

Consensus Conference on Clinical Practice in Chronic GVHD: Second-Line Treatment of Chronic Graft-versus-Host Disease

Daniel Wolff,¹ Michael Schleuning,² Stephanie von Harsdorf,³ Ulrike Bacher,⁴ Armin Gerbitz,⁵ Michael Stadler,⁶ Francis Ayuk,⁴ Alexander Kiani,⁷ Rainer Schwerdtfeger,² Georgia B. Vogelsang,⁸ Guido Kobbe,⁹ Martin Gramatzki,¹⁰ Anita Lawitschka,¹¹ Mohamad Mohty,¹² Steven Z. Pavletic,¹³ Hildegard Greinix,¹⁴ Ernst Holler¹

Steroid refractory chronic graft-versus-host disease (cGVHD) is associated with a significant morbidity and mortality. Although first-line treatment of cGVHD is based on controlled trials, second-line treatment is almost solely based on phase II trials or retrospective analyses. The consensus conference on clinical practice in cGVHD held in Regensburg aimed to achieve a consensus on the current evidence of treatment options as well as to provide guidelines for daily clinical practice. Treatment modalities are the use of steroids and calcineurin inhibitors as well as immunomodulating modalities (photopheresis, mTOR-inhibitors, thalidomide, hydroxychloroquine, vitamin A analogs, clofazimine), and cytostatic agents (mycophenolate mofetil, methotrexate, cyclophosphamide, pentostatin). Recent reports showed some efficacy of rituximab, alemtuzumab, and etanercept in selected patients. Moreover, tyrosine kinase inhibitors such as imatinib came into the field because of their ability to interfere with the platelet-derived growth factor (PDGF-R) pathway involved in fibrosis. An other treatment option is low-dose thoracoabdominal irradiation. Although different treatment options are available, the “trial-and-error system” remains the only way to identify the drug effective in the individual patient, and valid biomarkers are eagerly needed to identify the likelihood of response to a drug in advance. Moreover, the sparse evidence for most treatment entities indicates the urgent need for systematic evaluation of second-line treatment options in cGVHD.

Biol Blood Marrow Transplant 17: 1-17 (2011) © 2011 American Society for Blood and Marrow Transplantation

KEY WORDS: Allogeneic hematopoietic stem cell transplantation, Chronic GVHD, Bone marrow transplantation, Immunosuppressive therapy

INTRODUCTION

Chronic graft-versus-host disease (cGVHD) remains the leading cause for late morbidity and mortality after allogeneic hematopoietic stem cell transplantation (HSCT). Although half of the patients

respond to first-line treatment, prognosis of steroid refractory cGVHD remains poor [1-3]. Primary treatment of cGVHD is based on controlled trials and consists of prednisone given with or without a calcineurin inhibitor (CNI). In contrast, evidence in steroid refractory cGVHD is limited almost

From the ¹Department of Hematology and Clinical Oncology, University of Regensburg, Germany; ²DKD, Wiesbaden, Germany; ³Department of Internal Medicine III, University of Ulm, Germany; ⁴Interdisciplinary Clinic for Stem Cell Transplantation, University Cancer Center Hamburg (UCCH), Germany; ⁵Department of Internal Medicine III, Campus Benjamin Franklin, Charité-University Hospital Berlin, Germany; ⁶Department of Hematology, Hemostasis, Oncology and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany; ⁷Department of Internal Medicine I, University of Dresden, Germany; ⁸Johns Hopkins Oncology Center, Baltimore, Maryland; ⁹Department of Hematology, University of Duesseldorf, Germany; ¹⁰Department of Hematology, University of Kiel, Germany; ¹¹St. Anna Children's Hospital,

Vienna, Austria; ¹²Department of Hematology, University of Nantes, France; ¹³Experimental Transplantation and Immunology Branch, Center of Cancer Research, National Cancer Institute, Bethesda, Maryland; and ¹⁴Department of Internal Medicine I, Medical University of Vienna, Austria.

Financial disclosure: See Acknowledgments on page 13.

Correspondence and reprint requests: Daniel Wolff, MD, Department of Hematology and Oncology, University of Regensburg, F.J. Strauss Allee 11, 93053 Regensburg, Germany (e-mail: daniel.wolff@klinik.uni-regensburg.de).

Received February 12, 2010; accepted May 17, 2010

© 2011 American Society for Blood and Marrow Transplantation
1083-8791/\$36.00

doi:10.1016/j.bbmt.2010.05.011