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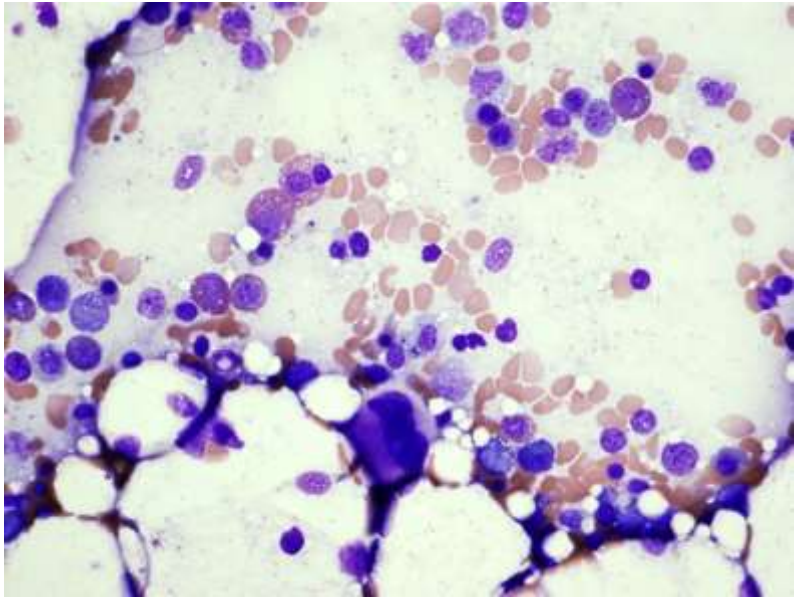
www.bhs.be

MDS

18th April 2026

Case 1

- 40 yr old male with Hodgkin lymphoma , 7 years prior
- Chronic fatigue and inability to focus
- Blood results
  - Hb 9.7 g/dL
  - MCV 95 fl
  - WBC 3.9 neutrophils 10%
  - Plt 151x109/L



Dysplasia in erythroid precursors and megakaryocytes

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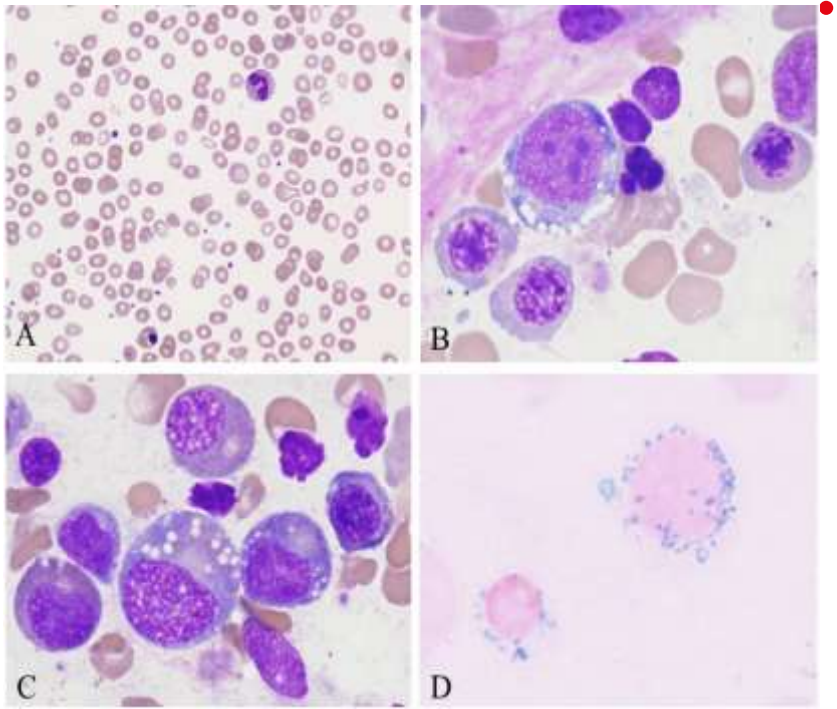
What is your next step

- A. You wait for karyotype and NGS results
- B. You ask your pathologist to have a second look
- C.You have watched the BHS seminar about MDS and decide to check the iron and vitamin levels



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Minimal diagnostic criteria

- Moderate or >10% dysplastic cells
- Persistent cytopenia(s) (> 4 months)
  - Hb < 10 g/dL
  - ANC < 1800/µL
  - Platelets < 100 x 10^9/L
- Diagnosis per exclusionem
  - Vitamin B12/folate deficiency
  - Iron deficiency
  - Copper deficiency
  - Alcohol abuse
  - Medication (chemotherapy, MTX, tacrolimus, MMF, cotrimoxazole…)
  - Heavy metals (lead, zinc, arsenic,…)
  - Hereditary BMF syndromes
  - Other hematological disorders (PNH, LGL, HCL, AA,…)
  - Autoimmune disorders (SLE, PAN, JRA,…)
  - Hypothyroidism, infections (Parvo, HIV, Hepatitis C,…)

Clinical history

Non-clonal disorders

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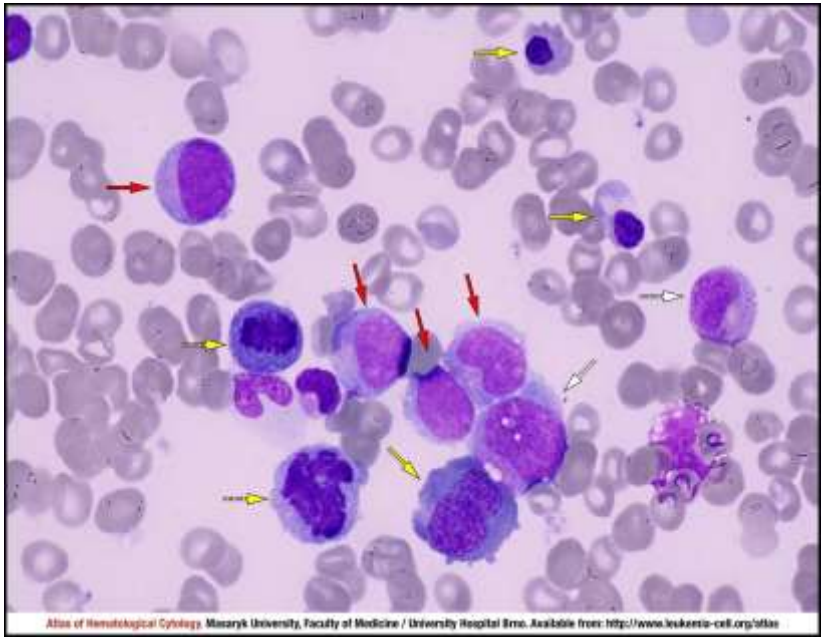
Case 2

- 74 yr old male
- Referral because of abnormal blood results
- Blood results
  - Hb 7.9 g/dL
  - WBC 1.0 x109/L neutrophils 0.5
  - Plt 51x109/L
  - Normal iron – and vitamine status



Severe dysplasia with 11% blasts

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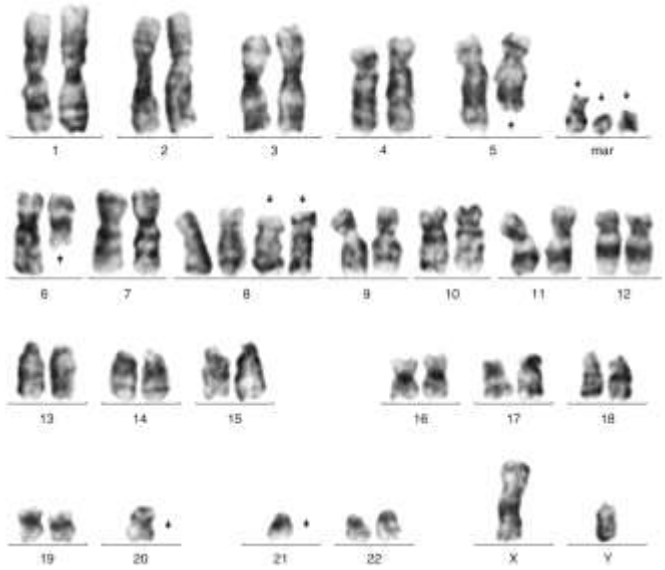
Case 2

- Karyotype
  - 47~49,XY,-Y,del(5)(q31q35), del(6)(q12q25),+8,+8,-20,-21,+mar1,+mar2,+mar3[cp12]/46,XY[8]
- NGS
  - TET2, NRAS, NPM1
- Diagnosis
  - MDS-EB2 with complex karyotype and several mutations



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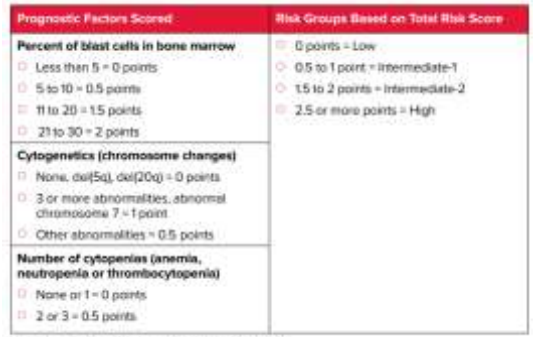
Next steps

- Risk scores
  - IPSS: high risk
  - IPSS-R: very high risk
  - IPSS-M: very high risk
- Conclusion
  - High risk MDS - azacitidine

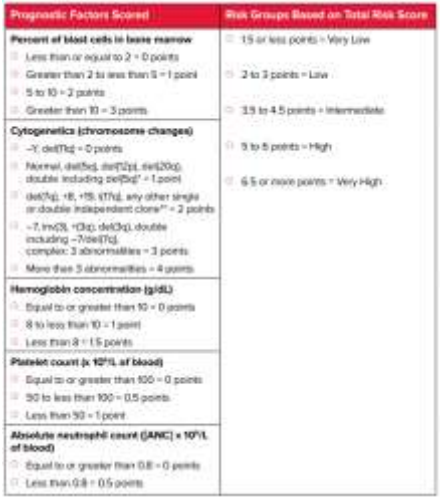
But is this correct

- A. Yes
- B. No



Prognostic Factors Scored	Risk Groups Based on Total Risk Score
Percent of blast cells in bone marrow Less than 5 = 0 points 5 to 10 = 0.5 points 11 to 20 = 1.5 points 21 to 30 = 2 points	0 points = Low 0.5 to 1 point = Intermediate-1 1.5 to 2 points = Intermediate-2 2.5 or more points = High
Cytogenetics (chromosome changes) None, del(5q), del(20q) = 0 points 3 or more abnormalities, abnormal chromosome 7 = 1 point Other abnormalities = 0.5 points	
Number of cytopenias (anemia, neutropenia or thrombocytopenia) None or 1 = 0 points 2 or 3 = 0.5 points	

Key: IPSS, International Prognostic Scoring System; del, deletion



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Cytogenetics (chromosome changes) –Y, del(11q) = 0 points Normal, del(5q), del(12p), del(20q), double including del(5q)* = 1 point del(7q), +8, +19, i(17q), any other single or double independent clone** = 2 points –7, inv(3), t(3q), del(3q), double including –7/del(7q), complex: 3 abnormalities = 3 points More than 3 abnormalities = 4 points	
Hemoglobin concentration (g/dL) Equal to or greater than 10 = 0 points 8 to less than 10 = 1 point Less than 8 = 1.5 points	
Platelet count (x 10^9/L of blood) Equal to or greater than 100 = 0 points 50 to less than 100 = 0.5 points Less than 50 = 1 point	
Absolute neutrophil count (ANC) x 10^9/L of blood) Equal to or greater than 0.8 = 0 points Less than 0.8 = 0.5 points	

IPSS-M
https://mds-risk-model.com/

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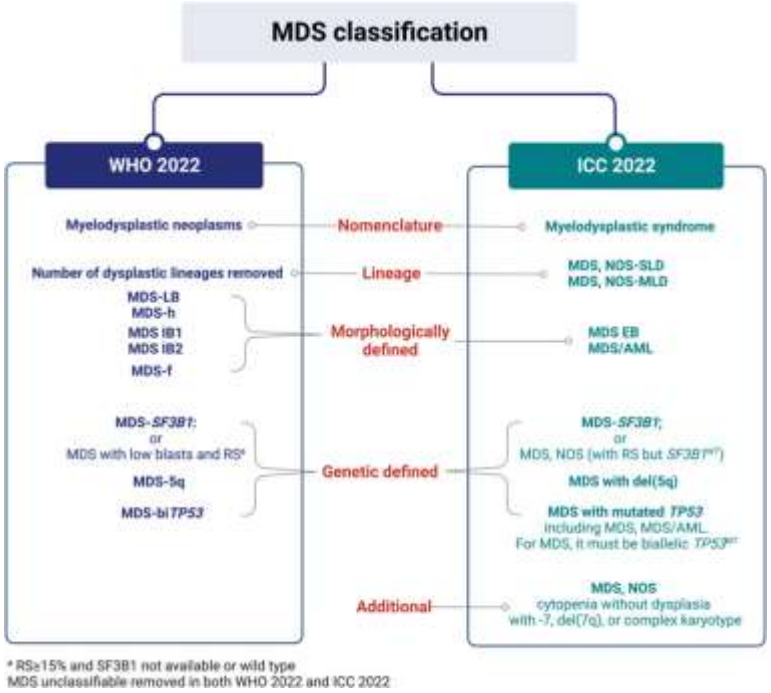
Classification



AML with defining genetic abnormalities

Acute promyelocytic leukemia with *PML::RARA* fusion
AML with *RUNX1::RUNX1T1* fusion
AML with *CBFB::MYH11* fusion
AML with *DEK::NUP214* fusion
AML with *RBM15::MRTFA* fusion
AML with *BCR::ABL1* fusion
AML with *KMT2A* rearrangement
AML with *MECOM* rearrangement
AML with *NUP98* rearrangement
AML with *NPM1* mutation
AML with *CEBPA* mutation

AML, myelodysplasia-related

AML with other defined genetic alterations

AML with *RUNX1T3::GLIS2* fusion
AML with *KAT6A::CREBBP* fusion
AML with *FUS::ERG* fusion
AML with *MNX1::ETV6* fusion
AML with *NPM1::MLF1* fusion

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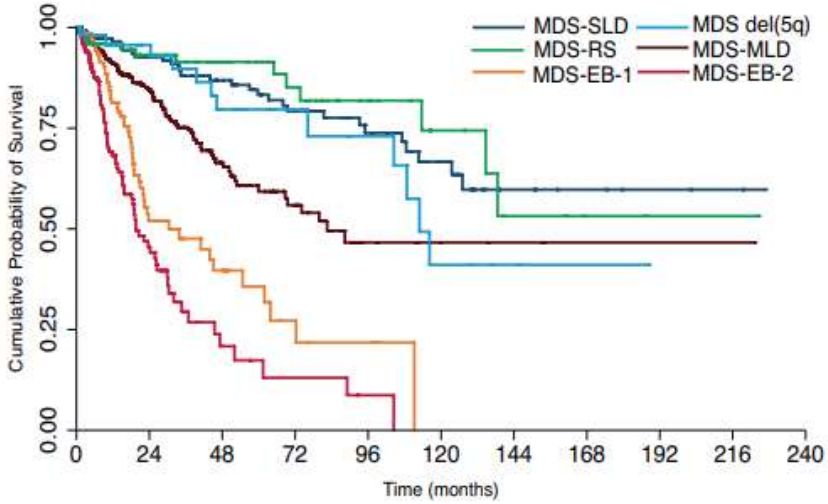
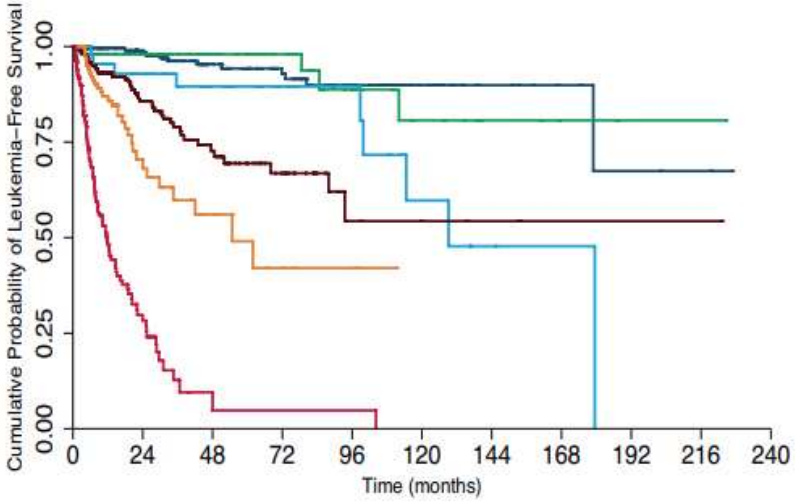
Stahl M et al. Blood Reviews 2023

Prognosis





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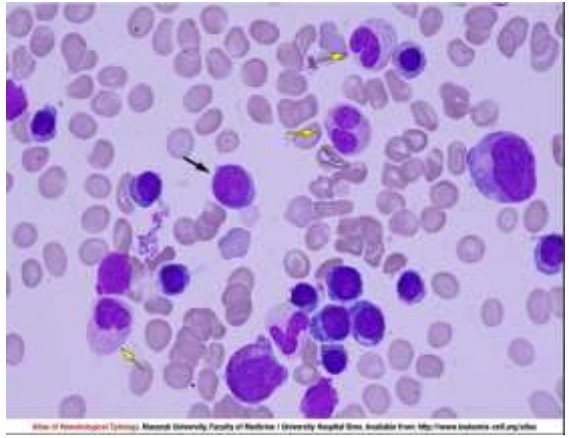
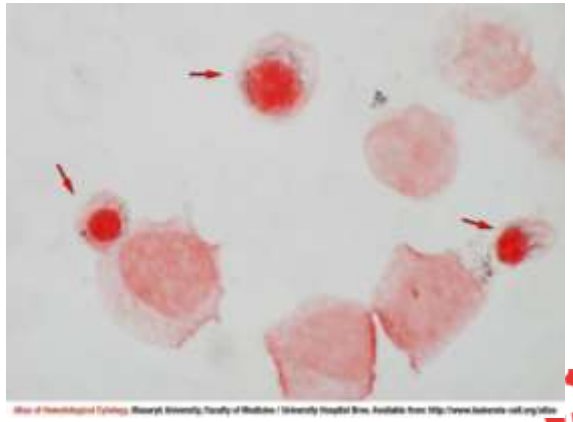
Cazzola M, et al. Blood. 2017

Case 3

- 81 yr female
- Fatigue
- Normal physical examination
- Blood results
  - Hb 10.5 g/dL
  - No other abnormalities
- Bone marrow
  - Blast count 4%
  - 40% ringsideroblasts
  - Dysplasia in several lines





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Case 3

- Risk score
  - IPSS: low
  - IPSS-R: low
  - IPSS-M: very low
- Epo-level 33.7 IU/L
- Diagnosis
  - MDS-RS-MLD

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IPSS-M
https://mds-risk-model.com/

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Which treatment

- A. EPO is low so I start with ESA
- B. Luspatercept
- C. Lenalidomide
- D. Transfusions

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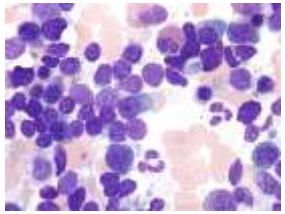
Which treatment

Patient



Disease

Treatment

- **Functional status of the patiënt:** psychological - geriatric profile
- **Biology of MDS** and prognostic impact
- **Risk and benefit of treatment**
- **Wishes of the patient** – social background
- Medical expertice of available treatment

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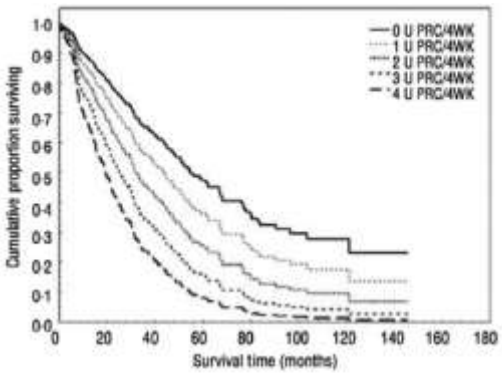
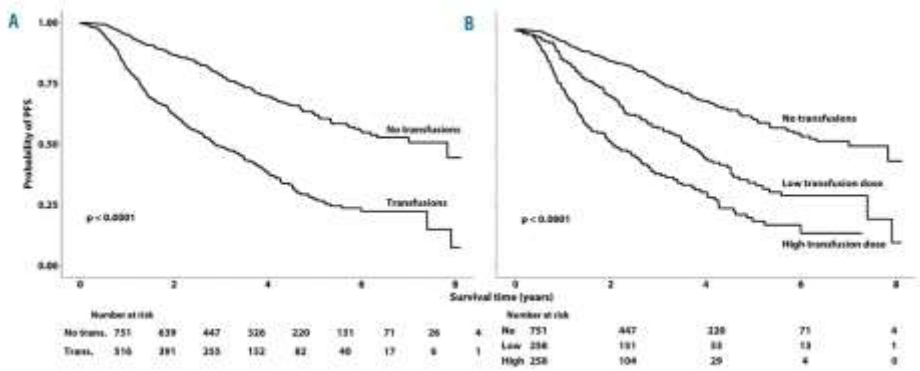
Treatment of LR-MDS: anemia

- Reduced QoL and prognosis with transfusions
- ESA = standard of care
  - Dose 40000U – 80000U/wk
- Response evaluation: 6 -12 wk
- Predictors of response
  - EPO level
  - <4U PC/ 8 wk
  - Lower IPSS-R score
  - ≤2 somatic mutations
  - Ringsideroblasts

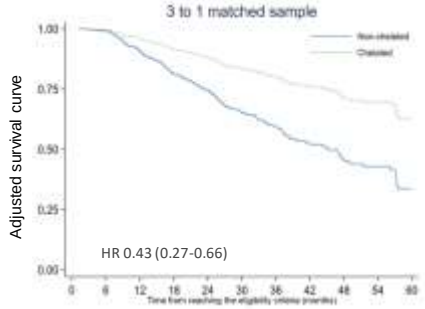




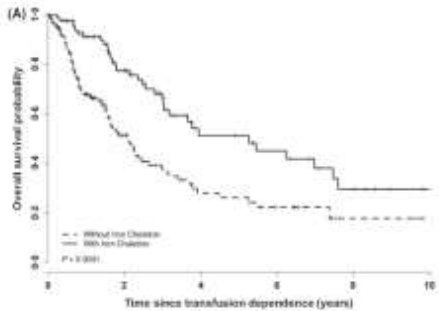
Malcovati et al, Haematologica, 2006
De Swart et al, Haematologica 2020
Killick et al Br J Haematol 2021

Iron chelation

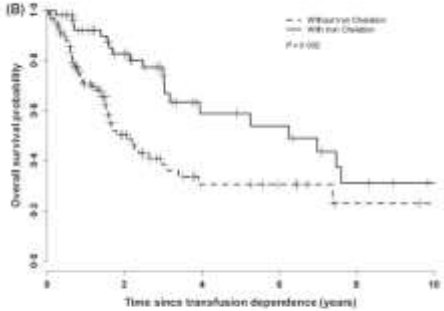
- Iron overload
  - Transfusion
  - Ineffective erythropoiesis
- Treatment
  - Deferasirox



All MDS



Only R-IPPS very low/low, intermediate, no ringsideroblasts



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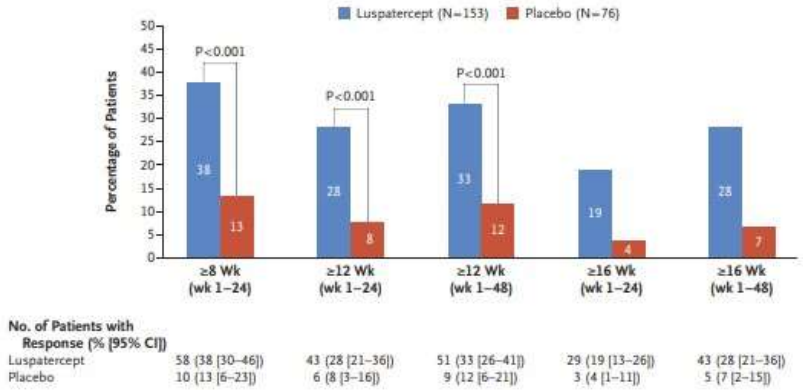
Leitch et al, Br J Haematol 2017
Hoeks et al, Haematologica, 2020

Treatment of LR-MDS: ESA failure

- Luspatercept
  - Medalist trial: phase 3 double blind, placebo controlled
  - IPSS-R : very low, low, intermediate
  - Primary endpoint: TI ≥ 8 weeks
  - Second endpoint: TI ≥ 12 weeks
  - Most common AE:
    - Fatigue
    - Nausea, diarrhea
    - Dizziness
  - Reimbursed



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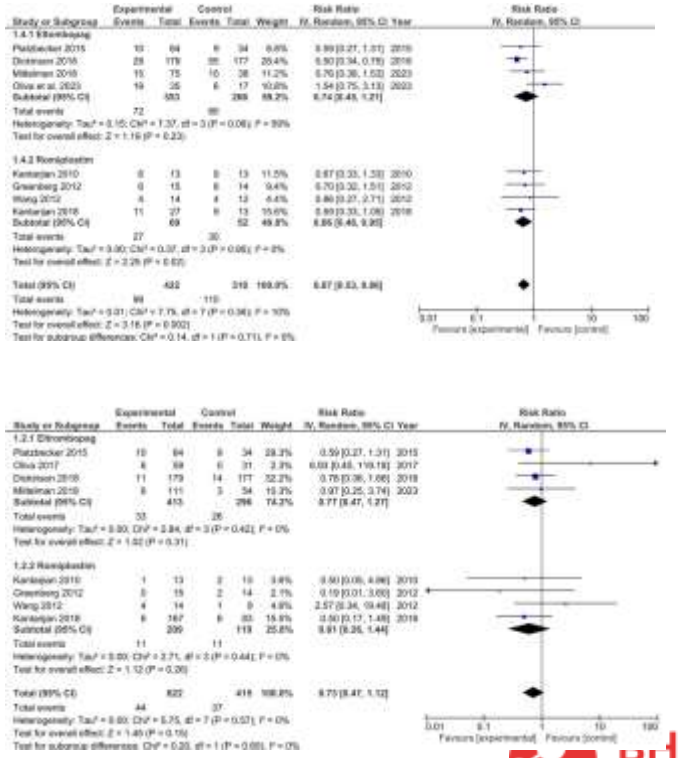
Fenaux P, et al. NEJM 2020

Treatment of LR-MDS: other cytopenias

- Neutropenia
  - G-CSF
  - Life treatening infections are rare
- Thrombocytopenia
  - Variation in clinical practice
  - Platelet transfusion
  - TPO agonists
    - Significant reduction in transfusion
    - No risk of AML progression



Aziz N, at al. 2025

Case 4

- 50 yr male patient
- Routine check-up
- Blood results
  - Hb 14 g/dL
  - WBC 3.0 neutrophils 0.5
  - Plt 80 x109/L
- BM: around 5% blast with moderate dysplasia
- NGS: no abnormalities
- Karyotyping
  - 46,XY,del(20)(q11q23)[7]/46,XY,ider(20)(q10)del(20)[4]/46,XY[1]
- IPSS-R: high risk (poor cytogenetics)
- IPSS-M: very low risk

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What would you do

- A. Start azacitidine
- B. Upfront alloSCT
- C. Watchful waiting and perhaps in the future transplantation

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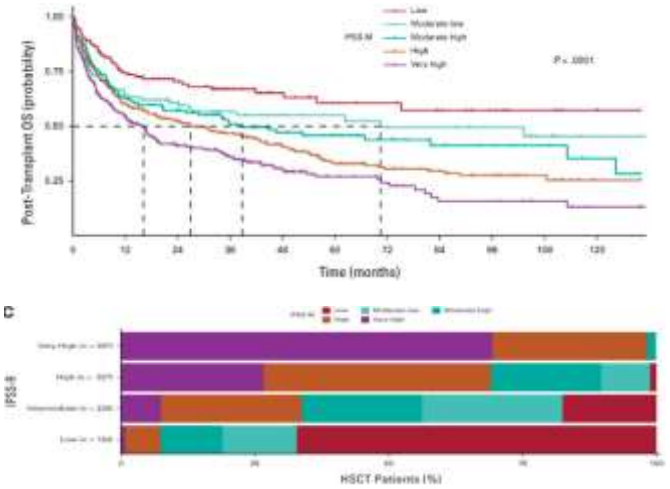
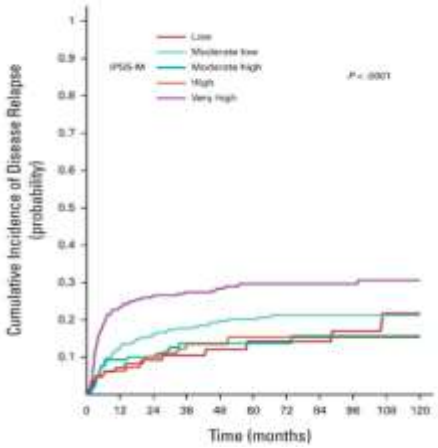
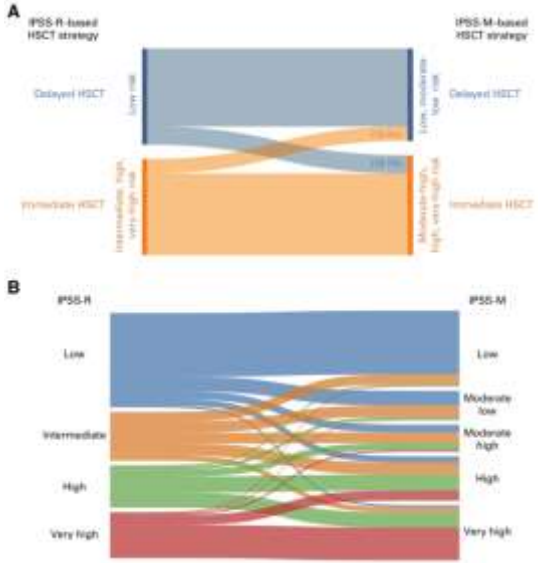
IPSS-M in patients receiving HSCT

- 2876 MDS patients from the GenoMed4All consortium retrospectively analyzed
- IPSS-M significantly improved the prediction of disease relapse and post- transplantation survival versus IPSS-R







Tentori C, et al. JCO 2024

Treatment of higher risk MDS

- Co-morbidities

- Fit for alloSCT
  - Yes: blast reduction if blasts >10%
  - No: azacitidine or BSC

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