



## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 723.ALLOGENEIC TRANSPLANTATION: LONG-TERM FOLLOW-UP AND DISEASE RECURRENCE

**Pre-Emptive Donor Lymphocyte Infusion As Optimal Treatment for Relapsed Acute Myeloid Leukemias and Myelodysplastic Syndromes Following Allogeneic Stem Cell Transplantation: Insights from a French-Italian Study on 134 Patients**

Eugenia Accorsi Buttini<sup>1</sup>, Cristina Doran<sup>2</sup>, Michele Malagola<sup>1</sup>, Mohamad Mohty, MDPH<sup>2</sup>, Vera Radici, MD<sup>1</sup>, Mirko Farina, MD<sup>1</sup>, Marco Galli<sup>1</sup>, Enrico Morello, MD<sup>1</sup>, Nicola Polverelli, MD<sup>3</sup>, Sofia Terlizzi<sup>1</sup>, Simona Bernardi, PhD<sup>4,5</sup>, Domenico Russo, MD PhD<sup>1</sup>, Eolia Brissot<sup>2</sup>

<sup>1</sup>Unit of Blood Diseases and Bone Marrow Transplantation, Cell Therapies and Hematology Research Program, Department of Clinical and Experimental Science, University of Brescia, ASST Spedali Civili di Brescia, Brescia, Italy

<sup>2</sup>Sorbonne Université Service d' Hématologie Clinique et Thérapie Cellulaire, Hospital Saint-Antoine, Centre de Recherche Saint-Antoine (CRSA), Paris, France

<sup>3</sup>Unit of Blood Diseases and Bone Marrow Transplantation, Department of Clinical and Experimental Sciences, University of Brescia, ASST Spedali Civili di Brescia, Brescia, Italy

<sup>4</sup>Department of Clinical and Experimental Sciences, University of Brescia, Bone Marrow Transplant Unit, ASST Spedali Civili, Brescia, Italy, Brescia, Italy

<sup>5</sup>Research Center Ail (CREA), Chair of Hematology Department of Clinical and Experimental Science, University of Brescia, ASST Spedali Civili di Brescia, Brescia, Italy

Disease relapse after allogeneic stem cell transplantation (allo-SCT) is the main challenge in achieving a cure for acute myeloid leukemias (AMLs) and myelodysplastic syndromes (MDSs). The treatment of disease relapse can be offered in case of full hematological recurrence or in the presence of minimal residual disease (MRD) positivity and/or mixed chimerism. The latter approach is defined as pre-emptive therapy. Overall, treatment strategies may include chemotherapy, molecular-target drugs, hypomethylating agents (HMAs), donor lymphocyte infusions (DLIs) or even a second allo-SCT.

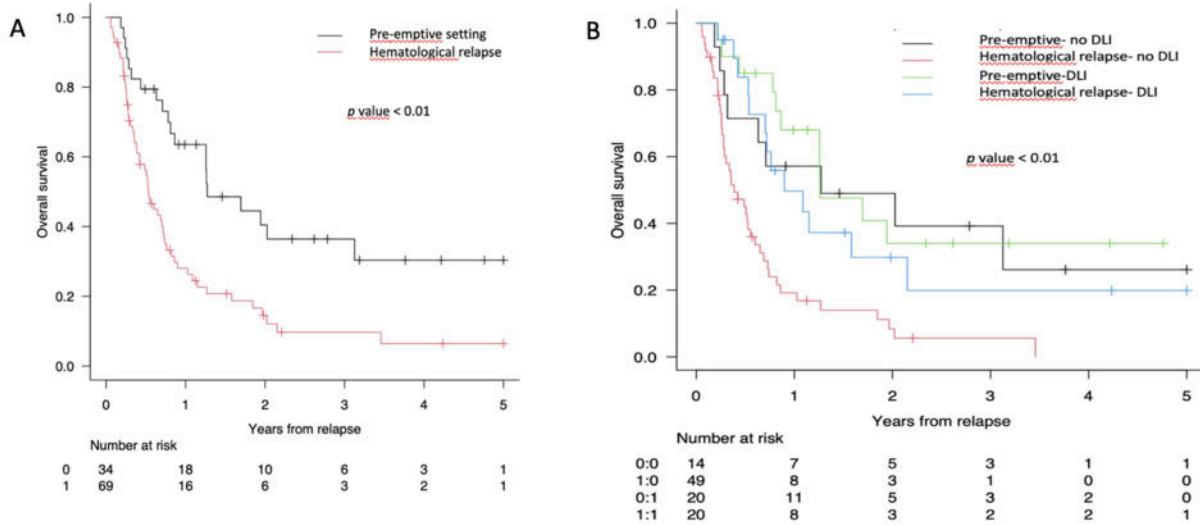
We retrospectively analyzed a cohort of 553 AML and MDS adult patients consecutively allotransplanted between January 1, 2015, and December 31, 2021, at Saint-Antoine University Hospital, Paris (France) (n=420) and Spedali Civili di Brescia, Brescia (Italy) (n=133). 134/553 (24%) patients relapsed and were included in this study. 103/134 (77%) were subsequently treated. Among patients who received treatment, 40/103 (39%) were treated with a DLI-based regimen. In this group, 9 received DLIs alone, while the others also received HMAs (4 cases), HMAs+ venetoclax (12 cases), FLT3-inhibitors (3 cases), intensive chemotherapy (5 cases), a second allo-SCT (5 cases), or other therapies (2 cases). The remaining 63/103 (61%) patients were treated with regimens that did not include DLIs. Of these, 10 received HMAs, 27 HMAs+ venetoclax, 4 FLT3-inhibitors, 6 intensive chemotherapy, 9 a second allo-SCT, and 7 other therapies.

With a median follow up of 1.6 years, the estimated 1-, 2- and 5-year OS rate of the 134 patients who relapsed after allo-SCT was 32%, 18 %, and 11 %, respectively. The OS of patients treated after allo-SCT relapse was 40 %, 20%, and 15% at 1, 2 and 5 years compared with 6 %, 3%, and 0 % for patients who did not receive therapy, respectively (  $p < 0.01$ ). Moreover, the OS was significantly better in patients treated in a pre-emptive setting than in those treated for a morphological relapse (OS at 1, 2 and 5 years was 60%, 36% and 30%, respectively, for patients treated in a pre-emptive setting versus 26%, 12%, and 6%, respectively, for patients treated in hematological relapse (  $p < 0.01$ ) (Figure 1A). Focusing on post-relapse treatment, patients who received DLI-based regimens had a 1-, 2- and 5-year OS of 55%, 32% and 32%, respectively, compared to 27%, 16% and 7% for patients treated with other therapies (  $p < 0.01$ ). Among patients who received DLIs, 50% of patients were treated in the pre-emptive setting. Conversely, in the group of patients treated without DLI, only 22% were treated in the pre-emptive setting, reflecting the more advanced phase of relapse in this group. Finally, when patients were analyzed by the treatment strategy (pre-emptive therapy vs therapy in hematological relapse) and DLI administration (yes vs no), the best outcome was achieved when the relapse was promptly detected and pre-emptive therapy was started, particularly if a DLI was administered. Indeed, the 1-year OS of patients treated in the pre-emptive setting was 67% for those receiving a DLI and 54% for those treated without DLI, while for patients with hematologic relapse, the 1-year OS was 43% for those treated with the DLI-based regimen and 17% for those treated without DLI (  $p < 0.01$ ) (Figure 1B). On multivariate analysis, treatment

with DLI after relapse, and pre-emptive setting were independent factors associated with better OS ( $p=0.03$  and  $p<0.01$ ), respectively.

Our data showed that relapse treatment with pre-emptive therapies is associated with improved outcomes and this effect is more evident when combined with a DLI. These results confirm the primary role of the graft- versus leukemia effect in the treatment of relapse and underscore the importance of its early identification through MRD monitoring.

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**Figure 1. A.** Overall survival of 34/103 (33%) patients treated after allo-SCT relapse in a pre-emptive setting *versus* overall survival of 69/103 (67%) patients treated in hematological relapse. **B.** Overall survival of the 103 patients treated after allo-SCT relapse according to the type of treatment (DLI based regimen *vs* therapy not including DLI) and the setting of treatment administration (pre-emptive therapy *vs* treatment in hematological relapse).

**Figure 1**

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