XIX CONGRESSO NAZIONALE SIES 2026

IMPATTO PROGNOSTICO DELLE VARIANTI DI *SRSF2* P95 NELLE SINDROMI MIELODISPLASTICHE CON MUTAZIONE DI *ASXL1*

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Firenze | **4-6 marzo 2026**
Palazzo degli Affari

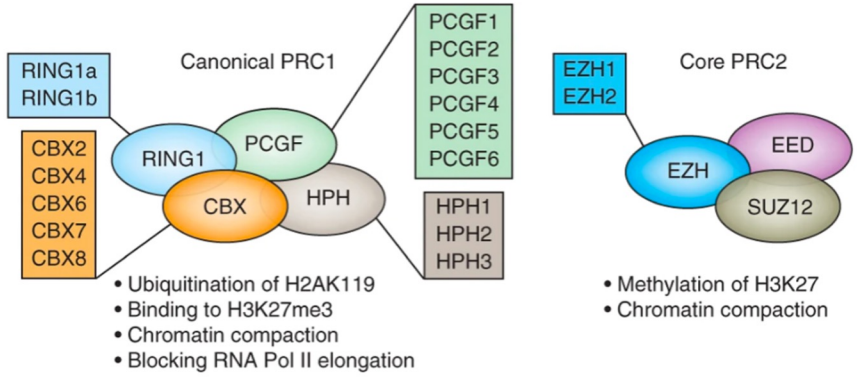
No disclosures

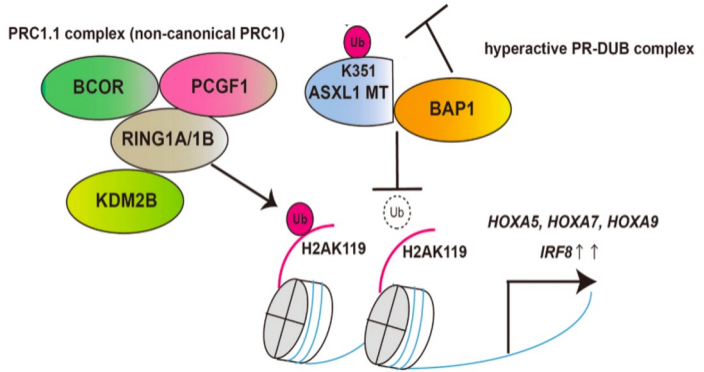
ASXL1: mutated in 20–30% of MDS cases

ASXL1mut

→ reduction in H3K27me3 levels

→ expression of genes normally silenced





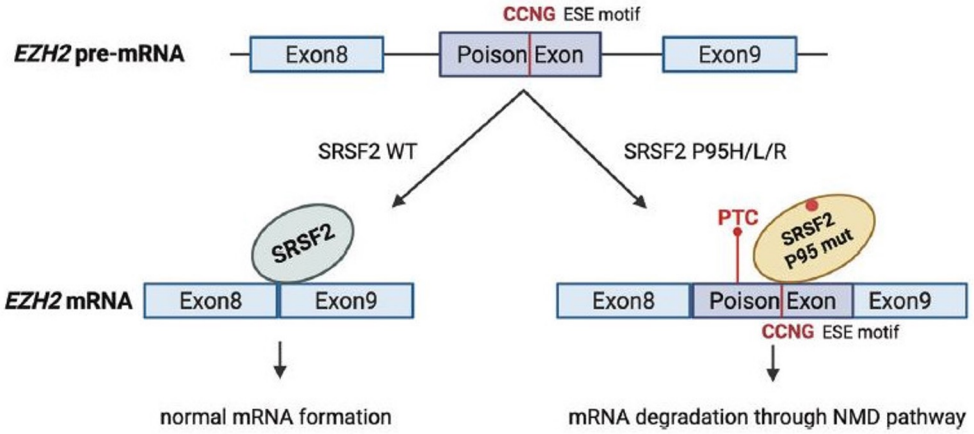
Di Croce, L., Helin, K., *Nat Struct Mol Biol* **20**, 1147–1155 (2013)

SRSF2: mutated in 15-20% of MDS cases

SRSF2^{P95} : Induce inclusion of an aberrant exon in the EZH2 transcript

↓

Reduced EZH2 levels.



*Yu, H., Hong, J., Shin, DY. et al. Leukemia **39**, 2329–2339 (2025)*

Aim of the study:

To analyze, in patients with MDS and ASXL1 mutation, the impact of SRSF2 mutation and of the individual P95 variants.

Methods

Study cohort: 853 patients

Inclusion criteria:

- MDS diagnose according to WHO 2016 criteria
- WBC <13x10^9/L;
- Presence of at least one pathogenic *ASXL1* mutation

Database	Cases
MDS Unit Careggi	394 patients with MDS and CMML
IPSS-M	2957 patients with MDS and CMML
GenoMed4All	1592 patients with MDS
Cleveland Clinic	1286 patients with MDS, CMML, MDS/MPN

Patients with diagnose of CMML were excluded

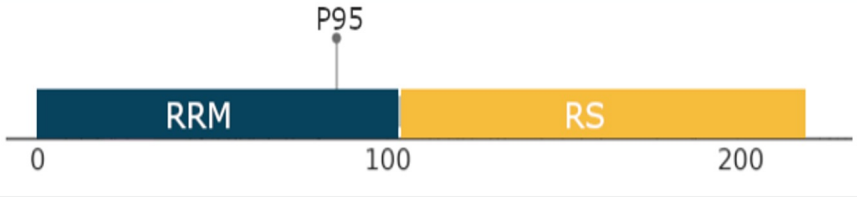
Patients with co-mutation of *ASXL1* and *EZH2* were analyzed in a different study

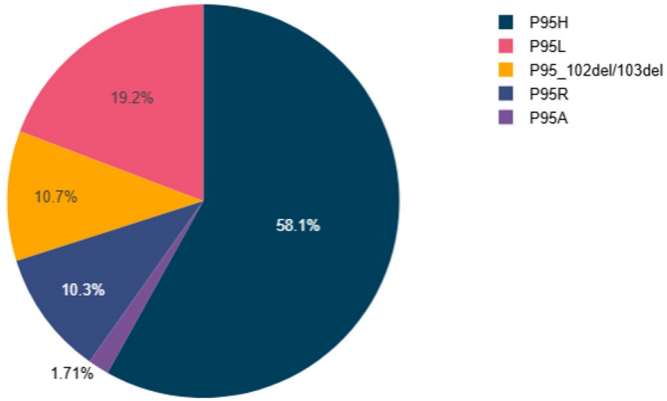
239 patients with co-mutation of ***ASXL1*** and ***SRSF2***

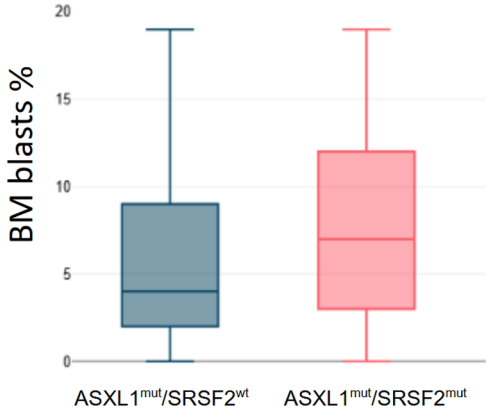
SRSF2: 95% *involved the P95 hotspot*

In 10.7% of cases, the mutation was an in-frame deletion between positions 95 and 102 or 95 and 103.

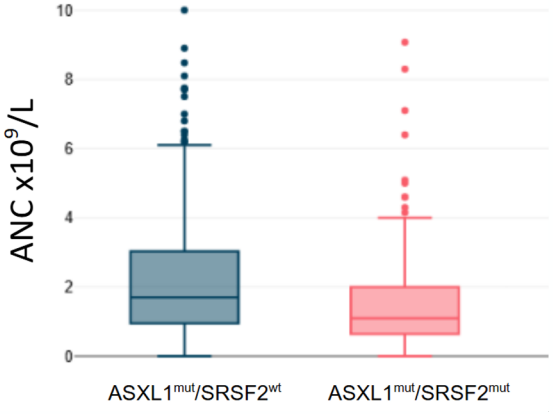
In the remaining cases: P95H (58.1%), P95L (19.2%), P95R (10.3%), P95A (1.7%).



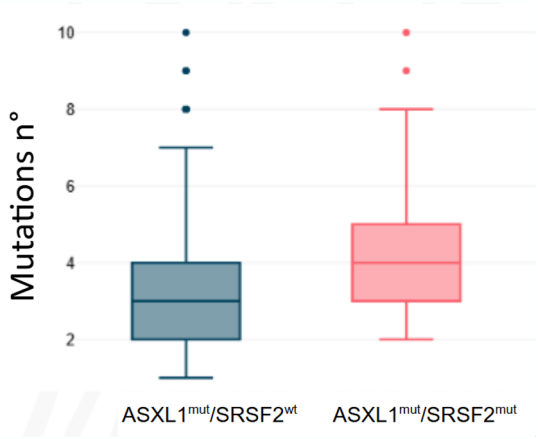




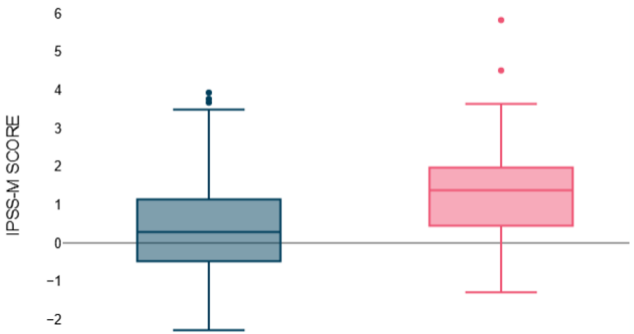
Groups	n	Median
ASXL1mut	505	4
ASXL1/SRSF2mut	239	7



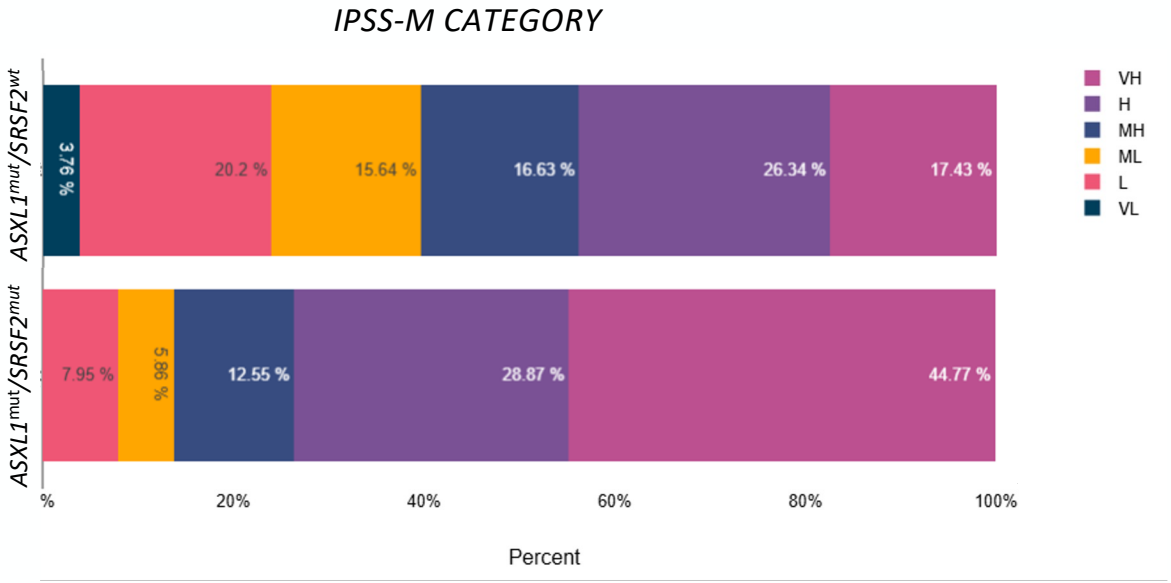
Groups	n	Median
ASXL1mut	325	1.7
ASXL1/SRSF2mut	142	1.09



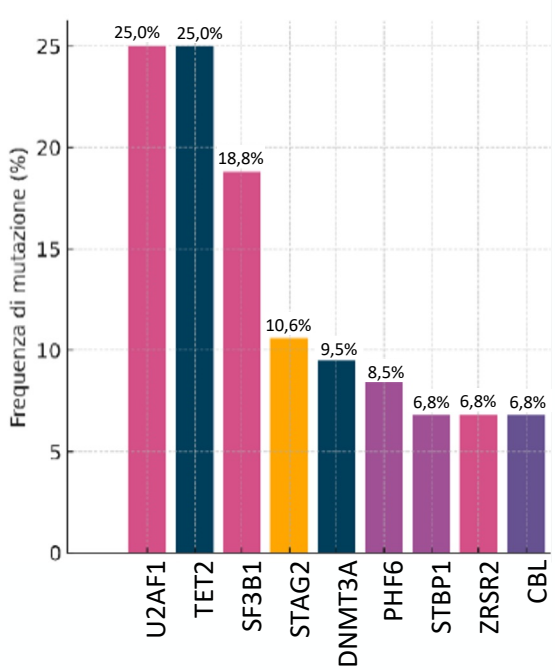
Groups	n	Median
ASXL1mut	503	3
ASXL1/SRSF2mut	237	4



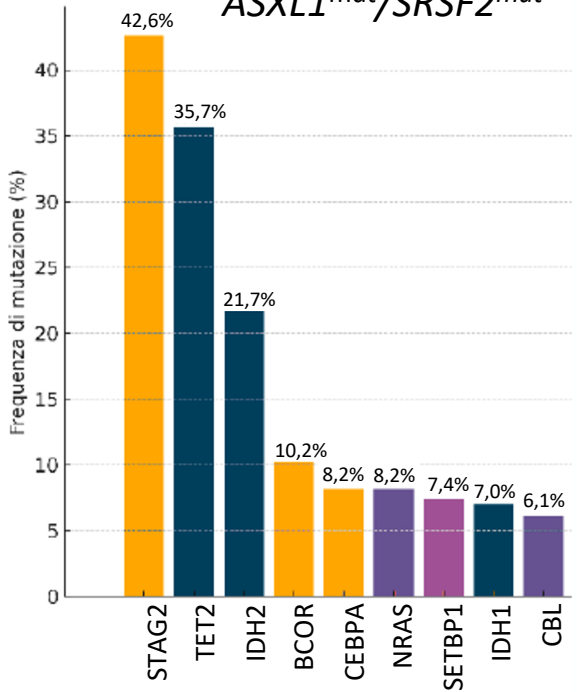
GROUP	Frequency	Median	Std. Deviation
ASXL1mut/SRSF2wt	505	0.29	1.17
ASXL1mut/SRSF2mut	239	1.38	1.11



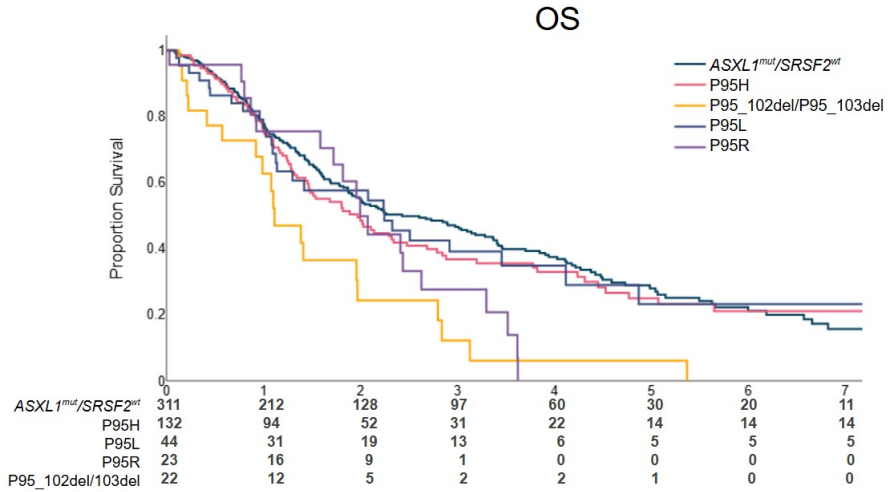
ASXL1^{mut}/*SRSF2*^{wt}

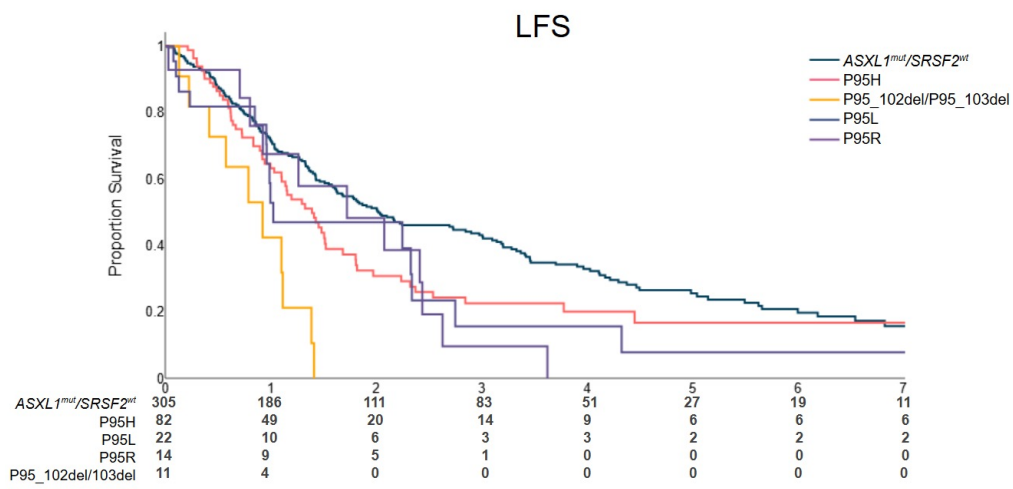


ASXL1^{mut}/*SRSF2*^{mut}



regolazione epigenetica
splicing
trascrizione/regolazione cromatinica/coesina
RAS pathway/Signaling
oncosoppressori/altro





P95_102del and P95_103del mutations are associated with a worse OS (HR = 2.30; IC 95% 1.44–3.68; p < .001) and LFS (HR= 2.42 IC 95% 1.26-4.64 p=0.008)

Independently of the IPSS-M score.

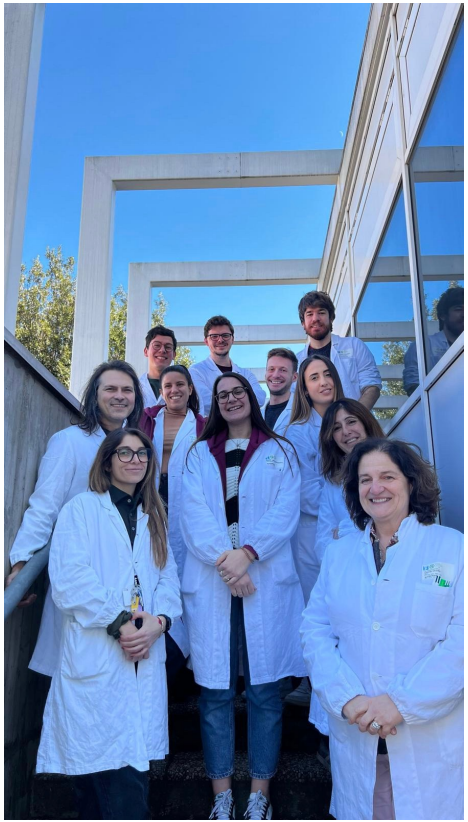
Conclusions

In *ASXL1*-mutated MDS, *SRSF2* co-mutation defines a distinct biological and clinical subset.

The prognostic impact of *SRSF2* is variant-specific:

- Deletion-type variants (p.P95_102del/p.P95_103del) identify patients with independently adverse outcomes

These findings highlight the need for variant-level annotation of SRSF2 mutations in MDS patients



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