

## Lenalidomide: From Bench to Bedside (Part 1)

For those of us involved in clinical research or the management of patients with hematologic malignancies, we realize that therapeutic advances emerge on the heels of discoveries clarifying disease biology. The myelodysplastic syndromes (MDS), however, have for years seemed somewhat immune to such progress, with forced reliance on supportive or symptomatic measures of care. As enigmatic as the name implies, this collection of stem cell malignancies or “syndromes” displays wide ranging variation in hematologic and pathologic presentation, natural history, and management goals.<sup>1</sup> Despite their relative frequency, insight into critical biological targets that might guide therapeutic development has until recently been lacking.

The past few years have witnessed watershed advancements for patients with MDS in which new therapeutics have moved the field from a strategy of supportive measures such as administration of red cell transfusions and recombinant growth factors, to the use of active therapy directed against the malignant clone. These include the US Food and Drug Administration (FDA) approvals of the DNA methyltransferase inhibitors, 5-azacitidine (Vidaza®; Pharmion Inc, Boulder, CO) and decitabine (Dacogen™; MGI Pharma, Minneapolis, MN), which have filled a critical void for MDS patients with higher risk disease. In 2005 the first of a new proprietary class of drugs called the immunomodulatory drugs, lenalidomide (Revlimid®; Celgene Corp, Summit, NJ), was approved by the FDA for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk MDS associated with a chromosome 5q deletion with or without additional cytogenetic abnormalities.<sup>2</sup> This agent belongs to a novel class of agents that have properties which impact the malignant clone as evidenced by the high frequency of cytogenetic response, immune response, microenvironment, and disease-specific angiogenic effects. This wide spectrum of pharmacologic effects is believed to account for the powerful remitting activity of lenalidomide in MDS. Lenalidomide has emerged as a novel and effective treatment alternative for patients with lower risk disease in whom cytokine therapy is ineffective.

This supplement to *Cancer Control* is titled Lenalidomide (Revlimid®) — A Novel Immunomodulatory Drug (IMiD®) From Bench to Bedside (Part 1:

Myelodysplastic Syndromes). The publication represents the first of a two-part series that will focus on the role of this novel compound in MDS. The companion supplement, which will appear later in 2007, will examine the role of lenalidomide in multiple myeloma and in malignancies beyond MDS.

This supplement includes four manuscripts that characterize the activity and safety of lenalidomide in MDS, biological targets of action, key issues in patient management, and finally lenalidomide's role in the emerging therapeutic algorithm for MDS. Opening the supplement is “Lenalidomide: Targeted Anemia Therapy for Myelodysplastic Syndromes” by Amanda F Baker, PhD, and Sylvan Green, MD (University of Arizona), William Bellamy, PhD (University of Arkansas), and me. We review the MDS clinical experience including the pivotal registration trial that gained FDA approval for lenalidomide for MDS patients with 5q deletion and, in addition, the results of a second trial for lower risk patients without the chromosome 5q deletion. The next manuscript, titled “Evolving Applications of Lenalidomide in the Management of Anemia in Myelodysplastic Syndromes,” discusses lenalidomide's role within the armamentarium of treatment alternatives for patients with MDS, and its placement in the new National Comprehensive Cancer Network (NCCN) Guidelines (version 4.2006) for the management of MDS patients with lower-risk disease.

These articles set the stage for the first pharmacoeconomic evaluation of lenalidomide titled “Cost Effectiveness of Lenalidomide in the Treatment of Transfusion-Dependent Myelodysplastic Syndromes in the United States” by Thomas F Goss, PharmD (Covance Market Access Service Inc) and colleagues. This report applies an economic model that utilizes the registration trial data to compare the relative pharmacoeconomic impact of lenalidomide with cytokine and best supportive care measures in the management of transfusion-dependent, low- or intermediate-1-risk MDS with deletion 5q. This manuscript is the first of its kind to offer an economic perspective of lenalidomide's impact, which is so critical today in the evaluation of new cancer therapies.

Closing out the supplement is “Practical Considerations in the Use of Lenalidomide Therapy for Myelodysplastic Syndromes” by Sandra Kurtin, RN, MS, AOCN,

ANP (University of Arizona), and Lubomir Sokol, MD, PhD (H. Lee Moffitt Cancer Center & Research Institute). This discussion, which is structured in a question and answer format, examines several clinically relevant and practical considerations concerning drug dosing, patient monitoring and follow-up, adverse events, and available support for lenalidomide patients and their prescribing practitioners. This piece should provide useful practical information for those hematology/oncology specialists managing MDS patients receiving lenalidomide treatment.

This supplement reflects the cumulative efforts of many talented individuals, without whom this publication would not have been possible. My sincere thanks to all the authors who contributed their time and knowledge and to Celgene Corporation for supporting this educational supplement. Finally, we extend our gratitude to John Horton, MB, CHB, the editor of *Cancer Control*, for his editorial review of these contributions, and the dedicated staff of *Cancer Control* for their coordination of this exciting issue.

The paradigm for the management of MDS continues to be redefined. Through this supplement, the contributors seek to raise awareness and facilitate discussion that will foster the incorporation of new and effective approaches, such as lenalidomide, in the treatment of MDS. It is our hope that this supplement will serve as a resource that clinicians will access and refer to for years to come.

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## References

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