Belgian Journal of Hematology

The Belgian Journal of Hematology is the official journal of the Belgian Hematological Society (BHS), the Belgian Society on Thrombosis and Haemostasis (BSTH), the Belgian Society of Paediatric Haematology and Oncology (BSPHO) and the Belgian Society for Analytical Cytology (BVAC-ABCA)

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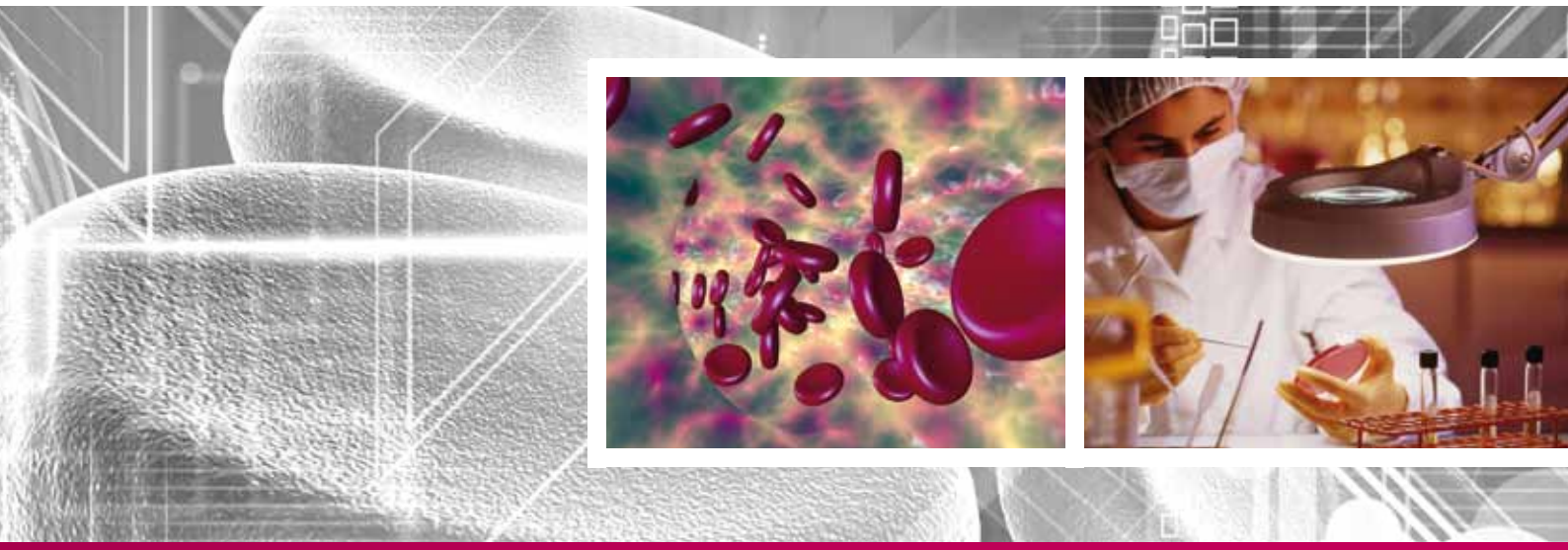

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Belgian transplantation clinical trials
A. Vandamme, R. Schots, Y. Beguin

Adoptive immunotherapy for viral infections after allogeneic stem cell transplantation
M.L. Zandvliet

2

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colophon

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De BJH aims to be a peer-reviewedhematology journal covering all aspects of the diagnostic and clinical management of hematology patients, reflecting a multidisciplinary approach to therapy. It aims informing clinicians active in the field of hematology in Belgium and Luxembourg, thereby giving clinicians a solid support for daily practice. The BJH targets al specialists and specialists in training with an active interest and participation in the clinical management and treatment of hematological diseases. The BJH is distributed for free via controlled circulation amongst all medical specialists working as clinicians in the field of Hematology in Belgium and Luxembourg. This includes fields as hemostasis and thrombosis, but also transfusion medicine and transplantation medicine. The BJH is also sent to clinical chemistry specialists, doctors working in transfusion departments and doctors performing research in the field of hematology, as well as to all specialists in training within these fields in Belgium and Luxembourg.
The content is determined by an independent Editorial Board, consisting of key opinion leaders within the field of hematology, to ensure that articles published in the BJH are truly objective and independent. The journal welcomes contributions from readers, however these will be evaluated for publication by reviewers from the Editorial Board or, occasionally, from outside the Board. For more information, please turn to the publisher, Ariez International.

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Volume 3, Issue 2, June 2012

Table of Contents

Introduction
J. Van Droogenbroeck — 33

Review Hematology
Less veno-occlusive disease after intravenous versus oral busulfan for autologous haematopoietic stem cell transplantation: The Belgian paediatric experience — 34
S. Huybrechts, Y. Beguin, V. Bordon, MF. Dresse, S. Dupont, A. Ferster, G. Laureys, al. Meyts, M. Renard, C. Vermylen

Practice Guidelines
Guidelines of the Belgian Hematological Society for newly diagnosed and relapsed follicular lymphoma 2012 — 41
S. Debussche, A. Van Hoof , A. Sonnet, C. Bonnet, , A. Janssens, G. Verhoef, D. Dierickx, V. De Wilde, D. Bron, W. Schroyens, E. Van Den Neste, F. Offner

Pharmacotherapy
Dasatinib (Sprycel®) use in daily clinical practice: a Belgian observational retrospective study in patients with chronic myeloid leukaemia and Philadelphia positive acute lymphatic leukaemia who are resistant or intolerant to prior therapies including imatinib — 51
P. Martiat, A. Bosly, L. Noens, G. Verhoef, B. Houssa, P. Lacante

Hematocase
Bilateral exophthalmia: first symptom of a Mantle-Cell Lymphoma — 59
M. Igala, B. Bailly B, R. Firescu , M-F. Dehou, S. Goldman, I. Vierasu I, O. Pradier, A. Kentos, D. Bron

Hematotrial
Belgian transplantation clinical trials — 62
A. Vandamme, R. Schots, Y. Beguin

Hematothesis
Adoptive immunotherapy for viral infections after allogeneic stem cell transplantation — 68
M.L. Zandvliet

Calendar of events — 71

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Volume 3, Issue 2, June 2012

Introduction

Dear Reader,

As I'm writing this foreword, a Mediterranean to subtropical climate has – finally – reached Belgium. Although the weather may not be 'classical Belgian', the word 'Belgian' is mentioned 4 (four!) times on the cover of this edition of the BJH.

Not only do we currently enjoy the weather we've waited for, this is also the direction we wanted to go with this journal: a forum for any scientist working in the Belgian field of clinical haematology. I'm very happy to see how many experts in their field collaborated in several contributions.

This issue is also proof of the fact that 'Belgian' is not a synonym for boring or narrow-minded, with articles covering a broad spectrum. You'll discover articles on topics as diverse as VOD, follicular lymphoma, CML and transplantation trials. The case report and hematothesis add some extra pigment.

I do wish you enjoyable reading.

Warm regards,

Jan Van Droogenbroeck
Editor in chief

Less veno-occlusive disease after intravenous versus oral busulfan for autologous haematopoietic stem cell transplantation: the Belgian paediatric experience

S. Huybrechts, Y. Beguin, V. Bordon, MF. Dresse, S. Dupont, A. Ferster, G. Laureys, I. Meyts M. Renard, C. Vermylen

Busulfan is commonly used in preparative conditioning regimens prior to haematopoietic stem cell transplantation in children and young adults for malignant and non-malignant disorders. For many years busulfan was only available in oral form, resulting in large inter- and intra-patients variability in plasma exposure, associated with higher graft failure rate as well as higher toxicity such as veno-occlusive disease. With the development of an intravenous formulation of busulfan, a more accurate control of both the inter- and intra-patient variability has been provided. The goal of this study was to evaluate the use and efficacy of intravenous busulfan in comparison with the oral formulation in children undergoing an autologous transplantation after conditioning with busulfan. Despite the small number of patients, this study confirmed the apparent benefit of intravenous busulfan in children undergoing an autologous HSCT. The use of a five-level dose schedule defined by body weight resulted in an efficient engraftment with marked reduction in the incidence of veno-occlusive disease compared with oral busulfan. In terms of disease-free outcome, survival and event-free survival, similar results have been obtained in both groups. The choice of this formulation of busulfan should therefore be considered.

(Belg J Hematol 2012;3:34-40)

Introduction

Busulfan (Bu) has been widely used as a chemotherapeutic agent in high-dose preparative regimens in children undergoing both allogeneic and autologous haematopoietic stem cell transplantation (HSCT) for malignant and non-malignant disorders.[1-9] For

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Conflict of interest: the authors have nothing to disclose and indicate no potential conflicts of interest.
Key words: autologous haematopoietic stem cell transplantation, intravenous and oral busulfan, combined regimen, children, solid tumours, veno-occlusive disease.

Guidelines of the Belgian Hematological Society for newly diagnosed and relapsed follicular lymphoma 2012

S. Debussche, A. Van Hoof, A. Sonnet, C. Bonnet, A. Janssens, G. Verhoef, D. Dierickx, V. De Wilde, D. Bron, W. Schroyens, E. Van Den Neste, F. Offner

Follicular lymphoma is an indolent lymphoma that has occurred more frequently over the last decades. In this article we present an overview of the diagnosis and initial work-up, prognostic scoring system and choice of therapy. For limited stage disease radiotherapy is the treatment of choice, and may have a curative potential. For advanced stages treatment should be initiated upon certain criteria, and is essentially based on immunochemotherapy, rituximab plus chemotherapy. The choice of chemotherapy depends on age, frailty, and specific toxicities of chemotherapy. Maintenance therapy with rituximab after induction has become standard practice. Since virtually all patients relapse eventually, an overview of the treatment in the relapsed setting is given. The treatment is then again based on immunochemotherapy but there is also a place for radio-immunotherapy, or immunotherapy alone. For young patients, high dose chemotherapy with autologous stem cell rescue should be considered. A brief overview on novel agents, and agents that are in the pipeline, is given. We conclude with some recommendations for follow-up.

(Belg J Hematol 2012;3:41-50)

Introduction

Follicular lymphoma (FL) is a B-cell non-Hodgkin's lymphoma (NHL), usually with an indolent clinical course. It is the most frequent of the low-grade lymphomas, and the incidence is increasing.

The introduction of rituximab in the treatment regimen has changed the picture of the disease, and resulted in an increase of progression-free survival

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Conflict of interest: Professor E. Van Den Neste is a member of the Advisory Board of Roche.

Key words: follicular lymphoma, guidelines.

Dasatinib (Sprycel®) use in daily clinical practice: a Belgian observational retrospective study in patients with chronic myeloid leukaemia and Philadelphia positive acute lymphatic leukaemia who are resistant or intolerant to prior therapies including imatinib

P. Martiat, A. Bosly, L. Noens, G. Verhoef, B. Houssa, P. Lacante

This study aimed to collect information on daily clinical use of dasatinib (Sprycel®) in Belgium, when used for treating patients with chronic myeloid leukaemia (CML) and Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) with resistance or intolerance to prior therapies including imatinib.

We used an observational retrospective approach to collect data from 84 patients (72 CML and 12 Ph+ ALL) from 23 Belgian centres who received dasatinib in the period between October 1, 2007 and October 31, 2009.

The majority of patients had been diagnosed with chronic phase CML (69%). All patients had received prior treatment with imatinib before initiation of dasatinib. Main reasons for switching to dasatinib were development of resistance (65%) or intolerance (31%). In 89% of chronic and accelerated phase CML patients, dasatinib therapy induced complete haematological response (CHR). Major cytogenetic response (MCyR) was observed in 63% and 67% of chronic and accelerated phase patients, respectively.

This study population is representative for patients receiving dasatinib treatment in Belgium. Dasatinib was well tolerated and patient outcome confirmed dasatinib use has significant clinical value in the treatment of CML and Ph+ ALL patients with resistance or intolerance to prior imatinib therapy.

(Belg J Hematol 2012;3:51-58)

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Conflict of interest: P. Martiat, A. Bosly, L. Noens and G. Verhoef had a consultancy or advisory role with Bristol-Myers Squibb; B. Houssa and P. Lacante are employees of Bristol-Myers Squibb.

Key words: dasatinib, imatinib, chronic myeloid leukaemia, clinical response.

Bilateral exophthalmia: first symptom of a Mantle-Cell Lymphoma

M. Igala, B. Bailly, M-F. Dehou, S. Goldman, I. Vierasu, O. Pradier, A. Kentos, D. Bron

Mantle-cell lymphoma (MCL), located in the central nervous system (CNS) was first described some twenty years ago. It is a rare lymphoma usually diagnosed in the context of a resistant or recurring illness. We report the case of a patient in whom bilateral exophthalmia and palpebral ptosis were the first manifestations of a MCL with retro-orbital and meningeal infiltration.
(Belg J Hematol 2012;3:59-61)

Introduction

Mantle-cell lymphoma (MCL) is a B cells non-Hodgkin's lymphoma (NHL) often diagnosed at an advanced stage with lymphnode, bone marrow, bone and splenic localisations. It represents between 3 and 10% of non-Hodgkin's lymphomas (1). The average age of patients diagnosed with this condition is 60; they are predominantly male, aged particularly between 55 and 65, with a male/female ratio greater than 6. The average survival is three to five years.[2] The cells express CD20, CD5 membranous antigens and intranuclear cycline D1. The infiltration of the CNS, which were only described for the first time some twenty years ago, are rare and with an incidence varying according to the series, from 4 to 26%.[1,3] These effects manifest themselves through neurological clinical signs, the presence of malignant cells in the cerebro-spinal fluid, or a parenchymatous or leptomeningeal infiltration revealed by magnetic resonance imaging (MRI).[4]

We report the case of a patient admitted for a problem of bilateral palpebral ptosis and exophtalmia. Work up revealed a stage-IV MCL with a bilateral retro-orbital and a meningeal infiltration from the onset.

Observation

The patient was 64 years old, had no particular previous medical history, was employed in the food industry and without addictive behaviour. In December 2009 he presented a bilateral exophthalmia complicated by a bilateral palpebral ptosis of increasing intensity with reduced visual acuity. The ophthalmological examination concluded there was a chalazion in the right eye, a reduction of visual acuity in the left eye and small papillae at the back of the eye. Following an evident loss of weight estimated to be about eight kilograms in three months, the attending physician had a blood test which revealed a deterioration of the liver function tests, and a thrombopenia. The examination was completed by an abdominal echograph which showed a hepatosplenomegaly. The liver biopsy revealed a diffuse infiltration by a non-Hodgkin mantle-cell lymphoma (CD20+, CD5+ and cycline D1+). He was then referred to the haematology department.

Upon admission, his general condition had deteriorated (performance status ECOG: 2) with fatigue, night sweats without fever, a weight of 97 Kg (a loss of eight Kg in three months), normal arterial blood pressure and a regular heart rate of 90/min.

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Conflict of interest: the authors have nothing to disclose and indicate no potential conflict of interest.

Key words: Non-Hodgkin's lymphoma, Mantle-cell lymphoma, Exophthalmia, Central Nervous System, 18F-FDG PET/CT.

Academic clinical trials run by the Transplant Committee of the Belgian Hematological Society

Belgian transplantation clinical trials

A. Vandamme, R. Schots, Y. Beguin

The Transplantation Committee of the Belgian Hematological Society (BHS) is supported by all university centres and nonuniversity centres with significant transplant activity. The committee is involved in the development of transplant guidelines and recommendations, the transplant peer review process, contacts with regulatory authorities, the introduction of expanded access and medical need programs and the initiation of academic studies addressing important questions in the transplant field. Since 2008, eight clinical trials have been initiated after approval by the Ethics Committees and the National Competent Authority (AFMPS/FAGG). So far, one of them has been completed and is being prepared for publication. In this paper, we briefly describe the rationale, objectives, treatment arms, major inclusion criteria and current status of these different trials. In addition and for each trial a link is provided to the BHS website to obtain more details regarding inclusion criteria, participating centres and administrative/contact information.

(Belg J Hematol 2012;3:62-67)

Introduction

The allogeneic stem cell transplantation (alloSCT) activity in Europe is continuously increasing. On the one hand, indications become more restricted as molecular techniques enable to identify subsets of patients who are more likely to benefit from the graft-versus-tumor (GVT) effect. On the other hand, the introduction in the mid-nineties of non-myeloablative alloSCT (NM-alloSCT) has allowed to expand the indications to more elderly patients or those with comorbidities. Despite improvements in supportive care, alloSCT remains a potentially dangerous treatment option because of the risk of infections and graft-versus-host disease. Many centers and/or collaborative groups are still initiating studies aiming at improving conditioning regimens and posttransplant immunosuppression as well as the use of donor lymphocyte infusions or other cel-

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Conflict of interest: The authors have nothing to disclose and indicate no potential conflicts of interest.

Key words: bone marrow transplantation, clinical trials, mesenchymal stem cells.

Adoptive immunotherapy for viral infections after allogeneic stem cell transplantation

M.L. Zandvliet

On the 22nd of March 2011, M.L. Zandvliet defended his thesis entitled 'Adoptive immunotherapy for viral infections after allogeneic stem cell transplantation' at the University of Leiden, The Netherlands. The research described in this thesis was supervised by professor H.-J. Guchelaar, PharmD, professor J.H.F. Falkenburg, MD, and Dr. P. Meij, PhD. The most important findings of his thesis research are summarised in this report.
(Belg J Hematol 2012;3:68-70)

Introduction

Patients who have undergone allogeneic stem cell transplantation are at an increased risk of viral complications for an extended period of time. This is caused by a lack of virus-specific T cells. The risk is even greater if patients have undergone T cell depletion to reduce the risk of graft-versus-host disease. The main viral pathogens causing serious illness and mortality by reactivation of the virus or by de novo infection are cytomegalovirus, Epstein-Barr virus, and, especially in children, human adenovirus. Pharmacotherapy can be effective, but application is limited by toxicity and is often insufficient for long-term viral control. Various studies have demonstrated that reconstitution of virus-specific T cells is associated with long-lasting protection against viral complications. Adoptive immunotherapy with virus-specific T cells derived from a stem cell donor can therefore be an effective strategy for post-transplant prophylaxis or treatment of viral disease. The transfer of unselected donor T cells via transplant or in the form of donor lymphocyte infusions can promote antiviral reconstitution, but is limited by the risk of simultaneous administration of alloreactive T cells, which may result in graft-versus-host disease. The research described in Zandvliet's thesis focused on the development of clinically applicable methods to isolate virus specific T cells from donor peripheral blood, to allow for effective anti-viral reconstitution with a minimum risk of graft-versus-host disease.

Isolation of virus-specific T cells

For the isolation of virus-specific T cells, mononuclear cells from peripheral blood were stimulated with pools of synthetic 15-mer peptides spanning whole viral proteins. Subsequently, activated T cells were labelled with antibodies, based on production of IFNγ or activation marker CD137, and linked to superparamagnetic beads, after which they could be isolated with a magnet. The advantage of this method is that both $CD8^+$ and $CD4^+$ T cells can be isolated for a wide repertoire of viral epitopes, irrespective of the patient's human leukocyte antigentype. Optimisation of this isolation methodology is described in several chapters.[1-4] Investigating the efficiency of activation of both $CD8^+$ and $CD4^+$ T cells after stimulation with various antigens shows that synthe-

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Conflict of interest: the authors have nothing to disclose and indicate no potential conflicts of interest.

Key words: adoptive immunotherapy, allogeneic stem cell transplantation, T cells, viral infections.

Calendar of events

International & national congresses	
July 7-12, 2012	**32nd International Congress of the International Society of Blood Transfusion (ISBT),** Cancun, Mexico For more information please visit: www.isbtweb.org
August 17-19, 2012	**5th Mayo Clinic Angiogenesis Symposium,** Minneapolis, United States For more information please visit: www.mayo.edu/cme/hematolgy-and-oncology
August 18-22, 2012	**The 30th World Congress of Biomedical Laboratory Science** Berlin, Germany For more information please visit: www.paragon-conventions.com
August 23-26, 2012	**41st Society for Hematology and Stem Cells (ISEH) Annual Scientific Meeting,** Amsterdam, The Netherlands For more information please visit: www.iseh.org
September 20-23, 2012	**European School of Haematology (ESH): ESH-iCMLf International Conference: Biology and Therapy,** Baltimore, United States For more information please visit: www.esh.org/conferences/
October 3-6, 2012	**15th European Society for Immunodeficiencies (ESID) Meeting** Florence, Italy For more information please visit: www.kenes.com/esid2012/
October 4-6, 2012	**European School of Haematology (ESH): ESH International Conference on Myeloproliferative Neoplasms,** Vienna, Austria For more information please visit: www.esh.org/conferences/
October 5-8, 2012	**44th Congress of the International Society of Paediatric Oncology** London, United Kingdom For more information please visit: www.siop2012.org
October 8-12, 2012	**28th Annual Meeting of the Histiocyte Society** London, United Kingdom For more information please visit: www.histiocytesociety.org
October 11, 2012	**4th Amsterdam's Symposium Haematology (IKNL)** Amsterdam, The Netherlands For more information please visit: www.hematologienederland.nl
October 28-30, 2012	**European School of Haematology (ESH): ESH International Conference on Lymphomas** Marseille, France For more information please visit: www.esh.org/conferences/
November 1-3, 2012	**4th International Symposium on Childhood, Adolescent and Young Adult Non- Hodgkin's Lymphoma,** New York, United States For more information please visit: https://www.kintera.org/site/apps/ka/rg/ecreg.asp?c=bjJULdNRJkL4H&b=7978079&en=felBllMnH9JCLNNuF6JBJQMpFelVl1NsF6LFJMMrEfKMJRMwFsG