TREATMENT OF MULTIPLE MYELOMA AND RELATED DISORDERS

Owing to major advances in understanding the biology and pathogenesis of the disease, the management of multiple myeloma is changing rapidly. New diagnostic and prognostic criteria have been introduced, and treatment options are multiplying with high-dose chemotherapy regimens, stem cell transplants, and the development of novel agents and immune-based strategies that target tumor cells directly.

This book is aimed at the practitioner who is looking to put these advances into clinical context. It will serve as an up-to-date resource for treatment of myeloma and related disorders. Chapters are written by international authorities and contain color photos, diagrams, and algorithms outlining preferred treatment strategies. Relevant scientific information is integrated throughout, but the focus here is on providing practical therapeutic guidance for oncologists and hematologists caring for myeloma patients. The book covers all myeloma subtypes and related disorders, including amyloidosis, Waldenström macroglobulinemia, plasmacytoma, MGUS, and POEMS syndrome.

Dr. S. Vincent Rajkumar is Professor of Medicine at Mayo Clinic College of Medicine and Chair of the Mayo Clinic Myeloma, Amyloidosis, and Dysproteinemia Group. He has authored more than 250 papers and book chapters, primarily in the field of myeloma and related plasma cell disorders. He has led several clinical trials investigating the role of new agents in myeloma. Dr. Rajkumar is a member of the American Society of Clinical Oncology Cancer Education Committee as well as the Scientific Advisory Board of the International Myeloma Foundation. Dr. Rajkumar is an associate editor of the Mayo Clinic Proceedings and is on the editorial boards of American Journal of Oncology Review and Leukemia Research.

Dr. Robert A. Kyle is Professor of Medicine and Laboratory Medicine at Mayo Clinic in Rochester, Minnesota. He served as the William H. Donner Professor of Medicine and Laboratory Medicine and was Section Head and Chairman of the Division of Hematology. Dr. Kyle is one of the most respected authorities in the field of multiple myeloma and related disorders and has authored more than 750 papers and book chapters, primarily in the field of myeloma and related plasma cell disorders. He has led several major clinical trials and epidemiological studies in the field. Dr. Kyle is currently Chairman of the Scientific Advisory Board of the International Myeloma Foundation, Chairman of the Scientific Advisory Committee of the International Waldenström's Macroglobulinemia Foundation, and President of the International Society of Amyloidosis.

During his career, Dr. Kyle has been recognized as the first recipient of the Robert A. Kyle Award for the Waldenstrom's Macroglobulinemia Foundation, first recipient of the Robert A. Kyle Lifetime Achievement Award from the International Myeloma Foundation, recipient of the Mayo Clinic's Henry S. Plummer Distinguished Internist Award, recipient of the Mayo Clinic's Distinguished Clinician Award, and recipient of the Mayo Clinic's Distinguished Alumni Award. He was also recipient of the 2007 David Karnofsky Award and Lecture at ASCO.
TREATMENT OF MULTIPLE MYELOMA
AND RELATED DISORDERS

Edited by

S. VINCENT RAJKUMAR
Mayo Clinic College of Medicine

ROBERT A. KYLE
Mayo Clinic College of Medicine
## CONTENTS

List of Contributors

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DIAGNOSIS AND GENETIC CLASSIFICATION OF MULTIPLE MYELOMA</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Rafael Fonseca and P. Leif Bergsagel</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>STAGING AND RISK-STRATIFICATION OF MULTIPLE MYELOMA</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>A. Keith Stewart</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>TREATMENT OF NEWLY DIAGNOSED MULTIPLE MYELOMA</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>S. Vincent Rajkumar and Robert A. Kyle</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MAINTENANCE THERAPY IN MULTIPLE MYELOMA</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>Sagar Lonial and Jonathan L. Kaufman</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>TREATMENT OF RELAPSED AND RELAPSED/REFRACTORY MULTIPLE MYELOMA</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>Marc S. Raab, Paul G. Richardson, and Kenneth C. Anderson</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>DIAGNOSIS AND TREATMENT OF MYELOMA BONE DISEASE</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>G. David Roodman</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>TREATMENT OF MYELOMA-RELATED COMPLICATIONS</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>Joan Bladé and Laura Rosiñol</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>AUTOLOGOUS TRANSPLANTATION FOR MULTIPLE MYELOMA</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>J.-L. Harousseau</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>ALLOGENEIC STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>William I. Bensinger</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>IMMUNOGLOBULIN LIGHT CHAIN AMYLOIDOSIS</td>
<td>112</td>
</tr>
<tr>
<td></td>
<td>Morie A. Gertz and Suzanne R. Hayman</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>WALDENSTRÖM MACROGLOBULINEMIA/LYMPHOPLASMACYTIC LYMPHOMA</td>
<td>129</td>
</tr>
<tr>
<td></td>
<td>Steven P. Treon and Giampaolo Merlini</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>DIAGNOSIS, RISK-STRATIFICATION, AND MANAGEMENT OF SOLITARY PLASMACYTOMA</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>Meletios A. Dimopoulos and Efstathios Kastritis</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE AND SMOLDERING MULTIPLE MYELOMA</td>
<td>164</td>
</tr>
<tr>
<td></td>
<td>Robert A. Kyle and S. Vincent Rajkumar</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>DIAGNOSIS AND TREATMENT OF POEMS SYNDROME</td>
<td>182</td>
</tr>
<tr>
<td></td>
<td>Angela Dispenzier</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Index</td>
<td>195</td>
</tr>
</tbody>
</table>
CONTRIBUTORS

Kenneth C. Anderson, MD
Kraft Family Professor of Medicine
Harvard Medical School
25 Shattuck St.
Boston, MA 02115

Chief, Division of Hematologic Neoplasia
Director, Jerome Lipper Myeloma Center and
LeBow Institute for Myeloma Therapeutics
Dana-Farber Cancer Institute
44 Binney St.
Mayer 557
Boston, MA 02115

William I. Bensinger, MD
Professor of Medicine
University of Washington
1959 NE Pacific
Seattle, WA 98195

Director, Autologous Stem Cell Transplantation
Clinical Research Division
Fred Hutchinson Cancer Research Center
1100 Fairview Ave. N
Seattle, WA 98109

P. Leif Bergsagel, MD, FRCPC
Professor of Medicine
Mayo Clinic College of Medicine
13400 E. Shea Blvd.
Scottsdale, AZ 85259

Consultant
Mayo Clinic
13400 E. Shea Blvd.
Scottsdale, AZ 85259

Joan Bladé, MD
Associate Professor of Medicine
University of Barcelona
Casanova 136
08036 Barcelona, Spain

Senior consultant
Department of Hematology
Hospital Clinic
Villarroel, 170
08036 Barcelona, Spain

Meletios A. Dimopoulos, MD
Professor and Chairman
Department of Clinical Therapeutics
University of Athens School of Medicine
80 V. Sofias Ave.
Athens, Greece 115 28

Director
Department of Clinical Therapeutics
Alexandra Hospital
80 V. Sofias Ave.
Athens, Greece 115 28

Angela Dispenzieri, MD
Associate Professor of Medicine
Division of Hematology
Mayo Clinic
200 First St. SW
Rochester, MN 55905

Rafael Fonseca, MD
Professor of Medicine
Division of Hematology–Oncology
Mayo Clinic
200 First St. SW
Rochester, MN 55905
Consultant
Division of Hematology-Oncology
Mayo Clinic
13400 E. Shea Blvd.
Scottsdale, AZ 85259

**Morie A. Gertz, MD**
Chair and Professor of Medicine
Department of Medicine, Division of Hematology
Mayo Clinic
200 First St. SW
Rochester, MN 55905

**J.-L. Harousseau, MD**
Professor
Department of Hematology
1 Place Alexis Ricordeau
Nantes, 44093, France
Head, Department of Hematology
1 Place Alexis Ricordeau
Nantes, 44093, France

**Suzanne R. Hayman, MD**
Consultant, Division of Hematology
Assistant Professor of Medicine
Mayo Clinic
200 First St. SW
Rochester, MN 55905

**Efstathios Kastritis, MD**
Professor and Chairman
Department of Clinical Therapeutics
University of Athens School of Medicine
80 V. Sofias Ave.
Athens, Greece 115 28
Director
Department of Clinical Therapeutics
Alexandra Hospital
80 V. Sofias Ave.
Athens, Greece 115 28

**Jonathan L. Kaufman, MD**
Assistant Professor
Department of Hematology and Medical Oncology
Emory University
1365C Clifton Rd. NE
Atlanta, GA 30322

**Robert A. Kyle, MD**
Professor of Medicine and Laboratory Medicine
Division of Hematology
Mayo Clinic
200 First St. SW
Rochester, MN 55905

**Sagar Lonial, MD**
Associate Professor
Department of Hematology and Medical Oncology
Emory University
1345 Clifton Rd. NE
Atlanta, GA 30322

**Giampaolo Merlini, MD**
Full Professor
Department of Biochemistry
University of Pavia
Viale Taramelli, 3/b
Pavia, Italy, 27100
Director
Center for Research and Treatment of Systemic Amyloidosis
Fondazione IRCCS Policlinico San Matteo
Viale Golgi, 19
Pavia, Italy, 27100

**Morie A. Gertz, MD**
Chair and Professor of Medicine
Department of Medicine, Division of Hematology
Mayo Clinic
200 First St. SW
Rochester, MN 55905

**Robert A. Kyle, MD**
Professor of Medicine and Laboratory Medicine
Division of Hematology
Mayo Clinic
200 First St. SW
Rochester, MN 55905

**Sagar Lonial, MD**
Associate Professor
Department of Hematology and Medical Oncology
Emory University
1345 Clifton Rd. NE
Atlanta, GA 30322

**Giampaolo Merlini, MD**
Full Professor
Department of Biochemistry
University of Pavia
Viale Taramelli, 3/b
Pavia, Italy, 27100
Director
Center for Research and Treatment of Systemic Amyloidosis
Fondazione IRCCS Policlinico San Matteo
Viale Golgi, 19
Pavia, Italy, 27100
List of Contributors

S. Vincent Rajkumar, MD
Professor of Medicine
Chair, Myeloma Amyloidosis
Division of Hematology
Mayo Clinic
200 First St. SW
Rochester, MN 55905

Paul G. Richardson, MD
Associate Professor of Medicine
Harvard Medical School
25 Shattuck St.
Boston, MA 02115

Clinical Director
Jerome Lipper Center for Multiple Myeloma
Dana-Farber Cancer Institute
44 Binney St., Dana 1B02
Boston, MA 02115

G. David Roodman MD, PhD
Professor of Medicine
Department of Hematology-Oncology
University of Pittsburgh
VAMC, University Dr. C, R&D 151U
Pittsburgh, PA 15240

Director, Center for Bone Biology at
UPMC and Myeloma
Medicine/Hematology-Oncology
University of Pittsburgh Medical Center
and University of Pittsburgh Cancer
Institution

Laura Rosiñol, MD, PhD
Specialist in Hematology
Department of Hematology
Hospital Clinic
Villardroel, 170
08036 Barcelona, Spain

A. Keith Stewart, MB, ChB
Professor
Division of Hematology-Oncology
Mayo Clinic
13400 E. Shea Blvd.
Scottsdale, AZ 85259

Consultant
Division of Hematology-Oncology
Mayo Clinic
13400 E. Shea Blvd.
Scottsdale, AZ 85259

Steven P. Treon, MD, MA, PhD
Associate Professor
Harvard Medical School
M547, 44 Binney St.
Boston, MA 02115

Director
Bing Center for Waldenström’s
Macroglobulinemia
Dana-Farber Cancer Institute
M547, 44 Binney St.
Boston, MA 02115