematology and Bone Marrow Transplantation, Department of Medical Area, University of Udine, Italy.

[†]Dr. M. Tiribelli and Dr. A. Sperotto share first authorship.

Correspondence

Mario Tiribelli, MD

Division of Hematology and Bone Marrow Transplantation

Department of Medical Area

Ospedale S. M. Misericordia

33100 Udine, Italy

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Phone: +39-0432-559604

Fax: +39-0432-559661

e-mail: mario.tiribelli@uniud.it

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To the Editor

In a recent manuscript entitled "Haploidentical transplant for patients with relapse after first allograft", Srour et al. reported on 29 patients that underwent an haploidentical transplantation (haplo-SCT) for relapse after a first allogeneic SCT for different hematological malignancies, mostly AML, with a 3-year overall survival (OS) of 40%. Moreover, they found that lower comorbidity index (HCT-CI) and lack of donor-specific anti-HLA antibodies were correlated with a significantly better outcome (3-year OS 60% in patients with HCT-CI < 3 and no detectable antibodies).1

Prompted by this remarkable outcome, we reviewed our database and identified 19 patients (7 males and 12 females) who received haplo-SCT for relapse after an allogeneic SCT between 2009 and 2019. Median age at haplo-SCT was 44 years (range: 23-72; majority of patients had acute leukemia (AML 13 and ALL 4, respectively), one patient had myelofibrosis (MF) and one Hodgkin lymphoma (HL). Median time from first SCT to relapse was 8 months (range: 3-34); type of first transplant was matched related donor in 6 (31.5%), matched unrelated donor in 11 (58%) and haploidentical in 2 (10.5%). Disease status at haplo-SCT was complete remission in 3 patients (16%) and active disease in 16 (84%), median HCT-CI was 2 (range: 1-5) and 7 patients (37%) had an HCT-CI ≥3. Stem cells source was peripheral blood (PB) in 15 cases (79%) and bone marrow (BM) in 4 (21%), conditioning regimen was myeloablative in 2 (10%) and reduced intensity in 17 (90%). GVHD prophylaxis consisted of post-transplantation cyclophosphamide, mycophenolate mofetil and tacrolimus.

With a median follow-up of 30 months (range: 12-64), 18 patients (95%) died, with a median OS of 8 months (95% confidence interval (CI): 2-8) and a 1-year OS of 16% (95% CI: 4-35) (Figure 1A). Cause of death was disease relapse/progression in 14 cases (78%) and non-relapse mortality in 4 (22%). We did not find any significant difference in survival according to age at transplant (p=0.40), disease status (p=0.27), HCT-CI (p=0.86), stem cell source (p=0.88) or conditioning regimen (p=0.78). The only factor associated with a shorter OS was diagnosis of AML: median survival after haplo-SCT was 6 months in the 13 AML cases compared to 13 months for other malignancies (p=0.003) (Figure 1B). The difference was confirmed also excluding the two cases with MF and HD, as median survival for the 4 ALL patients was 13 months (p=0.02).

Despite being comparable for most of patients and transplant characteristics, our data only partially confirm the brilliant results reported from colleagues at M. D. Anderson: while median OS was similar (8 months), our 1-year survival was only 16% compared to 40%. The only apparent difference between the two cohorts seems to be a wider use of PB-derived stem cells for haplo-SCT in our patients (79%,

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compared to 31%). If stem cell source may have an impact on long-term survival after haplo-SCT is still to be defined: a recent study on over 450 patients receiving an haplo-SCT for lymphoma did not find any difference in OS for PB or BM.[2] With the limits of a very small sample size, we observed a superior outcome of a second haplo-SCT in ALL patients compared to AML ones, despite similar patients and transplant features. If this difference is due to different disease biology or to other factors need further investigations and confirmation in larger studies.

In evaluating the role of a second haplo-SCT, we must keep in mind that the outcome of patients relapsing after an allogeneic SCT is generally poor. A study from the IBMTR on 1788 AML patients relapsing after a median of 7 months from an allogeneic SCT: 1231 patients (69%) received intensive therapy, with a 1-year survival of 23%; survival probability was directly associated with length of time from SCT to relapse.[3] Motabi et al. found, in a cohort of 100 AML or MDS patients relapsing after allogeneic transplant, a median OS of 6 month with intensive chemotherapy and 3.9 months with hypomethylating agents.[4]

Relapse after allogeneic SCT represent a challenge for hematologists; along with novel agents, such as small molecules and monoclonal antibodies, second transplant represent a feasible option and the choice of an haploidentical graft has the advantages of a widely and timely available source.

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Conflict of interests

Nothing to report.

Author Contributions

MT and AS designed the study, collected and analyzed the data, and wrote the manuscript; FP contributed to patient care and collection of data; DD and RF critically revised and edited the manuscript. All authors approved the submission of the manuscript.

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Figure legend

Figure 1. A. Overall survival in the entire population. B. Overall survival for patients with AML and other malignancies.

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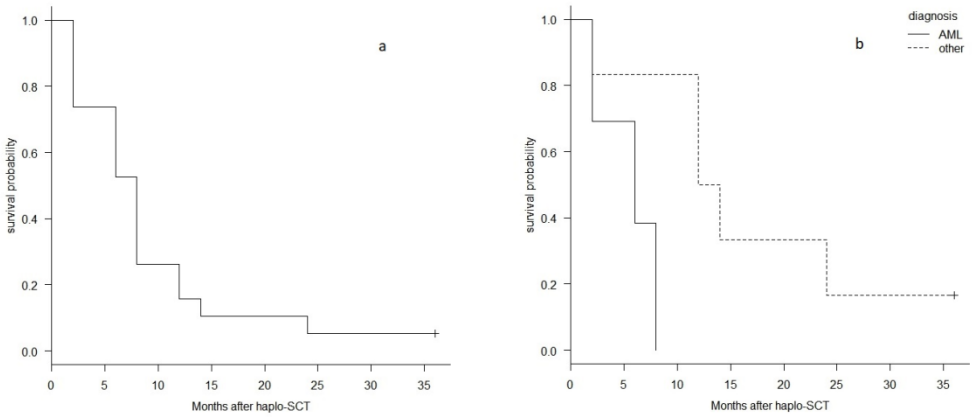

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