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Foreword

Current and emerging therapeutics for multiple myeloma

Noopur Raje & Sundar Jagannath

The evolution of therapies for the treatment of multiple myeloma and related plasma cell dyscrasias has succeeded in transforming myeloma into a chronic disease. The last decade has allowed us to use our insights into the biology of multiple myeloma with therapeutic intent and this has been largely responsible for the replacement of conventional chemotherapy with novel more targeted approaches impacting both the tumor cell and the microenvironment in which it resides [1,2].

We have had eight drugs or drug combinations approved for the treatment of myeloma. These include two major classes of drugs; the immunomodulatory drugs (IMiDs) [3] and the proteasome inhibitors (PIs) [4]. These are now routinely incorporated into the care of myeloma patients and in fact are even used in combination. With these combinations, we are now seeing unprecedented response rates where over 90% of patients are responding to treatment.

The introduction of the IMiDs in 1999 set the stage and we now have three drugs, thalidomide, lenalidomide and pomalidomide, approved for the treatment of newly diagnosed and relapsed refractory myeloma. The recent discovery of cereblon as a receptor for IMiDs has shed a new light into the mechanism of action of these drugs and spurred renewed interest in better defining the role of these agents in myeloma [5,6]. The PIs followed shortly with bortezomib, the first in its class, to be approved in 2003. Since then, carfilzomib has also recently been approved and waiting in the wings are

several oral PIs such as ixazomib and oprozomib. Marizomib is an irreversible PI with activity against all three proteasome subunits and is undergoing early clinical trial evaluation. These two classes of drugs will form the backbone of antimyeloma therapy for the foreseeable future.

Newer exciting targets in myeloma, including the histone deacetylases inhibitors, drugs targeting the AKT pathway, and CDK inhibitors, are in various phases of clinical development. In addition to these classes of small-molecule inhibitors, we are now at a stage where monoclonal antibodies are beginning to demonstrate promise. Among these, elotuzumab, daratumumab and tabalumab are the furthest in development.

The chapters included in this book highlight some of these advances. They tackle the current landscape of therapies available to patients, discuss the role of transplantation in the era of these novel agents, highlight the IMiDs and PIs and finally tackle relevant targets such as histone deacetylases inhibitors, the AKT pathway and other novel agents, such as monoclonal antibodies, being evaluated in early phase trials, which will soon become part of the standard armamentarium for multiple myeloma. The chapters included are a succinct overview of the evolving treatment paradigm of therapies in myeloma and will provide the readership a context for use of these therapies for patients.

The future will incorporate some of these agents in combination with the goal of transforming myeloma from a chronic disease into a curable one at least in a subset of patients.

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