Myeloma Bone Disease
Myeloma Bone Disease

Edited by

G. David Roodman

University of Pittsburgh Medical Center,
Pittsburgh, PA, USA
Multiple myeloma is the second most common hematologic malignancy and currently affects approximately 50,000 people in the United States. Each year about 20,000 people are diagnosed with myeloma. Although new treatments have been developed, which significantly prolong the survival of patients, myeloma bone disease still remains a major cause of severe morbidity and increased mortality in patients with myeloma. Myeloma bone disease is characterized by “punched out” lytic lesions caused by increased osteoclastic bone destruction accompanied by suppressed or even absent osteoblast activity. Advances in our understanding of both the pathophysiology of myeloma bone disease and the development of novel agents that target specific pathways involved in both the increased osteoclast formation and the suppressed osteoblast activity in myeloma provide new hope for these patients. The treatment of myeloma bone disease was revolutionized by clinical trials that demonstrated the significant benefit of intravenous bisphosphonate therapy in patients with myeloma bone disease. With the identification of many of the cytokines and chemokines involved in myeloma bone disease, novel therapies such as denosumab that blocks RANKL activity, anti-DKK1, which targets the inhibition of osteoblast activity by blocking Wnt signaling inhibition, and the potential anabolic effects of agents such as bortezomib and activin have greatly improved our potential to block the progression or reverse myeloma bone disease. These topics as well as new techniques for imaging myeloma bone disease, the use of new bone markers for monitoring myeloma bone disease, and surgical techniques to ameliorate pain and loss of vertebral height in patients with vertebral compression fractures are highlighted in this volume. With the survival of patients with myeloma increasing, treatments that are directed at preventing the progression of bone disease, fractures, and even repairing lytic lesions will have even a more profound impact on patients with myeloma. In this book, outstanding experts from a variety of backgrounds discuss the presentation of patients with myeloma bone disease, the underlying pathophysiology of both the increased osteoclast activity and the suppressed osteoblast activity that occurs in myeloma, murine models of myeloma bone disease, as well as therapeutic and diagnostic procedures for patients with myeloma bone disease.

Pittsburgh, PA

G. David Roodman
# Contents

1 Clinical Presentation of Myeloma Bone Disease ............................ 1
   Rebecca Silbermann and G. David Roodman

2 Imaging of Multiple Myeloma, Solitary Plasmacytoma,
   MGUS, and Other Plasma Cell Dyscrasias ............................ 15
   Ronald C.Walker, Laurie Jones-Jackson, Twyla Bartel, Tracy
   Brown, and Bart Barlogie

3 Biochemical Markers of Bone Remodeling
   in Multiple Myeloma .................................................. 63
   Evangelos Terpos

4 Radiation Therapy in Multiple Myeloma ............................. 91
   Joel S. Greenberger

5 Surgical Management of Bone Disease ............................ 101
   Mohamad A. Hussein

6 Bisphosphonates in the Treatment of Myeloma Bone Disease .... 117
   James R. Berenson

7 Osteonecrosis of the Jaw .............................................. 133
   Ashraf Badros

8 Murine Models of Myeloma Bone Disease: The Importance
   of Choice .............................................................. 151
   Peter I. Croucher, Karin Vanderkerken, Joshua Epstein,
   and Babatunde Oyajobi

9 RANK Ligand Is a Therapeutic Target in Multiple Myeloma ... 169
   William C. Dougall, Michelle Chaiisson-Blake, Howard Yeh,
   and Susie Jun

10 Osteoclast Activation in Multiple Myeloma .......................... 183
    Sonia Vallet and Noopur Raje
11 Potential Role of IMiDs and Other Agents as Therapy for Myeloma Bone Disease .......................... 199
Suzanne Lentzsch

12 Proteasome Inhibitors and the Wnt Signaling Pathway in Myeloma Bone Disease .......................... 211
Claire M. Edwards and Gregory R. Mundy

13 Mechanisms Involved in Osteoblast Suppression in Multiple Myeloma ................................. 231
Nicola Giuliani

Index .................................................................................................................................................. 243
Contributors

Ashraf Badros  Greenebaum Cancer Center, University of Maryland, Baltimore, MD, USA

Bart Barlogie  Myeloma Institute for Research and Therapy, Little Rock, AR, USA

Twyla Bartel  Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR, USA

James R. Berenson  Institute for Myeloma & Bone Cancer Research, West Hollywood, CA, USA

Tracy Brown  Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Michelle Chaisson-Blake  Amgen Inc., Seattle, WA, USA

Peter I. Croucher  Department of Human Metabolism, Faculty of Medicine, Dentistry and Health, University of Sheffield, Sheffield, UK

William C. Dougall  Amgen Inc., Seattle, WA, USA

Claire M. Edwards  Departments of Cancer Biology and Clinical Pharmacology/Medicine, Vanderbilt Center for Bone Biology, Vanderbilt University Medical Center, Nashville, TN, USA

Joshua Epstein  Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Nicola Giuliani  Department of Internal Medicine and Biomedical Science, Hematology and BMT Center, University of Parma, Parma, Italy

Joel S. Greenberger  Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA

Mohamad A. Hussein  Celgene Corporation, Summit, NJ, USA

Laurie Jones-Jackson  Department of Radiology & Radiological Sciences, Vanderbilt University Medical Center, Nashville, TN, USA
Susie Jun  Amgen Inc., Thousand Oaks, CA, USA

Suzanne Lentzsch  Division of Hematology/Oncology, University of Pittsburgh, Pittsburgh, PA, USA

Gregory R. Mundy  Departments of Cancer Biology and Clinical Pharmacology/Medicine, Vanderbilt Center for Bone Biology, Vanderbilt University Medical Center, Nashville, TN, USA

Babatunde Oyajobi  Departments of Cellular and Structural Biology, and Medicine, University of Texas Health Sciences Center, San Antonio, Texas, USA

Noopur Raje  Division of Hematology-Oncology, Harvard Medical School, Massachusetts General Hospital Cancer Center, Boston, MA, USA

G. David Roodman  Department of Medicine/Hematology-Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Rebecca Silbermann  Department of Medicine/Hematology-Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Evangelos Terpos  Department of Clinical Therapeutics, University of Athens School of Medicine, Alexandra Hospital, Athens, Greece

Sonia Vallet  Division of Hematology-Oncology, Harvard Medical School, Massachusetts General Hospital Cancer Center, Boston, MA, USA

Karin Vanderkerken  Department of Hematology and Immunology, Myeloma Center Brussels, Vrije Universiteit, Brussels, Belgium

Ronald C. Walker  Department of Radiology & Radiological Sciences, Vanderbilt University Medical Center and Tennessee Valley VA Healthcare System, Nashville, TN, USA

Howard Yeh  Amgen Inc., Thousand Oaks, CA, USA