Prognostic impact of *SF3B1* mutation and multilineage dysplasia in myelodysplastic syndromes with ring sideroblasts: a Mayo Clinic study of 170 informative cases

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Supplemental table 1: Phenotypic and genotypic characteristics of 170 patients with myelodysplastic syndromes with ring sideroblasts (MDS-RS), stratified by presence or absence of multilineage dysplasia

Variables	**All patients n=170**	**MDS-RS-MLD n=87 (51%)**	**MDS-RS-SLD n=83 (49%)**	**P value**
Age in years; median (range)	73 (41-94)	74 (47-94)	72 (41-89)	0.81
Males; n (%)	114 (67)	62 (71)	52 (63)	0.23
Hemoglobin (g/dl) median (range)*	9.6 (6.4-13.7)	9.3 (6.4-13.7)	9.9 (6.5-12.2)	0.19
Transfusion dependence; n (%)	38 (22)	23 (26)	15 (18)	0.19
Leukocytes x10^9/l; median (range)	N=169 5.1 (0.7-13.1)	N=87 4.4 (0.7-13.1)	N=82 5.6 (1.4-12.7)	**<0.01**
ANC x10^9/l; median (range)	N=167 2.8 (0.2-9.4)	N=87 2.6 (0.2-9.4)	N=80 3 (0.2-8.4)	0.06
ANC <1 × 10^9/l; n (%)	11 (7)	9 (10)	2 (2)	**0.02**
ALC x10^9/l; median (range)	N=166 1.3 (0.04-3.6)	N=86 1.2 (0.2-3.1)	N=80 1.6 (0.04-3.6)	**0.001**
ALC <1.2 × 10^9/l; n (%)	65 (39)	40 (47)	25 (31)	**0.04**
AMC x10^9/l; median (range)	N=165 0.4 (0.02-1.6)	N=85 0.4 (0.02-1.6)	N=80 0.5 (0.06-1.1)	0.15
Platelets x10^9/l; median (range)	N=169 229 (20-599)	N=87 202 (20-599)	N=82 275 (46-585)	**<0.01**

Platelets <100 × 10^9/l; n (%)	19 (11)	16 (18)	3 (4)	**<0.01**
Bone marrow blast %; median (range)	1 (0-4)	1 (0-4)	1 (0-4)	0.14
Peripheral blood blast %; median (range)	0 (0-1)	0 (0-1)	0 (0-0)	0.37
Karyotype (*n evaluable = 166)*				**<0.01**
Normal; n (%)	121 (73)	53 (63)	68 (83)	
Sole loss of "Y"; n (%)	9 (5)	5 (6)	4 (5)	
Sole trisomy 8; n (%)	8 (5)	3 (2)	5 (3)	
Sole 20q-; n (%)	7 (4)	4 (5)	3 (4)	
Complex; n (%)	5 (3)	5 (6)	0	
-7/7q-; n (%)	3 (2)	3 (4)	0	
Other; n (%)	13 (8)	11 (13)	2 (2)	
Mutations *(n evaluable = 145)***				
SF3B1; n (%)	126 (87)	59 (82)	67 (92)	0.08
TET2; n (%)	37 (25)	15 (21)	22 (30)	0.2
DNMT3A; n (%)	28 (19)	13 (18)	15 (21)	0.7
ASXL1; n (%)	16 (11)	7 (10)	9 (12)	0.61
SRSF2; n (%)	7 (5)	2 (3)	5 (7)	0.25
TP53; n (%)	7 (5)	3 (4)	4 (5)	0.73
IDH1; n (%)	3 (2)	3 (4)	0 (0)	0.08
CSF3R; n (%)	3 (2)	0 (0)	3 (4)	0.08
Erythropoietin IU/l; median (range)	N=122 69 (7-5461)	N=59 73 (13-5461)	N=63 61 (7-1648)	0.36
LDH U/l; median (range)	N=83 194 (112-538)	N=46 185 (112-413)	N=37 198 (112-538)	0.47
Bone marrow ring sideroblasts %; median (range)	40 (5-80)	35 (10-80)	45 (5-80)	0.11

Median follow-up for patients alive. **median years (range)**	5.2 (0.13-12.6)	5.4 (0.12-9)	5.0 (1.0-12.6)	0.93
Deaths; n (%)	104 (61)	63 (72)	41 (49)	**<0.01**
Leukemic transformation; n (%)	8 (5)	6 (7)	2 (2)	0.16
Allogeneic stem cell transplant; n (%)	7 (4)	5 (6)	2 (2)	0.27

*Hemoglobin for patients with transfusion independent anemia at time of diagnosis.

**mutations present in at least 3 patients.

Abbreviations: ALC, absolute lymphocyte count; ANC, absolute neutrophil count; AMC, absolute monocyte count; IPSS-R, Revised International Prognostic Scoring System; MDS-RS, MDS with ring sideroblasts; MDS-RS-MLD, MDS with ring sideroblasts and multilineage dysplasia; MDS-RS-SLD, MDS with ring sideroblasts and single lineage dysplasia

Supplemental table 2: Phenotypic and genotypic characteristics of 145 patients with myelodysplastic syndromes with ring sideroblasts (MDS-RS), stratified by presence or absence of *SF3B1* mutation

Variables	**All patients N=145**	***SF3B1* mutated n=126**	***SF3B1* wild-type n=19**	**P value**
Age in years; median (range)	72 (41-94)	72 (41-94)	72 (55-83)	0.6
Males; n (%)	98 (68)	82 (65)	16 (84)	0.08
Hemoglobin (mg/dl) median (range)*	9.6 (6.5-13.7)	9.5 (6.5-13.5)	10.2 (6.6-13.7)	0.2
Transfusion dependence; n (%)	36 (25)	33 (26)	3 (16)	0.31
Leukocytes x10^9/l; median (range)	5.2 (0.7-13.1)	5.5 (1.5-13.1)	3.7 (0.7-9.4)	**<0.01**
ANC x10^9/l; median (range)	3 (0.2-9.8)	3 (0.4-9.8)	1.9 (0.2-5.6)	**<0.01**
ANC <1 × 10^9/l; n (%)	9 (6)	5 (4)	4 (21)	**0.02**
ALC x10^9/l; median (range)	1.4 (0.04-3.6)	1.4 (0.2-3.6)	1 (0.04-3.1)	**0.03**
ALC <1.2 × 10^9/l; n (%) ***(n evaluable = 143)***	54 (38)	41 (33)	13 (68)	**<0.01**
AMC x10^9/l; median (range)	0.5 (0.04-1.6)	0.5 (0.06-1.6)	0.2 (0.04-0.9)	**0.02**
Platelets x10^9/l; median (range)	226 (20-599)	247 (25-599)	85 (20-406)	**<0.01**
Platelets <100 × 10^9/l; n (%)	15 (10)	4 (3)	11 (58)	**<0.01**
Karyotype (*n evaluable = 143)*				

Normal; n (%)	109 (76)	98 (79)	11 (58)	0.08
Sole loss of "Y"; n (%)	7 (5)	5 (4)	2 (11)	
Sole trisomy 8; n (%)	5 (4)	5 (4)	0	
Sole 20q-; n (%)	7 (5)	5 (4)	2 (11)	
Complex; n (%)	5 (4)	2 (2)	3 (16)	
-7/7q-; n (%)	2 (1)	2 (2)	0	
Other; n (%)	8 (6)	7 (6)	1 (5)	
Mutations**				
DNMT3A; n (%)	28 (19)	27 (21)	1 (5)	0.06
TET2; n (%)	36 (25)	28 (22)	8 (42)	0.08
ASXL1; n (%)	16 (11)	15 (12)	1 (5)	0.34
SRSF2; n (%)	7 (5)	2 (2)	5 (26)	**<0.01**
TP53; n (%)	7 (5)	4 (3)	3 (16)	**0.04**
RUNX1; n (%)	5 (3)	3 (2)	2 (10)	**<0.01**
IDH1; n (%)	3 (2)	0	3 (16)	**<0.01**
IDH2; n (%)	3 (2)	3 (2)	0	0.35
CSF3R; n (%)	3 (2)	3 (2)	0	0.35
CBL; n (%)	3 (2)	3 (2)	0	0.35
ZRSR2; n (%)	3 (2)	2 (2)	1 (5)	0.95
U2AF1; n (%)	2 (1)	0	2 (10)	**0.01**
EZH2; n (%)	2 (1)	2 (2)	0	0.45
Erythropoietin IU/l; median (range) ***(n evaluable = 106)***	68 (10-5461)	67 (10-5461)	81 (20-380)	0.54
LDH U/l; median (range) (*n evaluable = 65)*	198 (112-538)	181 (112-441)	225 (128-538)	0.1
Bone marrow ring sideroblasts %; median (range)	35 (5-80)	40 (5-80)	30 (15-70)	0.09
MDS-RS subclassification.				0.08
MDS-RS-MLD; n (%)	72 (50)	59 (47)	13 (68)	
MDS-RS-SLD; n (%)	73 (50)	67 (53)	6 (32)	

Median follow-up for living patients; median years (range)	5.1 (0.12-12.6)	5.2 (0.12-12.6)	4.6 (1.9-8.3)	0.09
Deaths; n (%)	88 (61)	79 (63)	9 (47)	0.2
Leukemic transformation; n (%)	6 (4)	4 (3)	2 (10)	0.2
Allogeneic hematopoietic stem cell transplant; n (%)	5 (4)	4 (3)	1 (5)	0.7

*Hemoglobin for patients with transfusion independent anemia at time of diagnosis.

**mutations present in at least 2 patients.

Abbreviations: ALC, absolute lymphocyte count; ANC, absolute neutrophil count; AMC, absolute monocyte count; IPSS-R, Revised International Prognostic Scoring System; MDS-RS-MLD, Myelodysplastic syndromes with ring sideroblasts and multilineage dysplasia; MDS-RS-SLD, Myelodysplastic syndromes with ring sideroblasts and single lineage dysplasia