Immunomodulating agents (ImiDs) are a novel class of anticancer drugs that have demonstrated impressive antitumor activity in various malignant disorders. Of this class, most recent research has been focused on the remarkably active agent, lenalidomide. Lenalidomide was designed to enhance immunologic and anticancer properties while potentially decreasing neurotoxic and teratogenic adverse effects of the parent compound thalidomide. The introduction of this novel agent has broadened the therapeutic landscape of hematologic malignant disorders including multiple myeloma (MM) and, more recently, other B-cell neoplasms.

In this issue, we focused on mechanisms of action and results from clinical investigation that report the relevance of lenalidomide for the treatment of B-cell disorders including MM, chronic lymphocytic leukaemia (CLL), and non-Hodgkin's lymphomas. In this issue, we focused on mechanisms of action and results from clinical investigation that report the relevance of lenalidomide for the treatment of B-cell disorders including MM, chronic lymphocytic leukaemia (CLL), and non-Hodgkin's lymphomas. In this issue, we focused on mechanisms of action and results from clinical investigation that report the relevance of lenalidomide for the treatment of B-cell disorders including MM, chronic lymphocytic leukaemia (CLL), and non-Hodgkin's lymphomas. In this issue, we focused on mechanisms of action and results from clinical investigation that report the relevance of lenalidomide for the treatment of B-cell disorders including MM, chronic lymphocytic leukaemia (CLL), and non-Hodgkin's lymphomas.

In this special issue, we invited papers on potential topics including, but are not limited to, lenalidomide: mechanism of action, lenalidomide as part of the induction therapy before hematopoietic stem cells transplantation (HSCT) as well as its use as extended maintenance therapy post-HSCT in patients with MM will be of great interest.

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host's immune response. The molecular mechanisms and targets of lenalidomide remain largely unknown, but recent evidence shows cereblon (CRBN) as a possible mediator of its therapeutic effects.

The paper entitled “Molecular action of lenalidomide in lymphocytes and hematologic malignancies” by J. M. McDaniel et al. summarizes the current information about lenalidomide in proliferative neoplasms and describes our understanding of the molecular mechanism of action in lymphocytes. Based on the overwhelming success of lenalidomide for the treatment of several hematologic malignancies, there is potential for therapies that augment host immune responses to be extended from the relapsed and refractory setting, to primary therapy.

The paper entitled “Secondary primary malignancies in multiple myeloma: an old nemesis revisited” by J. Yang et al. reviews the developmental history of myeloma therapy, with particular emphasis on the risk of secondary cancers, and examine the available data with regard to the risk of SPMs seen with lenalidomide. We also speculate about the mechanism(s) by which lenalidomide could increase the risk of second cancers. To conclude, we make some recommendations about how our current understanding affects our treatment decisions and suggest directions for future research. As new data emerge about lenalidomide and the risk of SPMs, it is our hope that this paper will help to put that information in proper perspective.

The paper entitled “Lenalidomide in the treatment of young patients with multiple myeloma: from induction to consolidation/maintenance therapy” by B. Lupo et al. presents an overview of the results achieved with lenalidomide-containing combinations in patients eligible for high-dose therapies, namely, young patients. The advantages obtained should always be outweighed with the toxicity profile associated with the regimen used. Therefore, here, we will also provide a description of the main adverse events associated with lenalidomide and its combination.

The paper entitled “Lenalidomide in the treatment of chronic lymphocytic leukemia” by A. Cortelezzi et al. provides a comprehensive summary regarding mechanism of action, efficacy, and safety of lenalidomide in CLL patients. Relevant clinical trials using lenalidomide alone or in combination are discussed. Lenalidomide shows good activity also in relapsed/refractory or treatment-naive CLL patients. Definitive data from ongoing studies are needed to validate overall and progression-free survival. The toxicity profile might limit lenalidomide use because it can result in serious side effects, but largely controlled by gradual dose escalation. Further understanding of the exact mechanism of action in CLL will allow more efficacious use of lenalidomide alone or in combination regimens.

The paper entitled “Lenalidomide in diffuse large B-cell lymphomas” by A. Chiappella et al. reports the most relevant clinical trials for the use of lenalidomide in DLBCL. Monotherapy with lenalidomide showed an activity in terms of overall response rate, with acceptable hematological and extrahematological toxicities in relapsed/refractory aggressive NHL. The role of lenalidomide as salvage therapy in both cell of origin patterns in DLBCL (germinat center B cell/activated B cell) was reported in preliminary data. Preliminary data regarding the role of lenalidomide in addition to chemoimmunotherapy (R-CHOP) in first-line clinical trials were discussed; data of safety, feasibility, and efficacy were promising.

The paper entitled “Therapeutic activity of lenalidomide in mantle cell lymphoma and indolent non-Hodgkin’s lymphomas” by M. Gunnellini et al. discusses the role of lenalidomide in the therapeutic armamentarium of patients with indolent NHL or MCL.

The tenth paper entitled “Lenalidomide before and after autologous hematopoietic stem cell transplantation in multiple myeloma” by S. A. Tuchman et al. summarizes existing data that pertains to lenalidomide in the specific context of ASCT, and we share our thoughts on how our own group applies these data to approach this complex issue clinically.

Anna Marina Liberati
Umberto Vitolo
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