

Sindromi mielodisplastiche: ricerca e nuovi trattamenti

Matteo G Della Porta

*Cancer Center
IRCCS Humanitas Research Hospital
& Humanitas University
Milano*

matteo.della_porta@hunimed.eu

MDS in Italia



GROM



7105 PAZIENTI (2008-2018)

Età mediana alla diagnosi 75 anni

il 30% dei pazienti ha >85 anni, il 6% meno di 50 anni

CLASSIFICAZIONE WHO

- MDS con displasia unilineare	19%
- MDS con sideroblasti ad anello	10%
- MDS con displasia multilineare	34%
- MDS con delezione 5q	6%
- MDS con eccesso di blasti	29%
- MDS non classificabile	2%

STATO DI MALATTIA

INIZIALE (IPSS basso / int 1)	83%
AVANZATO (IPSS int 2 / alto)	17%

TERAPIE

Trattamenti per l'anemia (pazienti a basso rischio):

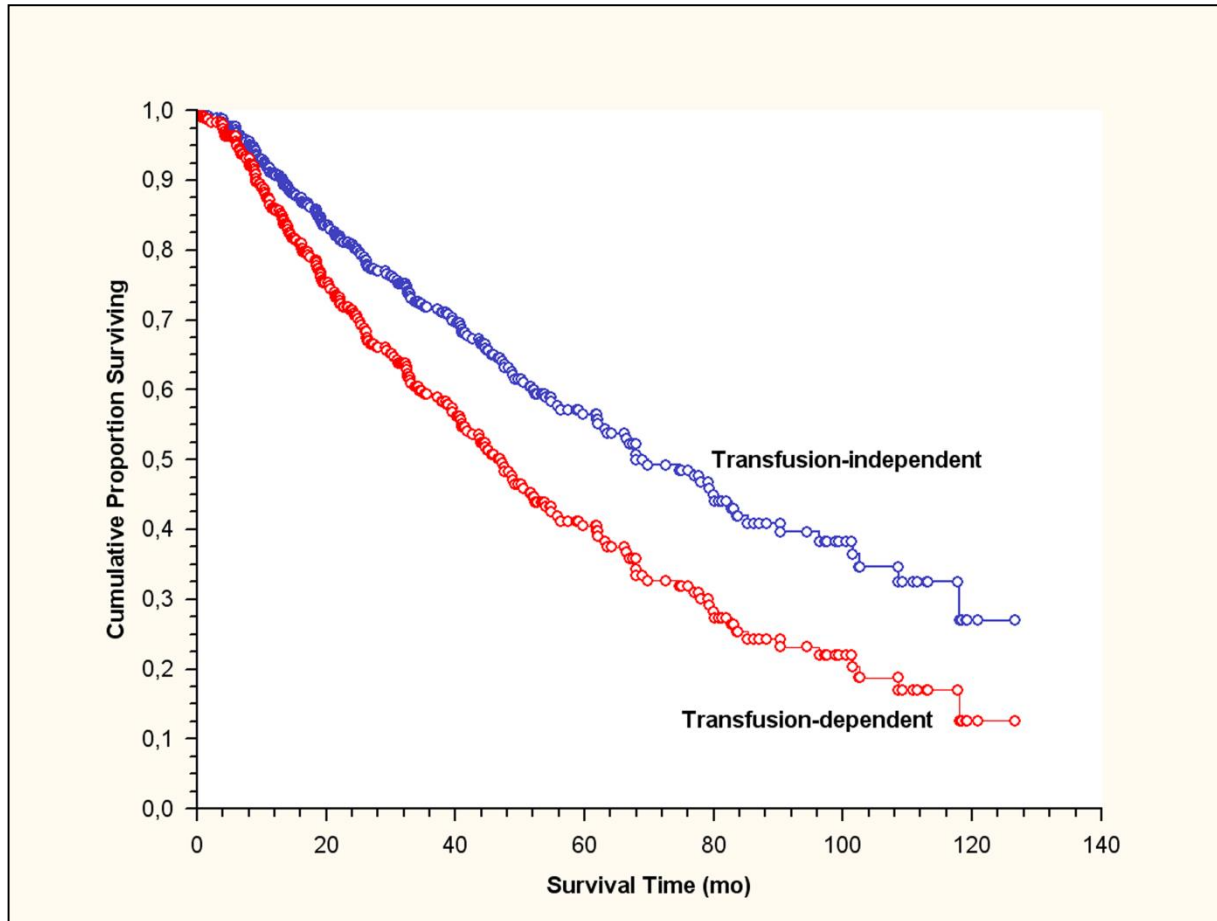
- trasfusioni 38%
- eritropoietina 36%
- lenalidomide 3%

Trattamenti per ridurre il rischio di evoluzione acuta (pazienti ad alto rischio)

- farmaci ipometilanti 15%
- chemioterapia 5%
- trapianto di cellule staminali 4%

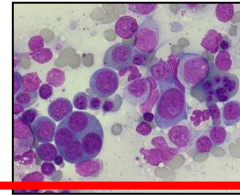
Pazienti in studi clinici sperimentali 3%

Sopravvivenza pazienti con MDS in accordo alla severità dell'anemia



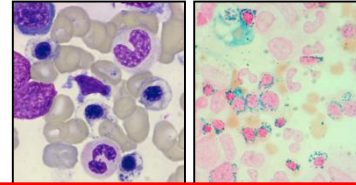
WHO Classification of Myelodysplastic Syndromes

Refractory Cytopenia with Unilineage Dysplasia (RCUD)

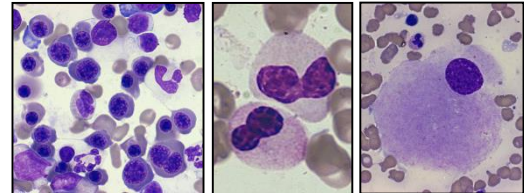


INIBITORI TGF β

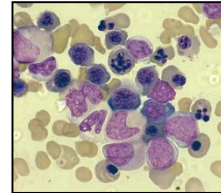
Refractory Anemia with Ring Sideroblasts (RARS)



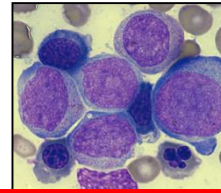
Refractory Cytopenia with Multilineage Dysplasia (RCMD)



Refractory Anemia with Excess Blasts type 1 (RAEB-1)

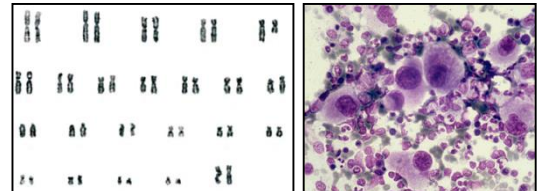


Refractory Anemia with Excess Blasts type 2 (RAEB-2)



LENALIDOMIDE

MDS with Isolated del(5q)





Lenalidomide in the Myelodysplastic Syndrome with Chromosome 5q Deletion

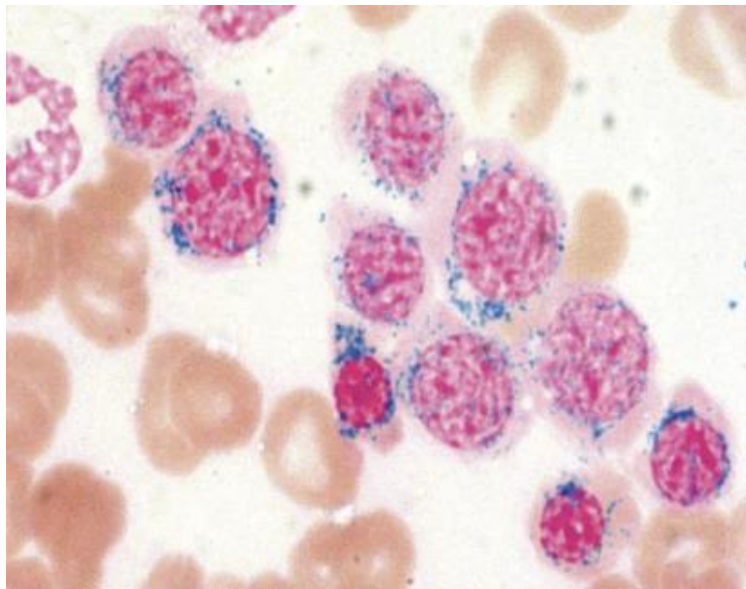
Alan List, M.D., Gordon Dewald, Ph.D., John Bennett, M.D., Aristotle Giagounidis, M.D., Azra Raza, M.D., Eric Feldman, M.D., Bayard Powell, M.D., Peter Greenberg, M.D., Deborah Thomas, M.D., Richard Stone, M.D., Craig Reeder, M.D., Kenton Wride, M.S., John Patin, M.S., Michele Schmidt, R.N., Jerome Zeldis, M.D., Robert Knight, M.D., for the Myelodysplastic Syndrome-003 Study Investigators

IPSS Low/Int-1 del(5)(q31), Trasmusione-dipendenti

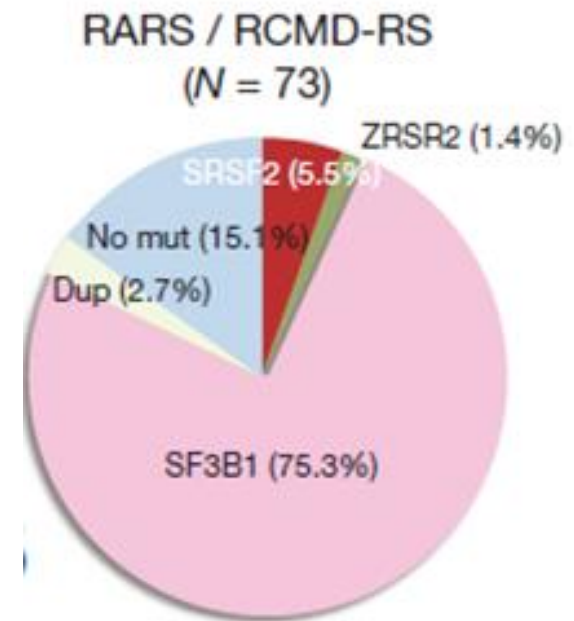
<i>Risposta Eritroide</i>	99/148 (67%)
Hb mediana basale	7.8 g/dL
Hb mediana alla risposta	13.4 g/dL

MDS con sideroblasti ad anello (11% dei casi)

Accumulo di ferro mitocondriale



Mutazioni SF3B1



Sotatercept and Luspatercept: nuovi farmaci per il trattamento dell'anemia

Sotatercept^{1,2}

Luspatercept^{3,4}

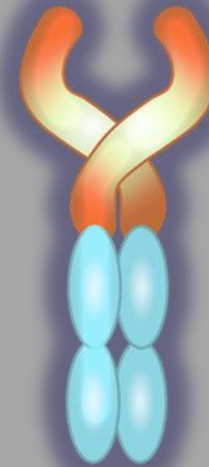
Fusion proteins with ligand trap activity toward the activin type 2 receptors^{2,3}

Do not bind EPO receptors^{2,3}



Extracellular domain of **ActRIIA**

Fc domain of human IgG₁ antibody



Modified extracellular domain of **ActRIIB**

Fc domain of human IgG₁ antibody

Heme effect^{2,3}

+

+

Bone effect⁵

+

-

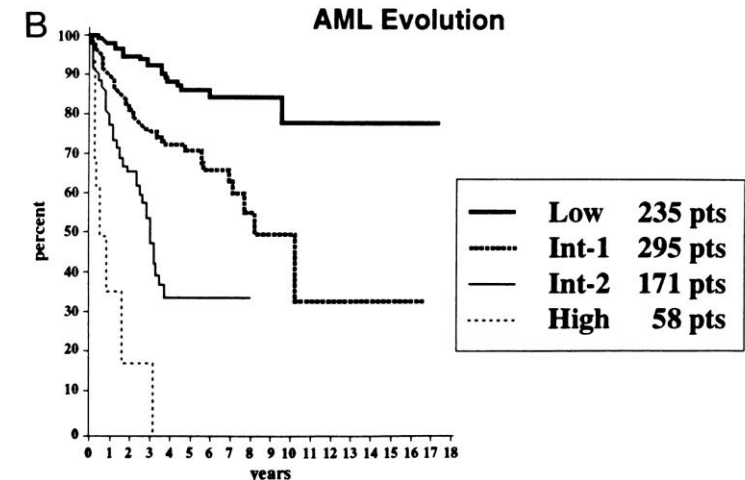
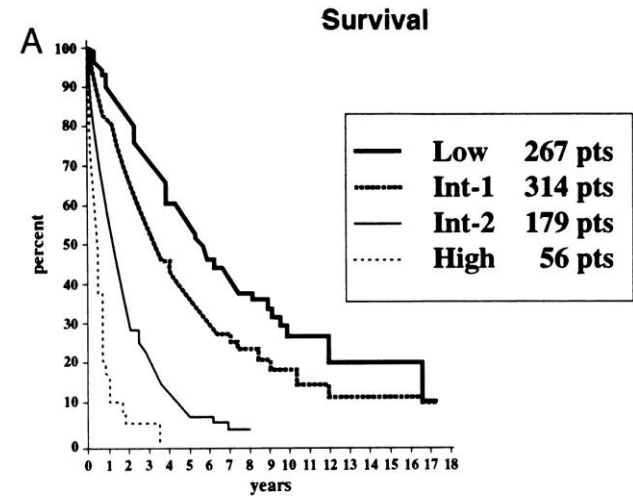
International Prognostic Scoring System - IPSS

Variable	0	0.5	1	1.5	2
BM blasts %	<5	5-10	-	11-20	21-30
Karyotype*	Good	Intermediate	Poor		
Cytopenias^o	0/1	2/3			

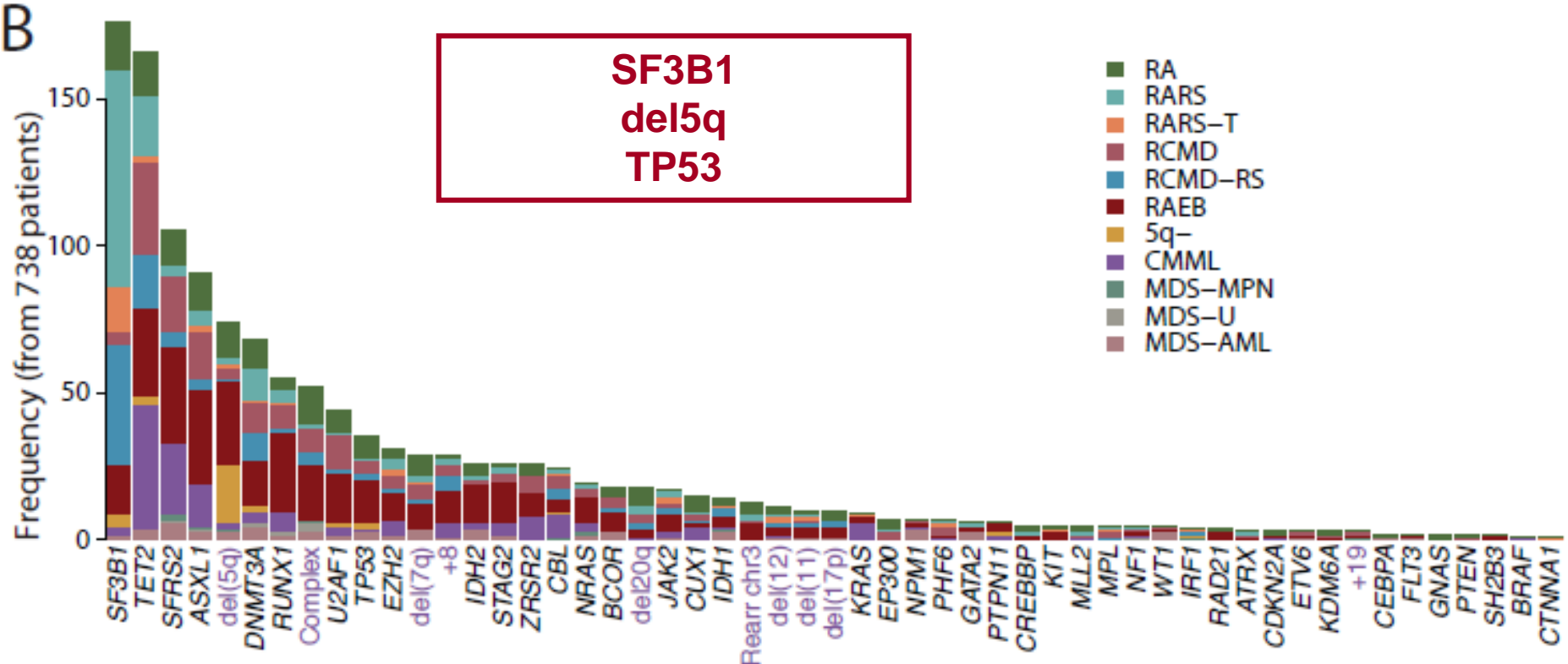
* *Good*: normal, -Y, del(5q), del(20q); *Poor*: complex, chromosome 7 anomalies; *Intermediate*: other abnormalities.

^oHemoglobin < 10 g/dL, absolute neutrophil count < 1,500/ μ L, platelet count < 100,000/ μ L.

Scores for risk groups are as follows: Low, 0; INT-1, 0.5-1.0; INT-2, 1.5-2.0; and High, 2.

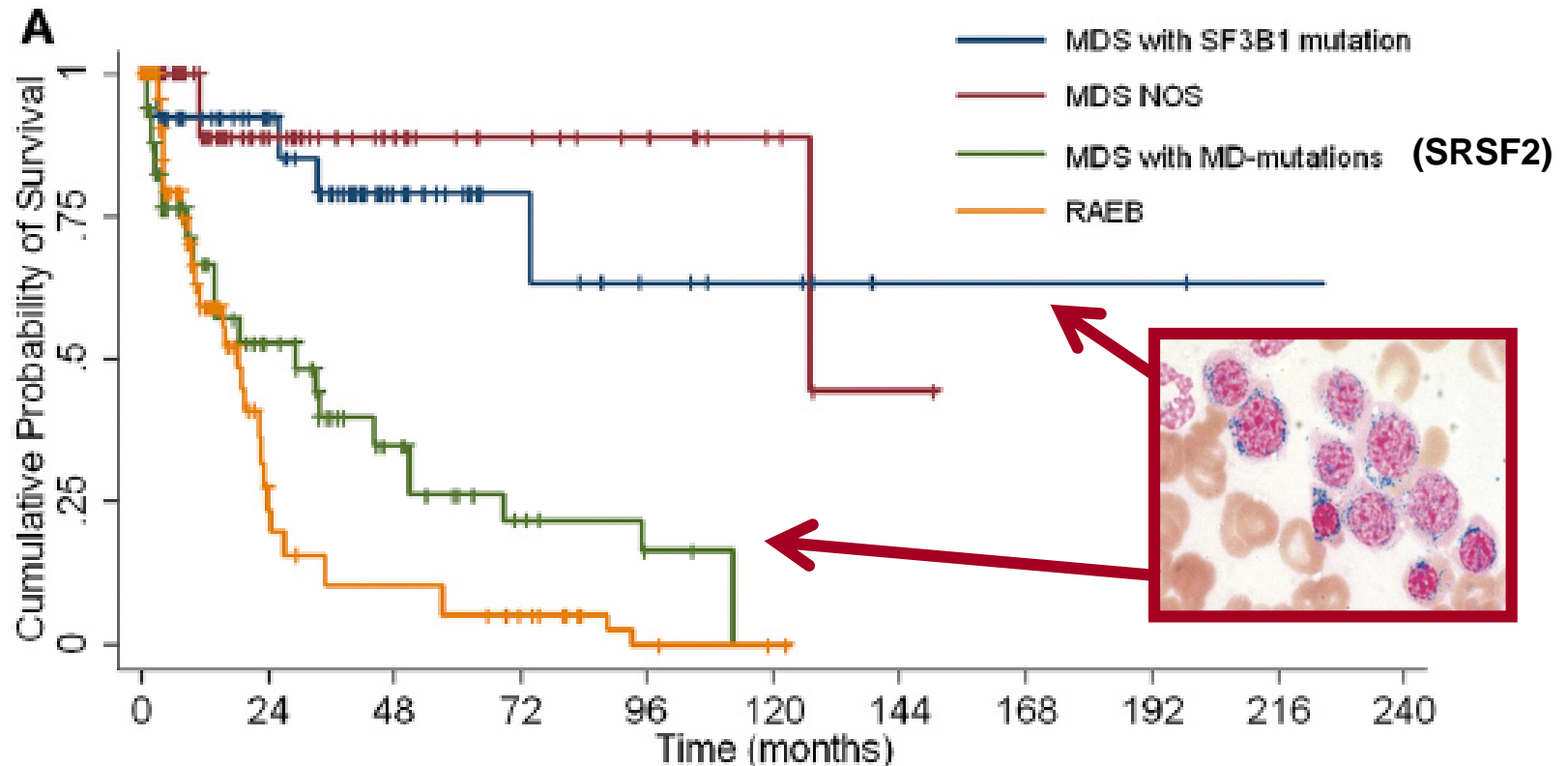


Mutazioni somatiche nelle MDS

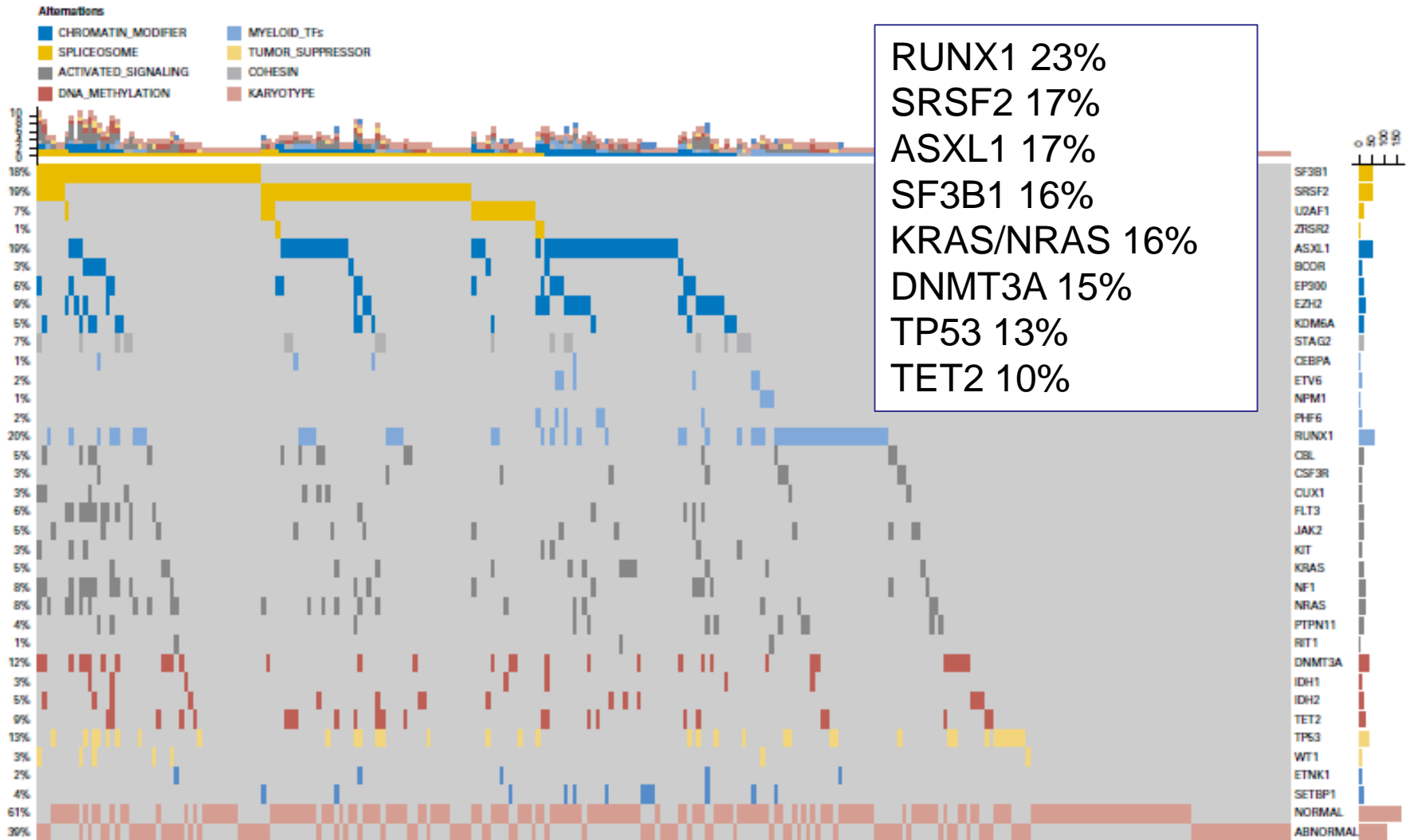


Papaemmanuil E et al. Blood. 2013;122:3616-27
Cazzola M, Della Porta MG, Malcovati L. Blood 2013;122:4021-34
Della Porta MG et al. Leukemia 2015;29:1502-13

Effetto prognostico delle mutazioni somatiche nei pazienti con MDS



Approccio trapiantologico personalizzato nelle MDS: ruolo delle mutazioni geniche





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