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POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Interest of Cytoreductive Therapy before Allogenic Hematopoietic Stem Cell Transplantation in Childhood Myelodysplastic Syndromes: A Retrospective Study on Behalf of the Société Francophone De Greffe De Moelle Et De Thérapie Cellulaire (SFGM-TC)

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Background:
Pediatric myelodysplastic syndromes (cMDS) are rare and biologically different from that seen in adults. In addition to a specific genomic landscape, they are characterized by the high frequency of hypoplastic forms, and the recurrent association with germline predispositions (Khoury et al. 2022; Locatelli et Strahm 2018). For most patients, allogenic hematopoietic stem cell transplantation (allo-HSCT) remains the only curative option. In case of cMDS with increased blasts (cMDS-IB), pre-tranplant cytoreductive chemotherapy may be considered, but remains controversial (Strahm et al. 2011).

Methods
This multicenter retrospective study included all cMDS patients (<18y.o.) reported to the SFGM-TC registry who underwent an allo-HSCT between 2000 and 2020. Data have been obtained through ProMISe (internet-based system shared by all EBMT transplantation centers). All patients have given signed informed consent.

Results
Eighty-four cMDS patients from 17 centers were included. Median age at transplant was 10.2 years (IQR: 7.2, 14.2). Fifty-two percent of patients presented with increased blasts at diagnosis. Germline predispositions were known in 24% of patients. GATA 2 mutations were the most frequent (14%). Eighty-two percent of patients presented with hematologic cytogenetic abnormalities, including 64% of monosomy 7. Myeloablative conditioning was used in most of cases (91%). Busulfan/melphalan was the most frequent conditioning regimen (58%). HSCT were performed from sibling donors in 29% of the cases, matched

unrelated donors (MUD) in 44%, umbilical cord blood (UCB) in 21% and haploidentical in 6%. Stem cell source was bone marrow in 68% of the cases.

Considering the whole cohort, 5y overall survival (OS) and disease-free survival (DFS) were 67% (IC95% 57-78%) and 63% (IC95% 54-74%) respectively (Figure 1). Five years cumulative incidences of non-relapse mortality (NRM) and relapse were 26% (IC95% 17-35%) and 12% (IC95% 5.6-20%) respectively. Of the 21 cases of reported toxic death, 15 were related to acute GVH (aGVHD). Six months cumulative incidences of grade II-IV and III-IV acute graft vs host disease were 46 % and 24 % respectively. In univariate analysis, patients under 12 years (p=0,018) or who received a BuCyMel conditioning (p=0,004) or a graft from a MUD (p=0,030) had worst 5y OS and PFS. As expected, OS increased with time (p=0,014) reflecting improvements in supportive care and HSCT procedures (Figure 2A). These results were confirmed in multivariate analysis, except for MUD.

Twenty-four patients received pre-transplant cytoreductive therapy, most often intensive chemotherapy (20/24). In the overall population, pre-transplant cytoreduction was not associated with an improved survival. However, subgroup analysis of the 40 patients with cMDS-IB showed a significant improvement of the OS probability (HR 0.18 [0.04-0.83], p=0.014) in patients who received a pre-transplant cytoreductive therapy in univariate analysis (Figure 2B). Cytoreductive therapy did not appear to be associated with a reduced risk of relapse, but with a lower risk of NRM. Although not statistically significant, the incidence of aGVHD was higher in patients who did not receive any cytoreductive therapy (HR 0.60 [0.09-3.85]).

Conclusion:

This retrospective study reports the outcomes of 84 patients who underwent allo-HCT for childhoodMDS. This study seems to show a benefit associated with the pre-transplant cytoreduction therapy in the subgroup of patients with cMDS-IB, notably through a reduction of aGVHD and NRM occurrence. BuCyMel conditioning, currently recommended for cMDS-IB, appears here, to be associated with excess of toxic mortality. This study also confirms the high aGVH-related toxic mortality rates already reported in cMDS (Strahm et al. 2011). Recent retrospective data have shown a benefit of post-transplantation cyclophosphamide (PTCy) in GATA2 patients transplanted with sibling or matched unrelated donors (Nichols-Vinueza et al. 2022). Prospective data on the use of PTCy in cMDS are therefore needed.

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Figure 1

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