Meet The Professors:
Myelodysplastic Syndromes Edition, 2016

CME Information

OVERVIEW OF ACTIVITY

The myelodysplastic syndromes (MDS) are a diverse group of hematologic disorders associated with ineffective production of myeloid blood cells. Patients with MDS generally experience resultant cytopenias, and their disease also has the significant potential for transformation to acute leukemia, leading to shortened survival. MDS is a disease that primarily affects older adults. Clinical care for the elderly is complicated by the myriad of physical, cognitive and psychosocial changes associated with aging, necessitating that medical oncologists and allied cancer professionals be able to individualize the treatment of these patients.

To offer optimal patient care — including the option of clinical trial participation — practicing medical oncologists, hematologists and hematology-oncology fellows must be well informed of advances in this field. *Meet The Professors* uses relevant case-based discussions between community oncologists and clinical investigators to assist practicing clinicians with the incorporation of this information into their management strategies for MDS.

LEARNING OBJECTIVES

- Develop an understanding of the various prognostic scoring systems, and use this information in counseling patients and treatment decision-making.
- Determine the optimal dosing schedule and treatment duration with azacitidine and decitabine.
- Appraise the role of bone marrow transplantation for patients with MDS.
- Evaluate available efficacy and safety data with the use of lenalidomide in patients with low- to intermediate-risk MDS with and without del(5q).
- Recognize the impact of patient-related factors, including age and cytogenetic abnormalities, on therapeutic planning and potential outcomes.
- Recall the emerging data with novel agents (eg, checkpoint inhibitors and TGF-beta inhibitors) being investigated in the treatment of MDS.

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Consulting Agreements: Amgen Inc, ARIAD Pharmaceuticals Inc, Celgene Corporation, Daiichi Sankyo Inc, Incyte Corporation, Janssen Biotech Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc, Seattle Genetics, Sunesis Pharmaceuticals Inc; **Contracted Research:** Agios Pharmaceuticals, Amgen Inc, Astellas Pharma Global Development Inc, Celator Pharmaceuticals Inc, Seattle Genetics, Takeda Oncology; **Data and Safety Monitoring Board:** GlycoMimetics Inc; **Speakers Bureau:** Celgene Corporation, Incyte Corporation, Novartis Pharmaceuticals Corporation.

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No relevant conflicts of interest to disclose.

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No relevant conflicts of interest to disclose.

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

A multi-center, randomized, double-blind, placebo-controlled clinical trial of deferasirox in patients with myelodysplastic syndromes (low/int-1 risk) and transfusional iron overload. NCT00940602

A phase I/IB study of ipilimumab or nivolumab in patients with relapsed hematologic malignancies after allogeneic hematopoietic cell transplantation. NCT01822509

A phase I/II study of ABT-199 in combination with low-dose cytarabine in treatment-naïve subjects with acute myelogenous leukemia who are ≥ 65 years of age and who are not eligible for standard anthracycline-based induction therapy. NCT02287233

A phase IB/II multi-arm study with venetoclax in combination with cobimetinib and venetoclax in combination with idasanutlin in patients aged ≥ 60 years with relapsed or refractory acute myeloid leukemia who are not eligible for cytotoxic therapy. NCT02670044

A phase II trial evaluating the combination of lirilumab and nivolumab with 5-azacitidine in patients with MDS. NCT02599649

A phase II trial evaluating the combination of nivolumab and ipilimumab with 5-azacitidine in patients with MDS. NCT02530463

A phase III trial to evaluate imetelstat (JNJ-63935937) in transfusion-dependent subjects with IPSS low or intermediate-1 risk MDS that is relapsed/refractory to erythropoiesis-stimulating agent (ESA) treatment. NCT02598661

Abel GA et al. **Patient-reported outcomes for the myelodysplastic syndromes: A new MDS-specific measure of quality of life.** *Blood* 2014;123(3):451-2.

Bejar R et al. **Somatic mutations predict poor outcome in patients with myelodysplastic syndrome after hematopoietic stem-cell transplantation.** *J Clin Oncol* 2014;32(25):2691-8.

Bejar R et al. **TET2 mutations predict response to hypomethylating agents in myelodysplastic syndrome patients.** *Blood* 2014;124(17):2705-12.

Cabrero M et al. **Discontinuation of hypomethylating agent therapy in patients with myelodysplastic syndromes or acute myelogenous leukemia in complete remission or partial response: Retrospective analysis of survival after long-term follow-up.** *Leuk Res* 2015;39(5):520-4.

Chesnais V et al. **Effect of lenalidomide treatment on clonal architecture of myelodysplastic syndromes without 5q deletion.** *Blood* 2016;127(6):749-60.

Daver N et al. **5-azacytidine (AZA) in combination with ruxolitinib (RUX) as therapy for patients (pts) with myelodysplastic/myeloproliferative neoplasms (MDS/MPNs).** *Proc ASH* 2015;**Abstract 823**.

Daver N et al. **FLT3 mutations in myelodysplastic syndrome and chronic myelomonocytic leukemia.** *Am J Hematol* 2013;88(1):56-9.

Giagounidis A et al. **Luspatercept treatment leads to long term increases in hemoglobin and reductions in transfusion burden in patients with low or intermediate-1 risk myelodysplastic syndromes (MDS): Preliminary results from the Phase 2 PACE-MDS extension study.** *Proc ASH* 2015;**Abstract 92**.

Giagounidis A et al. **Outcomes in RBC transfusion-dependent patients with low-/intermediate-1-risk myelodysplastic syndromes with isolated deletion 5q treated with lenalidomide: A subset analysis from the MDS-004 study.** *Eur J Haematol* 2014;93(5):429-38.

Greenberg PL et al. **A randomized controlled trial of romiplostim in patients with low- or intermediate-risk myelodysplastic syndrome receiving decitabine.** *Leuk Lymphoma* 2013;54(2):321-8.

Gurion R et al. **5-azacitidine prolongs overall survival in patients with myelodysplastic syndrome — A systematic review and meta-analysis.** *Haematologica* 2010;95(2):303-10.

Guryanova OA et al. **DNMT3A regulates myeloproliferation and liver-specific expansion of hematopoietic stem and progenitor cells.** *Leukemia* 2015;[Epub ahead of print].

Hollenbach P et al. **Lenalidomide promotes degradation of casein kinase 1a (CK1a) through cereblon: Implications for the efficacy of lenalidomide in MDS and AML.** *Proc ASH* 2014;**Abstract 3606**.

Jonasova A et al. **High level of full-length cereblon mRNA in lower risk myelodysplastic syndrome with isolated 5q deletion is implicated in the efficacy of lenalidomide.** *Eur J Haematol* 2015;95(1):27-34.

Kadia TM et al. **Final results of the phase II study of rabbit anti-thymocyte globulin, ciclosporin, methylprednisone, and granulocyte colony-stimulating factor in patients with aplastic anaemia and myelodysplastic syndrome.** *Br J Haematol* 2012;157(3):312-20.

Select Publications

Kantarjian HM et al. **Phase 2 study of romiplostim in patients with low- or intermediate-risk myelodysplastic syndrome receiving azacitidine therapy.** *Blood* 2010;116(17):3163-70.

Komrokji RS et al. **Phase I clinical trial of oral rigosertib in patients with myelodysplastic syndromes.** *Br J Haematol* 2013;162(4):517-24.

Lyons RM et al. **Hematologic response to three alternative dosing schedules of azacitidine in patients with myelodysplastic syndromes.** *J Clin Oncol* 2009;27(11):1850-6.

Nazha A et al. **Outcomes of patients with myelodysplastic syndromes who achieve stable disease after treatment with hypomethylating agents.** *Leuk Res* 2016;41:43-7.

Oliva EN et al. **Eltrombopag for the treatment of thrombocytopenia of low and intermediate-1 IPSS risk myelodysplastic syndromes: Interim results on efficacy, safety and quality of life of an international, multicenter prospective, randomized, trial.** *Proc ASH* 2015;**Abstract 91**.

Patel B et al. **Genetic and molecular characterization of myelodysplastic syndromes and related myeloid neoplasms.** *Int J Hematol* 2015;101(3):213-8.

Patnaik MM et al. **Predictors of survival in refractory anemia with ring sideroblasts and thrombocytosis (RARS-T) and the role of next-generation sequencing.** *Am J Hematol* 2016;91(5):492-8.

Raj K et al. **CDKN2B methylation status and isolated chromosome 7 abnormalities predict responses to treatment with 5-azacytidine.** *Leukemia* 2007;21(9):1937-44.

Remacha ÁF et al. **Evolution of iron overload in patients with low-risk myelodysplastic syndrome: Iron chelation therapy and organ complications.** *Ann Hematol* 2015;94(5):779-87.

Santini V et al. **The effect of lenalidomide on health-related quality of life (HRQoL) in patients with MDS: Results from the MDS-005 trial.** *Leuk Res* 2015;39(Suppl 1):60.

Santini V et al. **Efficacy and safety of lenalidomide (LEN) versus placebo (PBO) in RBC-transfusion dependent (TD) patients (Pts) with IPSS low/intermediate (Int-1)-risk myelodysplastic syndromes (MDS) without del(5q) and unresponsive or refractory to erythropoiesis-stimulating agents (ESAs): Results from a randomized phase 3 study (CC-5013-MDS-005).** *Proc ASH* 2014;**Abstract 409**.

Santini V et al. **Minimizing risk of hypomethylating agent failure in patients with higher-risk MDS and practical management recommendations.** *Leuk Res* 2014;38(12):1381-91.

Savona M et al. **Results of first in human (FIH) phase 1 pharmacokinetic (PK) guided dose-escalation study of ASTX727, a combination of the oral cytidine deaminase inhibitor (CDAi) E7727 with oral decitabine in subjects with myelodysplastic syndromes (MDS).** *Proc ASH* 2015;**Abstract 1683**.

Scott BL et al. **Results of a Phase III randomized, multi-center study of allogeneic stem cell transplantation after high versus reduced intensity conditioning in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML): Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0901.** *Proc ASH* 2015;**Abstract LBA-8**.

Sekeres MA et al. **Additional analyses of a randomized phase II study of azacitidine combined with lenalidomide or with vorinostat vs azacitidine monotherapy in higher-risk myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML): North American Intergroup study SWOG S1117.** *Proc ASH* 2015;**Abstract 908**.

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Silverman LR et al. **Clinical activity and safety of the dual pathway inhibitor rigosertib for higher risk myelodysplastic syndromes following DNA methyltransferase inhibitor therapy.** *Hematol Oncol* 2015;33(2):57-66.

Steensma DP et al. **Practical recommendations for hypomethylating agent therapy of patients with myelodysplastic syndromes.** *Hematol Oncol Clin North Am* 2010;24(2):389-406.

Toma A et al. **Lenalidomide with or without erythropoietin in transfusion-dependent erythropoiesis-stimulating agent-refractory lower-risk MDS without 5q deletion.** *Leukemia* 2016;30(4):897-905.

Yang H et al. **Expression of PD-L1, PD-L2, PD-1 and CTLA4 in myelodysplastic syndromes is enhanced by treatment with hypomethylating agents.** *Leukemia* 2014;28(6):1280-8.