The BMT Data Book

The BMT Data Book

2nd edition

Reinhold Munker

Hillard M. Lazarus

Kerry Atkinson

CAMBRIDGE
UNIVERSITY PRESS

CAMBRIDGE UNIVERSITY PRESS
Cambridge, New York, Melbourne, Madrid, Cape Town, Singapore, São Paulo, Delhi

Cambridge University Press
The Edinburgh Building, Cambridge CB2 8RU, UK

Published in the United States of America by Cambridge University Press, New York

www.cambridge.org
Information on this title: www.cambridge.org/9780521711005

First published 2009

Printed in the United Kingdom at the University Press, Cambridge

A catalogue record for this publication is available from the British Library

ISBN 978-0-521-71100-5 paperback

Contents

Contributors

Kerry Atkinson, MD
Professor of Medicine
University of Queensland
South Brisbane
Australia

Oscar F. Ballester, MD
Professor of Medicine
Edwards Comprehensive Cancer Center at Marshall University
Huntington, WV

Gary Brooke, PhD
Research Scientist,
University of Queensland,
South Brisbane,
Australia

Richard W. Childs, MD
Senior Investigator, Hematology Branch
National Heart, Lung, and Blood Institute
National Institutes of Health
Bethesda, MD

Daniel R. Couriel, MD
Director, Allogeneic Transplant and Apheresis Services
Tennessee Oncology
Nashville, TN

Nicholas R. DiPaola, PhD
Research Scientist, Department of Surgery
Ohio State University Medical Center
Columbus, OH

Alison G. Freifeld, MD
Professor of Medicine,
University of Nebraska Medical Center
Omaha, NE

Ramiro Garzon, MD
Assistant Professor of Medicine,
Ohio State University Medical Center,
Columbus, OH

Mary J. Laughlin, MD
Associate Professor of Medicine and Pathology, (in collaboration with R. Patrick Weitzel)
Case Western Reserve University
Cleveland, OH

Hillard M. Lazarus, MD
Professor of Medicine
Ireland Cancer Center, University Hospitals
Case Western Reserve University
Cleveland, OH

Anna Locasciulli, MD
Professor of Pediatrics, Ospedale S. Camillo-Forlanini
Rome
Italy

Reinhold Munker, MD
Associate Professor of Medicine,

Louisiana State University,
Shreveport, LA

Pavan Reddy, MD
Assistant Professor of
Medicine, University of
Michigan
Ann Arbor, MI

Vishwas Sakhalkar, MD
Assistant Professor of
Pediatrics, University of
Florida
Gainesville, FL

Shalini Shenoy, MD
Associate Professor of Pediatrics,
Washington University
St. Louis, MO

Amanda Sun, MD, PhD
Assistant Professor of Medicine,
Louisiana State University,
Shreveport, LA

Naoto T. Ueno, MD, PhD
Professor of Medicine,
M.D. Anderson Cancer Center
Houston, TX

Foreword

It is over 50 years since the basic concepts underpinning bone marrow transplantation were revealed in radiation protection experiments in mice. It seems curious to us now that in the 1950s the idea that marrow cells could grow and reconstitute hematopoiesis in an irradiated recipient was so revolutionary that it took careful experiments to prove the "cellular theory" and disprove the "humoral theory" of radiation protection. Equally remarkable is the fact that within a few years of this (and at a time before we knew what the thymus did or that lymphocytes could be divided into B and T cell subsets) the unique transplant-associated phenomena of graft-versus-host disease, graft-versus-leukemia and graft rejection were recognized as alloresponses. Fast forward to today; bone marrow transplantation has become stem cell transplantation (SCT) and the complexity of the field has increased exponentially as we define transplant biology increasingly at the molecular level. SCT is a treatment being continually extended to new malignant and nonmalignant diseases. More transplants are being performed, not only because more unrelated donor stem cell sources are available but also because mismatched transplants are beginning to be used more safely. As the mortality from transplant has fallen, SCT is applied increasingly to older and debilitated individuals. Luckily, expertise in the clinical SCT community has kept pace with this expanding field. There has been a general increase in transplant "know how" and many procedures are now standardized worldwide. However, to maintain our standards of care at the cutting edge, clinicians need to have access to more data than they can memorize to offer the best treatments to their patients. Recurrent issues that require detailed data for the best decision making are – Who should be offered transplant? What type of transplant should they receive? How should the transplant be performed, and how should the complications be managed? Drs. Munker, Lazarus, and Atkinson must be congratulated on compiling a guide which should help transplanters deal with these essential questions and in the process contribute substantially to the delivery of expert care to our patients.

John Barrett
Bethesda MD

Preface

The last 10 years have again seen a dramatic change and expansion in the discipline of clinical bone marrow and blood stem cell transplantation. New data have become available to support the decision for or against transplantation. The future has already started. Basic science has made progress: new genes and microRNAs have been characterized as risk factors in the outcomes of hematologic malignancies. The involvement of natural killer cells in the graft-versus-tumor reactions has been recognized. New cell populations like dendritic cells and mesenchymal stem cells have been characterized. Clinical science has made progress. New indications for transplants have been developed and evaluated. Examples are renal cell cancer, autoimmune disorders, and amyloidosis. New stem cell sources (e.g., from cord blood) were implemented. Owing to sophisticated typing methods, unrelated transplants have become safer. Owing to increased donor numbers, matched unrelated transplants can now be offered to more than 70% of patients who do not have a family match. Old indications (breast cancer) have almost become obsolete or are being reevaluated (chronic myelogenous leukemia) because of advances in the nontransplant arena. In the first edition of this book, transplant for multiple myeloma was put into context against "conventional" treatments. Now, autologous transplant has become the standard of care for multiple myeloma, which has to compete and will join forces with antiangiogenic agents or proteasome inhibitors. New treatment protocols for older patients or who have significant comorbidities were introduced (reduced-intensity conditioning). Overall, in the United States (2004–2006) 17 000, in Europe 22 000, and in Australia 1200 hematopoietic stem cell transplants are being performed each year. In addition to Europe and North America, South America, Mexico, China, and India have all started active transplant programs. The registry data evaluating the outcomes of autologous and allogeneic transplants are now based on thousands of patients instead of hundreds of patients. Therefore, in many instances, the promise of cure is being replaced or is supported by realistic long-term survival data.

The basic structure of the first edition of the *BMT Data Book* is conserved. In the first section, the biology of stem cells, other relevant cell populations,

and the science underlying transplantation are discussed. Next, the indications for transplant in different diseases (malignant and non-malignant) are given. Pediatric aspects are noted when indicated. Coauthors specialized in different areas have made contributions. All chapters are concise. The nontransplant options are briefly mentioned. Registry data are given when available. As in the first edition, major articles from respected journals were chosen for each topic and with the permission of the authors, one (or two) figures were reproduced. These articles not only support our recommendations but also illustrate current controversies. In the other two major sections, the practical aspects and the complications of allogeneic and autologous transplantation are discussed. The "BMT pharmacopoeia" of the first edition is updated with many new drugs, whereas standard-dose protocols (available in other textbooks) were removed. Finally, current transplant protocols and certain aspects of laboratory medicine are included. A new addition to the *BMT Data Book* is a guide to the Internet and printed databases. All chapters were reviewed by experts. This book is a work in progress. Owing to the enormous amount of literature and information available, we cannot be 100% complete. However, we hope, by providing recent and solid data, to help the physicians and patients to make informed decisions and choose the best individual treatment.

Reinhold Munker
Hillard M. Lazarus
Kerry Atkinson

Preface to the first edition

The use of hemopoietic stem cell transplantation to support high-dose chemotherapy or chemoradiotherapy is rapidly developing and fast changing. During the 1980s and 1990s, many marrow transplantation physicians had to start treating diseases they may not have treated for many years. Examples would be the use of autologous transplantation for breast, testicular, and ovarian cancer. Likewise, medical oncologists had to start becoming familiar with marrow and blood stem cell transplantation medicine.

In addition, effective new nontransplant treatments were introduced and made therapeutic decision making for an individual patient even more difficult. Examples included α-interferon for chronic myeloid leukemia and fludarabine for chronic lymphatic leukemia and low-grade non–Hodgkin lymphoma.

All this change occurred against a background of shrinking hospital budgets and an increasing concern for cost constraint.

These elements spurred the production of this book. Many long but useful hours were spent arguing such issues for individual patients in the weekly meeting of the marrow transplant program at St. Vincent's Hospital. It became clear that "change" was becoming the norm and marrow transplant physicians, like everyone else, had to adapt quickly. It thus seemed important to provide data-driven outcome analyses to help therapeutic decision making for individual patients.

Kerry Atkinson

Disclaimer: As in the first edition, the authors have attempted to provide the most accurate data and guidance possible. We recognize however that there may be unforeseen errors in drug dossage and modification recommendations. We always encourage treating physicians and their staff to consult the original source documents when developing specific treatment plans.

Acknowledgments

Katie James, Nick Dunton, and Deborah Russell (Cambridge University Press) helped realize the second edition of the *BMT Data Book*. Drs. Gary Burton, Michael Cockerham, Richard Creger, Marcos de Lima, Gerhard Hildebrandt, Erhard Hiller, Kathleen Hiller, Thomas Lin, Per Ljungman, Michael Lübbert, Grace Tenorio, Miguel Sanz, Roger Strair, Amanda Ranzino, and Francesco Turturro reviewed selected chapters. More than 60 authors (and their respective publishers) gave permission to use figures or graphs and provided valuable suggestions. Hillard Lazarus dedicates his contribution to his wife Joan and his sons Jeffrey and Adam for their unwavering encouragement and support. Kerry Atkinson dedicates this second edition to his dear wife Pauline. We would especially like to thank our patients and their families for their courage and trust.