About the Editors

Michael J Keating

Michael J Keating is Professor of Medicine in Hematology at the University of Texas MD Anderson Cancer Center (MDACC; TX, USA). He has been a member of the faculty of MDACC since 1977 and works as a physician in the Leukemia Department. In the earlier phases of his career, the importance of cytogenetics in predicting probability of response to treatment and survival in acute leukemia were foremost in his research interest. Since the mid-1980s, chronic lymphocytic leukemia (CLL) has been the major focus of his research. His career is marked by close collaboration with laboratory scientists but his major focus has been on delivery of effective, compassionate care to patients suffering from leukemia. In 1988, he won the Service to Mankind Award from the Leukemia Society of America and in 1993 was the recipient of the Faculty Achievement Award in Clinical Research at MDACC. In 1996, he was voted one of the best doctors in America by the American Health magazine. In January 2002, he was awarded the Charles A LeMaistre Outstanding Achievement Award in Cancer at MDACC and in March 2002, the Rai and Binet Award at the International Workshop on CLL. In March 2007, he was awarded the MDACC Gerald P Bodey, Sr Distinguished Professorship and in 2008 was awarded the Rofeh Yedid (Physician and Dear Friend) Award from the Aishel House and received the State of Israel Maimonides Award from the State of Israel Bonds. In 2009, he was presented with the Dr Jenaro Haddock Award by the Puerto Rico Society of Hematology. His major pursuits at the present time are developing new potentially curative therapies for CLL and developing rational combinations of new agents in the treatment of all leukemias and other hematologic malignancies.

Constantine S Tam

Constantine S Tam graduated from the University of Melbourne and completed a Leukemia Fellowship at the University of Texas MD Anderson Cancer Center (TX, USA). He is Consultant Hematologist at St Vincent's Hospital and a Senior Fellow at the University of Melbourne (Australia). His major research interests include the biology of CLL and novel therapies in CLL.

Foreword

Advances in the treatment of B-cell chronic lymphocytic leukemia

Michael J Keating &
Constantine Tam

The past two decades have seen substantial advances in our understanding of chronic lymphocytic leukemia (CLL). It has long been recognized that there is great heterogeneity in the clinical course of CLL: some patients have indolent disease and survival durations similar to that of healthy populations, whereas other patients experience rapid disease progression, treatment resistance and short survival. Advances in our understanding of the genetics and molecular biology of CLL have now uncovered some of the science behind this heterogeneity in clinical behavior. Thus, we now have the tools to genetically classify CLL, resulting in improved prognostication at the time of initial diagnosis, and allowing physicians to make personalized therapy decisions based on the biology of the disease. We now also have better understanding of interactions between the CLL cell and its antigenic and microenvironment, thus exposing new avenues for therapeutic targets and treatment strategies.

At the same time, the ability to treat CLL has improved. The number of active drugs have increased exponentially, and a series of Phase II and Phase III trials have explored the optimal combination of drugs in order to maximize synergy. The field has moved from treatment with alkylating agents (with complete remission rates of <5% and short remissions) to modern chemoimmunotherapy combinations, resulting in complete remission rates

of 45–72%, median remissions of 4–7 years, and improvements in overall survival. The success of modern chemoimmunotherapy has allowed physicians to define treatment subgroups where additional attention is required: elderly patients with comorbid conditions (where tolerance to treatment is poor), and patients with *TP53* deletions or mutations (where there is resistance to chemotherapy). Identification of the *TP53*-deleted and/or -mutated patient as being at particular high-risk has spurred the exploration of treatment options independent of the *TP53* gene, including allogeneic transplantation, immunomodulatory drugs, new monoclonal antibodies, and small molecules targeting the B-cell receptor signaling pathway.

Thus, a new dawn is rising upon those physicians and researchers working to understand and treat CLL. With the tools to molecularly dissect the CLL cell, treatment to debulk disease below the threshold of minimal residual disease, and an increasing armamentarium of nonchemotherapy agents, the cure of CLL may well be at hand. The field of CLL is vast and becoming increasingly complex: we are deeply indebted to the authors for their contributions in their respective fields. We recognize that there are other important topics in CLL biology and treatment that are not addressed in this book. Although regrettable, the numbers of forced omissions are in themselves a great testament to the activity and energy of the CLL research community.

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