Outcomes of Hypomethylating Agent (HMA)-Based Therapy in Patients with Myelodysplastic Syndrome with Fibrosis

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Introduction

- The 2022 WHO classification update redefined Myelodysplastic Syndrome with fibrosis (MDS-f) as a distinct morphological category
- MDS-F is characterized by either 5-19% bone marrow blasts or 2-19% peripheral blood blasts, along with MF grade 2-3 reticulin fibrosis.
- Historically, poor outcomes have been seen in cases of MDS associated with fibrosis

Objective

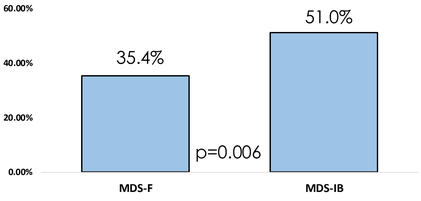
To evaluate the efficacy of HMA-based therapy in patients within the redefined WHO 2022 subgroup MDS-F.

Baseline Characteristics

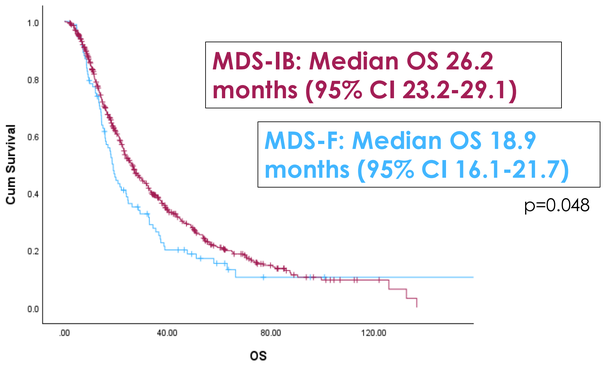
	Complete Cohort (n=821)	MDS-F (n=92)	MDS-IB (n=538)
Median Age at Diagnosis (yrs)	72	72.6	72.3
Gender			
Male	527 (64.2%)	63 (68.5%)	346 (64.4%)
Female	294 (35.8%)	29 (31.5%)	192 (35.%)
Race			
White	732 (89.2%)	78 (84.8%)	486 (90.3%)
Black	28 (3.4%)	4 (4.3%)	19 (3.5%)
Hispanic	28 (3.4%)	6 (6.5%)	16 (3%)
Others	26 (3.2%)	4 (4.3%)	13 (2.4%)
Not reported	7 (.09%)	0	4 (0.7%)
t-MDS	205 (25%)	24 (26.1%)	110 (20.4%)
WHO 2022 classification			
MDS-mTP53	191 (23.3%)		
IB-I	263 (32%)		538 (100%)
IB-II	275 (33.5%)		
MDS-F	92 (11.2%)	92 (100%)	
Cellularity			
Hypocellular	76 (9.3%)	11 (12%)	57 (10.6%)
Normocellular	145 (17.7%)	9 (9.8%)	114 (21.2%)
Hypercellular	572 (69.7%)	71 (77.2%)	345 (64.1%)
N/A	28 (3.4%)	1 (1.1%)	22 (4.1%)
BM Reticulin Fibrosis			
0-1	697 (84.9%)	0	353 (65.6%)
2-3	124 ((15.1%)	G2 67 (72.8%)	
		G3 25 (27.2%)	
R-IPSS Risk Category			
Good	27 (3.3%)	2 (2.2%)	24 (4.5%)
Intermediate	176 (21.4%)	13 (14.1%)	161 (29.9%)
High	218 (26.6%)	32 (34.8%)	175 (32.5%)
Very High	391 (47.6%)	40 (43.5%)	175 (32.5%)
N/A	9 (1.1%)	5 (5.4%)	3 (0.6%)
IPSS- M Mean Risk Category			
Very Low	1(0.1%)	1 (1.1%)	0
Low	29 (3.5%)	1 (1.1%)	28 (5.2%)
Moderate Low	48 (5.8%)	2 (2.2%)	45 (8.4%)
Moderate High	90 (11%)	10 (10.9%)	77 (14.3%)
High	225 (27.4%)	34 (37%)	181 (33.6%)
Very High	396 (48.2%)	37 (40.2%)	191 (35.5%)
N/A	32 (3.9%)	7 (7.6%)	16 (3%)
Baseline Lab Values Mean (Median)			
WBC (x 10^3/uL)	3.5 (2.6)	4.56 (2.91)	3.2 (2.5)
ANC (x 10^3/uL)	1.46 (1.06)	1.88 (1.2)	1.4 (0.99)
Platelets (x 10^3/uL)	102 (79)	109 (63)	107 (84)
PB blasts %	3.6% (2%)	4.2% (3%)	3.3% (2%)
BM Blasts %	10% (9%)	9% (8%)	10% (10%)
HgB (g/dL)	9.3 (9)	8.6 (8.4)	9.6 (9.5)

Results

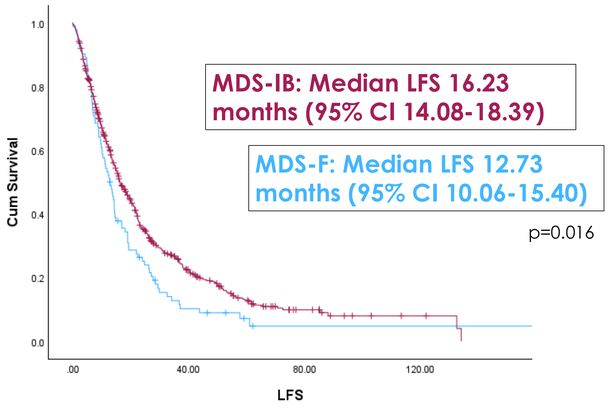
Overall Response Rate (IWG 2023)



Overall Survival



Leukemia-free survival



Overall Survival including biallelic TP53 inactivation

	Total patients	Median OS (months)	P-value
MDS-IB	538	26.2	0.048
MDS-F	92	18.9	
MDS-TP53-fibrosis	32	**10.9**	0.09
MDS-TP53-no fibrosis	159	**13**	

Discussion

- MDS-F patients have inferior response rates and survival after HMA therapy compared to MDS-IB.
- Biallelic *TP53* confers very poor prognosis irrespective of associated fibrosis
- Results support MDS-F as a distinctly poor prognostic subgroup of MDS.
- Toxicity assessment and computational genomic analyses are expected to generate further understanding of mechanisms behind poor prognosis in MDS-F.
- These results underscore the need to further develop and optimize treatment strategies in this poor prognostic MDS subgroup.

References

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