Myelodysplastic Syndromes Update

Volume 1, Issue 1 (Video Program)

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, radiation oncologists, nurses and other healthcare providers involved in the treatment of hematologic cancers.

OVERVIEW OF ACTIVITY

The clinical management of myelodysplastic syndromes remains a challenge from both a diagnostic and treatment standpoint, despite recent gains made in the understanding of this heterogeneous disease. Determining which treatment approach is most appropriate for a given patient requires careful consideration of patient-specific characteristics, physician expertise and available health system resources. To bridge the gap between research and patient care, this issue of *Myelodysplastic Syndromes Update* features one-on-one discussions with leading hematology-oncology investigators. By providing information on the latest clinical developments in the context of expert perspectives, this activity assists medical oncologists, hematologists and hematology-oncology fellows with the formulation of evidence-based and current therapeutic strategies, which in turn facilitates optimal patient care.

LEARNING OBJECTIVES

- Recognize the key cancer-defining features of MDS, and counsel patients accordingly regarding their prognosis, treatment goals and options.
- Appraise the role of molecular testing for MDS to facilitate diagnosis, prognostication and treatment decision-making.
- Formulate a treatment algorithm for patients with lower- and higher-risk MDS, considering patient- and disease-related factors, including cytogenetic abnormalities.
- Consider the available efficacy and safety data with the use of lenalidomide in patients with low- to intermediate-risk MDS with and without del(5q), and identify patients with MDS appropriate for this treatment.
- Evaluate the potential advantages of orally administered hypomethylating agents compared to standard parenteral administration of these drugs.
- Ascertain the utility of novel agents, such as luspatercept, in the management of anemia in patients with MDS, and consider its future role in clinical management.
- Recall promising investigational agents (eg, anti-PD-1/anti-PD-L1 monoclonal antibodies, venetoclax, IDH1/2 inhibitors) and combination strategies, and counsel appropriately selected patients regarding clinical trial enrollment.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.75 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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EDITOR — **Dr Love** is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

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This activity is supported by educational grants from Celgene Corporation.

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

Last review date: August 2017

Expiration date: August 2018

Select Publications

Almeida A et al. **Recent advances in the treatment of lower-risk non-del(5q) myelodysplastic syndromes (MDS).** *Leuk Res* 2017;52:50-7.

Arber D et al. **The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia.** *Blood* 2016;127(20):2391-405.

Bose P et al. **Phase-2 study of sotatercept (ACE-011) in myeloproliferative neoplasm-associated myelofibrosis and anemia.** *Proc ASH* 2016;**Abstract 478**.

Chen N et al. **Pharmacokinetics and exposure–response of luspatercept in patients with anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS): Preliminary results from Phase 2 studies.** *Proc ASH* 2016;**Abstract 1990**.

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

Fenaux P et al; MDS-004 Lenalidomide Del5q Study Group. **A randomized phase 3 study of lenalidomide versus placebo in RBC transfusion-dependent patients with low-/intermediate-1-risk myelodysplastic syndromes with del5q.** *Blood* 2011; 118(14):3765-76.

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(3):223-32.

Garcia-Manero G et al. **A Phase II study evaluating the combination of nivolumab (nivo) or ipilimumab (ipi) with azacitidine in pts with previously treated or untreated myelodysplastic syndromes (MDS).** *Proc ASH* 2016;**Abstract 344**.

Garcia-Manero G et al. **Efficacy and safety of extended dosing schedules of CC-486 (oral azacitidine) in patients with lower-risk myelodysplastic syndromes.** *Leukemia* 2016;30(4):889-96.

Garcia-Manero G et al. **Pembrolizumab, a PD-1 inhibitor, in patients with myelodysplastic syndrome (MDS) after failure of hypomethylating agent treatment.** *Proc ASH* 2016;**Abstract 345**.

Hendrix K et al. **Myelodysplastic/myeloproliferative neoplasms unclassified (MDS/MPN-U) overlap: Can we alter the natural history?** *Blood* 2016;128:3125.

Iwanaga M et al. **Risk of myelodysplastic syndromes in people exposed to ionizing radiation: A retrospective cohort study of Nagasaki atomic bomb survivors.** *J Clin Oncol* 2011;29(4):428-34.

Jabbour E et al. **A randomized Phase II study of low-dose decitabine versus azacitidine in patients with low- or intermediate-1-risk myelodysplastic syndromes: A report on behalf of the MDS Clinical Research Consortium.** *Proc ASH* 2016;**Abstract 226**.

Kantarjian H et al. **Decitabine improves patient outcomes in myelodysplastic syndromes: Results of a phase III randomized study.** *Cancer* 2006;106(8):1794-803.

Komrokji R et al. **A phase 2, dose-finding study of sotatercept (ACE-011) in patients with lower-risk myelodysplastic syndromes (MDS) or non-proliferative chronic myelomonocytic leukemia (CMML) and anemia requiring transfusion.** *Leuk Res* 2015;39:1(Suppl).

Kuendgen A et al. **Frequency and prognostic significance of cytogenetic abnormalities in 1269 patients with therapy-related myelodysplastic syndrome — A study of the International Working Group (IWG-PM) for Myelodysplastic Syndromes (MDS).** *Proc ASH* 2016;**Abstract 112**.

Lewinsohn M et al. **Novel germ line DDX41 mutations define families with a lower age of MDS/AML onset and lymphoid malignancies.** *Blood* 2016;127(8):1017-23.

List A et al. **Combined treatment with lenalidomide (LEN) and epoetin alfa (EA) is superior to lenalidomide alone in patients with erythropoietin (epo)-refractory, lower risk (LR) non-deletion 5q [del(5q)] myelodysplastic syndrome (MDS): Results of the E2905 Intergroup study—An ECOG-ACRIN Cancer Research Group study, Grant CA180820, and the National Cancer Institute of the National Institutes of Health.** *Proc ASH* 2016;**Abstract 223**.

Lübbert M et al. **Low-dose decitabine versus best supportive care in elderly patients with intermediate- or high-risk myelodysplastic syndrome (MDS) ineligible for intensive chemotherapy: Final results of the randomized phase III study of the European Organisation for Research and Treatment of Cancer Leukemia Group and the German MDS Study Group.** *J Clin Oncol* 2011; 29(15):1987-96.

Mittelman M et al. **Azacitidine-lenalidomide (ViLen) combination yields a high response rate in higher risk myelodysplastic syndromes (MDS)-ViLen-01 protocol.** *Ann Hematol* 2016;95(11):1811-8.

Park S et al. **Outcome of lower-risk patients with myelodysplastic syndromes without 5q deletion after failure of erythropoiesis-stimulating agents.** *J Clin Oncol* 2017;35(14):1591-7.

Select Publications

Platzbecker U et al. **Luspatercept increases hemoglobin and reduces transfusion burden in patients with low-intermediate risk myelodysplastic syndromes (MDS): Long-term results from Phase 2 PACE-MDS study.** *Proc ASH* 2016;**Abstract 3168**.

Polprasert C et al. **Inherited and somatic defects in DDX41 in myeloid neoplasms.** *Cancer Cell* 2015;27(5):658-70.

Saiki R et al. **NGS-based copy number analysis in 1,185 patients with myeloid neoplasms.** *Proc ASH* 2016;**Abstract 955**.

Santini V et al. **Randomized Phase III study of lenalidomide versus placebo in RBC transfusion-dependent patients with lower-risk non-del(5q) myelodysplastic syndromes and ineligible for or refractory to erythropoiesis-stimulating agents.** *J Clin Oncol* 2016;34(25):2988-96.

Santini V. **Treatment of low-risk myelodysplastic syndromes.** *Hematology Am Soc Hematol Educ Program* 2016;(1):462-9.

Sekeres MA et al. **Randomized Phase II study of azacitidine alone or in combination with lenalidomide or with vorinostat in higher-risk myelodysplastic syndromes and chronic myelomonocytic leukemia: North American Intergroup study SWOG S1117.** *J Clin Oncol* 2017;[Epub ahead of print].

Stein E et al. **Enasidenib (AG-221), a potent oral inhibitor of mutant isocitrate dehydrogenase 2 (*IDH2*) enzyme, induces hematologic responses in patients with myelodysplastic syndromes (MDS).** *Proc ASH* 2016;**Abstract 343**.

Tiu RV, Sekeres MA. **Making sense of the myelodysplastic/myeloproliferative neoplasms overlap syndromes.** *Curr Opin Hematol* 2014;21(2):131-40.

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.

Van de Loosdrecht A et al. **Lenalidomide with or without erythropoietin and granulocyte-colony stimulating factor shows efficacy in patients with low and intermediate-1 risk myelodysplastic syndrome with or without del 5q, refractory or unlikely to respond to erythropoietin. Results of a HOVON89 Phase II randomized multicenter study. (EudraCT 2008-002195-10).** *Proc ASH* 2016;**Abstract 224**.