

New Paradigm in the Management of Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) are now believed to be among the most common hematologic malignancies, affecting an estimated 15,000 persons annually in the United States.¹ This hematologically diverse spectrum of stem cell disorders demonstrates an equally diverse natural history.¹ Ineffective hematopoiesis is the hallmark of these disorders manifested by anemia, neutropenia, and thrombocytopenia. Evolution to acute myeloid leukemia occurs in approximately one third of unselected patients, but even in its absence patients succumb to complications of cytopenias and functional impairments including infection, bleeding, and iron overload.² Supportive care, which has been the empiric mainstay for most patients, involves the administration of transfusions and the use of recombinant erythropoietin and myeloid growth factors. However, the impact of such treatment on the natural history of the disease is uncertain, and growth factor therapy is most effective for patients with the lowest transfusion burden. Although hematopoietic stem cell transplantation offers the prospect for cure in younger patients with higher-risk disease, procedure-related mortality is excessive, and the majority of patients with MDS are not candidates for stem cell transplantation due to age, lack of a histocompatible donor, or comorbid medical factors.

Progress in the development of effective treatment for patients with MDS has until recent years been slow. We now recognize that the morphologic features applied to define these disorders identify a malignant phenotype that may arise from mechanistically diverse biological processes. This recognition has raised awareness that treatment strategies must be tailored to the pathobiology of the disease. The clinical and biological heterogeneity of MDS that initially challenged therapeutic advancement has now catapulted MDS to the center stage of drug development.

Indeed, years of empiric reliance on blood product transfusions and recombinant hematopoietic cytokines have given way to novel treatment strategies that offer the prospect to alter the natural history of the disease. Azacitidine (Vidaza®, Pharmion Corp; Boulder, Colo) is the first agent approved by the Food and Drug Administration for the treatment of MDS that is now expected to permanently change the therapeutic landscape of this disease.

This supplement provides an overview of the current treatment strategies for MDS and the evolution of the

treatment paradigm. Steven Gore, MD, of the Sidney Kimmel Cancer Center provides an opening discussion by summarizing therapeutic goals framed by prognostic features and expectations for survival. Second, Richard Stone, MD, of the Dana-Farber Cancer Center discusses currently available approaches and novel therapeutics on the horizon. Third, Lewis Silverman, MD, of Mount Sinai Medical Center and the lead investigator for the Cancer and Lung Group B (CALGB) cooperative group study in MDS, provides an overview of the pharmacology and results of clinical trials investigating methyltransferase inhibitors and azacitidine. Finally, I outline a new treatment algorithm for MDS built upon the incorporation of active therapy that represents consensus recommendations of thought leaders on this disease.

MDS is no longer an “orphan disease” without effective treatment options. Through this supplement, the contributors aspire to raise awareness and invite discussion that will lead to new and effective additions to the treatment paradigm.

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References

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