Current Strategies for the Management of Myelodysplastic Syndromes

European Nursing Module Series

The Myelodysplastic Syndromes Foundation Inc

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MDS-Foundation EU Nursing Advisory Board and the
EBMT Nurses Group

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Objectives

1. Describe the pathobiology, diagnosis and staging of MDS
2. Identify criteria for initiating active therapies for MDS
3. Describe the treatment options in MDS
4. Discuss treatment related complications

Objectives cont.

5. Discuss the considerations for the older adult with MDS
6. Describe symptom management strategies to maximize patient safety, quality of life, and adherence to the therapeutic regimen
7. Identify nursing management

Contents

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Current Strategies for the Management of Myelodysplastic Syndromes

SECTION 1: Pathobiology, diagnosis, classification and prognosis

Definition

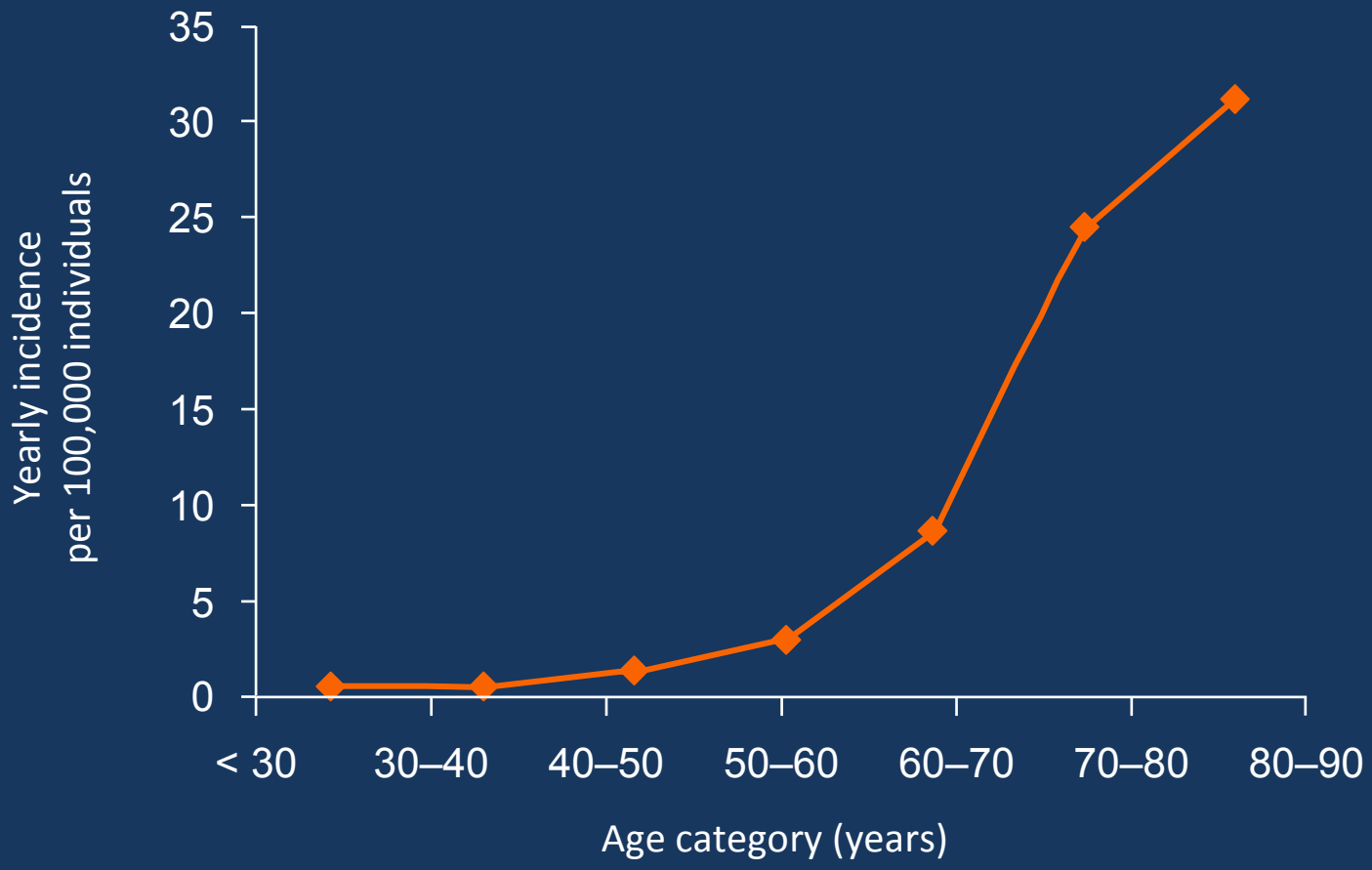
- The Myelodysplastic Syndromes (MDS) represent a spectrum of clonal, hematological stem cell malignancies that are characterized by:
  - Dysplastic and ineffective hematopoiesis
  - Peripheral cytopenias
  - Variable risk for leukemic transformation
- In general, as the disease progresses, bone marrow function declines

Kurtin 2006, List 2004, Steensma & Bennett 2006.

Epidemiology of the myelodysplastic syndromes

- Epidemiology of MDS
  - Peak incidence: 60–90 years of age
  - Median age: 74 years (EU-MDS registry)
  - 3.6–12.6 per 100,000 cases; > 20 per 100,000 cases at 70 years of age
- Typical MDS patient
  - Elderly
  - Has shortened life expectancy, even with low-risk MDS → ineffective hemotopoiesis
  - Male predominance

Incidence of MDS increases with age



Germing U et al. 2004, Jädersten M, Helström-Lindberg E. 2009

Risk factors

Heritable

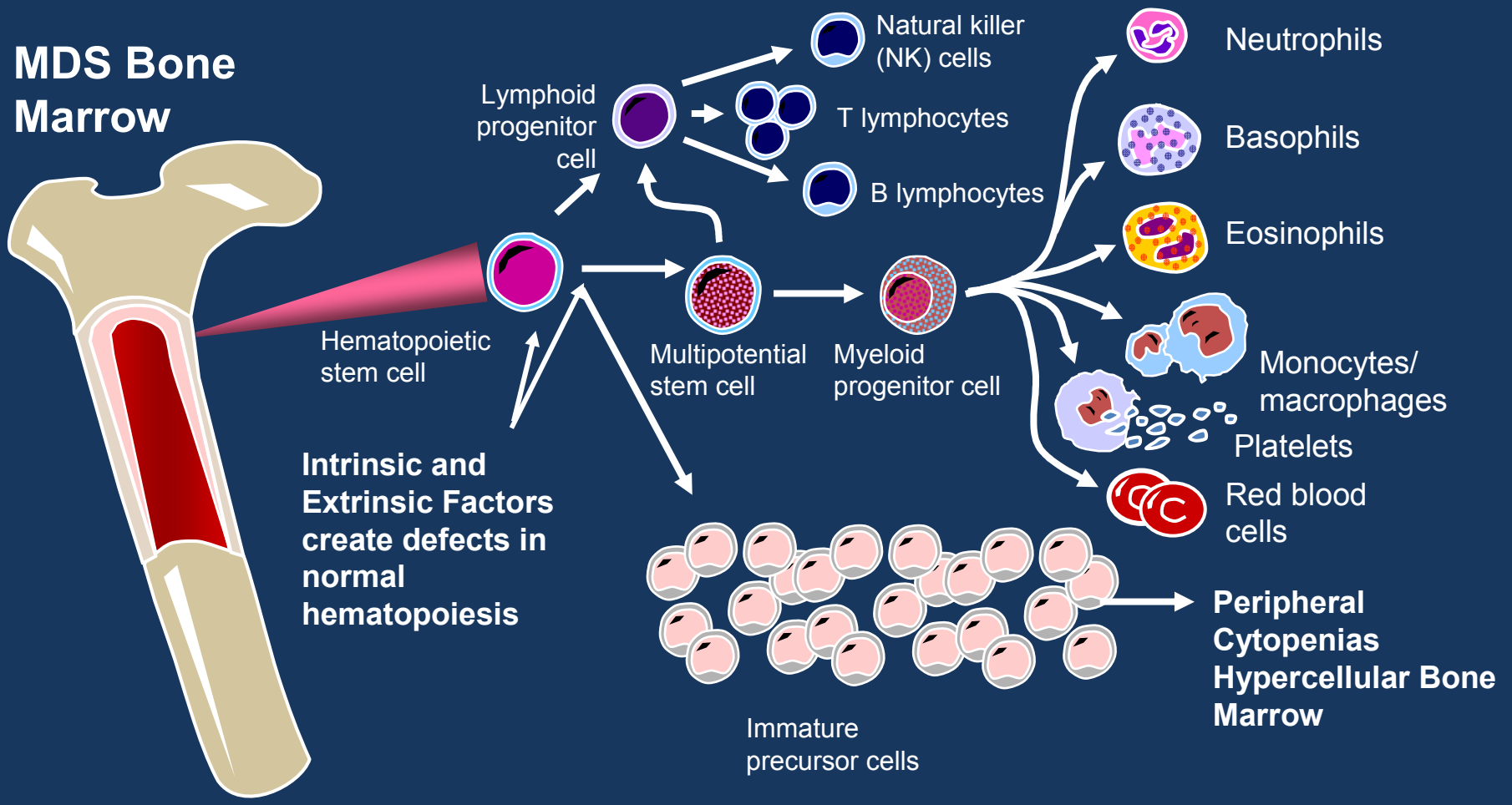
- Unknown in majority of patients
- Age > 70 years
- Male gender
- Inherited congenital abnormalities
  - Fanconi anemia
  - Familial MDS
- Immune dysfunction
- DNA Repair Deficiencies

Acquired

- Chemotherapy
- Environmental/occupational
- Tobacco (Benzene)
- Ionizing radiation

List AF et al. 2003, Pederson-Bjergaard et al. 2007.

In MDS intrinsic and extrinsic factors lead to ineffective hematopoiesis



http://stemcells.nih.gov/info/basics/basics4.asp. Accessed April 7, 2009.

Common presenting symptoms: MDS

- Many patients are asymptomatic
- 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*

Kurtin, S. 2007, Kurtin & Demakos, 2010.

Suspect MDS?

- Medical history
  - Onset of suspicious symptoms
  - Evaluation of co-morbid conditions
  - Historical labs
- Review of medication profile
- Physical exam
- Laboratory analysis
- Bone marrow biopsy and aspirate if high suspicion

Kurtin, S. 2007, Kurtin & Demakos, 2010.

MDS: diagnostic evaluation

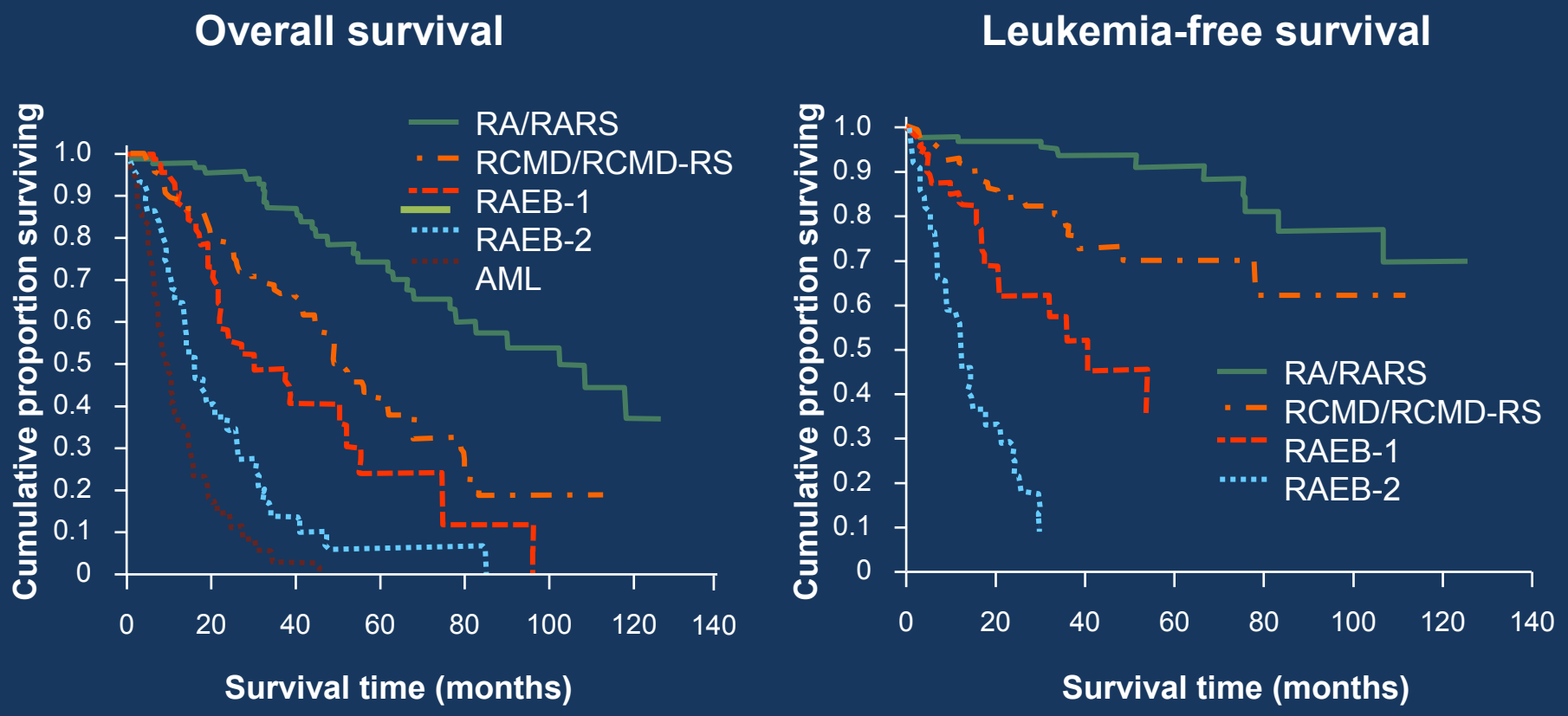
- Peripheral blood
  - Other possible causes of cytopenias, hemolysis, baseline erythropoietin level
- Bone marrow biopsy and aspiration
  - Classification and prognostic scoring

Update on classification of MDS: WHO 2008

New/updated category	Classification
Refractory cytopenia with unilineage dysplasia (RCUD)	New category. ≥10% dysplasia in one cell line. Patients have unicytopenia or bicytopenia but not pancytopenia. Includes refractory anaemia, refractory neutropenia, and refractory thrombocytopenia
MDS-U	Updated to include patients with no overt dysplasia with cytogenetic evidence of MDS; patients with pancytopenia and unilineage dysplasia; patients with RCUD and RCMD with <5% BM blasts and <1% peripheral blasts
RAEB-1	Updated to include patients with 5–9% BM blasts and 2–4% peripheral blasts. No Auer rods present
RAEB-2	Updated to include patients with 10–19% BM blasts and 5–19% peripheral blasts or patients with Auer rods
RARS and thrombocytosis (RARS-T; provisional category)	Subclassification of RARS with thrombocytosis. Up to 60% patients with RARS-T harbour the V617F mutation in *JAK2*
Idiopathic cytopenia of unknown significance (ICUS)	Includes patients with persistent cytopenia with no dysplasia or specific cytogenetic abnormalities

Bennett JM. 2009

Overall survival and risk of AML evolution in MDS classified according to WHO 2001



RCMD-RS = RCMD with ringed sideroblasts.

Malcovati L et al. 2005.

International Prognostic Scoring System (IPSS) in myelodysplastic syndromes

Prognostic variable	Score				
	0	0.5	1.0	1.5	2.0
Bone marrow blasts (%)	< 5	5–10		11–20	
Cytogenetics	Good	Intermediate	Poor		
Cytopenias*	0–1	2–3			

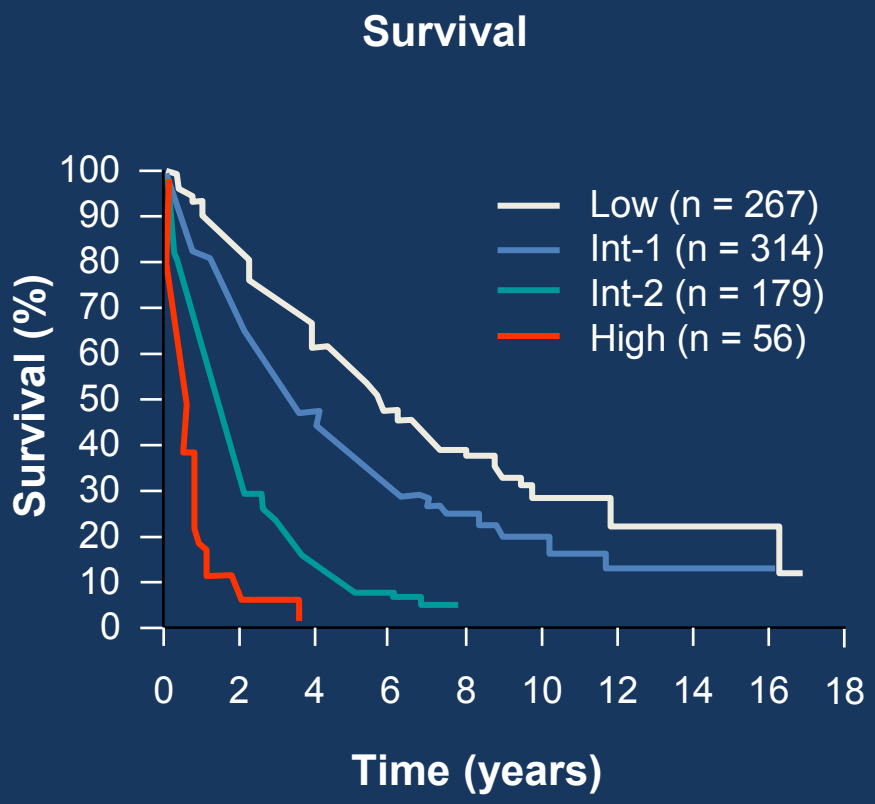
*Hb < 10 g/dL; 6.2 mmol/L; platelets < 100 x 10^9/L; ANC < 1.8 x 10^9/L

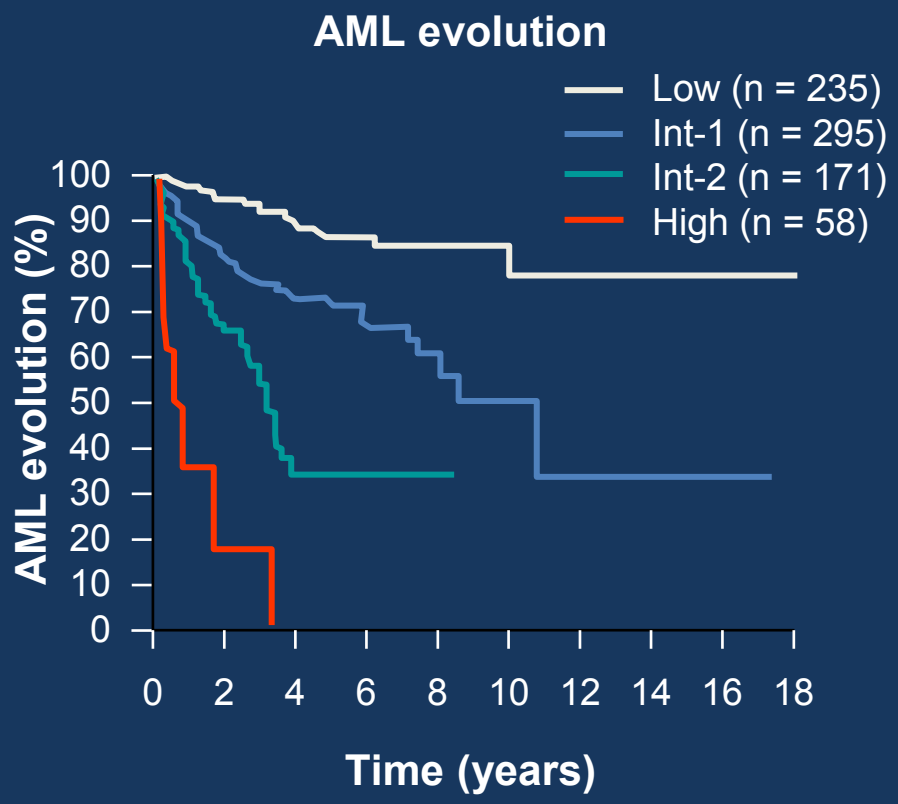
Risk groups:
Low (score = 0)
Intermediate-1 (score 0.5-1.0)
Intermediate-2 (score 1.5-2.0)
High (score ≥2.5)

ANC = absolute neutrophil count.

Greenberg P et al. 1997.

Cumulative survival of MDS patients by IPSS





Greenberg P et al. 1997.

WHO classification-based Prognostic Scoring System (WPSS) in MDS

Variable	0	1	2	3
WHO	RA, RARS, 5q–	RCMD ± RS	RAEB-1	RAEB-2
Karyotype	Good	Intermediate	Poor	–
Transfusions	No	Regular		

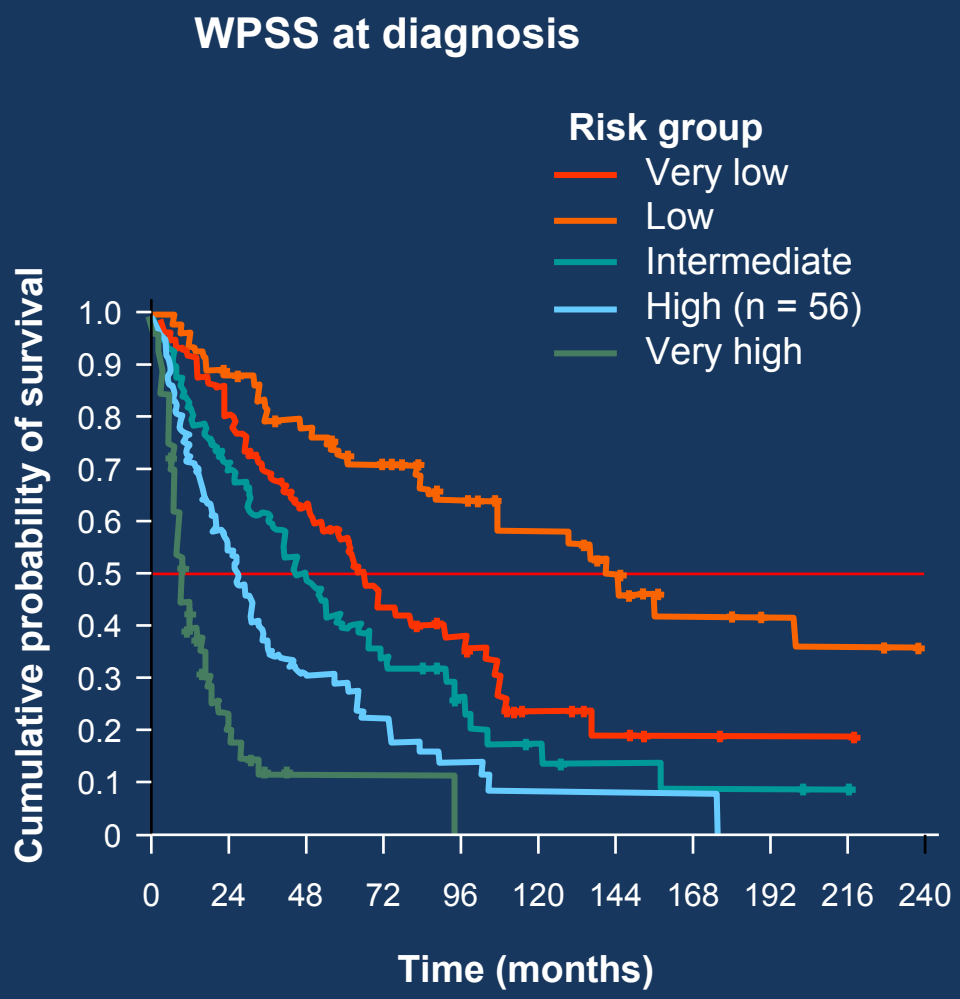
Risk groups

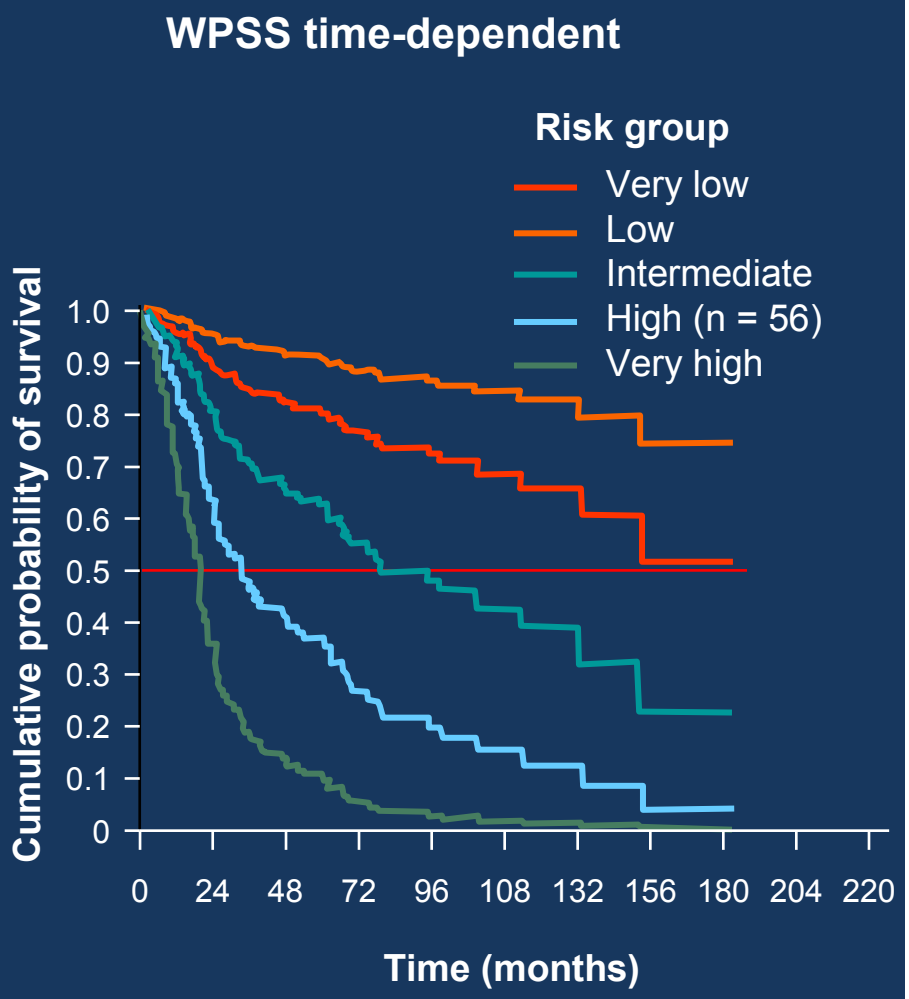
Very low (score = 0)
Low (score = 1)
Intermediate (score = 2)
High (score = 3–4)
Very high (score = 5–6)

RCMD ± RS = RCMD with or without ringed sideroblasts.

Malcovati L et al. 2007.

Time-dependent prognostic scoring system: validation cohort WPSS





Malcovati L et al. 2007.

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SECTION 2: Considerations for the older MDS patient

General considerations

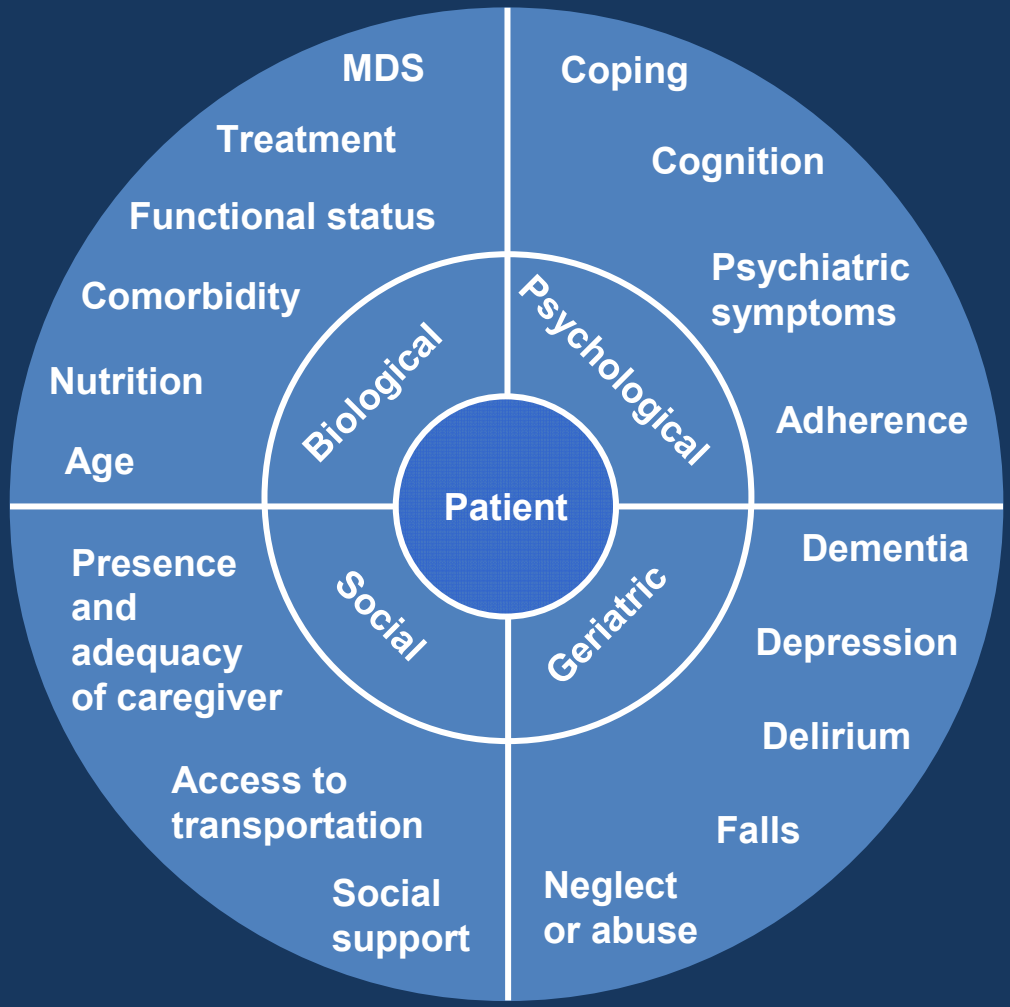
- MDS predominantly affects older patients, the incidence increases with age
- Ageing is associated with molecular, cellular and physiological changes that may influence the tolerance of treatment
- Identification of older patient who may benefit from curative option

Functional status, frailty and co-morbidities

- Functional status: Measures by ECOG and KPS
  - ADLs:
    - Ability to bathe, dress, toilet and maintain continence, transfer, and eat independently
  - IADLs:
    - Finances, shopping, housekeeping, transportation, and self-medication
- Co-morbidities
- Frailty:
  - Weight loss, weakness, poor nutritional intake, cognitive impairment and poor endurance, psycho-social aspects

Kumar et al. 2010, Balducci & Extermann. 2000.

Factors that determine treatment options in elderly patients with MDS



Fried LP et al. 2001, Tinetti ME, Fried T. 2004, Slaets JP. 2006, Gobbens RJ et al. 2007, Ossenkoppele G.J. 2010.

MDS in elderly: treatment approach

Patient Characteristics	Approach to Treatment
Functional independent without co-morbidities (also depending on age criteria)	Induction-chemotherapy followed by Allogeneic Hematopoietic Stem Cell Transplantation
Functional (in) dependent with/without co-morbidities	Individualized life prolonging pharmacological therapy
Functional independent and/or complex co-morbidities, and/or poor prognosis	Individualized palliative therapy, symptom management and supportive care

Saif & Lichtman, 2009, NCCN Senior Adult Oncology, 2010, Kurtin, S. 2010

Clinical trials and the older adult

- Historically, older adults have been under-represented in clinical trials, in particular registration trials for new drugs or new indications in cancer treatment
- More recent trials do not include advanced age in the exclusion criteria for participation

Carreca I, Balducci L. 2009, Wedding U. 2007, Kurtin S. 2010.

Clinical trials and the older adult

- Barriers to participation of the elderly in clinical trials continue:
  - Provider reluctance to recommend trials due to fear of toxicity
  - Limited expectation of benefit
  - Ageism
  - Patient reluctance to participate for similar reasons
  - Concern for cost and strain on caregivers
- Limited representation of the older adult in clinical trials impedes the development of evidenced-based practice guidelines specific to this population

Carreca I, Balducci L. 2009, Wedding U. 2007, Kurtin S. 2010.

Under-treatment of MDS in the older adult

- 310 online interviews conducted in North America and Europe
  - 153 in North America 157 in Europe
  - Age alone *is* often a factor for treatment
    - Less of a factor in North America – more focus on PS
  - Most treaters tend to be aggressive as is reasonable with older patients
  - Conservative treaters more likely to:
    - Consider age as a factor
    - Not treat with active therapy
    - Worry about treatment toxicity and active therapy tolerability
  - MDS treaters desire more tools to guide treatment choices

Life Beyond Limits Project – submitted for publication.

Removing age as a barrier to treatment

- Consideration of age-related physiological changes
- Co-morbidities
- Social and financial resources
- Development of co-morbidity and functional assessment tools specific to hematological malignancies
- Outcomes:
  - Identifications of patients who may benefit from aggressive therapy
  - Protection of at risk patients who may require less intensive therapy due to increased risk of morbidity and mortality

Kurtin, S. 2010.

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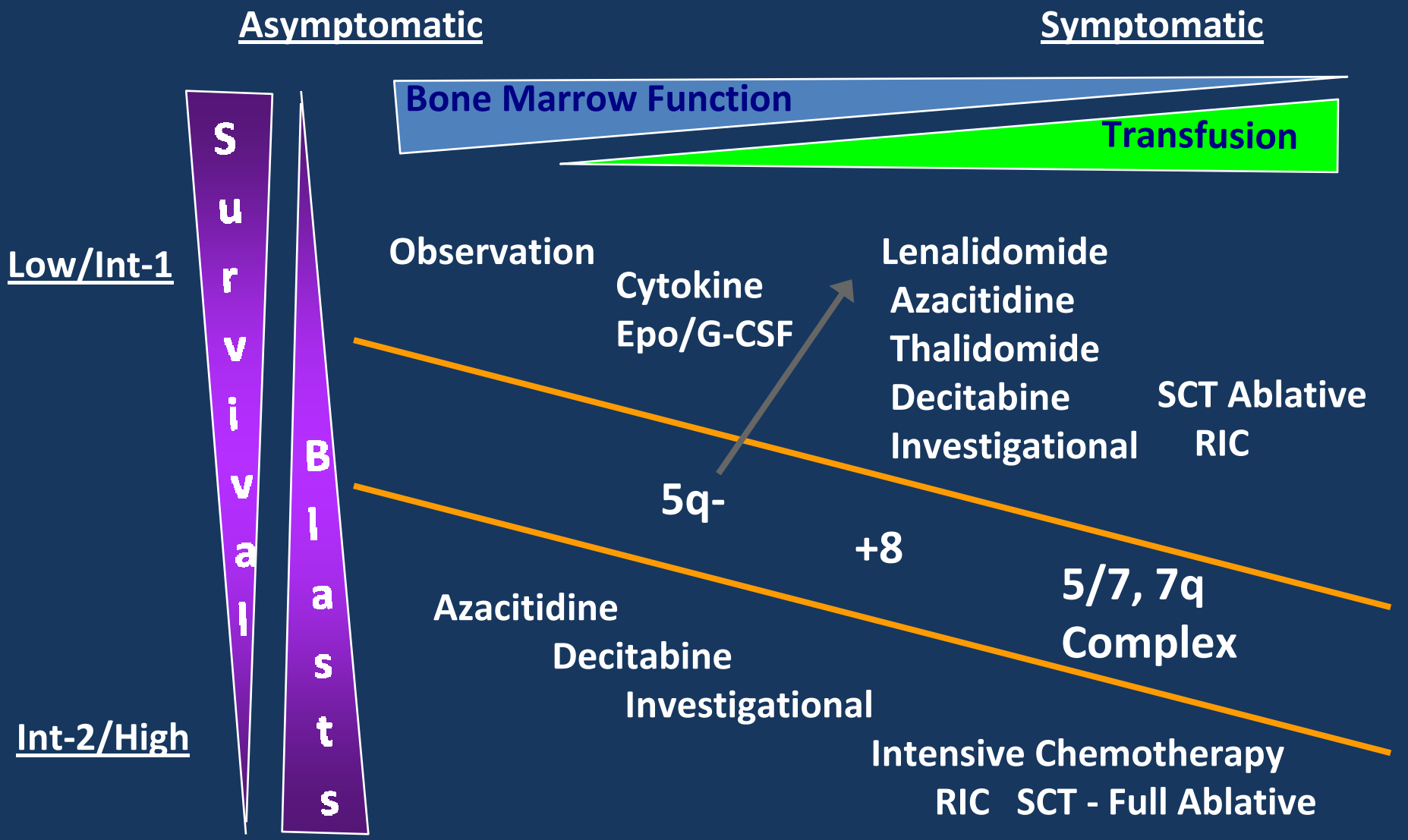
SECTION 3: MDS treatment

Key principles of therapy in MDS risk-adapted treatment selection

- Allogeneic bone marrow transplant remains the only potentially curative therapy
- Risk-adapted treatment selection is recommended:
  - IPSS/WPSS risk category
  - Disease specific attributes
  - Individual patient characteristics
    - Fit or frail
    - Age
    - Co-morbidities
    - Performance status
    - Quality of Life

Kurtin, S. 2010, Kurtin & Demakos. 2010.

Treatment algorithm for patients with MDS



Silverman. 2006.

Key principles of therapy in MDS treatment goals and duration

- MDS is not curable without allogeneic HCT
  - Not an option for the majority of patients
  - Not every patient will have a complete response
  - Hematologic improvement, stable disease, and transfusion independence are good things

Kurtin and Demakos. 2010, Kurtin S. 2011.

Key principles of therapy in MDS treatment goals and duration cont.

- Treatment should continue until disease progression or unacceptable toxicity
  - Methylation is a continuous process and is associated with leukemogenesis
  - Limited FDA approved agents currently available

Kurtin and Demakos. 2010, Kurtin S. 2011.

Key principles of therapy in MDS treatment duration

- A duration of 4-6 months of treatment is often required to evaluate initial response
  - Best response may not be evident until 9 months of therapy
- Myelosuppression is the most common toxicity in all types of active therapy for MDS
  - Cytopenias will often get worse before they better
  - Moderate asymptomatic cytopenias may persist for months or years in patients responding to treatment

Kurtin and Demakos. 2010, Kurtin S. 2011.

Strategies to minimize adverse events

- Supportive care is essential for all patients with MDS to improve quality of life
  - Transfusion support, growth factors, management of infections, management of co-morbidities, chelation therapy, referrals to supportive services
- Minimize AEs in patients on active therapies
  - Dose adjustment, drug holidays, or administration of growth factors to allow safe continuation of therapy
  - Clear guidelines to the patient and family for early reporting of AEs or strategies for independent management

Kurtin and Demakos. 2010, Kurtin S. 2011.

Setting expectations and empowering the patient and family

- Setting expectations:
  - Cytopenias are expected
  - Require close monitoring during therapy and follow up
  - Likely to improve with treatment response but may not return to normal - “new normal”
- Empower the patient and family to track, report and manage

Kurtin and Demakos. 2010, Kurtin S. 2011.

Treatment triggers

Initiation of active therapy should be decided on

- Transfusion dependence
- Progressive or symptomatic cytopenias
- Increasing blasts
- High-risk disease

Kurtin and Demakos. 2010, NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes—v.2.2011.

Supportive care: transfusion therapy and growth factors

Blood transfusions	Hemopoietic growth factors
• Improve symptoms of anemia • Correlates positively with quality of life • Eventually leads to iron overload	• EPO ± G-CSF can improve anemia • Best response in patients with low EPO and low transfusion dependence • Other growth factors under investigation

EPO = erythropoietin;
G-CSF = granulocyte colony-stimulating factor.

Hellström-Lindberg E. 2007.

Validated predictors of response to growth factor treatment (EPO/G-CSF) in Low-/Int-1-risk MDS

Serum EPO in U/L
< 100: +2
100–500: +1
> 500: –3

RBC transfusion
< 2 units/month: +2
≥ 2 units/month: –2

Score	Patients, n	Response
≥ 2	29	74%
± 1	31	23%
< –1	34	7%

Hellström-Lindberg E. 2003.

Novel agents

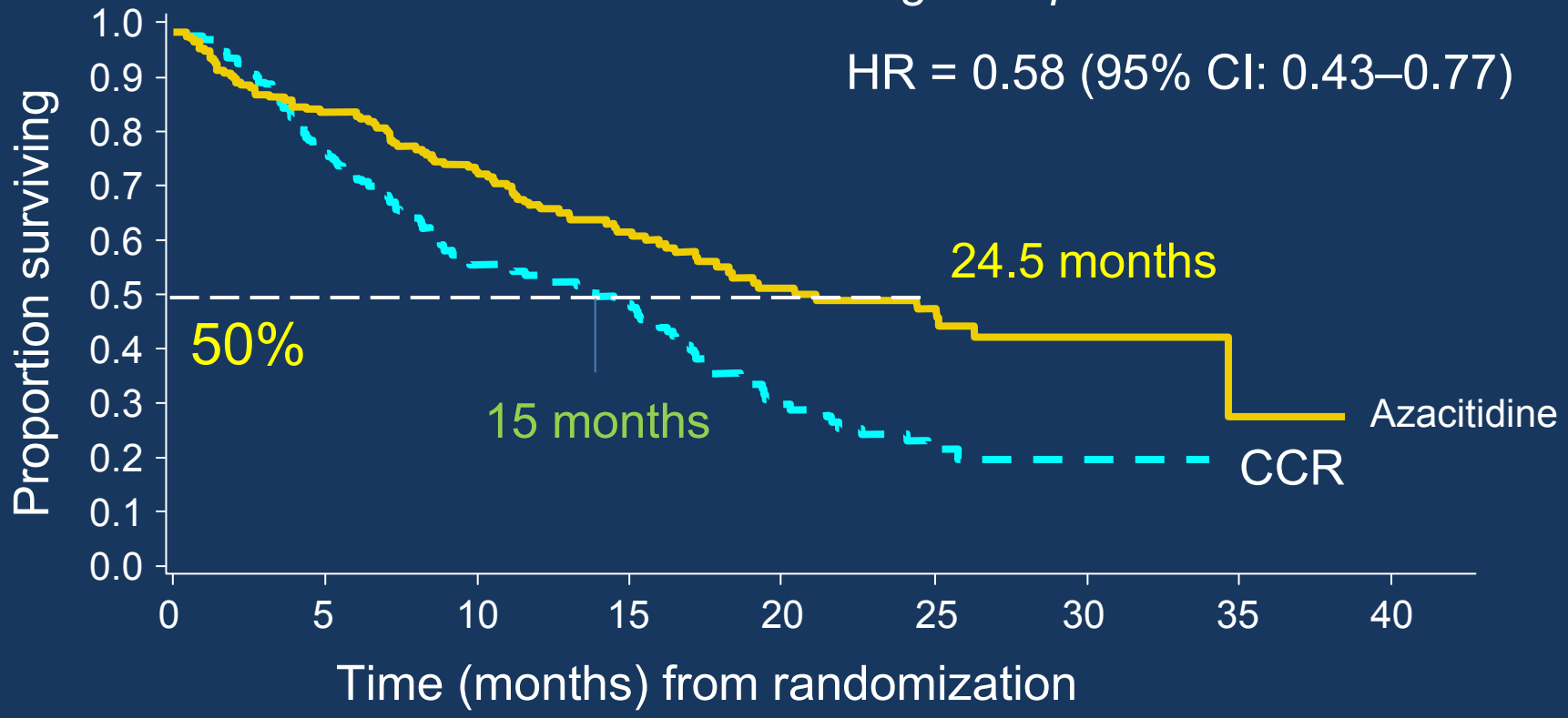
- Decitabine
- Thalidomide
- Lenalidomide

Azacitidine

- The recommended starting dose for the first treatment cycle is 75mg/m^2 s.c. for 7 days q.28d. for all patients regardless of baseline hematology laboratory values
- Hypomethylating agent
- It is recommended that patients should be treated for ≥6 cycles
- Patients should be monitored for hematological response/toxicity and renal toxicities

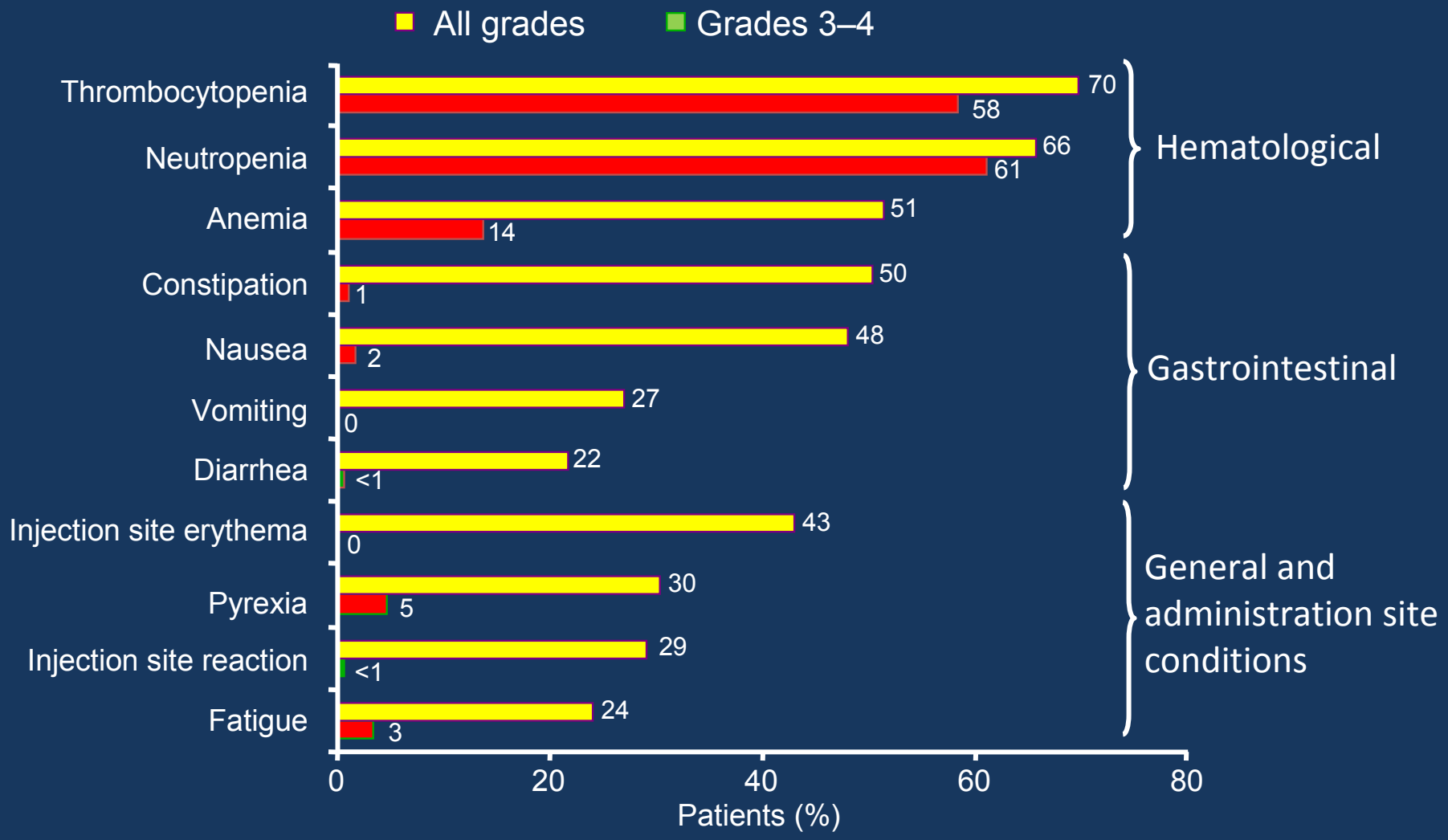
Vidaza EU SmPC.

AZA-001 trial



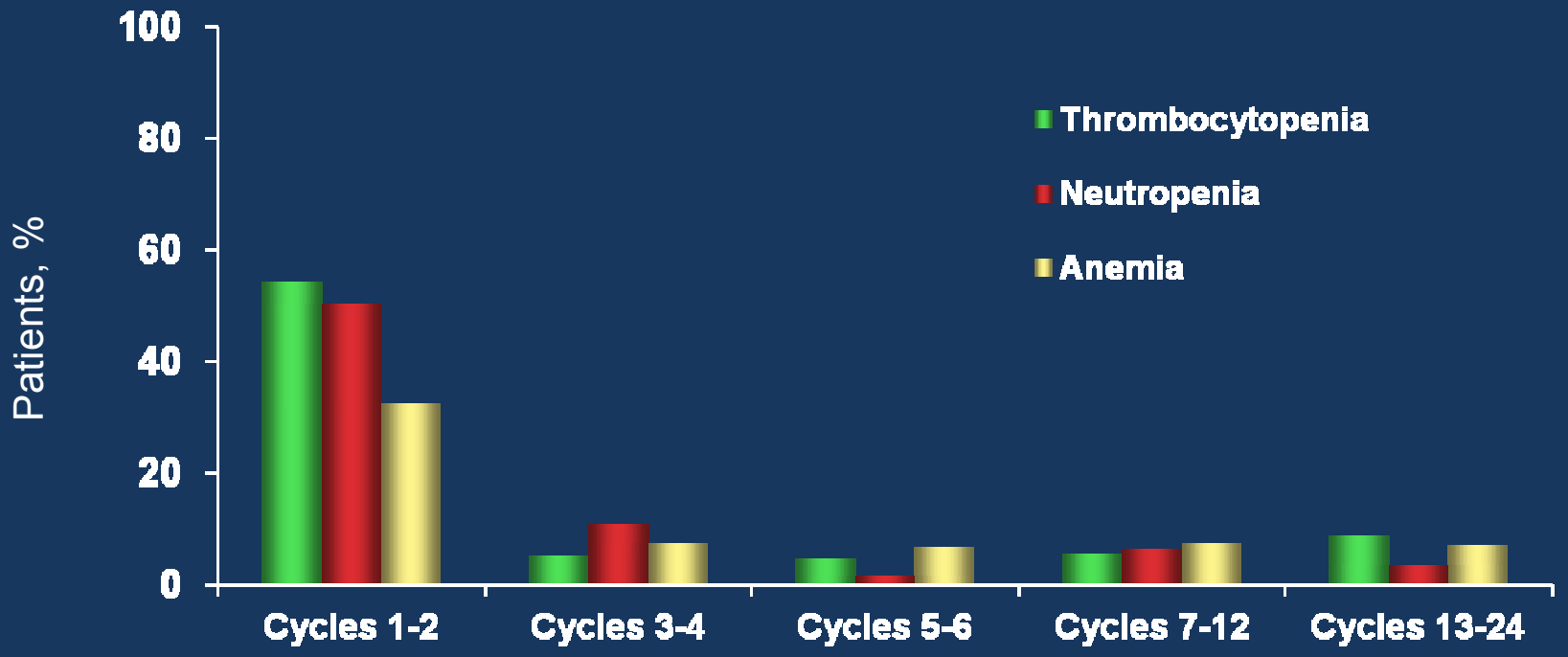
Fenaux et al. 2007, Fenaux et al. 2009.

AZA-001: AEs that occurred in >20% of patients given azacitidine (n=175)



Adapted from Santini V et al. 2008

Hematological AEs[a] occur early during azacitidine treatment in higher-risk patients

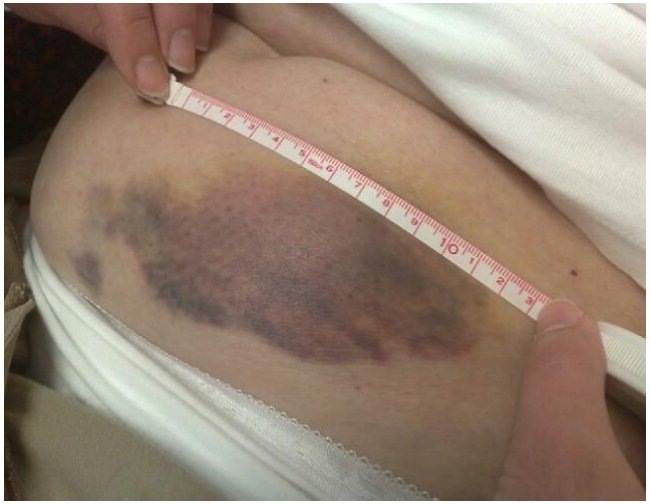


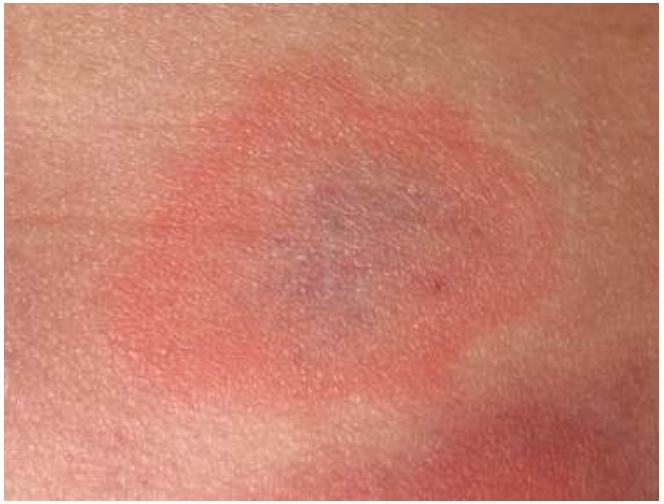
n (%)00	n = 175	n = 147	n = 130	n = 107	n = 56
Thrombocytopenia	95 (54.3)	8 (5.4)	6 (4.6)	6 (5.6)	5 (8.9)
Neutropenia	88 (50.3)	16 (10.9)	2 (1.5)	7 (6.5)	2 (3.6)
Anemia	57 (32.6)	11 (7.5)	9 (6.9)	8 (7.5)	4 (7.1)

[a]All grades.

Fenaux et al. 2009.

The majority of skin and subcutaneous AEs are local injection site reactions





Advice on management of azacitidine AEs

AE	Suggested action	Suggested medication
Hematological	• Monitoring • Delay of next cycle • Dose adjustment	• Prophylactic antibiotics • Growth factor support • Transfusions
Infections	• Microbiology work-up	• Anti-infectives plus growth factor support
Injection site reactions	• Injection technique • Supporting technique	• Antihistamines • Corticosteroids • Analgesics

Demakos EP, Linebaugh JA. 2005.

Advice on management of azacitidine AEs cont.

AE	Suggested action	Suggested medication
Nausea, vomiting	• Premedication	• Anti-emetics
Diarrhea	• Symptomatically	• Anti-diarrheals
Constipation	• Symptomatically	• Laxatives, stool softeners

Demakos EP, Linebaugh JA. 2005.

Side-effect management: lessons learned from AZA-001 and CALGB 9221 – conclusions

- The majority of AEs were transient, non-serious and were managed by
  - Dose delays for hematological events
  - Supportive care measures
- Most hematological events occurred during the first 1–2 cycles

Santini V et al. 2008.

Side-effect management: lessons learned from AZA-001 and CALGB 9221 – conclusions cont.

- Bleeding and infection rates were not increased in patients treated with azacitidine vs BSC
- Clinicians should be alert to the onset, duration and management of AEs so that they may be treated promptly
  - This may allow patients to prolong therapy and achieve maximum clinical benefit with azacitidine

Santini V et al. 2008, Santini V et al. 2009

Chemotherapy

- Hydroxyurea
- Tioguanine
- Low dose ara-C

Immunosuppressants

- ATG
- Ciclosporine

Hematopoietic stem cell transplant

- Curative potential for patients with MDS
- Many patients do not meet eligibility criteria:
  - Adequate PS and major organ function, limited co-morbidities
  - Treatment sensitive disease (MRD)
  - Suitable donor and consistent caregiver
- High upfront treatment-related mortality (30-50%)

Kurtin and Demakos. 2010, Scott and Deeg. 2010, Cutler. 2010.

Hematopoietic stem cell transplant cont.

- Reduced intensity conditioning (RIC) regimens are less toxic but carry a higher relapse risk
- Hypomethylating agents are sometimes used as a bridge to transplant
- Patients with higher-risk disease may have the greatest benefit

Kurtin and Demakos. 2010, Scott and Deeg. 2010, Cutler. 2010.

Approximation of life expectancy (years) for time of stem cell transplant

IPSS Risk	Transplant at Diagnosis	Transplant in 2 Years	Transplant at Progression
Low	6.51	6.86	7.21
Int-1	4.61	4.74	5.16
Int-2	4.93	3.21	2.84
High	3.20	2.75	2.75

Cutler et al. 2004.

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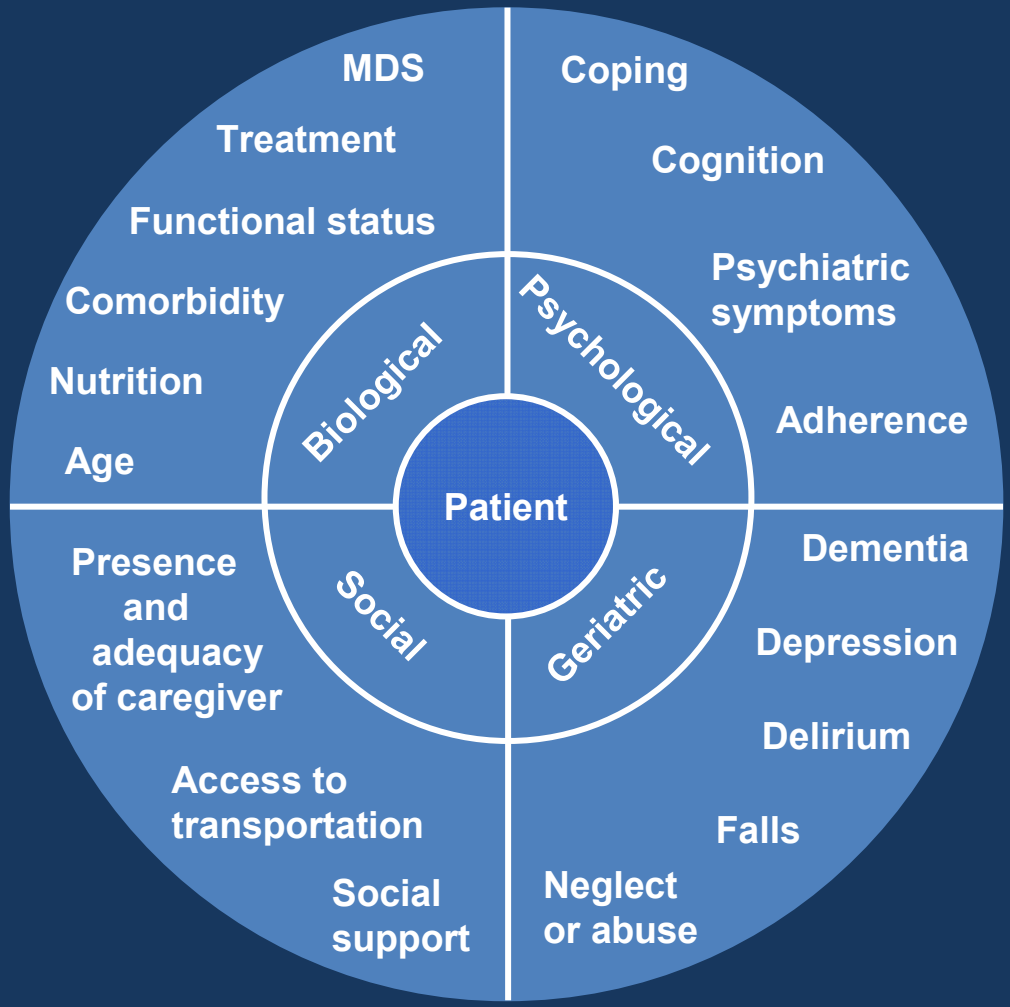
SECTION 4: Managing patients, symptoms and adverse events

Factors that determine treatment options in elderly patients with MDS



Fried LP et al. 2001, Tinetti ME, Fried T. 2004, Slaets JP. 2006, Gobbens RJ et al. 2007, Ossenkoppele G.J. 2010

Management of:

- Anemia
- Neutropenia
- Thrombocytopenia
- Gastrointestinal toxicity
- Pain
- Nutrition
- Fatigue
- Iron overload
- Quality of Life and psychosocial aspects
- End of Life

Managing anemia

- Signs and symptoms
  - Palpitations, chest pain, fatigue, dyspnea, dizziness, headaches
- Nursing considerations
  - Management of RBC transfusions
    - Patients with underlying cardiac disease are at increased risk for CHF exacerbation and may require diuresis with transfusions
    - Benefits are temporary and rarely restore Hct to normal
    - Transfusions should be based on symptoms not general Hct parameters
  - Administration of erythropoietin agents for patients with low risk MDS

Managing neutropenia

- Signs and symptoms
  - Fever, cough, dysuria, recurrent or refractory infections
- Nursing considerations
  - Monitoring of blood counts as clinically indicated by treatment choice and state of disease
  - Patients receiving active therapies may require withholding therapy or dose adjustment
  - Early recognition of infections
  - Administration of recombinant granulocytic growth factors for patients with low risk MDS
  - Antimicrobial therapy
    - Prophylactic or for active infections

Managing thrombocytopenia

- Signs and symptoms
  - Petechiae, ecchymosis, epistaxis, hemoptysis, hematuria
- Nursing management
  - Patients receiving active therapies may require withholding therapy or dose adjustment
  - Platelet transfusions based on risk of bleeding
  - Careful monitoring of concomitant medications with anti-platelet effect
  - Aminocaproic acid
    - Prophylactic or for active bleeding
  - Thrombopoietin stimulating hormones are in clinical trial

Managing gastrointestinal toxicities

- Nausea and vomiting
  - (Pre) medicate for nausea/vomiting
  - Encourage adequate hydration
  - Ensure baseline and ongoing renal function
- Constipation
  - Encourage adequate hydration
  - Dietary measures/consultation
  - Encourage exercise
  - Bowel regimen as indicated
  - Evaluate con-concomitant medications

Managing gastrointestinal toxicities cont.

- Diarrhea
  - Evaluate for infectious etiology
  - Encourage adequate hydration
  - Anti-diarrheal medications
  - Dietary measures/consultation

Patient education, when to alarm

- Fevers or shaking chills
- Sudden onset of shortness of breath or chest pain
- Skin changes
  - Bruises, petechiae, rash
- Head or vision change
  - Headaches, confusion, sleepiness
- Bleeding
  - Bleeding that does not stop after a few minutes, hematuria, melena
- Uncontrolled nausea, vomiting, diarrhea or constipation

Basic principles of cancer related fatigue

- Rarely an isolated symptom and commonly occurs with other symptoms
- A subjective experience
- Thorough baseline evaluation of normal activities will assist in evaluating fatigue
- Rehabilitation should begin with the cancer diagnosis

Wang, XS. 2008, NCCN. 2009c

Managing fatigue

Establish a baseline

- Focused history
- Disease status and treatment plan
- Psychosocial factors
- Assessment of treatable contributing factors
  - Activity level
  - Pain
  - Emotional distress
  - Sleep disturbance
  - Nutritional assessment
  - Medication review
  - Co-morbidities

Wang, XS. 2008, NCCN. 2009c, Breitbart et al. 2008.

Managing fatigue cont.

Interventions

- Activity enhancement and energy conservation
- Psychosocial interventions
  - Education and counseling
- Nutrition consultation
- Sleep evaluation
- Pharmacological interventions
  - Psychostimulants
  - Treatment of anemia
  - Sleep medications

Wang, XS. 2008, NCCN. 2009c, Breitbart et al. 2008.

Managing nutrition

- Changes in nutrition can occur due to the disease and/or to the treatment
  - Malnutrition, anorexia, weight loss, altered and/or loss of taste, reluctance, stomatitis, gastrointestinal toxicity
- Nursing considerations
  - Encourage adequate hydration
  - Dietary measures/consultation
  - Antiemetics

Managing pain

- Signs and symptoms
  - Bone pain, joint pain, headache, neuropathic pain
- Nursing considerations
  - Pain assessment
  - Administration of analgesic
  - TENS
  - Relaxation techniques
  - Pain consultation

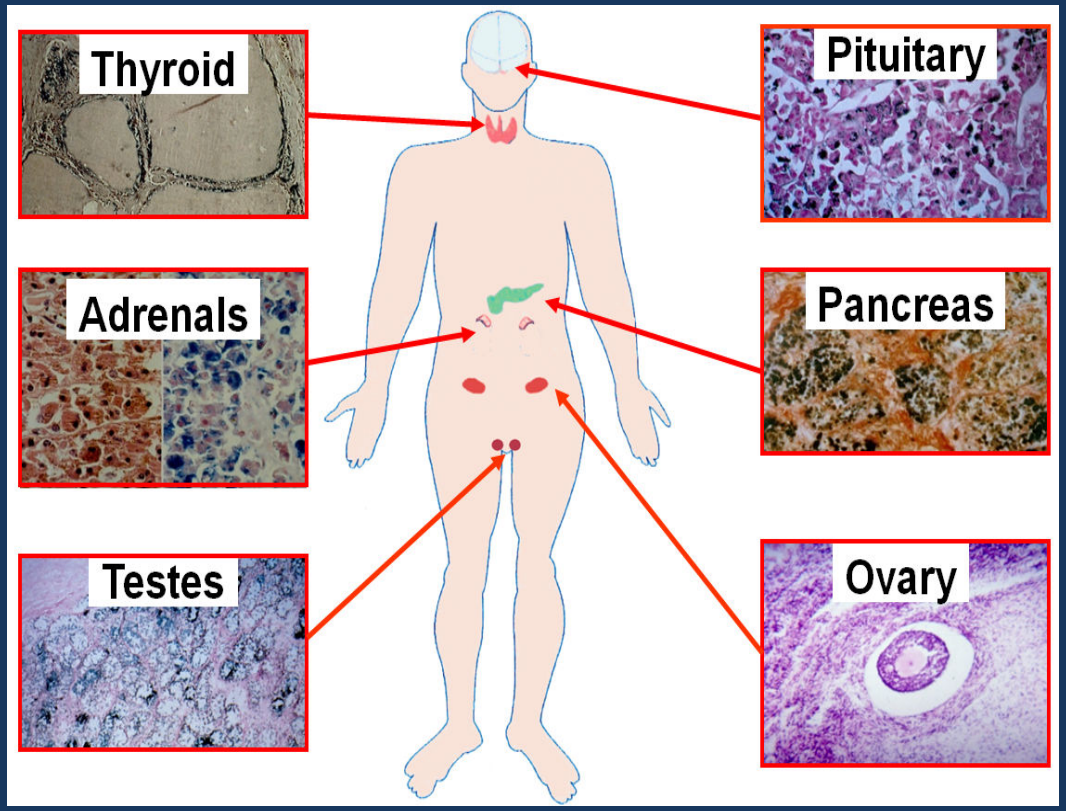
Potential causes for the effect of iron overload on survival and leukemic risk

- On survival[1]
  - Greater organ dysfunction
    - Cardiac
    - Hepatic
    - Endocrine
  - Higher infection rate
- On leukemic risk[2]
  - *In vitro* data suggest iron deposition increases malignant transformation of normal cells

Malcovati L et al. 2006, Calzolari A et al. 2007, Callens C et al. 2010

Endocrine complications in MDS

- Increase in diabetes in transfused patients
- Decrease in elevated blood glucose with chelation



Goldberg SL et al. 2010, Delea TE et al. 2009, Takatoku M et al. 2007

Which patients with MDS are likely to benefit most from management of iron overload?

Transfusion status	• Transfusion dependence • Requiring 2 units/month for > 1 year • Received 20–30 packed RBC units
Serum ferritin	• 1,000 ug/L (MDS Foundation) • > 2,500 ug/L (NCCN) • Or evidence of significant tissue iron overload with continued transfusion dependence
MDS risk	• IPSS: Low- or int-1 • WHO: RA, RARS, and 5q
Patient profile	• Candidates for allografts • Life expectancy > 1 year • Free of comorbidities that limit prognosis • A need to preserve organ function

NCCN, 2010; Jabbour et al. 2009.

Iron chelation therapy

- Deferoxamine (Desferral)
  - IV homepump for 5 days requires that patient has a central line, or SC also by homepump over 8-12 hours/ 5-7 days per week
- Deferasirox (Exjade)
  - Orally daily
- Defiriprone (Ferriprox)
  - Orally daily

Malcovati et al. 2005, Jabbour et al. 2009, Kurtin S. 2007, Kurtin S. 2008

Iron chelation therapy
safety and patient monitoring

- Pancytopenia -
  - Neutropenia, agranulocytosis, thrombocytopenia have been reported in MDS patients
    - Baseline and regular monitoring
- Auditory
  - High frequency hearing loss, decreased hearing
    - Baseline and yearly audiology evaluation
- Ocular
  - Cataracts, lens opacities, increased pressure, retinal disorders
    - Baseline and yearly slit eye and fundoscopic exam

Malcovati et al. 2005, Jabbour et al. 2009, Kurtin S. 2007, Kurtin S. 2008

Iron chelation therapy
safety and patient monitoring

- Renal toxicity
  - Increase in serum creatinine
    - Rare cases of acute renal failure have been reported
  - Intermittent proteinuria
    - Baseline and regular monitoring
    - Dose delay or reduction may be necessary
- Hepatotoxicity
  - Elevated transaminase levels
    - Baseline and regular monitoring
    - Dose delay or reduction may be necessary

Malcovati et al. 2005, Jabbour et al. 2009, Kurtin S. 2007, Kurtin S. 2008

Iron chelation therapy safety and patient monitoring

- Gastrointestinal toxicity
  - Diarrhea
    - May use anti-diarrheal medications
    - Dose reduction may be necessary
  - Nausea
    - Take at bedtime
    - Avoid taking with dairy products
- Adherence
  - IV and SC treatment interferes with patients' daily lives
  - Patients experiencing more side effects are more likely not to adhere to the treatment
    - Patient education is necessary

QoL and psychosocial aspects

- Negative impact on QoL
  - Diminished physical and mental capabilities
  - Symptoms caused by MDS, toxicity caused by treatment
  - Loss of independence
  - Relationships with family and others
  - Diminished role within the family
  - Emotional toll
  - Significantly more time spent on health-related care
  - Employment and economic challenges

Hepinstall K. 2008.

QoL and psychosocial aspects

- Positive Impact on Qol
  - Reassessing life's priorities
  - Improved relationships with family and friends
  - Adoption of positive health behaviors
  - Positive brighter outlook on life in general
  - Deeper more meaningful spiritual life
  - Feelings of hope when positive results of treatment

Hepinstall K. 2008.

Managing QoL and psychosocial aspects

- Assessment of QoL (EORTC QLQ C30, module ELD 15), distress (HADS)
- Multidisciplinary care and/or consultation social worker
- Family support
- Economic aid
- Patient organisation

Managing end of life

- Signs
  - Short life expectancy
  - Progressive disease
  - Depression and/or anxiety
  - Dimished QoL
- Nursing considerations
  - Identify patients' wishes and fears
  - Arrange discussion with multidisciplinary team and family

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Myelodysplastic Syndromes Foundation

Current Strategies for the Management of Myelodysplastic Syndromes

SECTION 5: Literature list

Literature List

- Balducci L, Extermann M. Management of cancer in the older person: a practical approach. Oncologist. 2000;5:224–237
- Bennett JM. Leuk Res 2009;33(Suppl. 1):S6–7
- Breitbart W, Alici Y. Pharmacological Options for Cancer-Related Fatigue: Current State of Clinical Research. Clin J Oncol Nurs. 2008;12(suppl)5:27-36
- Calzolari A et al. Blood Cells Mol Dis 2007;39:82-91; Callens C et al. J Exp Med 2010;207:677-680.
- Carreca I, Balducci L. Urologic Oncology: Seminars and Original Investigations 2009;27:633-642.
- Cutler, C. (2010) Patient Selection for Transplantation in the Myelodysplastic Syndromes. *Hematol Oncol Clin N Am,*24,469-476. Doi:10.1016/j.hoc.2010.02.006.
- Delea TE et al. Curr Med Res Opin 2009;25:139-47.
- Demakos EP, Linebaugh JA. Clin J Oncol Nurs 2005;9:417–23.

Literature List

- Fenaux, P., Gattermann, N., Seymour, J.F., Hellstrom-Lindberg, H., Mufti G.J., Duehrsen, U., et al. (2010a). Prolonged survival with improved tolerability in higher-risk myelodysplastic syndromes: azacitidine compared with low dose ara-C. *British Journal Haematology.* DOI: 10.1111/j.1365-2141.2010.08082.x.
- Fenaux P et al. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher risk myelodysplastic syndromes: A randomised, open-label, phase III study. Lancet Oncol 2009; 10: 223-32.
- Germing U et al. Haematologica 2004;89:905-10.
- Gobbens RJ et al. Frail elderly. Identification of a population at risk.
- Goldberg SL et al. J Clin Oncol 2010; 28(17):2847-52.
- Greenberg P et al. Blood 1997;89:2079-88.
- Hellström-Lindberg E et al. Br J Haematol 2003;120:1037-46.

Literature List

- Hellström-Lindberg E. ASH Education Book 2007. American Society of Hematology.
- Hepinstall,K. Quality of Life in Myelodysplastic Syndromes: A Special Report From the Myelodysplastic Syndromes Foundation, Inc. Oncology Nurse Edition, 22(2), 13-18.
- Jabbour E, Garcia-Manero G, Taher A, & Kantarjan H. Managing Iron Overload in Patients with Myelodysplastic Syndromes with Oral Deferasirox Therapy. The Oncologist, 2009;14:489-496
- Jädersten M, Helström-Lindberg E. J Intern Med 2009;265:307-28.
- Kumar S, Katheria V, Hurria A. Evaluating the Older Adult with Cancer: Understanding Frailty and the Geriatric Assessment. CA Cancer J Clin. 2010. Doi:10.3322/caac.20059.

Literature List

- Kurtin, SE: Advances in the management of low to intermediated risk myelodysplastic syndrome: Integrating the National Comprehensive Cancer Network Guidelines. Clin J Oncol Nurs 10(2): 197-208, 2006.
- Kurtin SE. Myelodysplastic Syndromes: Diagnosis, Treatment Planning, and Clinical Management. Oncology: Nurse Edition, 2007, 21(11), 41-48 @http://cancernetwork.com/oncology/showArticle.jhtml?articleId=202402608
- Kurtin S: A time for hope: Promising advances in the management of anemia, neutropenia, thrombocytopenia, and mucositis. J Support Oncol 5(suppl 2):085–088, 2007.
- Kurtin S. Updates and Strategies for the Management of MDS, CLL, and MM. Meniscus Educational Institute, August, 2008. @ https://www.meniscus.com/mds-cll-mm

Literature List

- Kurtin, SE. Leukemia and Myelodysplastic Syndromes. In Yarbro C, Wujick D, & Holmes-Gobel B, Ed. Cancer Nursing: Principles and Practice, 7th Ed. 2010; Jones and Bartlett Publishers LLC. MA. 1369-1398.
- Kurtin S & Demakos E. An Update in the Treatment of Myelodysplastic Syndromes. Clin J Oncol Nurs. 2010. doi:10.1188/10.Clin J Oncol Nurs.E24-E39.
- Kurtin, S. Risk Analysis in the Treatment of Hematological Malignancies in the Elderly. J Adv Pract Oncol. 2010;1:119-129.
- Kurtin S. Journal of the Advanced Practitioner in Oncology, 2010;1:119-129.
- Kurtin S. JAdPrO submitted for publication June, 2011.
- Larson R. Etiology and management of Therapy-Related Myeloid Leukemia. Hematology. 2007;453-458.

Literature List

- Life Beyond Limits - http://www.mdslifebeyondlimits.org/wp-content/uploads/2011/06/Survey_Trends_Treating_MDS-Brochure_Full.pdf
- List AF, Sandberg AA, Doll DC: Myelodysplastic Syndromes, in Lee GL, Bithell T, Forester J et al (eds). Wintrobes Clinical Hematology, 11th ed. Philadelphia, Pennsylvania, Lippincott Williams and Wilkins, 2004, pp 2207-2234.
- Malcovati L et al. J Clin Oncol 2005;23:7594-603.
- Malcovati L, Porta MG, Pascutto C, et al. Prognostic factors and life expectancy in myelodysplastic syndromes classified according to WHO criteria: a basis for clinical decision making. J Clin Oncol. 2005;23:7594-7603.
- Malcovati L et al. J Clin Oncol 2007;23:3503-10.

Literature List

- NCCN Practice Guidelines in Oncology - Cancer and Chemotherapy Induced Anemia v2.2010 @ http://www.nccn.org/professionals/physician_gls/PDF/anemia.pdf
- NCCN Practice Guidelines in Oncology - Cancer Related Fatigue v1.2010 @ http://www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf
- National Comprehensive Cancer Network. (2010). NCCN Clinical Practice Guidelines in Oncology™. Myelodysplastic syndromes. V.2.2010. Retrieved February 19, 2010, from http://www.nccn.org/professionals/physician_gls/PDF/mds.pdf
- Ossenkoppele G.J. Infocus Myelodysplastisch syndroom. Alphen a/d Rijn, Van Zuiden Communications BV, 2010.
- Pederson-Bjergaard et al, 2007;Hematology;392-397.

Literature List

- Saif M, Lichtman S. Chemotherapy options and outcomes in older adult patients with colorectal cancer. Crit Rev Oncology/Hematology. 2009;72:155-169
- Santini V et al. Poster presentation at ASH 2008, San Francisco, CA, USA
- Santini V et al. Leuk Res 2009;33(Suppl. 1):s133.
- Scott and Deeg. Myelodysplastic Syndromes. *Annu Rev Med*. 2010;53:345-58.
- Slaets JP. Vulnerability in the elderly: frailty. Med Clin North Am. 2006 Jul;90(4):593-601
- Silverman. In: Cancer Medicine 7th ed. 2006.
- Steensma D. & Bennett JM: The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

Literature List

- Stem cell basics. National Institutes of Health Stem Cell Information Web site. Available at: http://stemcells.nih.gov/info/basics/basics4.asp. Accessed April 7, 2009.
- Tefferi A & Vardiman JW, N Eng J Med, 2009
- Tinetti ME, Fried T. The end of the disease era. Am J Med. 2004 Feb 1;116(3):179-85
- Takatoku M et al. Eur J Haematol 2007;
- Tijdschr Gerontol Geriatr. 2007 May;38(2):65-76
- Vidaza EU SmPC. Available at http://www.emea.europa.eu/humandocs/PDFs/EPAR/vidaza/H-978-PIen.pdf
- Wang, XS. Pathophysiology of Cancer-Related Fatigue. Clin J Oncol Nurs. 2008;12(suppl):5, 11-20.
- Wedding U. Cancer Control 2007;14(1):44-56.
- www.cancer.gov/help

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