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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Post Allogeneic Stem Cell Transplant Outcomes Following Response to Hypomethylating Agent Therapy in Myelodysplastic Syndromes Are Predicted By Persistent International Prognostic Scoring System-Molecular Risk

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Introduction: The International Prognostic Scoring System-Molecular (IPSS-M) (*Bernard NEJM Evidence 2022*) and the 2023 International Working Group (IWG) response criteria for myelodysplastic syndrome (MDS) (*Zeidan Blood 2023*) are used to more accurately assess prognosis and therapeutic response in MDS. However, it is unknown if these tools can be used to predict outcomes post-allogeneic hematopoietic stem cell transplant (HCT). We sought to understand the impact of pre-HCT IPSS-M on post-HCT outcomes in patients (pts) with MDS who responded to hypomethylating agent (HMA) therapy.
Methods: Pts with MDS treated with HMA (azacitidine or decitabine) who received an HCT post-HMA at Dana-Farber Cancer Institute from January 2014 to December 2020 were included. Response to HMA was assessed by 2023 IWG response criteria and was defined as complete remission (CR) + CR with bi-lineage blood count recovery (CRbi) + CR with uni-lineage blood count recovery (Cruni) + CR with partial hematological recovery (CRh). Combined clinical and molecular risk was assessed by IPSS-M at times of diagnosis and of HCT, the latter using the bone marrow biopsy and sequencing data collected closest to HCT. High risk was defined as IPSS-M moderately high, high, and very high, whereas low risk was defined as IPSS-M very low, low, and moderately low.
Results: A total of 148 pts with MDS who received HMA and underwent subsequent HCT were included. Median age was 64 years (range 26-79) and 61.5% were men. Pts were diagnosed with MDS-EB1 (26.4%), MDS-EB2 (45.3%), and other MDS subtypes (28.3%). IPSS-M at time of diagnosis was very low (2%), low (10.1%), moderate low (6.1%), moderate high (8.8%), high (31.8%), and very high (22.3%). IPSS-M pre-HCT was very low (12.8%), low (8.8%), moderate low (10.8%), moderate high (12.8%), high (20.3%), and very high (10.8%). IPSS-M at diagnosis and pre-HCT could not be calculated because of missing molecular data in 18.9% and 23.6% of pts, respectively. Pts received a median of 4 HMA cycles (range 1-20) and were treated with azacitidine for 7 days (54.1%), decitabine for 5 days (39.2%), and other schedules (6.7%). Prior to HCT, IWG 2023 responses were: CR (15.5%), CRbi (14.9%), CRuni (19.6%), CRh (0.7%), partial remission (PR: 1.4%), hematological improvement (HI: 9.5%), and no response (38.5%). Most pts received HCT from either a matched unrelated (60.8%) or matched related

donor (18.2%) with reduced intensity conditioning (74.3%). Pts received graft versus host disease prophylaxis with tacrolimus (tac)/methotrexate (MTX) (54.7%), tac/MTX/sirolimus (19.6%), post-transplant cyclophosphamide/mycophenolate mofetil/tac (15.5%), tac/sirolimus (8.1%), other (2%). Median HCT-comorbidity index (CI) was 2 (range 0-13) and 48.6% pts had HCT-CI $\geq$ 3. For the entire cohort, the median follow-up time among ongoing survivors was 48.3 months (range 5.5-101.3). Among pts who responded to HMA per IWG 2023 criteria (CR/CRbi/CRuni/CRh), those who had high risk by IPSS-M prior to HCT had significantly shorter median overall survival (OS) (27 months; 95% CI 7.5-51) compared to pts with a low risk by IPSS-M (not reached; p=0.016) (**Figure A**). Cumulative incidence of relapse (CIR) at 4 years was 66% for pts with high risk and 31% for low risk (p=0.034) (**Figure B**). Pts with response to HMA with high risk by IPSS-M had lower OS (4-year OS: 27% versus 53%; p=0.016) and progression-free survival (4-year PFS: 19% versus 50%; p=0.018) but similar non-relapse mortality (NRM) (4-year NRM: 16% vs. 19%; p=0.66) post-HCT compared to pts with low risk at time of HCT.

Conclusion: For pts with MDS who achieve a response to HMA prior to HCT, combined clinical/molecular risk, as assessed by IPSS-M, has an important prognostic impact on post-HCT outcomes. Pre-HCT risk should be evaluated for prognostication and to guide patient care, including future prospective studies evaluating novel agents for post-HCT therapy.

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Figure: Outcomes post-HCT for patients who achieved a CR/CRbi/CRuni/CRh to HMA therapy per IWG 2023 response criteria and were found to have low vs. high clinical/molecular risk based on IPSS-M prior to HCT: (A) Overall survival (OS) and (B) Cumulative incidence of relapse
Low risk: IPSS-M very low, low, and moderate low; High risk: IPSS-M moderate high, high, and very high. CR, complete remission; CRbi, CR with bi-lineage blood count recovery; CRuni, CR with uni-lineage blood count recovery; CRh, CR with partial hematological recovery; HCT, hematopoietic stem cell transplant; HMA, hypomethylating agent; IPSS-M, International Prognostic Scoring System-Molecular.

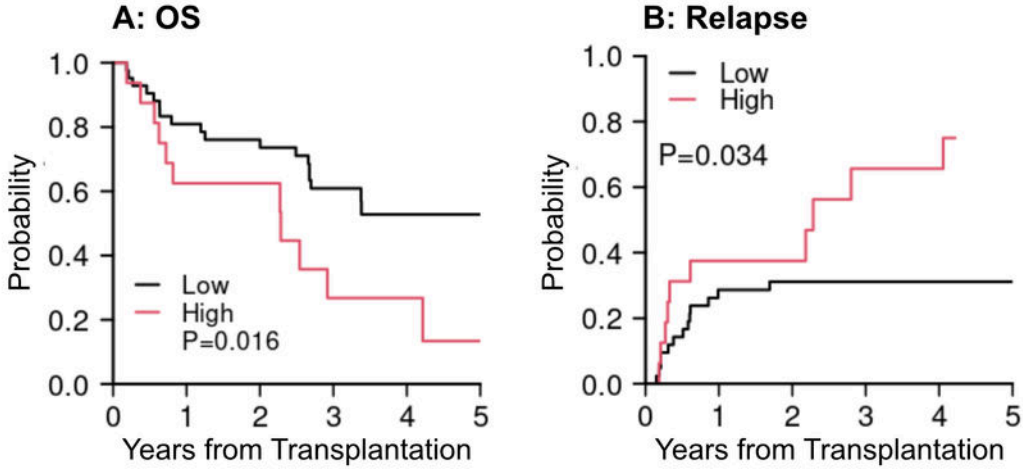

Figure 1

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