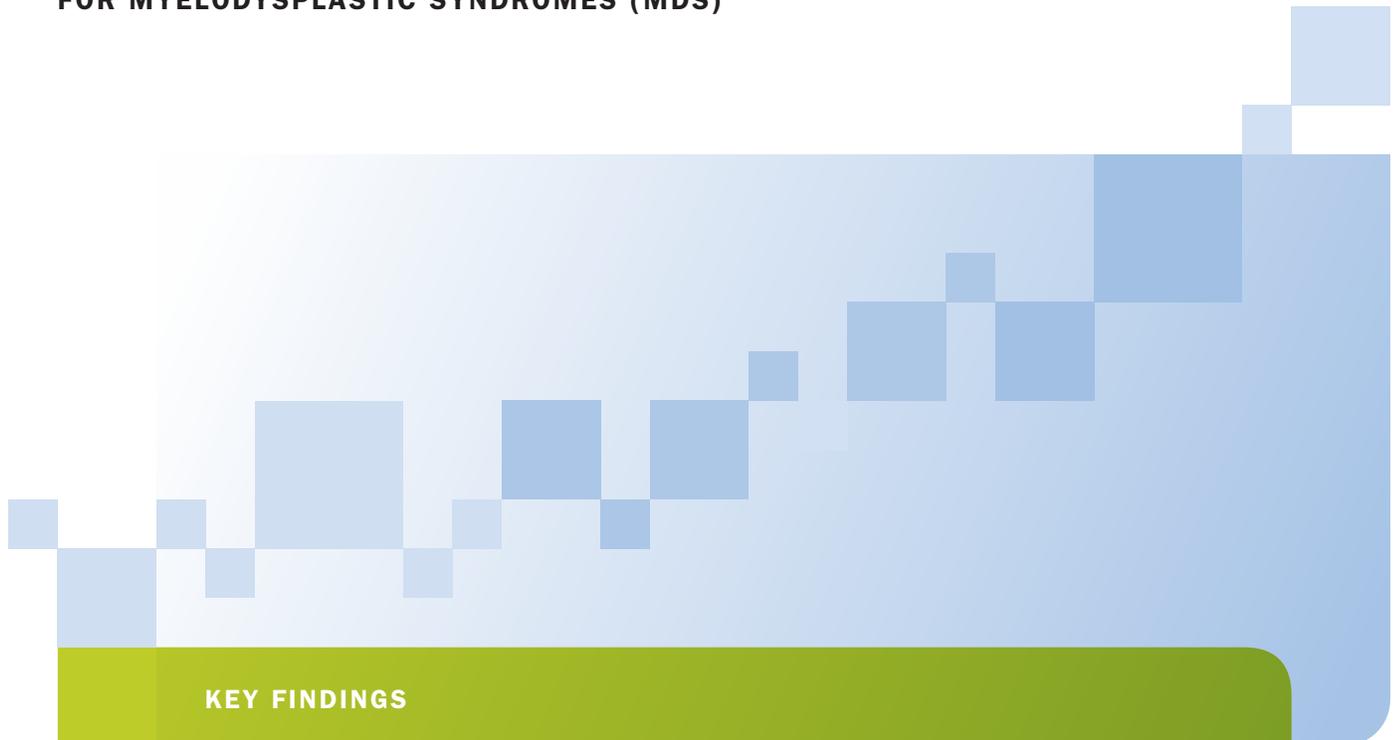


# HCT in MDS

TRENDS IN HEMATOPOIETIC CELL TRANSPLANTATION  
FOR MYELODYSPLASTIC SYNDROMES (MDS)



## KEY FINDINGS

1

***Revised risk assessment tools improve prognostic stratification of MDS patients***

A revised IPSS further refines prognostics and progression risk.

2

***Improved HCT outcomes in MDS; increasing number of older patients eligible***

Advances in clinical care and HLA matching have improved overall outcomes.

3

***Early planning for transplant is critical***

Novel agents to control progression and timely transplant consultation allow for transplant when optimal for the patient.



# Trends in HCT for MDS

As the general population ages, the prevalence of MDS is increasing, and more patients with MDS are undergoing allogeneic hematopoietic cell transplantation (HCT) to treat their disease with curative intent. [1,2]

Major trends driving the growing use of HCT in patients with MDS include:  
 1) Reduced-intensity conditioning regimens that permit more MDS

patients to undergo HCT; 2) Advances in post-transplant clinical care that have improved outcomes; 3) The use of hypomethylating agents to slow or stabilize disease progression, allowing a bridge to transplant for many patients; and 4) A decision by the Centers for Medicare and Medicaid Services (CMS) to cover transplants for MDS when performed on clinical studies approved by Medicare.

## Advances in MDS

### New scoring system

The International Prognostic Scoring System (IPSS), in use since 1997 to determine the prognosis of MDS patients and predict outcome after allogeneic HCT, was updated and revised in 2012. The new IPSS-R:

- Increases the number of major prognostic categories from 4 to 5
- Increases the number of cytogenetic prognostic subgroups from 3 to 5
- Splits low marrow blast percentage into 2 ranges: 0-2%, >2-<5%
- Takes into account the depth of cytopenias [3]

Figure 1 shows a highly significant correlation between IPSS-R category and survival. [3]

IPSS-R category correlates with survival

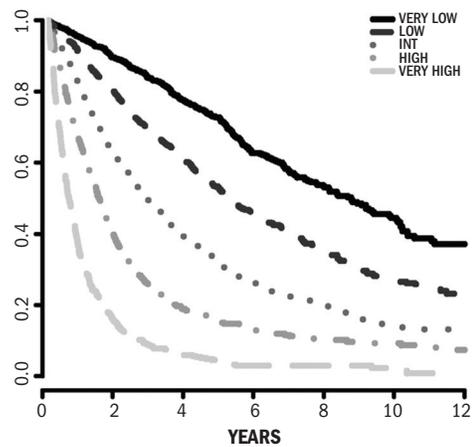


Figure 1. Survival related to prognostic risk categories of MDS patients (n=7,012, Dxy=0.43, p<0.001). (From Greenberg PL, et al. [3] Reprinted with permission.)

### New application of MDS drugs

Hypomethylating agents such as 5-azacitidine (AZA) and decitabine have been shown to be active in controlling the progression and symptoms of MDS. Some physicians are therefore using hypomethylating agents as a bridge to transplant, i.e., stabilizing disease to allow time for a planned transplant.

A 2010 study found that AZA was useful in stabilizing patients with MDS and allowed them to proceed to transplant, where they achieved

outcomes comparable to patients not pre-treated with AZA. [4] And a 2012 study found that either AZA or induction chemotherapy prior to HCT resulted in similar outcomes. [5]

Post-transplant AZA may also prevent or delay hematologic relapse in patients transplanted for MDS. [6]

### Improved survival

Several clinical factors have led to improved HCT outcomes in general, most notably better management of complications following HCT and enhanced patient-donor human leukocyte antigen (HLA) matching using DNA-based methods. [7-9] These same factors have also improved outcomes for patients with MDS.

Table 1 shows the improvement in two-year survival in unrelated donor transplants facilitated by the National Marrow Donor Program® (NMDP) for adults with MDS.

Improved two-year survival in HCT for MDS

TIME PERIOD	# OF TRANSPLANTS	2-YEAR SURVIVAL
2008 - 2010	1,016	47%
2004 - 2007	788	44%
1999 - 2003	453	39%
1987 - 1998	265	34%

Table 1. Two-year survival of MDS patients undergoing unrelated donor HCT at U.S. transplant centers. [10] Two-year survival is significantly improved for patients transplanted in 2004-2007 and 2008-2010 compared to patients transplanted during the two previous time periods (log-rank p-value <0.001).

# Patient selection changing, Medicare coverage approved

## Older patients eligible

The average age at diagnosis in MDS is approximately 70 years. The reduced-intensity and non-myeloablative conditioning regimens in use for more than a decade have permitted older patients and those with comorbidities to undergo HCT. A study published in 2012 shows similar outcomes using myeloablative compared to reduced-intensity regimens for transplants for AML or MDS. [11]

Research shows that chronological age alone should not serve as a barrier to allogeneic HCT in patients with MDS, and that instead, physical function and organ co-morbidities should be considered as factors in patient selection for transplant. [12,13]

## Medicare-approved study

Medicare patients with MDS can receive coverage from Medicare for HCT through a clinical study approved by the Centers for Medicare and Medicaid Services (CMS) under Coverage with Evidence Development.

The NMDP and its research arm, CIBMTR (Center for International Blood and Marrow Transplant Research), opened a CMS-approved clinical study to prospectively compare outcomes of allogeneic HCT in MDS patients  $\geq 65$  years of age with outcomes in younger patients.

As of October 2012, more than 630 patients have enrolled in this CIBMTR study. Visit [CIBMTR.org/HCTforMDS](http://CIBMTR.org/HCTforMDS) for enrollment information.

# Evidence-based HCT guidelines

## Optimal transplant timing for MDS

A landmark study demonstrated that IPSS high and intermediate-2 (INT-2) patients benefit most from immediate transplantation, whereas INT-1 and low-risk patients maximize their transplant outcomes by delaying HCT until disease progression. [14]

This transplant strategy is recommended by guidelines developed by the National Comprehensive Cancer Network (NCCN), as well as by a position statement developed by the American Society for Blood and Marrow Transplantation (ASBMT), which were based on evidence-based reviews. [15-17] ASBMT also recommends HCT for low-risk MDS patients (INT-1) who have poor prognostic features not included in the IPSS (e.g., older age, refractory cytopenias).

## Timing for transplant consultation

Based on ASBMT evidence-based reviews, the NMDP and the ASBMT developed guidelines to identify when patients should be referred for HCT consultation for autologous or allogeneic transplantation. [18] For some patients, early transplant may be indicated; for others, transplant may be needed later or not at all. Because appropriate planning and early donor identification are critical for optimal outcomes, early consultation is appropriate, even for patients who may never need HCT.

Table 2 shows an excerpt of these transplant consultation guidelines relating to patients with MDS.

### Recommended Timing for Transplant Consultation

#### MYELODYSPLASTIC SYNDROMES

Intermediate-1 or -2 (INT-1 or INT-2) or high IPSS score

Any MDS with poor prognostic features, including:

- Older age
- Refractory cytopenias
- Adverse cytogenetics
- Transfusion dependent

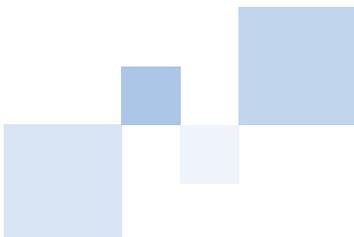
Table 2. Excerpt from NMDP/ASBMT guidelines highlighting patients at risk for disease progression who should be referred for transplant consultation. [18]

### ACCESS MDS RESOURCES

When considering transplant as a treatment for patients with MDS, quickly access:

- Outcomes data
- Clinical guidelines
- Research to help guide decision-making
- Education

Visit [marrow.org/md-MDS](http://marrow.org/md-MDS)



### CLINICAL ACTION POINTS

1

Review or revise treatment regimens for MDS, based on new research and updated prognostic scoring system.

2

Describe current HCT outcomes to patients with MDS; consider MDS patients for Medicare-approved HCT clinical study.

3

Use guidelines to identify patients who should be referred for HCT consultation.

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