Treating Anemia in MDS

A pocket guide on active treatments for anemia in patients with MDS

Goals of Treatment

Many patients with MDS become transfusion-dependent, resulting in complications. Active treatments can be used to help manage anemia associated with MDS. The primary goals of active treatment for LR-MDS are to increase patient quality of life by improving cytopenias and decreasing transfusion burden.[1]

Active Treatments

Official recommendations describing the use of active treatments for MDS continue to evolve. **Please review the latest NCCN Guidelines® for more information. Scan QR code here.**

	Mechanism of action	Role in MDS	Potential characteristics & limitations
Erythroid Maturation Agents (EMAs)[2-4] **Luspatercept**	Fusion proteins that inhibit the activity of TGF-β ligands, allowing for erythroid maturation through differentiation and increased erythroid precursors, thereby increasing RBC production and improvement of anemia	EMAs can be used for the treatment of anemia associated with MDS in patients with transfusion-dependent, LR-MDS regardless of previous exposure to ESAs	• May improve anemia associated with MDS • May facilitate transfusion independence and increased hemoglobin • Can be used regardless of prior ESA use • Risk of AEs including hypertension, fatigue, diarrhea, nausea, and dizziness
Erythropoiesis-Stimulating Agents (ESAs)[5-11] **Epoetin alfa, Darbepoetin alfa**	Recombinant human glycoproteins that mimic the effect of EPO, promoting differentiation, proliferation, and survival to drive production of mature RBCs	ESAs are not indicated for treatment of anemia associated with MDS within the US, however there are clinical data to support their use in this setting	• May improve anemia associated with MDS • Can reduce the need for RBC transfusions • Not FDA-approved for MDS • Some patients are or may become treatment refractory • Risk of AEs including asthenia, fatigue, and dyspnea
Hypomethylating Agents (HMAs)[1,12-15] **Azacitidine, Decitabine, Cedazuridine**	Small molecules that are incorporated into nucleic acids, inhibiting DNA methylation and inducing hypomethylation to prevent the silencing of tumor suppressor genes	• HMA use for treatment of LR-MDS is limited to late stages of treatment after failure of 1L ESAs • HMAs are the only approved therapeutics for patients with HR-MDS who are not suitable for intensive treatment options	• May lead to achievement of transfusion independence • Can be used as a low dose, 3-day regimen based on prospective studies • Patients may be at risk for developing resistance and relapse • Risk of AEs including cytopenias, embryo-fetal toxicity, hepatotoxicity, renal toxicity, tumor lysis syndrome, and myelosuppresion
Immunomodulatory Agents (IMiDs)[5,9,16,17] **Lenalidomide**	Modulate E3 ubiquitin ligase substrate specificity, inhibiting proliferation and inducing apoptosis of MDS cells, as well as modulating immune cells in the bone marrow microenvironment to decrease cytopenias	IMiDs are used for the treatment of low- or intermediate-1 risk transfusion-dependent MDS with del(5q) with or without additional cytogenetic abnormalities	• May lead to achievement of transfusion independence • Clinical data demonstrated complete cytogenetic response • Limited efficacy in patients without del(5q) • **Black box warning for embryo-fetal toxicity, hematologic toxicity, and venous and arterial thromboembolism**

The material herein is presented side-by-side for convenience purposes only. Head-to-head comparisons should not be made across products.

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Targeted Therapy

	Mechanism of action	Role in MDS	Potential characteristics & limitations
Telomerase Inhibitors[4,18-20] **Imetelstat**	Inhibit telomerase activity and prevent the continual growth of malignant cells, promoting cell death	Telomerase inhibitors can be used to treat adult patients with transfusion-dependent, LR-MDS who are unresponsive to or ineligible for ESA use	• May lead to achievement of transfusion independence • May reduce underlying population of malignant clones • Risk of AEs, including severe thrombocytopenia or neutropenia, infusion-related reactions, infections or sepsis, fracture, cardiac failure, hemorrhage, elevated liver enzymes, and fatigue
IDH1/IDH2 Inhibitors[21-28] **Ivosidenib (IDH1), Olutasidenib (IDH1), and Enasidenib (IDH2)**	Block the activity of mutant IDH1 or IDH2 to induce myeloid differentiation and hematopoietic recovery	IDH1 inhibitors are used for treatment of adult patients with relapsed/refractory MDS and a susceptible *IDH1* (or *IDH2*; under investigation) mutation confirmed by molecular testing	• May reduce blast cell counts and increase mature myeloid cells • May lead to achievement of transfusion independence • Potential achievement of complete remission within ~6 months • Risk of AEs, including irregular heart rhythm, Guillain-Barré syndrome, fatigue, rash, leukocytosis, and laboratory abnormalities • **Black box warning for differentiation syndrome**

For all therapies described, please see the full US Prescribing Information for more details, including warnings and adverse events.

Abbreviations: 1L, first-line; AE, adverse event; EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; FDA, U.S. Food and Drug Administration; HR-MDS, higher-risk MDS; IDH, isocitrate dehydrogenase; IMiD, immunomodulatory drugs; LR-MDS, lower-risk MDS; MDS, myelodysplastic syndromes; QoL, quality of life; RBC, red blood cell; TGF, transforming growth factor.

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