MYELODYSPLASTIC SYNDROMES TREATMENT REGIMENS (Part 1 of 3)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

First-Line Treatment[1]

Note: All recommendations are Category 2A unless otherwise indicated.

Relatively Lower-Risk Patients[ab]

Symptomatic Anemia With del(5q) ± Other Cytogenetic Abnormalities

REGIMEN	DOSING
Lenalidomide[2-5c]	**Days 1–21:** Lenalidomide 10mg orally once daily. Repeat cycle every 28 days (or 28 days monthly). Assess response 2–4 months after initiation of treatment.

Symptomatic Anemia Without del(5q) and Serum Erythropoietin ≤500mU/mL

rHu-Epo ± G-CSF[6-11]	rHu-Epo 40,000-60,000 subcutaneous units 1–3 times weekly. Repeat cycle 6–8 weeks. Add G-CSF if no response occurs during treatment. G-CSF 1–2mcg/kg subcutaneously daily 1–3 times weekly. Repeat cycle for 6–8 weeks. If no response observed after this treatment course, discontinue treatment.
Darbepoetin alfa ± G-CSF[8-15]	Darbepoetin alfa 150–300 mcg subcutaneously weekly. Repeat cycle for up to 24 weeks. Add G-CSF if no response occurs during treatment. G-CSF 1–2mcg/kg subcutaneously daily 1–3 times weekly. Repeat cycle for 6–8 weeks. If no response observed after this treatment course, discontinue treatment.

Symptomatic Anemia Without del(5q), Serum Erythropoietin >500mU/mL, Likely to Respond to IST[d]

ATG + Cyclosporine A[16-19]	**Days 1–4:** ATG (rabbit or equine) 40mg/kg IV daily, **plus** Cyclosporine 5–6mg/kg (initial dose) orally twice daily, and adjusted for blood levels between 100–300ng/mL per institutional guidelines.

Symptomatic Anemia Without del(5q), Serum Erythropoietin >500mU/mL, Unlikely to Respond to IST[e]

Azacitidine[20-23]	**Days 1–7:** Azacitidine 75mg/m² IV infusion or subcutaneous injection once daily. Repeat cycle every 4 weeks. After 2 cycles, dose can be increased to 100mg/m² if no beneficial effect is seen and no toxicity other than nausea and vomiting has occurred. Patients should be treated for a minimum of 4–6 cycles. Complete or partial response may require additional treatment cycles.
Decitabine[24-26]	**Days 1–3:** Decitabine 15mg/m² IV infusion over 3 hours, repeated every 8 hours. Repeat cycle every 6 weeks for minimum of 4–6 cycles. **OR** **Days 1–5:** Decitabine 20mg/m² IV infusion daily over 1 hour. Repeat cycle every 4 weeks for minimum of 4–6 cycles.
Lenalidomide[2-5]	**Days 1–21:** Lenalidomide 10mg orally once daily. Repeat cycle every 28 days (or 28 days monthly). Assess response 2–4 months after initiation of treatment.

Higher-Risk Patients[bf]

Transplant candidate with available donor stem cells[g]

Allogeneic HCT[27-29]	HLA-matched sibling is preferred donor, but HLA-matched unrelated donor can be considered. High-dose conditioning is typically used for younger patients, whereas reduced intensity conditioning is generally used for older patients (≥60 years).
High-Intensity Chemotherapy + HCT[30h]	**Days 1–3:** An anthracycline (daunorubicin 60–90mg/m² IV infusion OR idarubicin 12mg/m²), **plus** **Days 1–7:** Cytarabine 100–200mg/m² IV infusion. **AND** HCT upon reduction of bone marrow blast count.

continued

MYELODYSPLASTIC SYNDROMES TREATMENT REGIMENS (Part 2 of 3)

First-Line Treatment[1] (continued)

Higher-Risk Patients[bf]

Transplant candidate with available donor stem cells[g]

REGIMEN	DOSING
Azacitidine + HCT[20-23h]	**Days 1–7:** Azacitidine 75mg/m² IV infusion or subcutaneous injection once daily. Repeat cycle every 4 weeks. After 2 cycles, dose can be increased to 100mg/m² if no beneficial effect is seen and no toxicity other than nausea and vomiting has occurred. Patients should be treated for a minimum of 4–6 cycles. Complete or partial response may require additional treatment cycles. **AND** HCT upon reduction of bone marrow blast count.
Decitabine + HCT[24-26h]	**Days 1–3:** Decitabine 15mg/m² IV infusion over 3 hours, repeated every 8 hours. Repeat cycle every 6 weeks for minimum of 4–6 cycles. **OR** **Days 1–5:** Decitabine 20mg/m² IV infusion daily over 1 hour. Repeat cycle every 4 weeks for minimum of 4–6 cycles. **AND** HCT upon reduction of bone marrow blast count.

Transplant candidate with no available donor stem cells or not a transplant candidate[i]

Azacitidine (Category 1)[20-23]	**Days 1–7:** Azacitidine 75mg/m² IV infusion or subcutaneous injection once daily. Repeat cycle every 4 weeks. After 2 cycles, dose can be increased to 100mg/m² if no beneficial effect is seen and no toxicity other than nausea and vomiting has occurred. Patients should be treated for a minimum of 4–6 cycles. Complete or partial response may require additional treatment cycles.
Decitabine[24-26]	**Days 1–3:** Decitabine 15mg/m² IV infusion over 3 hours, repeated every 8 hours. Repeat cycle every 6 weeks for minimum of 4–6 cycles. **OR** **Days 1–5:** Decitabine 20mg/m² IV infusion daily over 1 hour. Repeat cycle every 4 weeks for minimum 4–6 cycles.

Abbreviations: ATG: antithymocyte globulin; *EPO:* erythropoietin; *ESA:* erythropoiesis-stimulating agent; *G-CSF:* granulocyte-colony stimulating factor; *HCT:* hematopoietic cell transplantation; *HLA:* human leukocyte antigen; *IPSS:* International Prognostic Scoring System; *IPSS-R:* International Prognostic Scoring System-Revised; *IST:* immunosuppressive therapy; *rHu-Epo:* recombinant human erythropoietin; *WPSS:* Work Health Organization Prognostic Scoring System.

a Includes patients classified as IPSS Low or Intermediate-1; IPSS-R Very Low, Low, or Intermediate; or WPSS Very Low, Low, or Intermediate.

b Patients classified as IPSS-R Intermediate can be treated using the regimens for either risk group, depending on additional risk factors such as age, performance status, and serum ferritin and serum lactate dehydrogenase levels.

c Lenalidomide should be avoided in patients with a clinically significant decrease in neutrophil or platelet counts. An initial trial of ESAs can be considered instead of lenalidomide in patients with serum erythropoietin <500mU/mL.

d Factors associated with a higher likelihood of a good response include age ≤60 years; ≤5% marrow blasts or hypocellular marrows; HLA-DR15 positivity; PNH clone positivity; or presence of STAT-3 mutant cytotoxic T cell clones.

e Patients lack features associated with features listed in footnote d.

f Includes patients classified as IPSS Intermediate-2 or High; IPSS-R Intermediate, High, or Very High; or WPSS High or Very High.

g High-intensity chemotherapy, azacitidine, or decitabine are administered before HCT when tumor burden needs to be reduced before performing HCT.

h Even a partial remission following treatment might be sufficient to enable HCT.

i Patients who show clinical benefit with azacitidine or decitabine should continue treatment with a hypomethylating agent as maintenance therapy.

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