

Mielodisplasie: vecchi e nuovi farmaci

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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

- IPSS basso / intermedio 1 83%
- iPSS intermedio 2 / alto 17%

GROM-L



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)

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

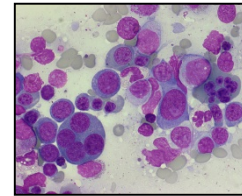
Pazienti in studi clinici sperimentali	3%
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GROM-L

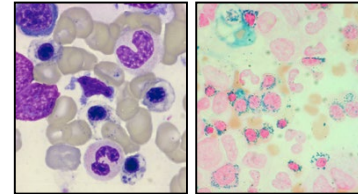


WHO Classification of Myelodysplastic Syndromes

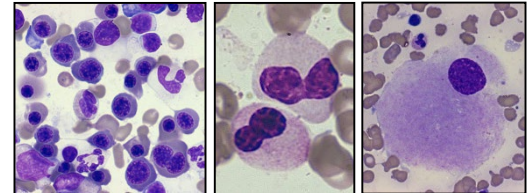
Refractory Cytopenia with Unilineage Dysplasia (RCUD)



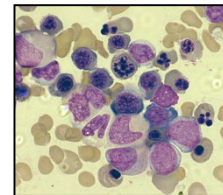
Refractory Anemia with Ring Sideroblasts (RARS)



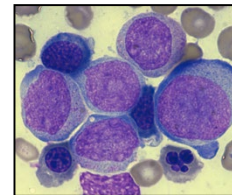
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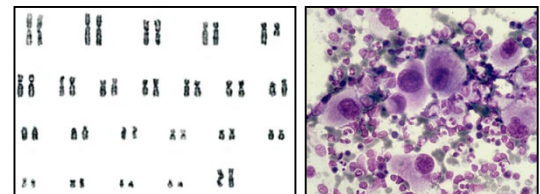
Refractory Anemia with Excess Blasts type 1 (RAEB-1)



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



MDS with Isolated del(5q)



Modello decisionale per il trattamento dell'anemia con Eritropoietina ricombinante

Variable	Value	Score	Value	Score
Transfusion need*	< 2 U/month	0	2 U/month	1
Serum-Epo*	< 500 U/liter	0	500 U/liter	1

- Predicted response rate:
 - Score 0=74%
 - Score 1=23%
 - Score 2=7%



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

Eligibility: IPSS Low/Int-1 del(5)(q31), Transfusion dependent

Erythroid response	99/148 (67%)
Median baseline Hb	7.8 g/dL
Median Hb at response	13.4 g/dL
Complete cytogenetic remission	38/85 (45%)



MEDALIST Trial

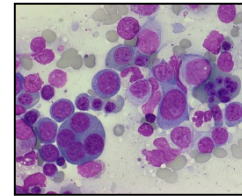
Primary Endpoint Met: Red Blood Cell – Transfusion Independence e 8 Weeks

RBC-TI \geq 8 weeks	Luspatercept (n = 153)	Placebo (n = 76)
Weeks 1–24, n (%)	58 (37.9)	10 (13.2)
95% CI	30.2–46.1	6.5–22.9
<i>P</i> value ^a	< 0.0001	

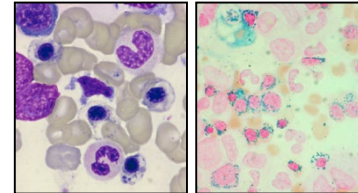
^a Cochran–Mantel–Haenszel test stratified for average baseline RBC transfusion requirement (\geq 6 units vs $<$ 6 units of RBCs/8 weeks) and baseline IPSS-R score (Very Low or Low vs Intermediate).
CI, confidence interval.

WHO Classification of Myelodysplastic Syndromes

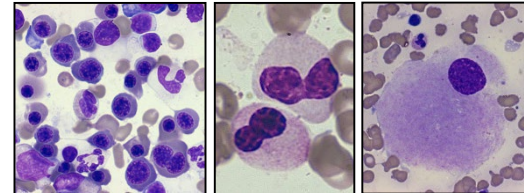
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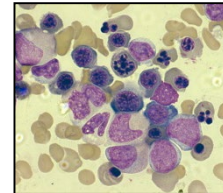
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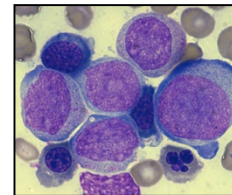
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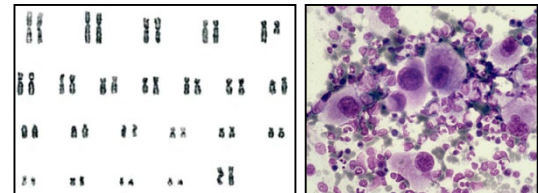
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GROM-L



Combinazioni basate sull'uso di farmaci ipometiaenti in sperimentazione clinica

Combination therapies with HMAs in patients with IPSS higher risk MDS			
Drugs	No of patients	ORR (%)	
Azacitidine + phenylbutyrate	32	34	
Azacitidine + valproic acid + all- <i>trans</i> retinoic acid	62	46	
Azacitidine + entinostat	136	43	
Azacitidine + lenalidomide - phase I	18	67	
Azacitidine + lenalidomide - phase II	36	72	
Azacitidine + thalidomide	36	58	
Decitabine + gentuzumab ozogamicin	33	42	
Azacitidine + etanercept	32	72	
Azacitidine + erythropoietin	32	44	
Azacitidine + romiplostim	40	23 (*)	
Decitabine + romiplostim	29	16	
Azacitidine + mocetinostat	22	59	
Azacitidine + panabinostat	10	50	
Decitabine + vorinostat	11	60	
Decitabine + valproic acid	87	55	
Azacitidine + eltrombopag	12	66	