Myelodysplastic Syndromes in Older Adults: Treatment Options and Support Strategies

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The planners and speakers have the following financial disclosures.

Name	Role	Disclosure
Ilene Galinsky BSN, MSN, NP-C	Speaker	Honorarium, Advocacy Board – Celgene, Jazz, Novartis and Pfizer
Marlise R. Luskin, MD, MSCE	Speaker	None
Jackie Foster, MPH, RN, OCN	Planner	Stock ownership - Pfizer
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Alice Houk, MPS	Planner	None
Stacy Stickney Ferguson, MSW, LICSW	Planner	None

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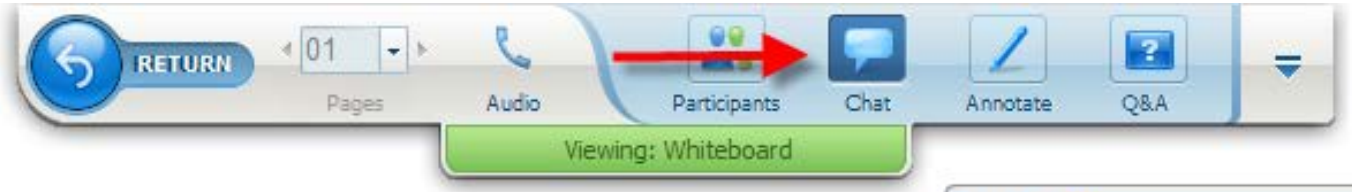
- All other health professionals will be issued a certificate of completion.

Webinar Evaluation

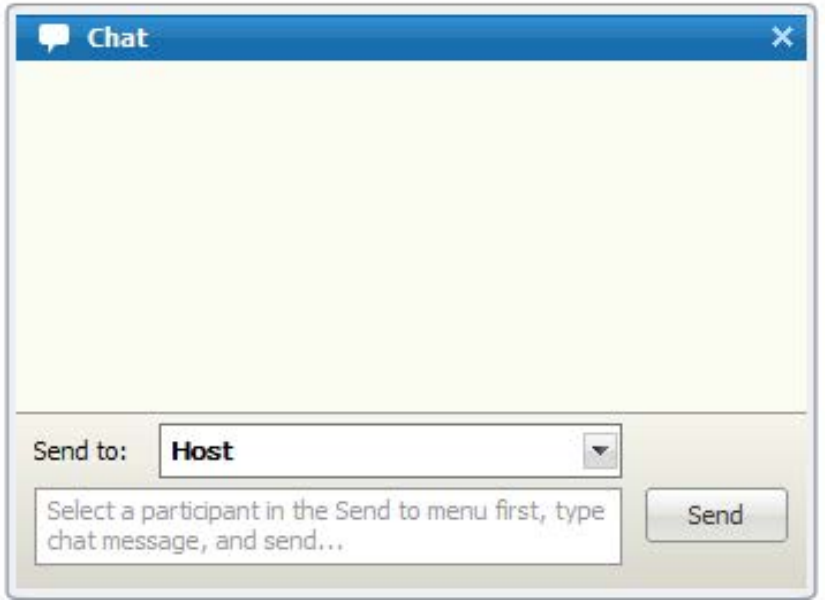
- Attendees will receive an email following the webinar with a link to the evaluation.
- All attendees completing the online program evaluation will receive a statement of continuing education or a certificate of attendance within 30 days.

Attendance and Questions



Utilize the chat feature to:

- Let us know the number of additional attendees listening as a group at your location.
- Ask a question.
  - Access the toolbar at the top of your screen. Click on the  icon.



For questions, support or concerns during the webinar, please email: nmdpeducation@nmdp.org

Learning Objectives

After attending this webinar, participants will be able to:

1. Outline treatment considerations for older patients with myelodysplastic syndromes (MDS) based on comorbidities, disease risk level and patient risk stratification.
2. Discuss evidence-based definitions of fitness to inform treatment decisions.
3. Identify supportive care considerations for older adults undergoing treatment for MDS.
4. Describe strategies for psychosocial support and education for older patients and their families.

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Myelodysplastic Syndromes in Older Adults: Treatment Options and Support Strategies

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Myelodysplastic Syndromes (MDS)

- Group of chronic, myeloid-lineage hematologic neoplasms characterized by ineffective, clonal hematopoiesis.

- **Diagnosis:** Requires bone marrow biopsy with karyotype
  1) Cytopenias (Hg < 10 g/dL, platelets <100, ANC < 1.8)
  2) An MDS-defining abnormality:
     -Dysplasia (≥10% in 1 or more lineage)
     -MDS-defining cytogenetic abnormality
     -Excess blasts: BM (≥5% to <20%) or PB (≥ 1% to <20%)

Arber et al. Blood 2016; 127: 2391-401

Myelodysplastic Syndromes (MDS)

- Hallmarks of the disease ("the ABCs")
  - Risk of progression to **A**ML.
  - **B**one marrow failure (progressive cytopenias).
  - **C**lonality indicates **c**ancer (almost all have abnormal karyotype and/or molecular gene mutation).
- Widely varied presentation and risk of progression.
- Some patients are asymptomatic, others experience substantial symptom burden.

Arber et al. Blood 2016; 127: 2391-401; Papaemmanuil et al. Blood 2013; 122:3616-27
Haferlach et al. Leukemia 2014; 28: 241-7

MDS is a Disease of Older Adults

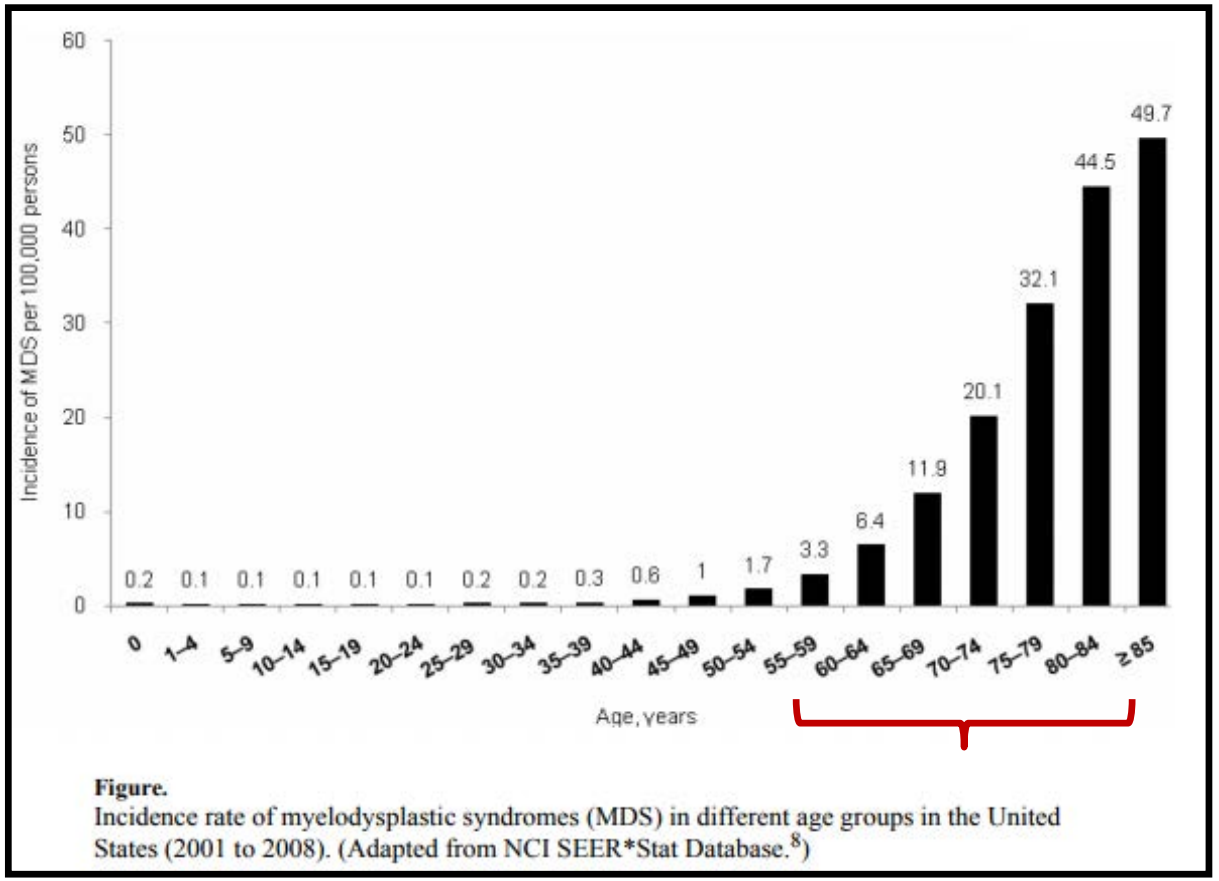


Figure.
Incidence rate of myelodysplastic syndromes (MDS) in different age groups in the United States (2001 to 2008). (Adapted from NCI SEER*Stat Database.[8])

- Median age at MDS diagnosis: 76 years
- Cancer registries: 10,000 new cases per year in US.
- MDS underreported to cancer registries – may be 3-4x higher.
- Cytopenias in older adults often incompletely evaluated.

Ma X. et al. Cancer 2007; 109: 1536-42; Goldberg et al. J Clin Oncol 2016; 28: 2847-52; Cogle et al. Blood: 2011: 117: 7121-5; Cogle et al. Leuk res 2014; 38:71-5

MDS is a Disease of Older Adults

- **Age is primary risk factor for developing MDS.**
- **Over time, hematopoietic stem cells accumulate mutations.**
  - Clonal hematopoiesis ("CHIP") → 10% of adults ≥ 70 years.
  - Accumulation of additional mutations → progression to frank myeloid disorder (MDS or AML).
- **Other risk factors:**
  - Modest association with smoking.
  - Exposure to chemotherapy, radiation, toxins.

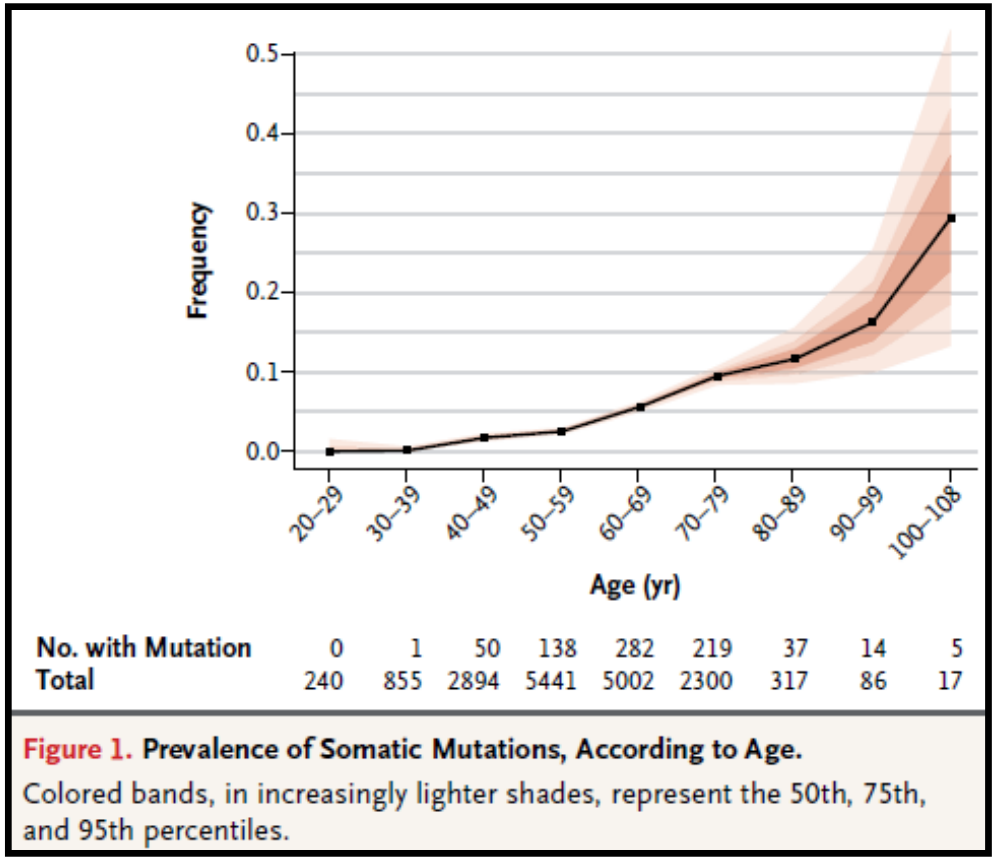


Figure 1. Prevalence of Somatic Mutations, According to Age.
Colored bands, in increasingly lighter shades, represent the 50th, 75th, and 95th percentiles.

Ma X et al. Cancer 2007; 109: 1536-42; Ugai et al. Br J Haematol 2017; 178: 747-55; Jaiswal et al. N Eng J Med 2014; 371: 2488-98

At Diagnosis:
Assess Disease AND Patient

- Prognosis and treatment decisions in MDS guided by combination of disease and patient characteristics.
- Disease: Assess MDS risk.

  Question: *How soon is patient expected to develop progressive cytopenias and/or progression to AML?*
- Patient: Assess degree of comorbidity and frailty.

  Question: *How likely is a patient to be able to tolerate treatment?*
- Integrate disease risk, patient characteristics, and patient preferences to determine treatment recommendation.

MDS Disease Risk Scores

- **Predict natural history (OS and risk of progression to AML).**
- **Integrate individual disease features associated with risk:**
  - Number and degree of cytopenias.
  - Presence and degree of excess blasts.
  - Karyotype (cytogenetic risk).
- **International Prognostic Scoring System (IPSS) and Revised IPSS-R most commonly used.**
  - Other scoring systems include additional factors: performance status, age, transfusion-dependence, pathologic classification (MD Anderson Risk model, WHO prognostic scoring system)

Greenberg et al. Blood 1997; 89: 2079-88; Greenberg et al. Blood 2012; 120: 2454-65;
Kantarjian et al. Cancer 2008; 113: 1351; Della Porta et al. Leukemia 2015; 29: 1502-13

IPSS

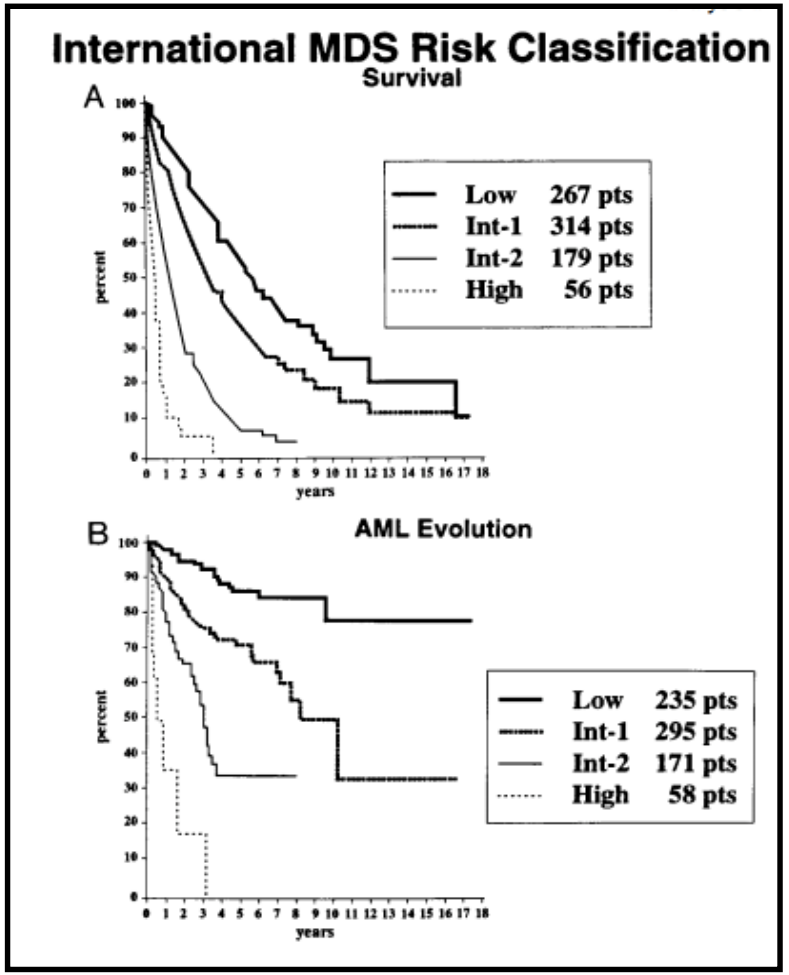
Table 1. International Prognostic Scoring System (IPSS): prognostic variables

	0	0.5	1.0	1.5	2.0
Marrow blasts, %	<5	5-10	—	11-20	21-30
Karotype	Good	Intermediate	Poor		
Cytopenias	0/1	2/3	—	—	—

— indicates not applicable; Good = normal, -y, del(5q), del(20q); Poor = complex (≥3 abnormalities) or chromosome 7 anomalies; and Intermediate = any other abnormalities.

Table 2. International Prognostic Scoring System (IPSS): clinical outcomes

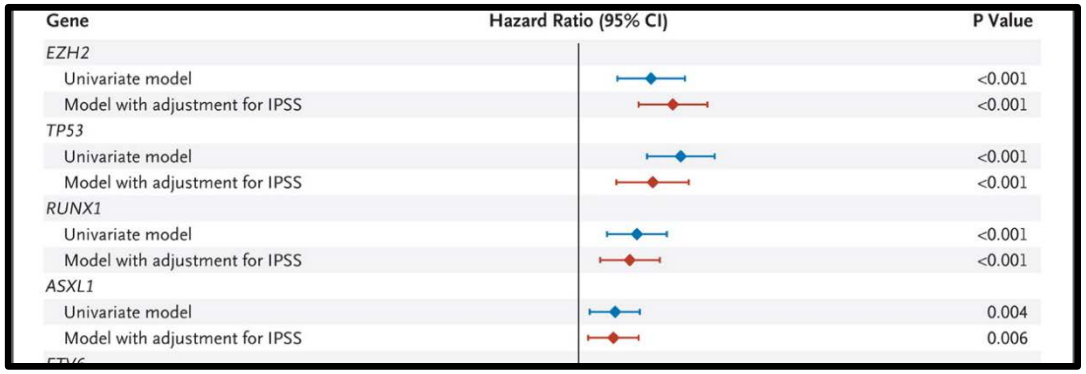
Risk group	Total score	Median survival, y	Time for 25% to progress to AML, y
Low	0	5.7	9.4
Intermediate-1	0.5-1.0	3.5	3.3
Intermediate-2	1.5-2.0	1.2	1.1
High	≥ 2.5	0.4	0.2

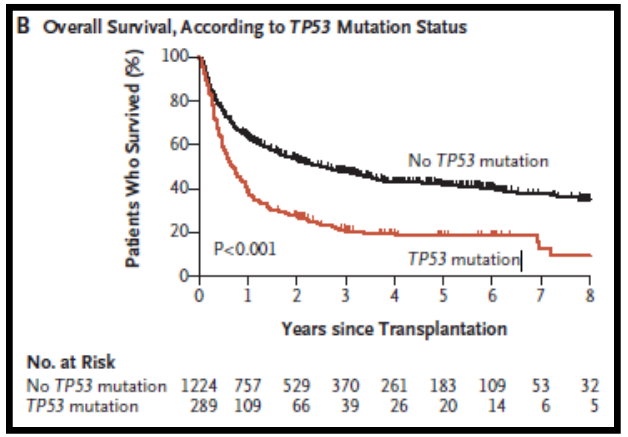


Greenberg et al. Blood 1997; 89: 2079-88

Molecular Genetics and MDS Risk

- Molecular gene level alterations increasingly relevant for understanding disease biology AND for prognostication.
- Specific mutations, and mutation number associated with outcomes.
- No consensus integrated model yet.





Bejar et al. N Eng J Med 2011; 364: 2496-506; Bejar et al J Clin Oncol 2012; 30: 3376-82;
Papaemmaneuil et al. Blood 2013; 122: 3616-27; Lindsley et al. N Eng J Med 2017; 376: 536-47

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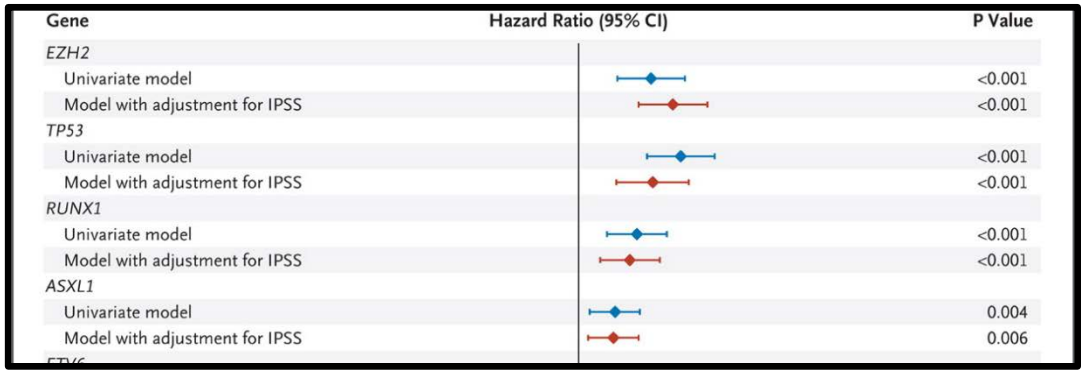

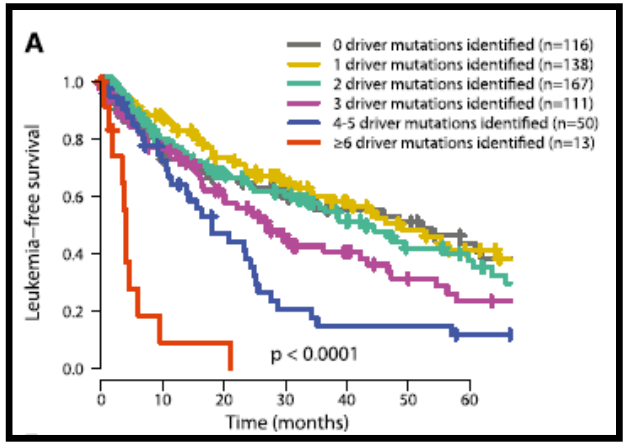

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Assessing the Patient

- Comorbidity
  - MDS-CI; HCT-CI; Charlson Comorbidity Index
- Frailty
- Performance status

Comorbidity Is Common in MDS Patients

- MDS patients frequently have comorbidities.
- A 2010 analysis by Goldberg *et al.* reported that MDS patients have more comorbidity than age-matched Medicare population.
  - Cardiac events (73.2 vs 54.5%, *P* <.01)
  - Dyspnea (49.4 vs 28.5%, *P* <.01)
  - Diabetes (40.0 vs 33.1%, *P* <.01)
  - Sepsis (22.5 vs 6.1%, *P* <.01)
  - Hepatic conditions (0.8 vs 0.2%, *P* <.01)

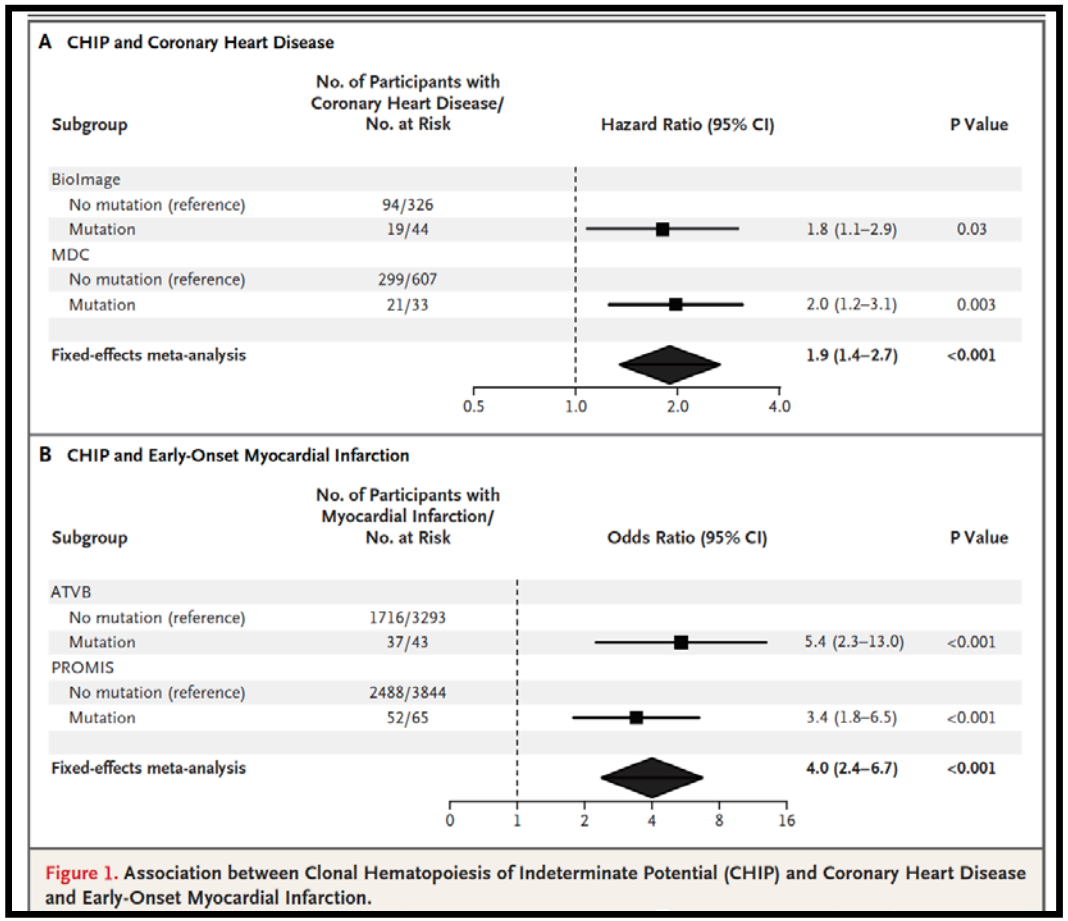
Goldberg et al. J Clin Oncol 2010; 28: 2847-52; Abel and Buckstein. Am Soc Clin Oncol Educ Book; 2016; 35:e337-44; Wang et al. Leuk Res 2009; 33:1594-8; Bammer et al. J Geriatric Oncol 2014;5:299-306;

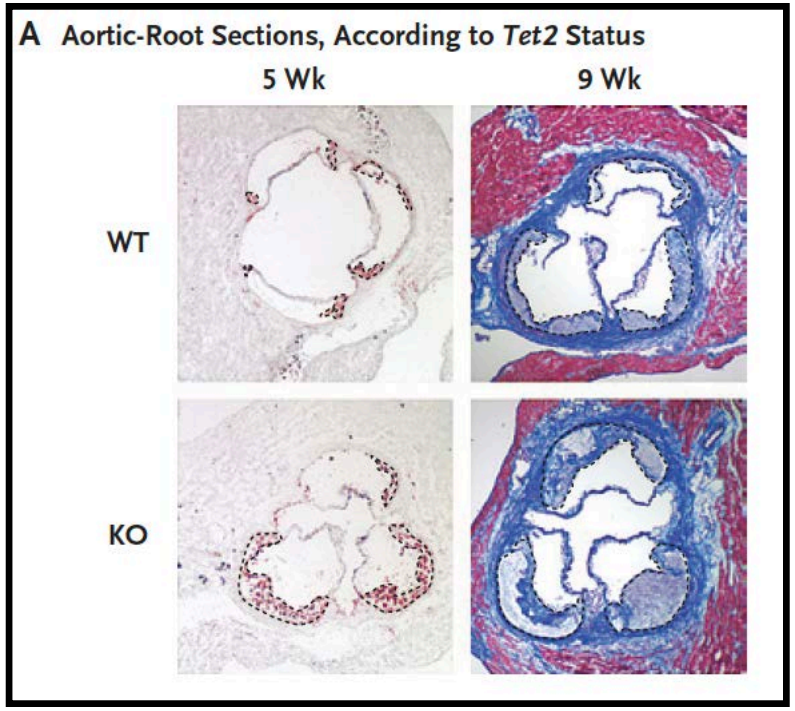
Comorbidity Is Common in MDS Patients

- **Some comorbidities are independently related to age.**
  - Increased contact with health care system → increased diagnoses?
- **Other comorbidities may be consequent to cytopenias**
  - Neutropenia → infections
  - Anemia → dyspnea, cardiovascular events
- **Researchers are now defining a pathophysiologic connection between clonal hematopoiesis and cardiovascular disease.**
  - In case control analysis, clonal hematopoiesis is associated with CAD and early MI.
  - In mouse models, *TET2* mutations associated with aberrant macrophage function and accelerated atherosclerosis.

Jaiswal et al. N Eng J Med 2017; 377: 111-21; Fuster et al. Science 2017; 355: 842-7

Comorbidity Is Common in MDS Patients





Jaiswal et al. N Eng J Med 2017; 377: 111-21; Fuster et al. Science 2017; 355: 842-7

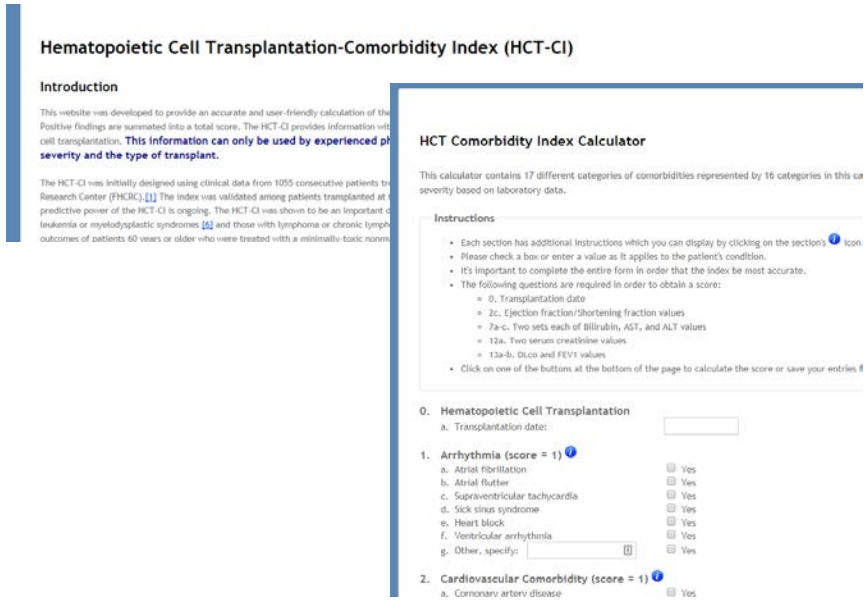
Comorbidity Is Associated with Prognosis in MDS Patients

- Increased comorbidity shown to have a negative impact on OS in MDS patients, *after* accounting for disease risk.
- Integration of comorbidity assessment into patient evaluation can improve prognostic accuracy.
- Two scores:
  - **HCT-CI** (Widely known, developed for transplant but validated in MDS)
  - **MDS-CI** (myelodysplastic syndrome-specific comorbidity index). Enhanced risk stratification in patients stratified by WPSS disease risk index.

Della Porta et al. Haematologica 2011; 96:441-9; Naqvi et al. J Clin Oncol 2011; 29:2240-6;
Breccia M et al. Leuk Res 2011; 35:159-62; Daver et al. Am J Hematol 2014; 89: 509-16;
Balleari et al. Leuk Res 2015; 39: 846-52; Van Spronsen et al. Eur J Cancer 2014; 50: 3198-205

Quantifying Comorbidity: HCT-CI

http://www.hctci.org/Home/Calculator



Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI)

Introduction

This website was developed to provide an accurate and user-friendly calculation of the
Positive findings are summated into a total score. The HCT-CI provides information wit
cell transplantation. **This information can only be used by experienced ph**
severity and the type of transplant.

The HCT-CI was initially designed using clinical data from 1055 consecutive patients tr
Research Center (FHCRC).[1] The index was validated among patients transplanted at
predictive power of the HCT-CI is ongoing. The HCT-CI was shown to be an important
leukemia or myelodysplastic syndromes [6] and those with lymphoma or chronic lymph
outcomes of patients 60 years or older who were treated with a minimally-toxic nonm

HCT Comorbidity Index Calculator

This calculator contains 17 different categories of comorbidities represented by 16 categories in this ca
severity based on laboratory data.

Instructions

- Each section has additional instructions which you can display by clicking on the section's icon
- Please check a box or enter a value as it applies to the patient's condition.
- It's important to complete the entire form in order that the index be most accurate.
- The following questions are required in order to obtain a score:
  - 0. Transplantation date
  - 2c. Ejection fraction/Shortening fraction values
  - 7a-c. Two sets each of Bilirubin, AST, and ALT values
  - 12a. Two serum creatinine values
  - 13a-b. DLco and FEV1 values
- Click on one of the buttons at the bottom of the page to calculate the score or save your entries f

0. Hematopoietic Cell Transplantation
   a. Transplantation date:
1. Arrhythmia (score = 1)
   a. Atrial fibrillation — Yes
   b. Atrial flutter — Yes
   c. Supraventricular tachycardia — Yes
   d. Sick sinus syndrome — Yes
   e. Heart block — Yes
   f. Ventricular arrhythmia — Yes
   g. Other, specify: — Yes
2. Cardiovascular Comorbidity (score = 1)
   a. Coronary artery disease — Yes

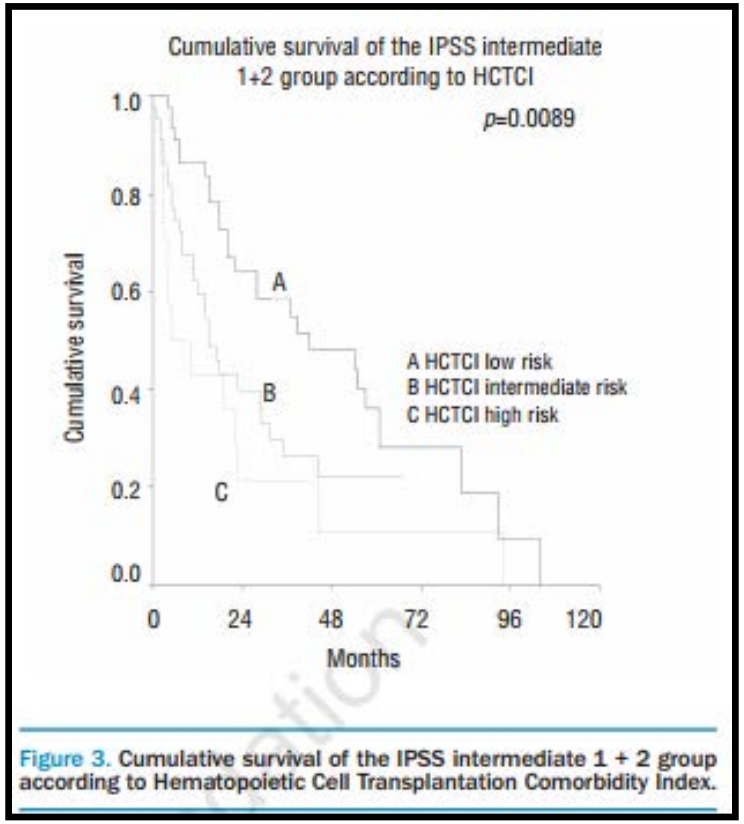


Figure 3. Cumulative survival of the IPSS intermediate 1 + 2 group according to Hematopoietic Cell Transplantation Comorbidity Index.

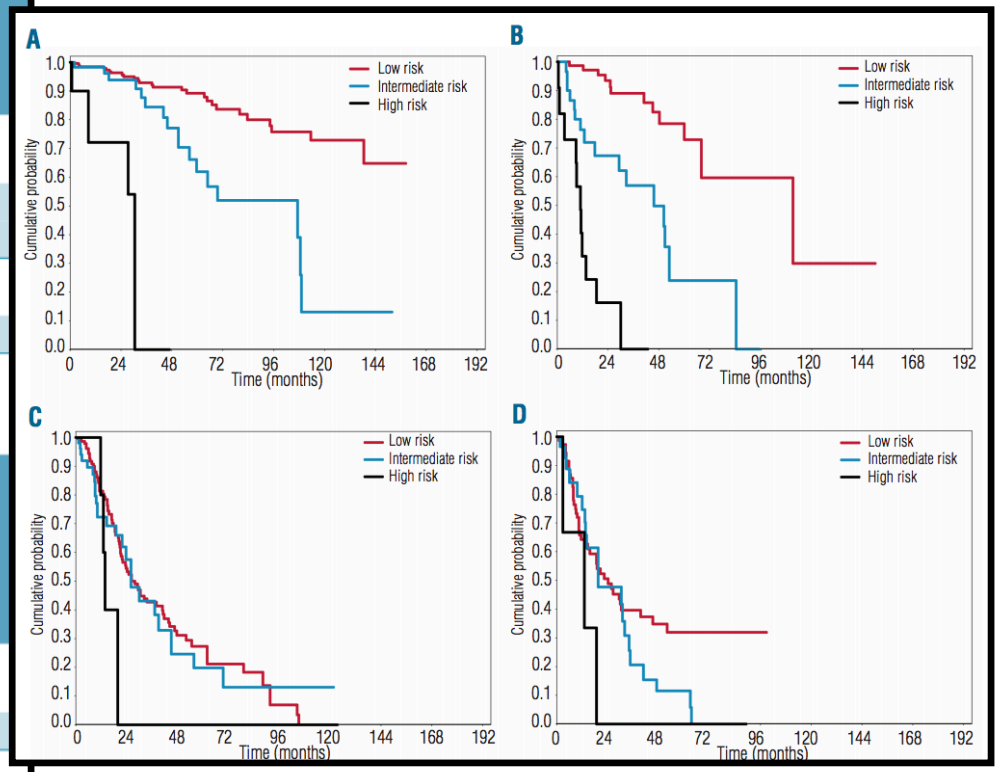
Sorror et al. Blood 2005; 106: 2912-9; Zipperer et al. Haematologica 2009; 94: 729-32

Quantifying Comorbidity: MDS-CI

Comorbidity	HR obtained through a multivariable Cox's survival analysis with NLD as an outcome	Variable weighted score (to be taken into account if the specific comorbidity is present)
Cardiac disease	3.57 (P<0.001)	2
Moderate-to-severe hepatic disease	2.55 (P=0.01)	1
Severe pulmonary disease	2.44 (P=0.005)	1
Renal disease	1.97 (P=0.04)	1
Solid tumor	2.61 (P<0.001)	1

MDS-CI risk	Sum of individual variable scores	Proportion of patients in the learning cohort belonging to the risk group (%)
Low risk	0	546/840 (65%)
Intermediate risk	1-2	244/840 (29%)
High risk	>2	50/840 (6%)

NLD: non-leukemic death.



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Assessing the Patient

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- Frailty
- Performance status

Assessing Frailty in MDS patients

- Frailty is a state of physiologic decline that results in a "state of high vulnerability to adverse health outcomes" in the face of medical stressor events.
- Frailty is common in older adults with cancer.
- Associated with poor tolerability of treatment and shorter survival.

Fried et al. J Gerontol A Biol Sci Med Sci 2005; 59 255-63; Handforth et al. Ann Oncol 2015; 26: 1091-201
Fega et al. J Geriatr Oncol 2015;6:299-98; Buckstein et al. Br J Haematol 2016; 174: 88-101

Assessing Frailty in MDS patients

- Frailty has been shown to be prognostic in MDS patients.
- Buckstein *et al*. assessed frailty in 445 patients using the Clinical Frailty Scale (CFS) and multiple direct physical measures.
- Found that frailty only modestly correlated with comorbidity, performance status, and IPSS-R but was associated with survival on multivariate analysis (HR 2.7).

Fried et al. J Gerontol A Biol Sci Med Sci 2005; 59 255-63; Handforth et al. Ann Oncol 2015; 26: 1091-201
Fega et al. J Geriatr Oncol 2015;6:299-98; Buckstein et al. Br J Haematol 2016; 174: 88-101

Assessing Frailty: CFS

Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Rockwood et al. CMAJ 2005; 173: 489-95.

Approach to Treating MDS

- **Supportive care**
  - **Goal:** Improve quality of life.
  - **Who:** All patients with symptoms, regardless of disease risk.

- **Disease modifying treatment**
  - **Goal:** Lengthen life, possibly cure
  - **Who:** Consider for fit patients with higher risk disease.

Supportive Care



- **Anemia – erythropoietin stimulating agents (ESAs) and transfusions**
  - Consider ESA if low EPO level and transfusion burden.
  - Iron overload can be a complication of transfusions. Benefit of iron chelation is not certain; consider in those with heavy transfusion burden and long expected survival.

Hellstrom-Lindberg et al. Br J Haematol 2003; 120:1037-46; Steensma et al. Best Pract Clin Haematol 2013; 26: 431-44. Lyons et al. Leuk Res 2017; 56: 88-95

Supportive Care



- **Thrombocytopenia**
  - Transfusion support
  - Thrombopoietin agonists are under study.
- **Neutropenia**
  - Appropriate antibiotics as necessary.
  - No benefit to routine GCSF prophylaxis.

Giagounidis et al Cancer 2014; 120: 1838-46; Kantarjian et al. J Clin Oncol 2010; 28: 437-44; Fenaux et al. Br J Haematol 2017; 178: 906-13

Impaired QOL Independent of Cytopenias

- Increasing recognition that MDS impairs QOL independent of symptoms attributable to cytopenias.
- Fatigue is particularly troublesome, independent of symptomatic anemia.
  - Other factors (cytokines, sleep disturbance) may be causative.
- Efficace *et al.* recently showed that self-reported fatigue in high risk MDS was associated inferior OS independent of IPSS classification.

Efficace *et al.* Br J Haematol 2015; 168: 361-70; Jansen *et al.* Br J Haematol 2003; 121: 270-4; Steensma *et al.* Leuk Res 2008; 32: 691-8; Efficace *et al.* Lancet Oncol 2015; 16: 1506-14

Quality of Life in Myelodysplasia Scale: QUALMS

- Need more research to understand, measure, and treat impaired QOL in MDS patients.
- QULAMS is a 38-item MDS-specific assessment tool developed for patients with MDS.
- Being incorporated into a large, prospective observational study of the natural history of MDS being conducted by the NHLBI (NCT02775383).
- Currently a research tool but may become a clinical tool.

Abel et al. Haematologica 2016; 101: 781-8

Disease Modifying Therapy

- **Consider in patients with high MDS risk**
  - High risk by disease risk score

- **Disease modifying treatment arsenal**
  - Hypomethylating agents: decitabine, azacitidine
  - Lenalidomide (especially del 5q)
  - Clinical trial – whenever possible!
  - Consider allogeneic stem cell transplant referral

Hypomethylating Agents

- Multi-center AZA-001 study.
- Aza versus conventional care
  - Physician choice: BSC, low-dose ara-c, or chemotherapy.
- **Responses:**
  - Heme improvement (49%),
  - CR (18%)
- **Median OS** improved from 15 to 24 months.

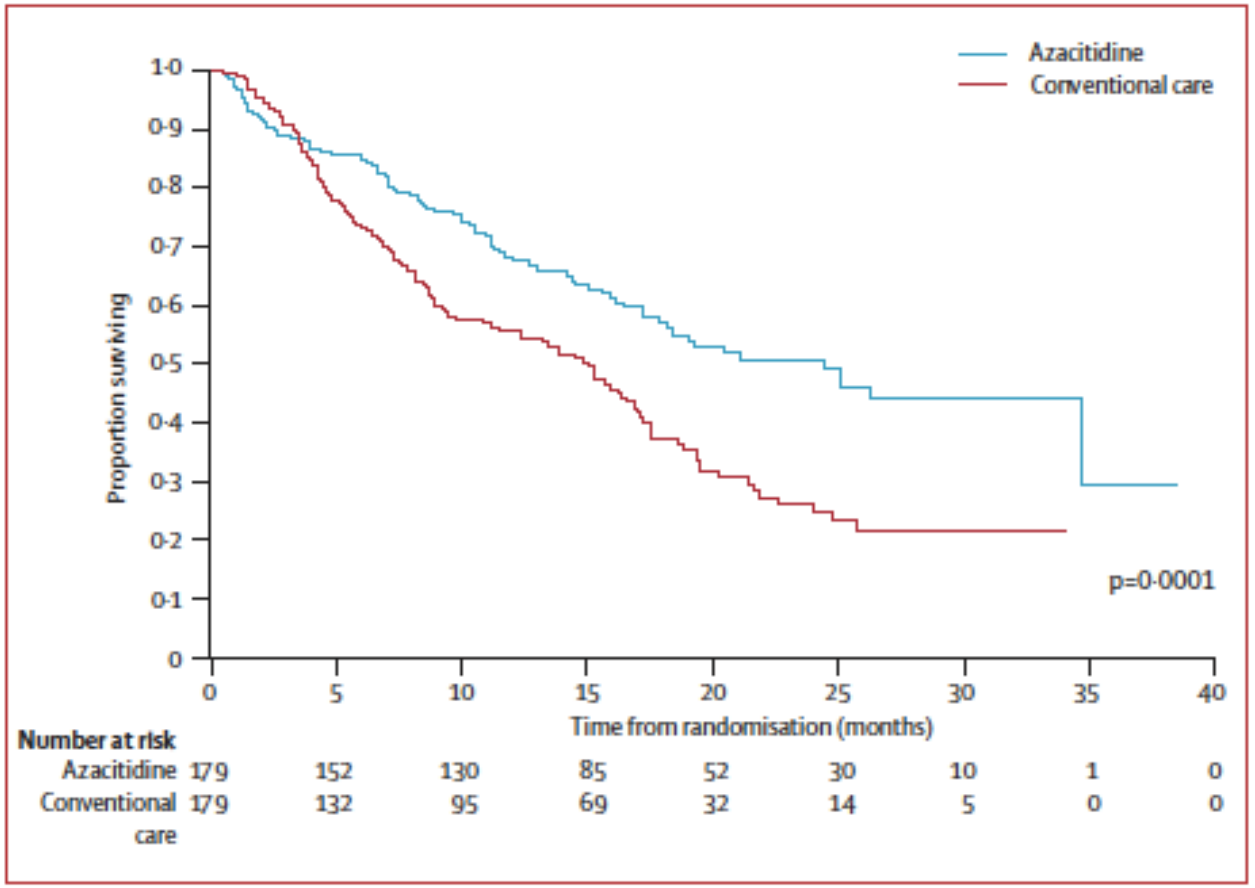


Figure 3: Overall survival

Fenaux et al. Lancet Oncol. 2009; 10: 223-32

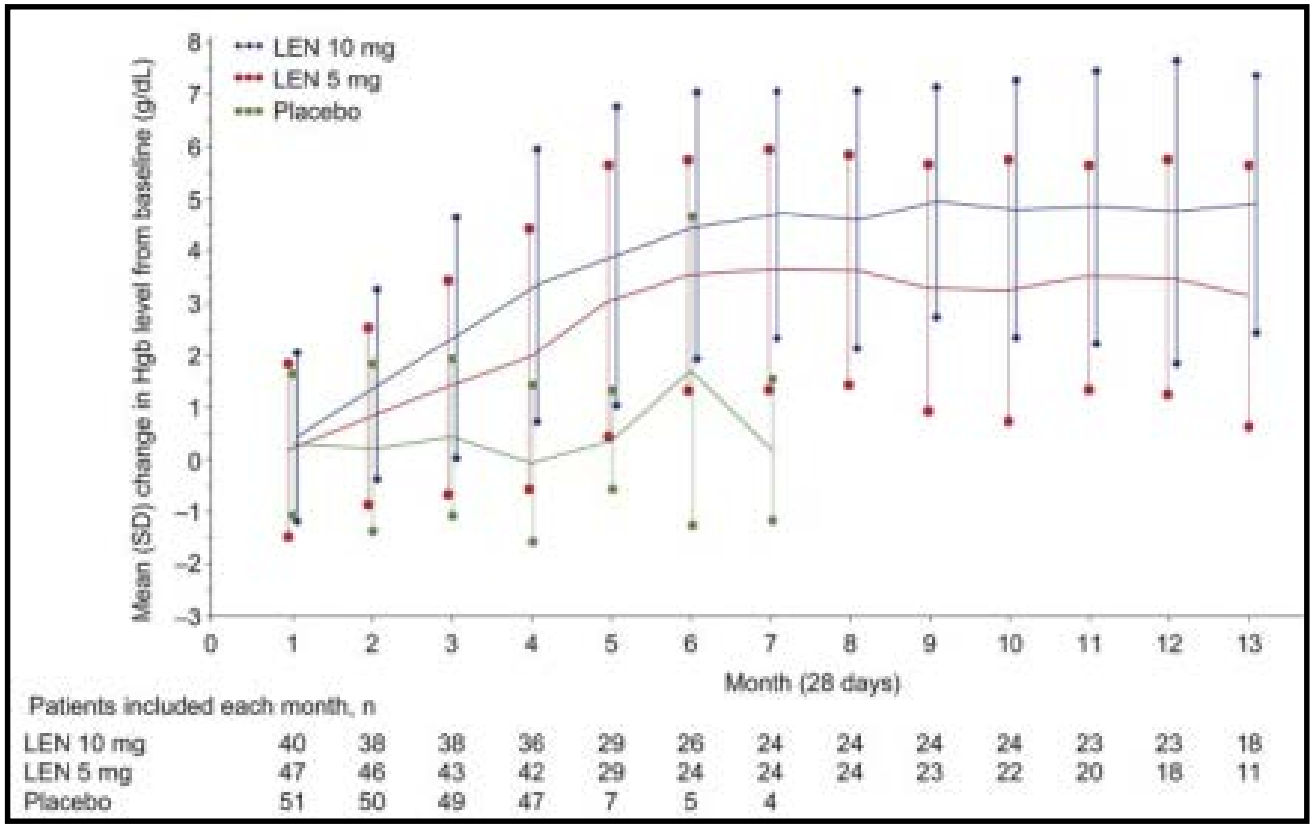
Hypomethylating Agents

- Randomized trial of decitabine versus best supportive care showed similar activity to azcitidine (survival benefit not confirmed).
- SEER analysis suggests equivalent efficacy between azaciditine and decitabine.
- Whether real-world benefit of HMAs match clinical trial data is not certain.
- Generally well-tolerated; main complication is cytopenias.
- Must be continued indefinitely until progression to sustain any achieved benefit.
- Benefit demonstrated even among patients over age 75. Age alone should not be an exclusion.

Lubbert et al. J Clin Oncol 2011; 29:1987-96; Zeidan et al. Br J Haemtaol 2016; 175: 829-40;
Zeidan et al. Leuk Lymphoma 2017; 58: 982-85; Seymour et al. Crit Rev Oncol Hematol 2010; 76: 218-27

Lenalidomide

- del(5q) → ~70% heme response
  - Median Hg rise 5.4 g/dL
  - Median response duration >2 years.
- Responders → decreased risk of death and AML progression
- Cytogenetic responses.



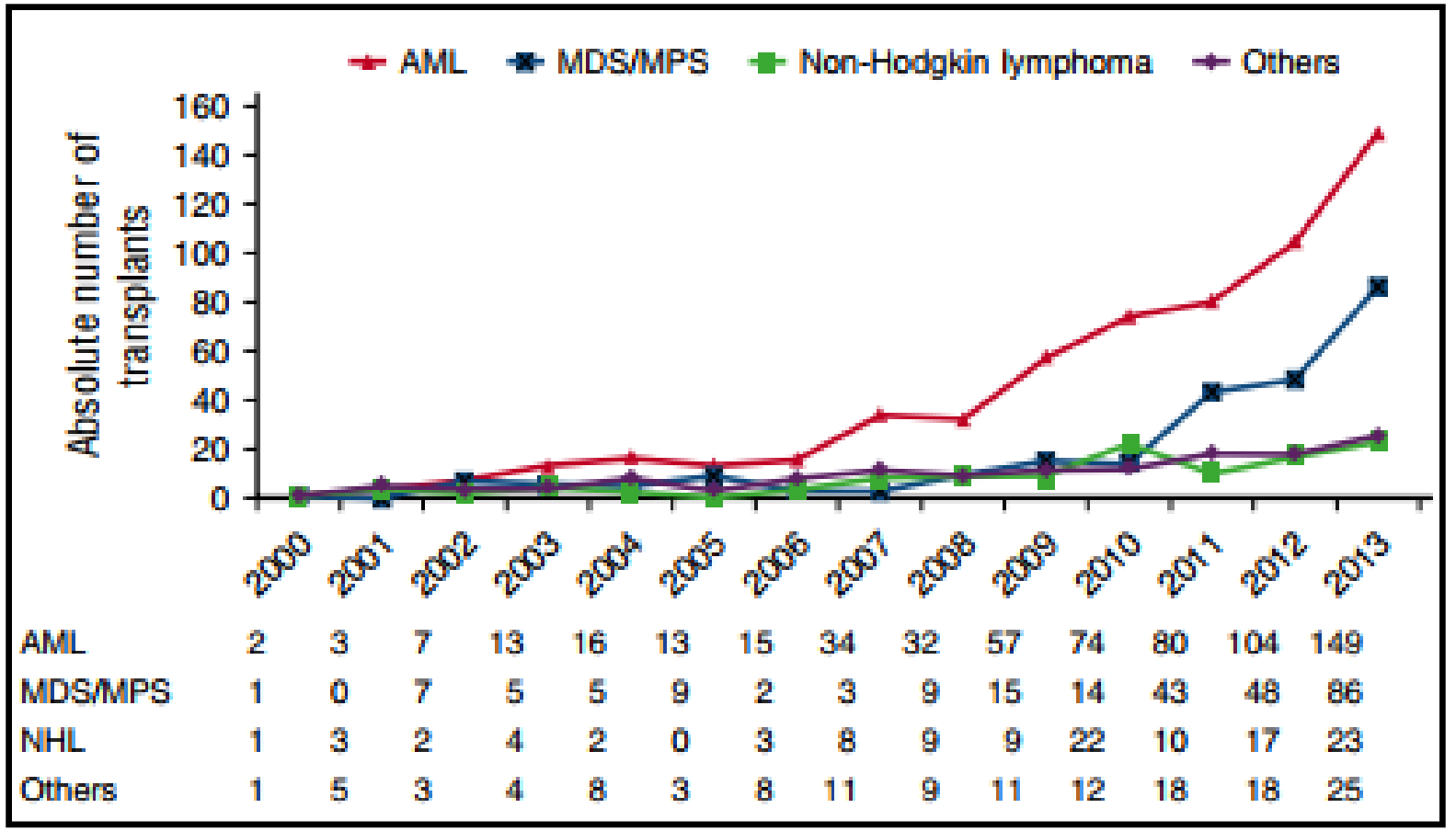
List et al. N Engl J Med. 2006; 355: 1456-65; Fenaux et al. Blood. 2011; 118:3765-76

Allogeneic SCT

- Allogenic SCT is only curative treatment modality for MDS.
- Historically, myeloablative conditioning regimens precluded transplant in older adults.
- Development of reduced intensity conditioning (RIC) approaches has made HCT available to fit older adults up to age 75 years.
- HSCT increasingly being used for treatment of older adults with MDS.

Sorror et al. JAMA 2011; 306: 1874-83; Laport GG et al. Biol Blood Marrow Transplant 2008; 14: 246-55; Kroger. Blood 2012; 119: 5632-9; Deeg et al. J Natl Compr Canc Netw 2013; 11: 1227-33;

Allogeneic SCT



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
AML	2	3	7	13	16	13	15	34	32	57	74	80	104	149
MDS/MPS	1	0	7	5	5	9	2	3	9	15	14	43	48	86
NHL	1	3	2	4	2	0	3	8	9	9	22	10	17	23
Others	1	5	3	4	8	3	8	11	9	11	12	18	18	25

Muffly et al. Blood 2017; 130: 1156-64

Allogeneic SCT

- Allogeneic HSCT indicated for higher-risk MDS. Demonstrated in a Markov model using IPSS to assess risk.
- Increasingly clearly that age itself should not be barrier to transplant as it has not been correlated with outcomes.
- HCT-CI comorbidity score predicts survival in older patients undergoing RIC transplants.
- Recommend that all fit patients up to age 75 years with higher-risk MDS be referred for formal allogeneic HSCT consultation.

Cutler et al. Blood 2004; 104: 579-85; Koreth et al. J Clin Oncol 2013; 31: 2662-70; Sorror et al. JAMA 2011; 306: 1874-83; Abel and Koreth et al. Curr Opin Hematol 2013; 20: 150-6; McClune et al. J Clin Oncol 2010; 28: 1878-87; Koreth et al. Biol Blood Marrow Transplant 2010; 16: 792-800

Putting It All Together: Approach to MDS Treatment in Older Adults

- **Characterize MDS disease risk**
  - Use IPSS, IPSS-R, or other disease risk stratification tool (based on institutional preference).
  - Consider obtaining molecular data to complement standard risk stratification.
- **Assess patient fitness and comorbidity**
  - Comorbidity, frailty assessment, performance status.
  - Consider referral for comprehensive geriatric assessment (CGA).
- **Assess patient psycho-social factors and preferences**
  - Consider social work assessment.

Luskin and Abel. J Geriatr Oncol 2017 [Epub Ahead of Print]

Putting It All Together: Approach to MDS Treatment in Older Adults

Table. Approach to the Older Patient with MDS

Patient Status*	MDS Disease Risk%	Treatment Approach
Robust	Lower	Supportive care
	Higher	Supportive care + hypomethylating agent + HSCT evaluation if age <70-75 years
Pre-Frail	Lower	Supportive care +/- CGA
	Higher	Supportive care +/- hypomethylating agent therapy and HSCT evaluation if age <70-75 years +/- CGA
Frail	Lower	Supportive care + CGA
	Higher	Supportive care + CGA *(consider disease modifying intervention if patient status improves)*

*Frailty screening using instruments such as CFS (Clinical Frailty Scale)

%Disease assessment as per one of the following: IPSS, IPSS-R, WPSS

Luskin and Abel. J Geriatr Oncol 2017 [Epub Ahead of Print]

Clinical Trials for Older Adults Needed

- Recent analysis of the NIH clinical trial registry found that among clinical trials for hematologic malignancies, only 5% focused on elderly or unfit patients, 27% of trials excluded patients by age alone, and exclusions for organ function (51%) and performance status (16%) were also common.
- Clinical trials that enroll older adults, including adults with some frailty and comorbidity needed.
- Endpoints of importance to older adults (including QOL) should be considered.

Hamaker et al. Oncologist 2014; 19: 1069-75

Key References

- Abel GA and Klepin HD. Frailty and the management of hematologic malignancies. *Blood* 2018; 131: 515-524.
- Luskin MR and Abel GA. Management of older adults with myelodysplastic syndromes (MDS). *J Geriatr Oncol* 2017 [Epub] doi: 10.1016/j.jgo.2017.12.002.
- Abel GA, Buckstein R. Integrating Frailty, Comorbidity, and Quality of Life in the Management of Myelodysplastic Syndromes. *Am Soc Clin Oncol Educ Book* 2016; 35: e337-44.
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- Klepin HD, Rao AV, and Pardee TS. Acute myeloid leukemia and myelodysplastic syndromes in older adults. *J Clin Oncol* 2014; 32: 2541-52.

Thank You!

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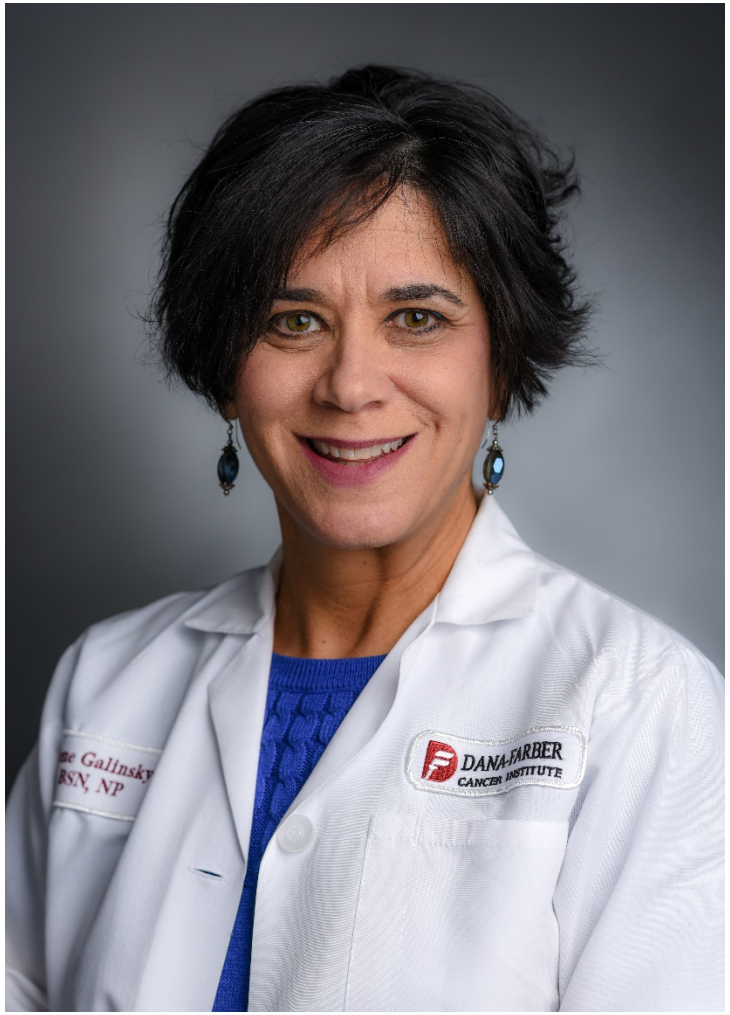

Common Presenting Symptoms: MDS

- Many patients are asymptomatic
  - diagnosed on routine screening
- Others present with vague symptoms
- Most common presenting symptoms are associated with one or more cytopenias
  - Fatigue, shortness of breath, palpitations—anemia
  - Fever, recurrent or prolonged infections—neutropenia
  - Bruising, petechiae, or bleeding—thrombocytopenia

Required Testing

- History and Physical
- CBC
- Reticulocyte count
- Bone Marrow aspirate and biopsy – chromosomes, Flow cytometry, Iron Stain
- Serum Erythropoietin
- Folate, serum B12,Serum ferritin, iron, Total Iron Binding capacity
- Transfusion History
- TSH
- Copper level, HIV, HLA typing

Source: NCCN Guidelines (2018 version)

Who the patient is matters as much as the biology of the disease

- AGE
- Physical Status
- Quality of Life

Mr. Crimson

- 75 year old gentleman – very physically active
- PS = 0
- Routine Physical – low platelet count slightly anemic
- Increased Creatinine
- Fluid Retention

Clinical Diagnostics

- WBC: 13.4
- HGB/HCT: 13/39.7 GM/DL
- PLTS: 88 k/ul
- BLASTS 0%
- POLY: 51%
- RBC Morphology: slight anisocytosis and slight poiklocytosis
- Lytes and LFT’s WNL’s
- Epo Level WNL’s

Bone Marrow Results

- FLOW CYTOMETRY: population of immature cells (6% of total events) that is positive for CD45(dim), CD34, HLA-DR, myeloid markers CD13, CD33 (dim), and CD117, monocytic marker CD11b
- ASPIRATE/BIOPSY: Approximately 10% of the cellularity are blast forms. Small clusters of CD34-positive blast forms.
- CHOROMSOME ANALYSIS: KARYOTYPE: 46xy

1997 International Prognostic Scoring System (IPSS) - still used for many clinical trials and for transplant

	Score				
Prognostic Variable	**0**	**0.5**	**1.0**	**1.5**	**2.0**
Marrow blasts (%)	<5%	5-10%	--	11-20%	21-30%***
Karyotype class*	Good	Intermediate	Poor	--	--
# of cytopenias**	0 or 1	2 or 3	--	--	--

***Karyotype risk groups**: **Good** = normal, -Y, del(5q) alone, del(20q) alone; **Poor** = chromosome 7 abnormalities or complex; **Intermediate** = other karyotypes

****** **Qualifying Cytopenias**: Hb < 10 g/dL, ANC <1800/µL, platelets <100,000/µL

*** 20% or more blasts now (WHO) considered **AML**, but was still MDS (FAB) at the time this system was developed

Score sum	IPSS Risk Category	Median survival for over age 60 group (years)	Time until 25% get AML (years)
0	**Low**	**5.7**	9.4
0.5-1.0	**Int-1**	**3.5**	3.3
1.5-2.0	**Int-2**	**1.2**	1.1
>=2.5	**High**	**0.4**	0.2

Source: Greenberg P et al *Blood* 1997; 89:2079-2089 (correction 1998; 91:1100)

IPSS-R calculation

Parameter	Categories and Associated Scores				
Cytogenetic risk group	Very good	Good	Intermediate	Poor	Very Poor
	0	1	2	3	4
Marrow blast proportion	≤2%	>2 - <5%	5 - 10%	>10%	
	0	1	2	3	
Hemoglobin	≥10 g/dL	8 - <10 g/dL	<8 g/dL		
	0	1	1.5		
Absolute neutrophil count	≥0.8 x 10^9/L	<0.8 x 10^9/L			
	0	0.5			
Platelet count	≥100 x 10^9/L	50 - 100 x 10^9/L	<50 x 10^9/L		
	Possible range of summed scores: 0-10				

Source: Greenberg P et al *Blood* 2012 Sep 20;120(12):2454-65. Epub 2012 Jun 27

What is Mr. Crimsons' risk score?

- Next Steps:
  - Discussion with patient and family members
  - Education - disease and "treatment"; supportive tools
  - Appropriate consults after complete assessment – remember to look at the whole person

- Treatment options?
  - Supportive Care
  - Chemotherapy
  - Hypomethylating agent

HYPOMETHYLATING AGENTS

AZACITIDINE

- Sub q administration or IV
- 7 consecutives days or 5 days off x 2 administer +2= 7 days
- Mildly emetic
- Can be myelosuppressive
- 28 day cycles
- May take up to 3 cycles to see a response
- Supportive care

DECITABINE

- IV bolus
- 5 consecutive days or 10 days for higher risk/AML
- Mildly emetic
- Can be myelosuppressive
- 28 day cycles
- May take up to 3 cycles to see a response
- Supportive care

TOOLS FOR MYELOSUPPRESSION MANAGEMENT

- Consider blood counts with possible transfusions 1-2 times per week (at least for the first two cycles) – use institute standard for transfusions
- Educate your patients on neutropenic precautions
- Give clear instructions of what they need to look for- temperature >=100.5; bleeding or bruising; blood in urine or stool; chills; SOB; dizziness
- Contact information for 24/7 access to care team
- Consider growth factors or prophylactic anti microbials per institutional guidelines

Tools for Management of Fatigue

- Individualized assessment
  - Sleep, nutrition, depression, medications, activity, comorbidities
- Individualized Interventions
  - Balance between activity enhancement and energy conservation
  - Psychosocial interventions
  - Nutrition consultation
  - Sleep evaluation
  - Pharmacologic interventions
    - Psychostimulants, sleep medications

Tools for Managing Common Gastrointestinal Toxicities

Nausea and Vomiting

- Ensure baseline and ongoing renal and hepatic function assays
- Pre-medicate for anticipated nausea/vomiting
- Encourage adequate hydration- electrolyte
- Dietary measures/consultation
- IV fluid in clinic

Constipation

- Adequate hydration- electrolyte
- Bowel regimen as indicated
- Evaluate concomitant medications
- Dietary measures/consultation
- IV fluid in clinic
- Consider less constipating emetic therapy- tailor to patient

Empowering the Patient and Family

- Expectations
- Low blood counts are expected
  - May get worse before they improve
  - Will require close monitoring – minimal once per week
- Present clear and upfront schedule of visits
- Clear communication of all involved, for questions and care- contact information written out, identification of care team
- Supportive care- not only medical but psychosocial- involves not just the patient but the entire family- frequent visits, change in quality of life (QOL)
  - Learning the new normal

Treatment Course

- During first cycle mild nausea with drug administration, controlled with Compazine, did not require in cycle 2 at all
- Counts became neutropenic in cycle 1, required a 5 day admission for f/n. Cultures negative – admission day +12
- Continued twice weekly labs and possibles in cycle 2- Began cycle 2 with normal cbc- no f/n
- Cycle 3 once weekly labs and possibles – however did not require any
- Marrow after cycle 3 showed <5 % blasts, normal cbc, ps=0. Patient out golfing
- We are continuing with vidaza q 28 days, labs checked on days 1 +7, no transfusions needed for past 5 cycles, counts are WNL's, marrowing every 3-4 cycles. Feels great

Educational and Supportive Resources

- Aplastic Anemia and MDS International Foundation – www.aamds.org
- Be The Match Patient Support Center – www.bethematch/one-on-one
- CancerCare – www.cancercare.org/support_groups
- Global Patient Support Groups-MDS Foundation- https://www.mds-foundation.org/global-patient-support-groups
- MDS and You – www.mds-and-you.info
- The Leukemia & Lymphoma Society – www.LLS.org
- Your local institute/state organizations

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Alice Houk, MPS
Senior Director of Health Professional Programs
Aplastic Anemia and MDS International Foundation (AAMDSIF)

AAMDSIF Mission

To support patients, families and caregivers coping with aplastic anemia, myelodysplastic syndromes (MDS), paroxysmal nocturnal hemoglobinuria (PNH) and related bone marrow failure diseases.

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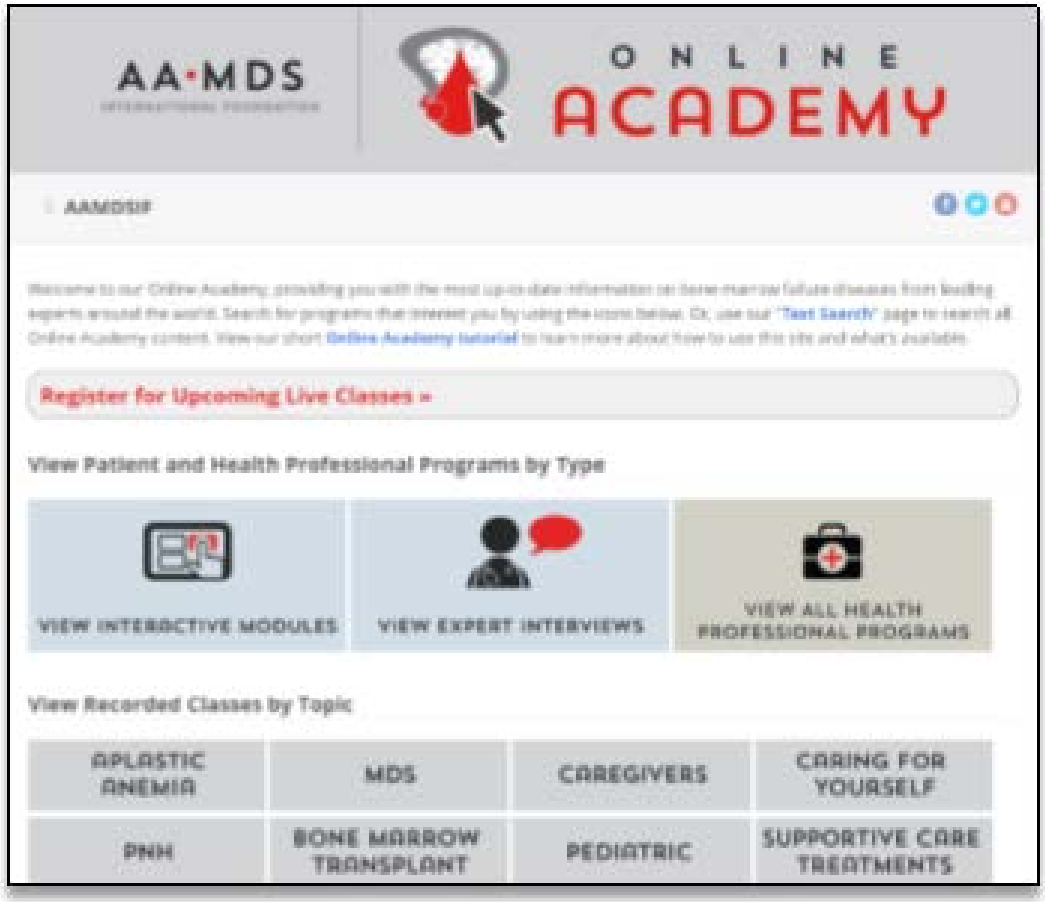
AAMDSIF Health Professional Education

- Biennial Scientific Symposium
- Satellite Symposium at ASH Annual Meeting
- Satellite Symposium at ONS Congress
- Regional Bone Marrow Failure Disease Symposia
- **"MDS Rounds"** CE program for community hospitals

AA·MDS INTERNATIONAL FOUNDATION

Online Academy for Professionals and Patients
www.aamds.org/learn



AA·MDS INTERNATIONAL FOUNDATION

AAMDSIF Patient Support and Education

- Free patient education materials
- Print and electronic newsletters
- Patient information specialist
- Peer support network
- Community Connection support groups

www.aamds.org

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Living with Aplastic Anemia, MDS and PNH

2018

National Patient and Family Conferences

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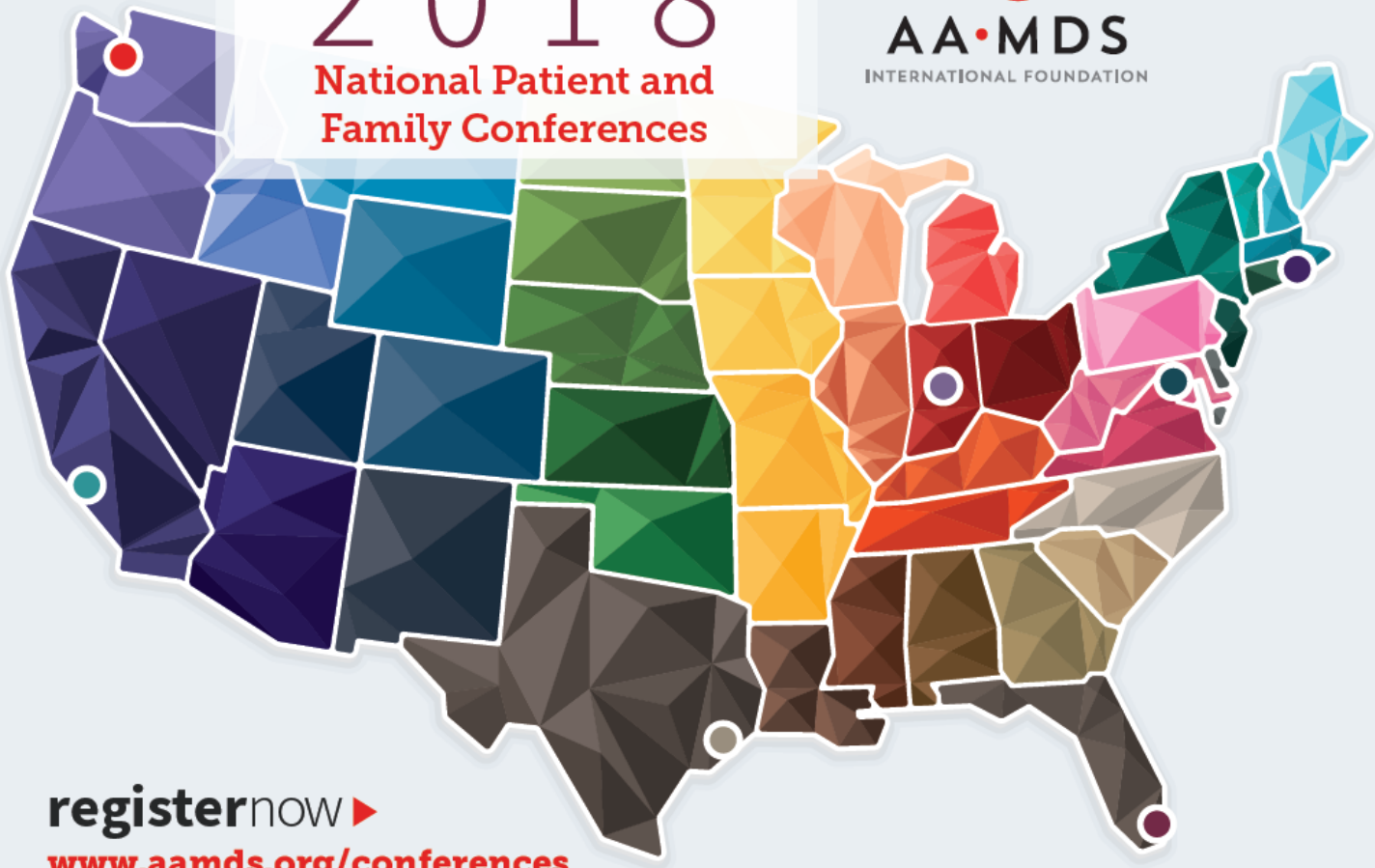

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Programs and resources for you and your patients

Stacy Stickney Ferguson, MSW, LICSW
Manager, Education and Outreach,
Patient and Health Professional Services
National Marrow Donor Program /Be The Match

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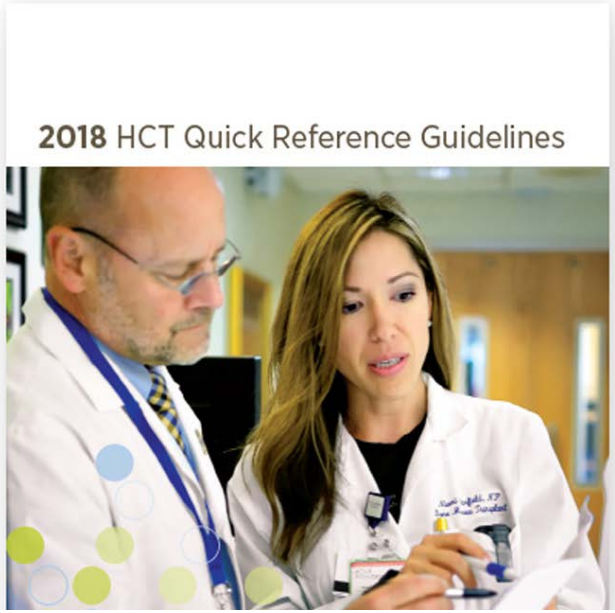
HCT Quick Reference Guidelines



2018 Clinical Guidelines include:

- HCT referral guide for autologous and allogeneic transplant for 20+ diseases
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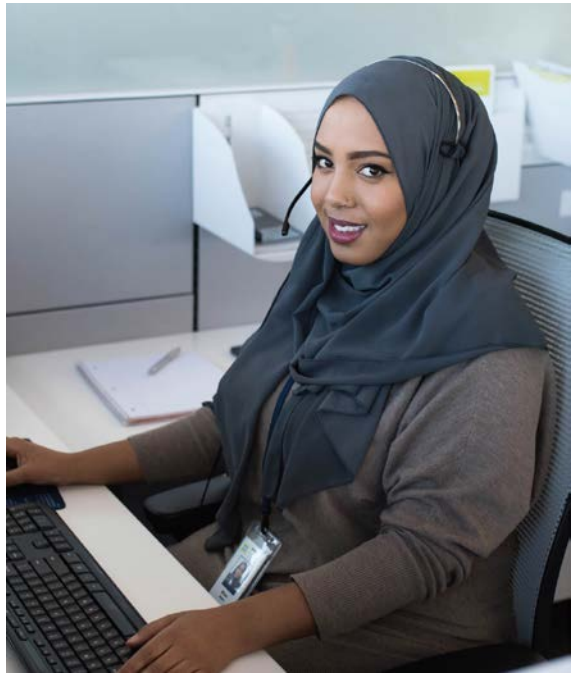

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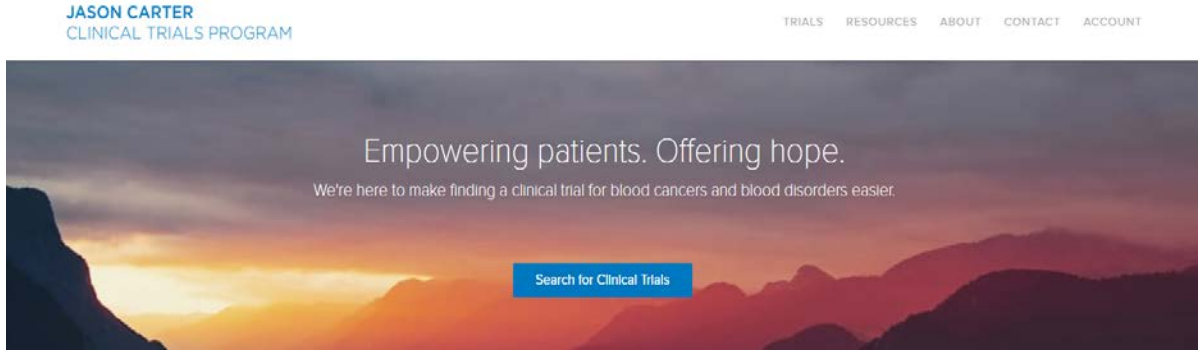

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Questions

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Ilene Galinsky, BSN, MSN, NP-C

To ask a question, use the chat  icon

or

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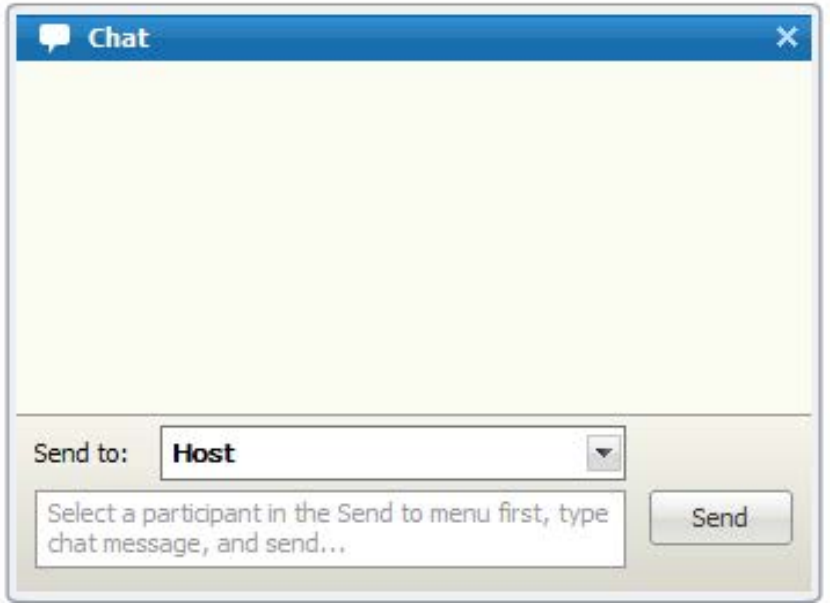

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