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## Myelodysplastic Syndrome

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### Abstract

The last decade has witnessed a multistep evolution in the understanding of the natural history, clinical manifestations, and some of the molecular mechanisms that underlie the ineffective hematopoiesis and leukemic transformation in the myelodysplastic syndrome (MDS). The international prognostic scoring system, FAB, and WHO classifications have helped define specific subgroups with their characteristic cytogenetic, molecular and immunological abnormalities. Until recently the mainstay of the treatment has been entirely supportive with blood and platelet transfusions. What is increasingly manifest now is the considerable excitement generated by the emergence of novel therapeutic strategies based on painstaking research findings from the laboratories.

In Section I, Dr. Alan List reviews the therapeutic strategies with the specific emphasis on the relevance of molecular mechanism of apoptosis and targeted therapies using small molecules. Of particular interest is the excitement surrounding the clinical benefit obtained from potent immunomodulatory derivative (IMiD) of thalidomide CC5013. The review provides an update of the role of small molecule inhibitors of VEGF receptor tyrosine kinase, arsenic trioxide, oral matrix metalloprotease inhibitors, farnesyl transferase inhibitors, and imatinib mesylate in the treatment of MDS subgroups.

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In Section II, Dr. Steven Gore describes the results of clinical trials of inhibitors of DNA methylation such as 5 azacytidine (5 AC) and 5-aza 2-deoxycytidine (Decitabine). The review also provides an update on the rationale and results obtained from the combination therapy using histone deacetylases (HDAC) and DNA methyltransferase inhibitors in the treatment of MDS.

In Section III, Professor Ghulam Mufti and Dr. Aloysius Ho describe the role of bone marrow transplantation with particular emphasis on recent results from reduced-intensity conditioned transplants, exploiting the graft versus leukemia effect without significant early treatment-related mortality. The section provides an update on the results obtained from the manipulation of the host's immune system with immunosuppressive agents such as ALG and/or cyclosporine A.

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