Myelodysplastic Syndromes (MDS) "Enhancing the Nurses Role in Management"

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Agenda

- **MDS Disease background:**
  - What is MDS and how common?
  - How and why do we stage patients?
- **MDS treatment options:**
  - Goals of therapy.
  - Lower risk MDS Treatment.
  - Higher risk MDS treatment.
  - Clinical trials.
- **Factors influencing treatment choice:**
  - Physical.
  - Psychosocial.
- **The Nurse's responsibilities in shared decision making:**
  - Assessment.
  - Education.

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What is MDS?

- A group of malignant hematopoietic disorders characterized by[1]
  - Bone marrow failure with resultant cytopenias and related complications
  - Macrocytic anemia is the most common presentation
  - The disease has a tendency to progress to Acute Myeloid Leukemia.
  - Of Greek origin “Myelo” prefix means marrow and “dysplasia” is a term to describe abnormal looking blood cells.
- Diagnostic Criteria
  - Dysplasia in ≥ 10% of all cells in 1 of the following lineages in the bone marrow smear: erythroid, neutrophilic, or megakaryocytic or > 15% ring sideroblasts (iron stain)
  - 5% to 19% myeloblast cells.
  - Specific chromosomal abnormality (by conventional karyotyping or FISH).

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Is MDS a "malignant neoplasm" ?

- MDS is a cancer diagnosis according WHO.
- Cancer is a term that describes disease(s) in which a mutation of a normal cell proliferates uncontrollably and invades surrounding tissues, or blood and lymphatic systems.
- MDS is spectrum of disorders.
- In a recent survey
  - 10% of patients agreed that MDS represented "cancer" compared with 46% of HCP and 59% of physicians.

Steensma et al, Cancer. 2014 Jun 1;120(11):1670-6.

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How common is MDS?

- One of the most common hematological malignancies or “Blood Cancers”.
- Estimates of 40,000 new cases in the US are diagnosed every year.
- The majority of patients are above the age of 60.
- Presents slightly more in males.

Goldberg et al. J Clin Oncol. 2010 Jun 10;28(17):2847-52

IPSS is the most common tool used for staging of MDS

	Score Value				
Prognostic variable	**0**	**0.5**	**1.0**	**1.5**	**2.0**
Bone marrow blasts	< 5%	5% to 10%	--	11% to 20%	21% to 30%
Karyotype*	Good	Intermediate	Poor	--	--
Cytopenias†	0/1	2/3	--	--	--

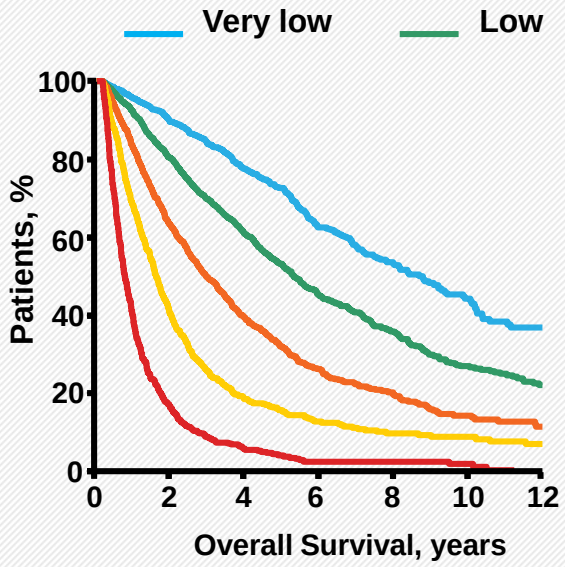
	Total Score					
	0	**0.5**	**1.0**	**1.5**	**2.0**	**≥ 2.5**
Risk	Low	Intermediate I		Intermediate II		High
Median survival, yr	5.7	3.5		1.2		0.4

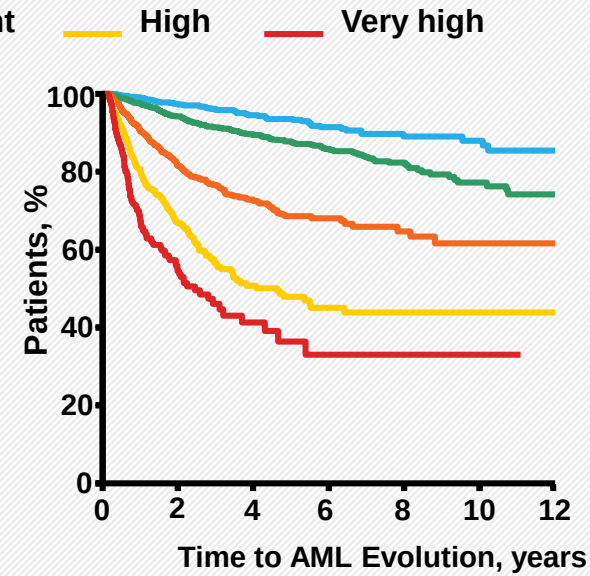
*Good = normal, -Y, del(5q), del(20q); intermediate = other karyotypic abnormalities; poor = complex (≥ 3 abnormalities) or chromosome 7 abnormalities.
†Hb < 10 g/dL; ANC < 1800/μL; platelets < 100,000/μL.

Greenberg P, et al. Blood. 1997;89:2079-2088.

Revised IPSS

Risk group	Points	% of Patients	Median survival, years	Time until 25% of patients develop AML, years
Very low	≤ 1.5	19 %	8.8	Not reached
Low	> 1.5 – 3	38 %	5.3	10.8
Intermediate	> 3 – 4.5	20 %	3.0	3.2
High	> 4.5 – 6	13 %	1.6	1.4
Very High	> 6	10 %	0.8	0.73





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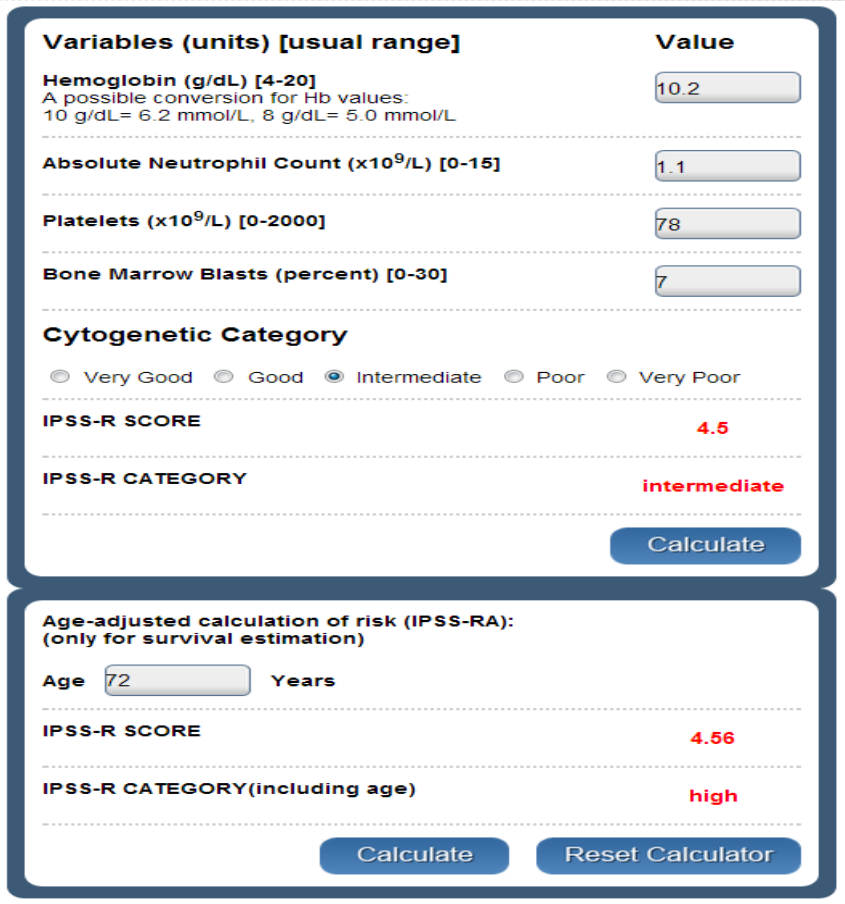
Age Dependence of the IPSS-R



www.ipss-r.com

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Therapeutic Objectives for Patients with MDS

MDS Type (IPSS)	Treatment Goals
lower-risk	• Achieving RBC-TI • Hematologic improvement • Improving QoL
higher-risk	• Overall survival and AML transformation • Altering disease's natural history • Improving QoL

Int, intermediate; IPSS, International Prognostic Scoring System; CR, complete remission; MDS, myelodysplastic syndromes; OS, overall survival; PR, partial remission; QoL, quality of life; RBC, red blood cell; TI, transfusion independence.

1. Cheson BD, et al. *Blood*. 2000;96:3671-3674.
2. Cheson BD, et al. *Blood*. 2006;108:419-425.

Treatment of Lower Risk MDS

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When do we need to treat lower risk MDS?

- The goal of treatment in lower risk MDS is to improve the patient's blood counts and alleviate related symptoms.
- In asymptomatic patients with adequate counts treatment may not be needed or indicated.
  - Providing confidence to patients in observation as an acceptable option is a major educational role for nurses.
  - There is no evidence that early treatment benefit the patients.
  - A majority of patients will need treatment for anemia to reduce or eliminate red blood cell transfusions.
  - Occasionally, treatment is directed to improve platelets or neutrophils.

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Supportive Care

- RBC transfusions are used for anemic patients who experience fatigue and/or shortness of breath. The frequency varies from patient to patient.
- MDS patients who require periodic red cell transfusions typically receive two units. Most of doctors will transfuse RBC if hemoglobin is less than 8 g/dl.
  - **The role of the nurse is to assess the patient's need for transfusion**
    - Anemia related symptoms.
    - Comorbidities.
- There are several concerns related to RBC transfusions
  - Iron overload
  - Risk of retaining excess fluid
  - Transmission of infection

    The role of the nurse is to assess and educate patients about transfusion complications, reactions.
- Despite the concerns, red cell transfusions improve the quality of life for patients with symptomatic anemia.
- Some patients may need platelets transfusion.

Erythroid Stimulating Agents (ESA)

- Used in lower risk MDS patients.
- First step for managing anemia.
- No difference between epoietin and darbepoietin. (dose equivalence).
- Start with a 8-12 weeks trial, if no response is elicited consider adding G-CSF weekly.
- Epoietin starting dose is 40,000 units weekly and may be escalated to 60,000 weekly.
- Average duration of response is 12-18 months among patients.
- No indication to continue with subsequent line of therapy.

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ESA Nursing implications

- Idenitfying those patients who will benefit from ESA.
  - Symptomatic anemia: typically Hgb < 10 g/dl.
  - Assessing factors that predict higher response:
    - serum erythropoietin level.
    - Transfusion burden.
- Educating the patient about ESAs and its side effects.
- Montioring patients during therapy:
  - Assess response by checking blood counts every 1-3 weeks based on baseline and treatment schedule.
  - Continuously assess for side effects and manage accordingly.

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Lenalidomide in MDS

- Lenalidomide is the standard of care for lower risk MDS with del 5 q[1,2]
  - Transfusion independence by IWG (67%).
  - 90% of patients respond within 3-4 months and duration of response is almost 3 years.
  - MDS-004 supports 10 mg as appropriate starting dose:
    - Higher TI for 10 mg.
    - Greater proportion of cytogenetic responses vs 5 mg (41% vs 17%).
    - No significant differences in hematological toxicity.
- MDS-001, MDS-002 and MDS-005 provided evidence that lenalidomide could be a choice for anemia treatment in lower-risk non-del(5q) pts with adequate platelets and neutrophil count[3,4]

1. Fenaux P, et al. Blood. 2011;118:3765-3776. 2. List AF, et al. N Engl J Med. 2006;355:1456-1465. 3. List AF, et al. N Engl J Med. 2005;352:549-557. 4. Raza A, et al. Blood. 2008;111:86-93. 5. Sekeres MA, et al. J Clin Oncol. 2008;26:5943-5949

Lenalidomide: Nursing Implications

- Idenitfying those patients who will benefit from lenalidomide.
  - Lower risk MDS with del 5 q chromosomal abnormality.

- Educating patients about Lenalidomide:
  - Revassist program.
  - Setting patients expectations:
    - There is a high chance of response
    - Expected 3-4 months of treatment before response.
    - Anticipating cytopenia with treatment and need for holding treatment but reassuring patient that this is a sign of response.

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Lenalidomide: Nursing Implications

- Expected side effects:
  - Cytopenia
  - Rash
  - GI: upset and diarrhea
  - Hypothyroidism.
  - Leg cramps

- Monitoring patients during therapy:
  - Weekly CBC/diff first 8 weeks and then monthly after.
  - 80% of patients will need dose interruption within 3 weeks and on average treatment is held for 3 weeks then restarted with 5 mg po daily.
  - Continuously assess and manage other adverse events.

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Immunosuppressive Therapy (IST)

- One course Anti-thymocyte globulin (ATG) +/- Cyclosporine-A (CSA)
- Positive variable for IST response[1,2]
  - Age is the strongest variable for response (< 60 year)
  - HLA-DR 15 status
  - Short Duration of disease.
  - Trisomy 8
  - Hypoplastic MDS
  - PNH clone
- Responses are durable and trilineage responses are observed[2]

1. Sauntharajah Y, et al. Blood. 2002;100:1570-1574. 2. Sloand EM, et al. J Clin Oncol. 2008;26:2505-2511.
3. Sloand E, et al. ASH 2004. Abstract 1431.

IST: Nursing Implications

- Idenitfying those patients who will benefit from ATG/CS:
  - Young < 60 year, lower risk MDS and HLA-DR15 positive.
- Educating patient about ATG/CSA:
  - Setting patients expectations:
    - Hospitalization- 5 days for ATG
    - Expected 4-6 month after starting treatment achieve a response.
  - Expected side effects:
    - ATG
      - Infusion reactions
      - Cytopenia
      - Serum sickness
      - Infections
    - Cyclosporine
      - Renal toxicity.
      - Hypertension.
      - Electrolytes imbalance.
      - Neurological toxicity .
      - GI toxicity.
      - Hisutism.
      - Infection.
- Monitoring patients during therapy
  - ATG is administered in the hospital, monitor for infusion and anaphylactic reactions.
  - Weekly CBC, CMP, cyclosporine trough levels at the beginning and then as needed clinically.
  - Continuously assess and manage other adverse events.

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Iron Chelation Therapy in MDS

Characteristic	NCCN[1]	MDS Foundation[2]
Transfusion status	▪ Received > 20 RBC transfusions ▪ Continuing transfusions	▪ Transfusion dependent, requiring 2 units/mo for > 1 yr
Serum ferritin level	▪ > 2500 µg/L	▪ 1000 µg/L
MDS risk	▪ IPSS: low or intermediate-1 risk	▪ IPSS: Low- or Int-1 ▪ WHO: RA, RARS and 5q-
Patient profile	▪ Candidates for allografts	▪ Life expectancy > 1 yr and no comorbidities that limit progress ▪ A need to preserve organ function ▪ Candidates for allografts

1. NCCN. Clinical practice guidelines in oncology. MDS. v2.2013.
2. Bennett JM, et al.. *J Hematol.* 2008;83:858-861.

ICT

Table[1]	Deferoxamine	Deferasirox	Deferiprone
Administration	SC or IV, continuous infusion 5-7 days/wk	Oral suspension	Oral tablet
Common AEs	Local skin reaction, hearing loss, late bone problems	Rash, GI disturbances, diarrhea, mild changes in creatinine, proteinuria, transaminases	GI disturbances, joint pain, arthritis
Severe AEs	Retinopathy, acute pulmonary distress	Peptic ulcers, liver or renal dysfunction leading to failure, cytopenias	Agranulocytosis, neutropenia
Cost	$$	$$$$	$-$$

- Box warnings
  - Noted more often when administered in excess of iron burden
- Deferoxamine: ocular and auditory disturbances, acute renal failure, hepatic dysfunction, adult respiratory distress syndrome, growth retardation in children
- Deferasirox: renal failure, hepatic failure, gastrointestinal hemorrhage
- Deferiprone: agranulocytosis, infection (leading to death)

Neufeld EJ. Hematology Am Soc Hematol Educ Program. 2010;2010:451-455.

ICT: Nursing Implications

- Identifying those patients who will benefit from ICT:
  - Patients with evidence of iron overload due to RBC transfusions typically present after 15-20 units.
  - Elevated serum ferritin levels in laboratory studies.
  - Lower risk MDS.

- Educating patients about ICT:
  - Monitoring Iron overload.
  - Options of ICT : Desferral pump versus oral iron chelation.
  - Expected side effects.

- Monitoring patients during therapy:
  - Weekly CBC, CMP for first 1-2 month and monthly thereafter.
  - Observe renal function and GI toxicity with Deferasirox.
  - Continuously assess and manage adverse events.

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Treatment of Higher Risk MDS

Hypomethylating Agents

- Two medications approved by FDA:
  - Azacitidine: First FDA approved drug for MDS.
  - Decitabine.
- Administered subcutaneously or intravenously.
- Low dose chemotherapy with unique mechanism of action.
- In general well tolerated by patients.
- Response rates of 40-50%.

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Hypomethylating Agents (HMA)

- Azacitidine is the preferred HMA given OS data in higher risk MDS.
- HMA are standard of care for higher risk MDS
    - 7 day regimen is preferred
- HMA are treatment option for lower risk MDS patients
    - Thrombocytopenia
    - 5 day regimen is accepted for administration.

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HMA: Nursing Implications

- Identifying those patients who will benefit from HMA:
  - Higher risk MDS patients.
  - Lower risk MDS patients with thrombocytopenia or a subsequent line of therapy for anemia.
- Educating patients about HMA:
  - Setting patients expectations:
    - Responses seen at 4-6 month.
    - Worsening of blood counts during the first two cycles.
    - Need to continue therapy among responders.
  - Expected side effects:
    - Myelosuppression.
    - Nausea and vomiting.
    - Constipation.
    - Injection site reactions.
- Montioring patients during therapy:
  - Weekly CBC at the beginning of therapy.
  - Assessing responses after 4-6 cycles.

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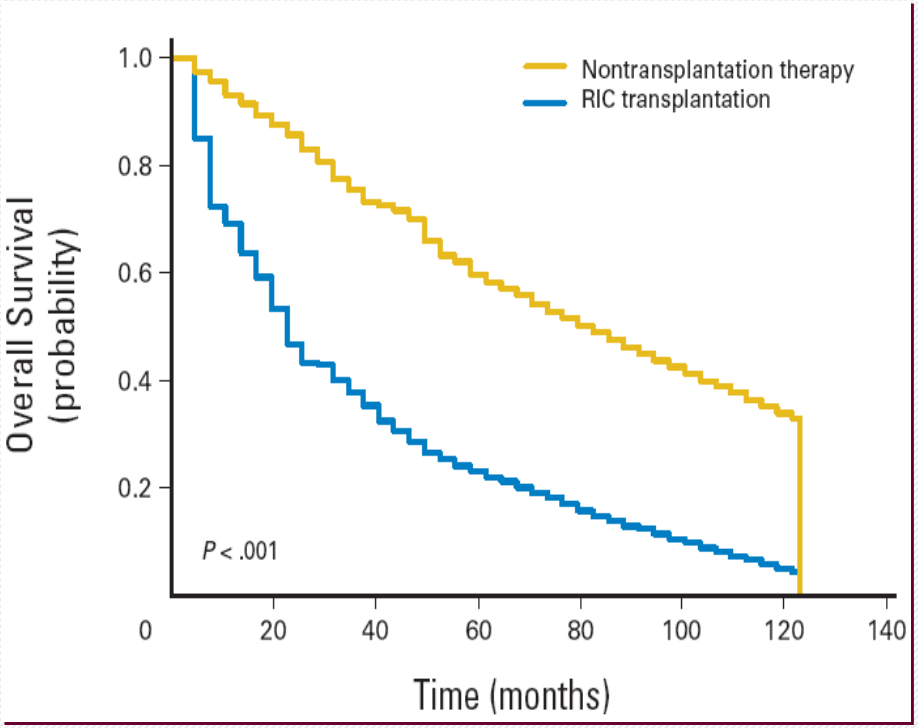
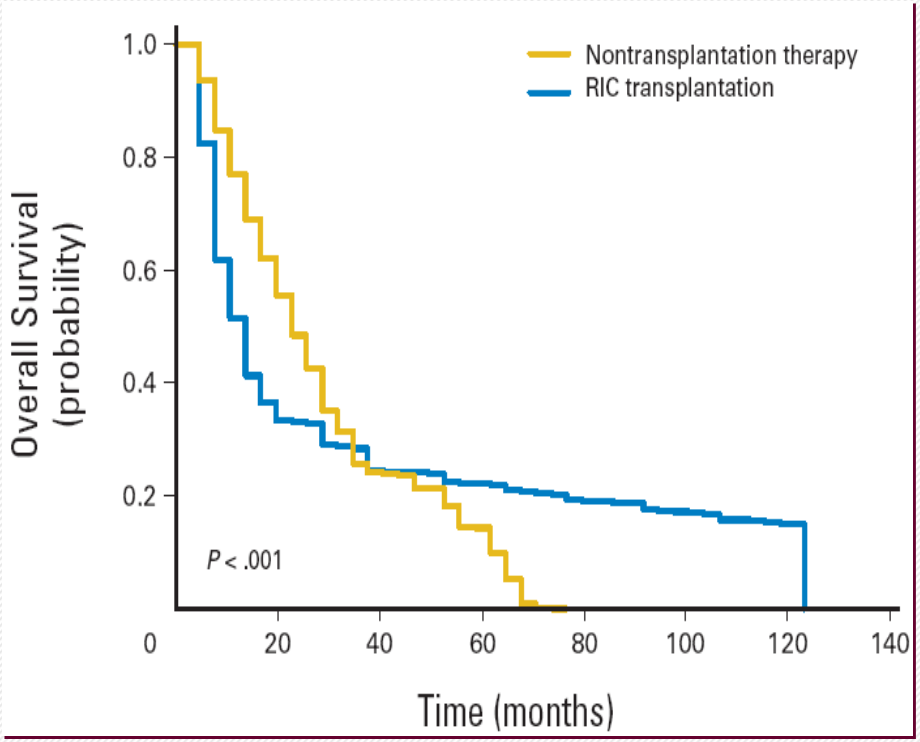
Allogeneic Hematopoietic Stem Cell transplant





Koreth J, et al. J Clin Oncol. 2013;31:2662-2671.

Allogeneic Stem Cell Transplant (HSCT): Nursing Implications

- Identifying those patients who will benefit from HSCT:
  - Fit and no major comorbidities.
  - Higher risk MDS.
  - Decision about pursuing allo SCT is complex and is a multi-disciplinary approach including active participation of the patient/family need to be involved.
- Educating the patients about HSCT:
  - Setting patients expectations:
    - Transplant procedure.
    - Transplant logistics.
    - Quality of life issues and need for caregiver.
  - Expected side effects:
    - Chemotherapy related.
    - Infections.
    - GVHD.
- Monitoring patients after HSCT:
  - After transplant intense monitoring up to 1 year with frequent visits, and bone marrow aspirate/biopsy repeats.

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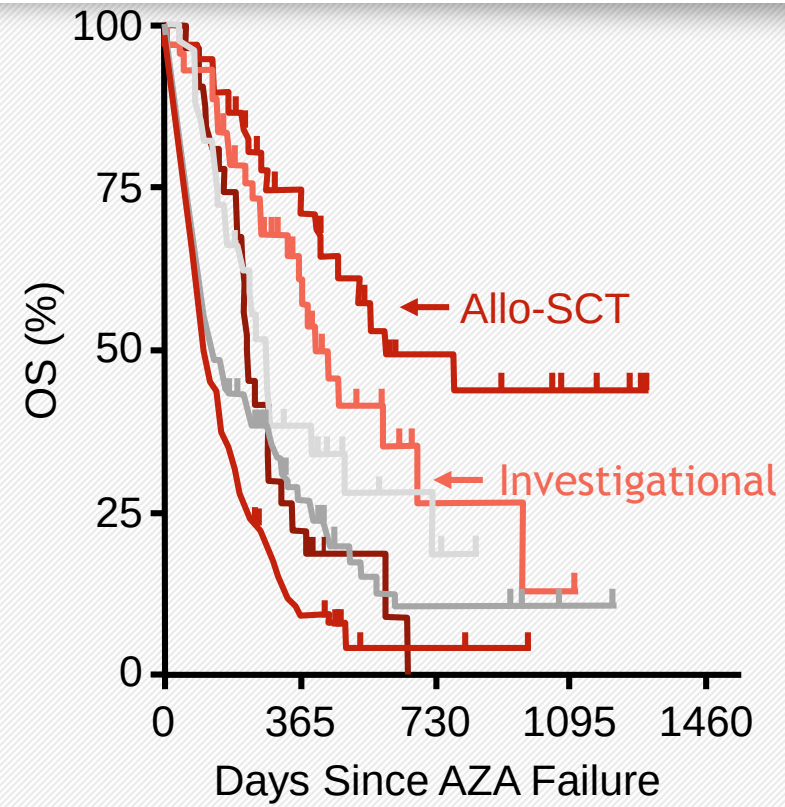
Salvage Therapy After Azacitidine Failure: Clinical Trials offers best non transplant outcome



Type of Salvage	N	ORR	Median OS, Mos
Unknown	165	NA	3.6
Best supportive care	122	NA	4.1
Low-dose chemotherapy	32	0/18	7.3
Intensive chemotherapy	35	3/22	8.9*
Investigational therapy	44	4/36	13.2*†
Allogeneic transplantation	37	13/19	19.5*†

*Log-rank comparison of BSC vs intensive CT (P = .04), investigational therapy (P < .001), or alloSCT (P < .001).
†Comparison of intensive CT vs investigational therapy (P = .05), intensive CT vs ASCT (P = .008), or IT vs ASCT (P = .09).

Prébet T, et al. J Clin Oncol. 2011;29:3332-3327.

Clinical Trials: Nursing Implication

- Clinical trials are considered the standard of care for treating MDS patients.
- Nurses play a crucial role in educating patients about the process of clinical trials, expectations and clearing any misconceptions.
- Moffitt Cancer Center Malignant Hematology SLIC project.

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Factors Influencing Treatment Choice Physical and Psychosocial

Physical Factors Influencing Treatment: Nursing Implications

- Age:
  - Goal and selection of therapy.
- Functional status.
- Comorbidities:
  - Selection of therapy.
  - Adjustment of treatment doses.
  - Addressing impact of MDS on comorbidities.

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Psychosocial Factors Influencing Treatment: Nursing Implications

- Patient disease perception.
- Coping with Disease.
- Quality of life.
- Patient support: Family and caregivers
- Logistics of treatment.
- Financial implications for patients.

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Disparity in Perceptions of Disease Characteristics, Treatment Effectiveness, and Factors Influencing Treatment Adherence

- Only 29% of patients reported that MDS was ever "curable" compared with 52% of physicians ($P < .001$).
- Physician, nurses, and patient perceptions of specific MDS therapies were significantly different, especially regarding health-related quality of life during treatment, adverse events, and the impact of treatment on patient activities.
- HCP viewed the potential benefits of active treatment as being significantly greater than did patients.
- Patients perceived the actual treatment experience more positively than physicians or nurses.
- Nurses were less sanguine about the benefit of specific therapies and were more aware of the burdens on patients than physicians, possibly because of more frequent contact with patients undergoing therapy.

Steensma et al, Cancer. 2014 Jun 1;120(11):1670-6.

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Q.U.A.L.M.S.-1 (DRAFT) © Dana-Farber Cancer Institute, Boston, MA

The Quality of Life in Myelodysplasia Scale version 1

- Several non disease specific tools used for QOL assessment in MDS.

- QUALMS-1 is MDS disease specific Quality of Life Scale developed at Dana Farber and being validated externally.

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Nurse Responsibility in Shared Decision Making

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To Summarize

- Maintain a major influence in the patients education.
  - Disease.
  - Treatment.
  - Coping.
- Identifying most appropriate therapy options for patients based on:
  - Disease risk.
  - Efficacy and adverse events of therapies.
  - Physical factors such as comorbidities.
  - Psychosocial factors.
- Educating patients and caregivers about disease expectations.
- Monitoring and addressing adverse events.
- Assessing patient benefit from therapy.

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Question One

1. Which of the following is true about patients and health care providers perception for Myelodysplastic syndromes (MDS):
   a. All doctors and health care providers recognize MDS as cancer but only 50% of patients do.
   b. Physician, nurses, and patient perceptions of specific MDS therapies were similar regarding health-related quality of life during treatment, adverse events, and the impact of treatment on patient activities.
   c. Nurses are more aware of the disease burden on patients than physicians, possibly because of more frequent contact with patients undergoing therapy.

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Question Two

1. Which of the following is false regarding use of Lenalidomide in del 5 q lower risk MDS:

a. Lenalidomide yields 67% transfusion independence rate with median duration of response 2-3 years.

b. Almost 80% of patients will need dose interruption in first 8 weeks but cytopenias on therapy predict the response.

c. Major side effects with Lenalidomide in MDS include myelosuppression, rash, GI upset and diarrhea.

d. Lenalidomide response is observed at 4 weeks in 90% of the patients.

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