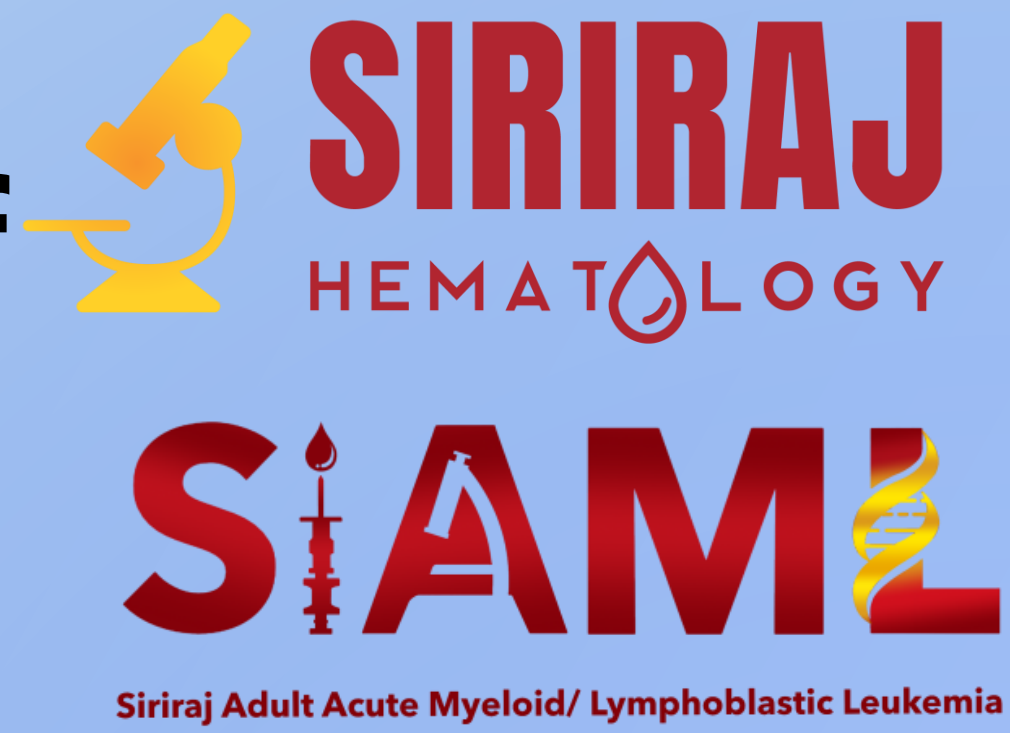




Comparison genetic profiling between myelodysplastic syndrome (MDS) and pre-MDS patients and the study of genetic mutation predicting of response to low-dose erythropoietin therapy in pre-MDS patients



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BACKGROUND

Myelodysplastic syndromes (MDS) are clonal hematopoietic disorders characterized by ineffective hematopoiesis and risk of progression to acute myeloid leukemia. Pre-MDS conditions show dysplastic features in >10% of blood cells, but the genetic relationship between pre-MDS and MDS remains unclear.

OBJECTIVE

Primary objective:
To compare the genetic profiling of MDS and pre-MDS

Secondary objective:
To study the genetic mutation predicting the response to low-dose erythropoietin therapy in MDS and pre-MDS patients

METHODS

In this retro-prospective cohort study, patients diagnosed with MDS and pre-MDS underwent bone marrow studies, cytogenetics, and next-generation sequencing (NGS). Data on hemoglobin levels and ESA response were collected to evaluate relationships between genetic profiles and clinical outcomes.

RESULTS

Among 350 patients (178 females, 172 males), 171 had MDS and 179 had pre-MDS. The mean age was comparable between groups (MDS: 69.87 ± 14.55 years; pre-MDS: 70.47 ± 12.28 years, p=0.672). Laboratory findings showed significant differences between MDS and pre-MDS groups in WBC (3700 vs. 4600 cells/mm³, p=0.003), ANC (1965 vs. 2490 cells/mm³, p=0.005), and platelet counts (103 vs. 160 x10³/mm³, p<0.001). EPO treatment patterns differed significantly (50.9% in MDS vs 35.2% in pre-MDS, p=0.003), with higher initial doses in the MDS group (10000 vs. 5000 units/week, p=0.004). Hemoglobin levels were consistently lower in MDS patients at baseline (9.00 vs. 9.90 g/dL), 3 months (9.11 vs. 10.42 g/dL), and 6 months (9.69 vs. 10.88 g/dL), all p<0.001. Nine genes were identified as more likely presence in MDS compared to pre-MDS: *ASXL1* (p=0.01), *DDX41* (p=0.039), *IDH2* (p=0.033), *RUNX1* (p<0.001), *SF3B1* (p<0.01), *SRSF2* (p=0.005), *TET2* (p=0.008), *TP53* (p=0.003), and *U2AF1* (p=0.001). ESA response patterns revealed *RUNX1* (p=0.012), *SF3B1* (p=0.006), and *SRSF2* (p=0.031) showed significantly associated with poor response to low-dose ESA (≤10,000 units/week) of the entire cohort.

Table 1 patient characteristics

Category	All patients (n = 350)		MDS (n = 171)		Pre-MDS (n = 179)	
All patients(%)	350	(100)	171	(48.9)	179	(51.1)
Sex(%)						
Male	172	(49.1)	96	(56.1)	76	(42.5)
Female	178	(50.9)	75	(43.9)	103	(57.5)
Age (years)Median	70.18 ± 13.42		69.87 ± 14.55		70.47 ± 12.28	
WBC (cells/mm³)	4000	(2900 - 5915)	3700	(2700 - 5480)	4600	(3170 - 6100)
ANC (cells/mm³)	2285	(1532.5- 3787.5)	1965	(1240 - 3437.5)	2490	(1725 - 3980)
Platelet count (x10³/mm³)	137	(76 - 228.5)	103	(56 - 203)	160	(93 - 236)
BUN (mg/dL)	17.90	(12.60 - 27.50)	16.80	(12.25 - 25.20)	19.10	(12.90 - 31.20)
Creatinine (mg/dL)	1.00	(0.77 - 1.49)	0.96	(0.72 - 1.41)	1.09	(0.80 - 1.57)
EPO treatment	150	(42.9)	87	(50.9)	63	(35.2)
Type of EPO, (n = 150)						
Alpha	111	(74.0)	60	(69.0)	51	(81.0)
Beta	39	(26.0)	27	(31.0)	12	(19.0)
Dose						
Initial dose (unit/week), (n = 150)	10000	(4000 - 10000)	10000	(4000 - 10000)	5000	(4000 - 10000)
≤10,000	129	(86.0)	72	(82.8)	57	(90.5)
>10,000	21	(14.0)	15	(17.2)	6	(9.5)
Average dose (unit/week), (n = 150)	10000	(4000 - 10000)	10000	(5000 - 14250)	8000	(4000 - 10000)
Adjusted dose, (n = 150)						
No	54	(36.0)	31	(35.6)	23	(36.5)
Increase	73	(48.7)	46	(52.9)	27	(42.9)
Decrease	23	(15.3)	10	(11.5)	13	(20.6)
Hemoglobin (g/dL) at baseline	9.46 ± 2.11		9.00 ± 2.05		9.90 ± 2.08	
Hemoglobin (g/dL) at 3 months	9.77 ± 2.20		9.11 ± 2.07		10.42 ± 2.15	
Hemoglobin (g/dL) at 6 months	10.29 ± 2.18		9.69 ± 2.08		10.88 ± 2.11	

Table 2 Genetic profiling between MDS and pre-MDS

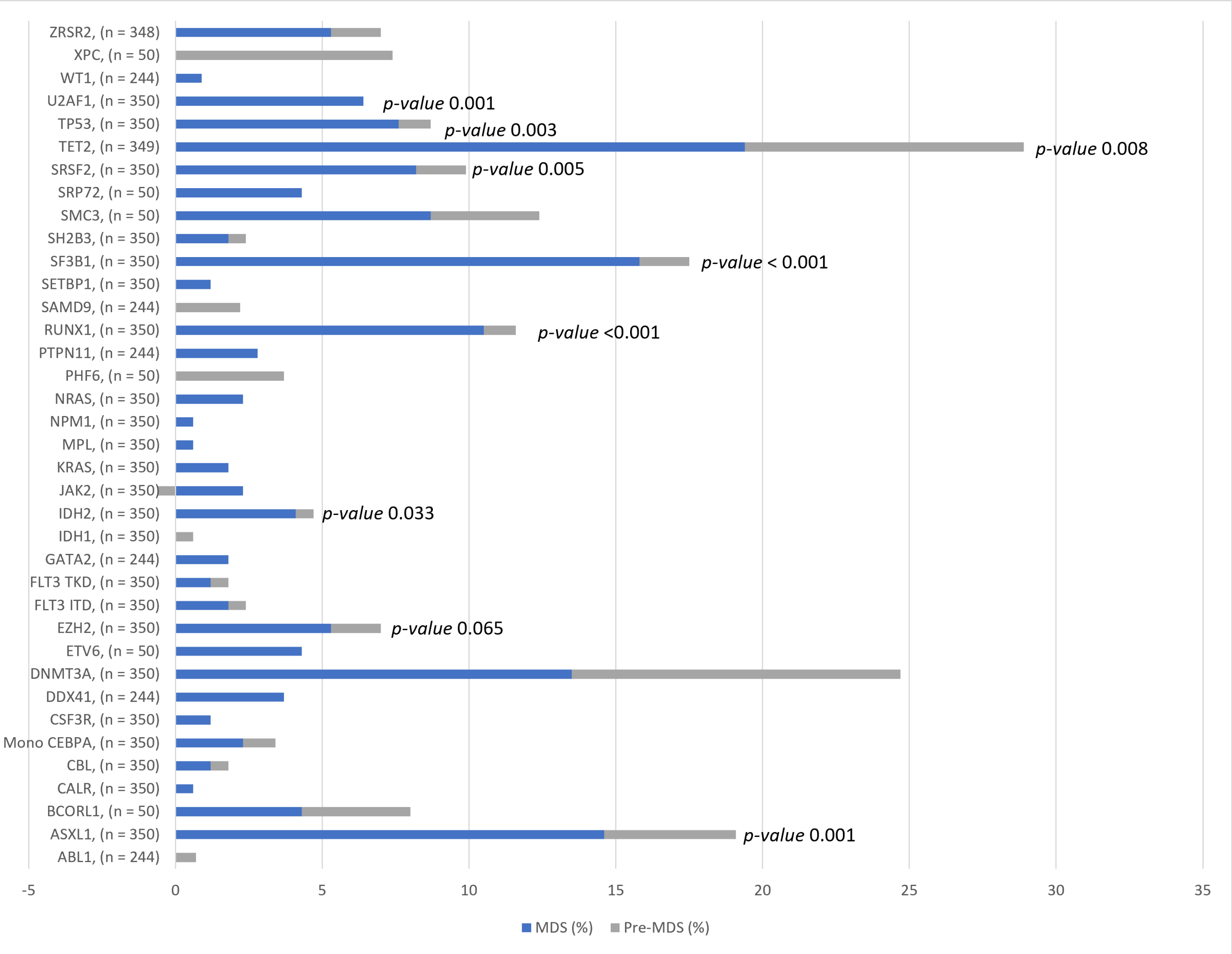
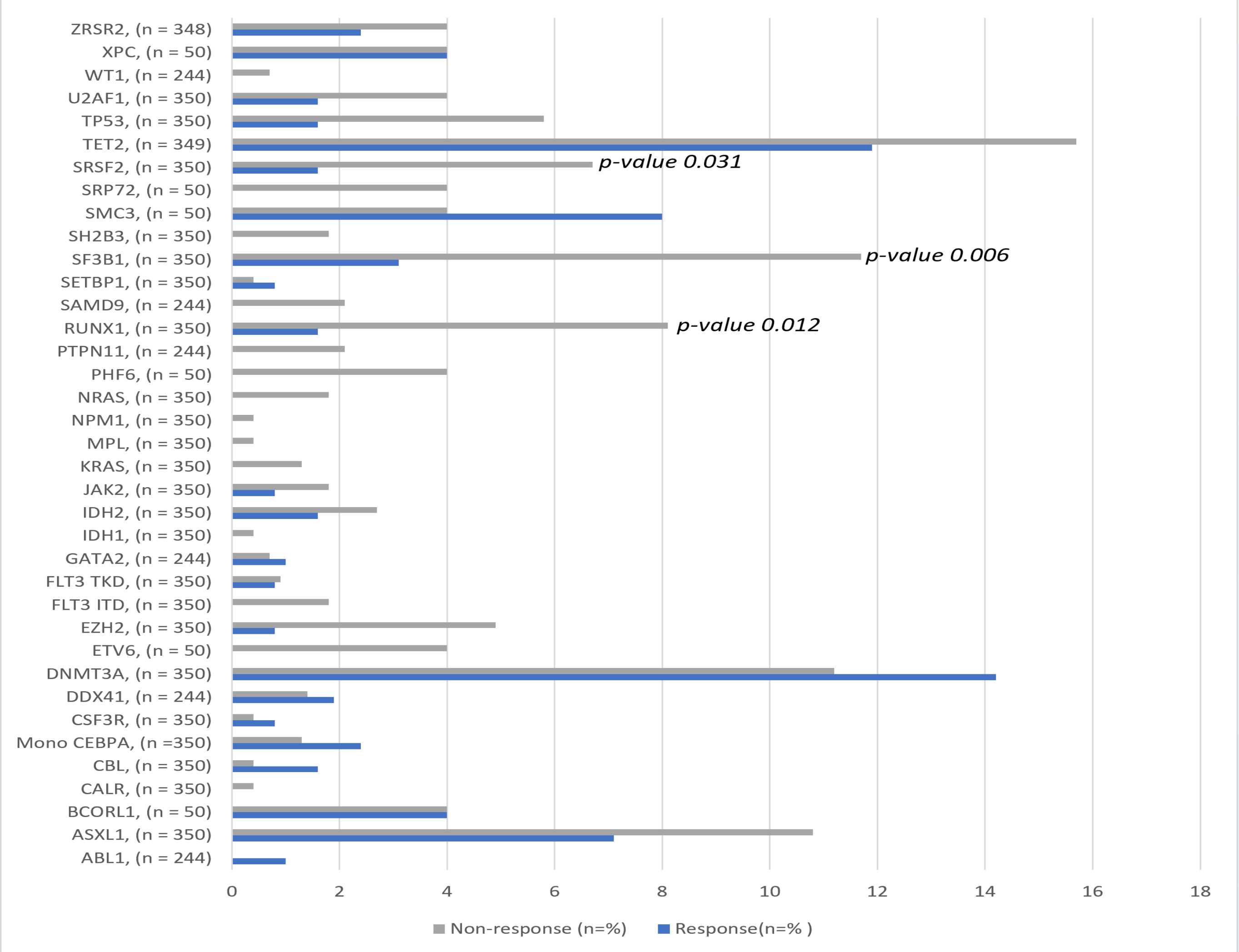


Table 3: Factor associated with well response to low-dose ESA (≤10,000 unit/week) in myelodysplastic syndrome (MDS) and pre-MDS



CONCLUSIONS

- This comprehensive analysis identifies several mutations more commonly found in MDS than pre-MDS. Additionally, mutations in splicing factor genes (*SF3B1*, *SRSF2*) and *RUNX1* are associated with poor response to low-dose ESA therapy.