Abstract: PB2429

Title: DOES MRD ASSESSMENT ALLOW FOR EARLY PREDICTION OF EXTRAMEDULLARY RELAPSE IN PATIENTS WITH MYELOID NEOPLASM AFTER ALLOGENEIC STEM CELL TRANSPLANTATION?

Abstract Type: Publication Only

Topic: Acute myeloid leukemia - Clinical

Background:

Extramedullary (EM) relapse of myeloid neoplasms is defined by the presence of leukemic cells at other sites than the bone marrow (BM). While in general rare, EM relapse after allogeneic hematopoietic stem cell transplantation (HSCT) affects up to 10-20% of acute myeloid leukemia (AML) patients (pts) with very poor outcomes. Measurable residual disease (MRD) detection allows the prediction of BM relapse and potentially initiation of pre-emptive treatment, but its' feasibility to predict EM relapse has not been evaluated.

Aims:

To evaluate the feasibility of MRD analyses to predict extramedullary relapse and detect systemic disease after allogeneic HSCT.

Methods:

We analyzed 10 patients (9 AML, 1 myeloproliferative neoplasm) who underwent myeloablative (n=4) or reduced intensity (n=6) allogeneic HSCT (median age 56.9, range 21.5-70.7, years [y]) and suffered a histologically proven EM relapse after HSCT. 50% of pts already had EM manifestations at diagnosis, and 50% had new EM involvement at relapse post HSCT. European LeukemiaNet 2022 risk at diagnosis was favorable (50%), intermediate (10%) or adverse (40%). At HSCT, 50% of pts had active disease and 50% were in complete remission (CR, 40% MRDpos, 10% MRDNA). 18Fluori-deoxy-Glucose Positron Emission Tomography/Computed Tomography (PET/CT) scans confirmed EM relapse (n=9). Post-HSCT molecular MRD was analyzed using pts-individual digital droplet PCR assays for assessable mutation (mut) or gene fusions known at diagnosis (n=9). MRD thresholds were 0.01% for *NPM1/ABL* (n=4) and *CBFB::MYH11/ABL1* (n=1) and 0.05% VAF for all other mut (*CEBPA, IDH2*, *JAK2, KIT, U2AF1*, each n=1).

Results:

The EM relapse occurred at a median of 0.76 (range 0.2-4.4) y as 1st (80%) or 2nd (20%) relapse after HSCT. PET/CT showed single (22%) or multiple (78%) EM lesions. In concurrent BM assessment, 40% had morphologic relapse (all positive for the MRD marker), 60% were in BM CR (30% MRDpos, 20% MRDneg, 10% MRDNA). There was no association between the PET/CT detection of single *vs* multiple EM lesions at relapse and the concomitant BM morphologic/MRD status (*P*=.67). EM relapse was preceded by an MRDpos test result in 67% of all pts at a median of 143 (range 23-214) d, and one pt was MRDneg in the last sample 59 days prior to simultaneous EM and BM relapse. Two pts remained MRDneg prior to, and at time of EM relapse. In pts with EM relapse alone, EM relapse was preceded by an MRDpos test result in 60% of pts. In all pts for whom DNA could be assessed, the EM relapse site was positive for the tracked MRD mut (n=8, including both pts with MRDneg BM at relapse, Fig. 1A). 20% received best supportive care only, while 80% of pts received systemic therapies (quizartinib [n=1], azacitidine alone [n=1] or + venetoclax [n=5], or intensive chemotherapy [n=1]). Still, 70% of pts died from progression (after a median of 0.3 y). Only pts receiving donor lymphocyte infusion (10%) or a second HSCT (30%) had overall survival (OS) longer than one year after EM relapse (Fig. 1B), of whom only the 2 pts who were BM MRDneg at EM relapse are alive in metabolic and molecular CR at last follow up (Fig. 1C).

Summary/Conclusion:

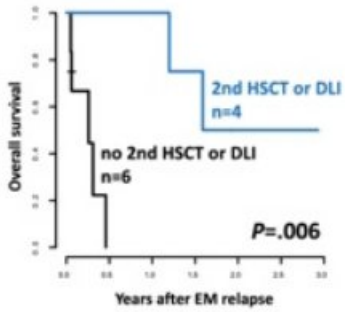
Molecular MRD evaluation allowed the prediction of EM relapse in 67% of all, and 60% of pts without concurrent morphologic BM relapse at a median of 143 and 149 days early, potentially enabling preemptive treatments in these pts. PET/CT seems to complement molecular MRD in assessing disease burden at relapse. Our data suggest better outcomes in pts without molecular evidence of BM involvement at EM relapse, which should be evaluated in larger trials.

A Extract of the molecular profile in bone marrow at diagnosis and extramedullary site at relapse

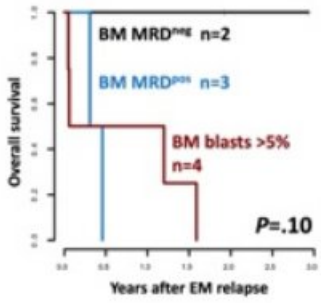
	NPM1		*TET2*		*FLT3-TKD*		*ASLX1*		*CEBPA*		*DNMT3A*		*EZH2*		*FLT3-ITD*		*IDH2*		*JAK2*		*KIT*		*NRAS*		*PTPN11*		*RUNX1*		*SRSF2*		*U2AF1*	
UPN	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM	Dx	EM
776	X	X	X	X	X	O	O	O	O	X	X	X	O	O	O	O	O	O	O	O	O	O	X	X	O	O	O	O	O	O	O	O
1084	X	X	X	X	O	NA	X	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	X	X	O	NA
643	X	X	O	O	X	O	O	O	O	O	X	X	O	O	X	X	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
1111	O	X	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
911	O	NA	X	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	O	NA	X	X	O	NA	O	NA	O	NA	O	NA	X	X
1031	O	O	O	O	X	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	X	O	O	O	O	O	O
1166	O	O	O	O	O	O	X	X	O	O	O	O	X	X	O	O	O	O	X	X	O	O	O	O	O	O	X	X	O	O	O	O
785	O	O	O	O	O	O	O	O	X	X	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
904	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	X	X	O	O	O	O	O	O	O	X	O	O	X	X	O	O
1010	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O

Dx *– bone marrow at diagnosis*
EM *– extramedullary site at relapse*
X *– mutated*
O *– wild type*
GREEN – concomitant mutation between diagnosis and relapse
RED – non-concomitant mutation between diagnosis and relapse

B According to 2nd HSCT/DLI



C According to BM at EM relapse



Keywords: Allogeneic hematopoietic stem cell transplant, MRD, Relapse, Myeloid malignancies