

2013



The 7th Annual Haematology Oncology Conference

Conference Programme and Abstracts

**and The 11th Annual South African Stem Cell
Transplantation Society Conference**



**Thursday 24 - Saturday 26 October 2013
The Birchwood Hotel, Boksburg - Johannesburg**

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Welcome Address

Dear Friends and colleagues,

You may have seen that this year the format of two popular meetings of the SA Clinical Haematology Society and the SA Stem Cell Transplantation Society have merged "in tandem", the one following the other. Due to time pressures in an academically busy calendar and a response to overall funding pressures, we have tested the concept of a single meeting joining forces among Haematologists with interest in general Haematology and those with a focus on stem cell transplantation. The initial impression is that having the two meetings together seems valuable. We will analyse the outcome of the meeting based on feedback that the delegates will provide. Please take a few minutes to fill in the form that will be distributed at the conference, making your opinions count.

We have local and international speakers who will review topics of great interest in the management of patients with HIV and blood disorders. In this regard, on Thursday 24 October, we have put together a program that focuses on the biology, management of HIV as well as some discussions on topics on the treatment of lymphomas. Friday afternoon and Saturday will be dedicated to discussing topics on stem cell transplantation and transplant immunology. We are thus grateful that Professors Michele Spina, Michele Cavo, Nicolaus Kröger, Jakob Passweg and Dr Peter Donnelly who have travelled from Europe to be with us and share their clinical experience and research work. Please feel free to interact with them informally and participate during question time so that we all get the maximum benefit from their visit. Last, but not least, have an enjoyable few days in Johannesburg and an academically fulfilling meeting.

Kind regards,

Nicolas Novitzky

Organizational and Administrative Support

ORGANIZING COMMITTEE:

HAEMATOLOGY ONCOLOGY CONFERENCE (SACHaS):

Prof Nicolas Novitzky

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Activity Programme

HAEMATOLOGY ONCOLOGY SYMPOSIUM

Thursday 24 October 2013

Time	Speaker	Topic	Chair person
08:00 – 08:05	Prof Nicolas Novitzky	Welcome address	
Mini-symposium of HIV in Haematology			
08:05 – 08:35	Dr Elizabeth Mayne	Guerrilla warfare: HIV and the subversion of the immune system.	Prof Moosa Patel
08:35 – 09:15	Dr Francois Venter	Update on Management of HIV.	
09:15 – 10:00	Prof Michelle Spina	Diagnostic pitfalls and progress in the treatment of HIV Lymphomas.	
10:00 – 10:30	Tea		
10:30 – 11:15	Dr J Thomson Dr M du Toit	<i>Debate 1: In patients with Lymphoma, should ARVs be started early during chemotherapy or at the end of the Lymphoma treatment?</i>	Prof Vernon Louw
11:15 – 12:00	Prof Michele Spina	Treatment of Hodgkin's Lymphoma in patients with HIV.	
12:00 – 13:00	Novartis - Tasigna 1st line Launch		Prof N Novitzky Prof M Patel
13:00 – 14:00	Lunch		
14:00 – 15:30	Dr W Van Schalkwyk Dr F Fazel Dr N Vawda Dr Z Mohamed Prof V Louw	Proffered papers 1	Dr Nazeer Alli
15:30 – 16:00	Tea		
16:00 – 17:00	Prof Michele Spina	The balance of benefit / tolerability in eradicating CNS disease in Lymphoma.	Dr David Brittain
17:30 – 18:30	AGM		

Activity Programme *(continued)*

Friday 25 October 2013

Time	Speaker	Topic	Chair person
08:00 – 08:50	Prof Michele Cavo	Current perspectives in post-transplant intensification and in maintenance therapy in transplant-eligible patients with multiple myeloma.	Prof Nicolas Novitzky
08:50 – 09:30	Dr D Moodley Dr N Sewpersad	Debate 2: <i>Second generation TKIs have now been registered as first line therapy in CML. However, with the advent of imatinib generics it is not worth changing...</i>	
09:30 – 10:10	Prof Michele Cavo	Multiple myeloma: Tackling relapse and resistance in clinical practice	
10:10 – 10:40	Tea		
10:40 – 11:30	Prof Michele Spina	Treatment of unfit and frail elderly patients with NHL.	Dr Jaimendra Singh
11:30 – 12:15	Prof Nicolaus Kröger	Role of Allo SCT in MM in the era of new agents.	
12:15 – 12:20	Closure		
12:20 – 13:00	Lunch		

International Speakers

Michele Spina, MD

Address: Via Andrea Benedetti, 2 - 33170 Pordenone (Italy)
Telephone and fax: 434-659730/284 (work); 434-659531 (Fax at work)
E-mail: mspina@cro.it
Date and place of birth: 14 December 1963 in Palermo - Italy



MEDICAL EDUCATION

Achievement of the medical degree at the University of Palermo in 1988.

Specialist in Haematology, University of Palermo, Italy 1991.

Specialist in Oncology, University of Udine, Italy 1997.

Scientific and Professional activity

- January 1986 to December 1989: he was involved in research programmes on HIV and AIDS at the Institute of Haematology of the University of Palermo, under the supervision of Prof. A. Cajozzo. In particular, he investigated the haematological abnormalities in patients with HIV infection.
- June 1989: he was awarded a study grant on HIV infection in intravenous drug users and in other risk groups in Italy from the Istituto Superiore di Sanità, Ministry of Health, Italy.
- January 1990 and March 1990: he was awarded a study grant on AIDS and Prostitution from the Istituto Superiore di Sanità, Ministry of Health, Italy.
- July 1990 to June 1991: he was awarded an annual study grant on AIDS and Prostitution from the National Cancer Institute of Aviano, Italy.
- June 1991 to June 1992 he was awarded an annual study grant on AIDS and Prostitution from the National Cancer Institute of Aviano, Italy.
- Since June 1992 he has been working as Assistant to the Director at the Division of Medical Oncology A of the National Cancer Institute of Aviano, Italy, involved in AIDS and related tumours, head and neck tumours, genitourinary tract tumours, haematological tumours, cancer in the elderly.
- Since April 2002, he is Chief of the Lymphoma Unit at the Division of Medical Oncology A of the National Cancer Institute of Aviano, Italy.
- Since January 2007, he is Co-director of the Division of Medical Oncology A of the National Cancer Institute of Aviano, Italy.

Present appointments:

- Member of the GICAT (Gruppo Italiano Cooperativo AIDS e Tumori) since 1990.
- Member of the ASCO (American Society of Clinical Oncology) since 1994.
- Member of the ASH (American Society of Hematology) since 2002.
- Member of the AIOM (Associazione Italiana di Oncologia Medica) since 1994.
- Member of the ESMO (European Society for Medical Oncology) since 1994.
- Member of the EORTC (European Organization for Research and Treatment of Cancer) AIDS and Tumors Study Group since 1994
- Member of the EORTC (European Organization for Research and Treatment of Cancer) Genitourinary Study Group since 1994
- Member of the EORTC (European Organization for Research and Treatment of Cancer) Lymphoma Study Group since 1999
- Member of the ANLAIDS (Associazione Nazionale per la Lotta contro l'AIDS) since 1999.
- Secretary of the Gruppo Oncoematologico Linfomi (GOL) since 2000.
- Member of the Scientific Committee of the Intergruppo Italiano Linfomi (IIL) since 2004.
- Chairman of the Elderly Subcommittee of the Intergruppo Italiano Linfomi (IIL) since 2007.

Training:

Attended the Division of Infectious Disease and AIDS Program of the San Francisco General Hospital from April to June 1994.

Attended the Division of Medical Oncology of the Stanford University from April to June 1994 and from November to December 2000.

Publications:

As of September 2013, 210 publications on the most important international journals on the following items: AIDS (neoplastic complications, sexual transmission, discrimination), tumours (in particular tumours in elderly patients, malignant lymphomas and new antineoplastic drugs).

Communications:

He gave lectures at the most important national and international congresses on tumours, AIDS.

Michele Cavo

“Seràgnoli” Institute of Hematology, Bologna University School of Medicine, Bologna, Italy



Michele Cavo, MD, is Professor of Hematology at the University School of Medicine, Bologna, Italy. He received his medical degree cum laude from Bologna University School of Medicine, where he was also awarded his postgraduate degree in Hematology. In 1991, he became Assistant Professor of Hematology, and in 1998 he was appointed Associate Professor of Hematology at Bologna University School of Medicine. From January 2000 to June 2005, Professor Cavo served as Director of Postgraduate Residency in Hematology at Bologna University School of Medicine. Between 2004 and 2009, Professor Cavo has been a member of the Board of the Italian Society of Hematology and has served as Treasurer of the society. Starting from November 2012, Professor Cavo has been appointed Director of “Seràgnoli” Institute of Hematology, Bologna University School of Medicine. Professor Cavo is a member of the European Group for Blood and Marrow Transplantation (EBMT), the American Society of Hematology (ASH) and the Italian Society of Hematology (SIE). Since many years, Professor Cavo is the Head of the Myeloma Research Unit at “Seràgnoli” Institute of Hematology, Bologna, and he actually Co-Chairs the GIMEMA Italian Myeloma Network. He authored many papers published in peer-reviewed journals, including the New England Journal of Medicine, the Lancet, Blood, the Journal of Clinical Oncology, Leukemia, British Journal of Haematology, Haematologica and others. Professor Cavo is a member of the Editorial Board of the Journal of Clinical Oncology and Haematologica/ the Hematology Journal.

International Speakers *(continued)*

Nicolaus Martin Kröger

Professor
 Medical Director
 Dept of Stem Cell Transplantation
 University Hospital Hamburg-Eppendorf/ Germany



EDUCATION AND TRAINING

Institution And Location

Year Conferred Field Of Study

Degree

(If Applicable)

University Hospital Hamburg-Eppendorf, Hamburg, Germany	MD	1982-1988	Medicine
MD Anderson Hospital, Houston/TX, USA	Research	1988	Hematology
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Internal Medicine	1994	Internal Medicine
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Hematology / Oncology	1996	Board Certified
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Assistant Medical Director, BMT	since 1997	
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Medical Director	Since 2011	

RESEARCH AND PROFESSIONAL EXPERIENCE

1988	MD Anderson Hospital, Houston / TX, USA
1988 – 1992	Internal Medicine, Israelite Hospital, Hamburg, Germany
1993 – 1996	Dept. of Hematology and Oncology, University Hospital Hamburg-Eppendorf, Germany
1995	Exam of the European Society of Medical Oncology (ESMO)
1997-2010	Assistant Medical Director, Bone Marrow Transplantation, University Hospital Hamburg-Eppendorf, Hamburg, Germany
1999	Scientific Secretary of the 25th annual EBMT meeting
2006 -2011	Chair of the MDS subcommittee of the European Group for Blood and Marrow Transplantation (EBMT)
Since 2011:	Medical Director, Bone Marrow Transplantation, University Hospital Hamburg-Eppendorf, Hamburg, Germany
Since 2012	Chair of the Chronic Malignancies Working Party of EBMT
2013	Organizing Committee of the 2. NCI Workshop Relapse after Stem Cell Transplantation, Bethesda, USA

Memberships

- European Society of Medical Oncology
- American Society of Clinical Oncology
- European Group for Blood and Marrow Transplantation
- American Society of Hematology
- MDS Foundation: Center of Excellence
- International Working Group Myelofibrosis Research and Treatment (IWG-MRT)
- International Myeloma Working Group (IMWG)

Honors

2010	Award Hamburger Cancer Society
2005	Poster-Award: 3rd International Congress on Myeloproliferative Diseases. Washington / DC, USA
2005	Award Werner-Otto-Foundation for Medical Research
2003	Center of Excellence: International MDS Foundation
2002	Poster-Award: International Symposium Transplantation in Hematology and Oncology

Publications: more than 300 publications in peer reviewed journals

International Speaker Abstracts

Hodgkin lymphoma in patients with HIV infection

Michele Spina, MD
Co-director Division of Medical Oncology A
National Cancer Institute – Aviano - Italy

Hodgkin lymphoma (HL) represents one of the most common non AIDS-defining cancers with an increasing incidence overtime. Clinically, patients present advanced stages of disease with extranodal involvement in the majority of cases. In the last years, significant improvements in the treatment of patients with HL and HIV infection have been achieved. In the lack of randomized trials, several phase II studies have showed that in the era of highly active antiretroviral therapy (HAART) the same regimens employed in HIV-negative patients with HL can be used in HIV setting with similar results. Moreover, in the last years the feasibility of high dose chemotherapy and peripheral stem cell rescue has allowed to save those patients who failed the upfront treatment.

Finally, in the near future, a better integration of diagnostic tools (including PET scan) chemotherapy (including new drugs), radiotherapy, HAART and supportive care will significantly improve the outcome of these patients.

Balancing risks and benefits of CNS prophylaxis in DLBCL

Michele Spina, MD
Division of Medical Oncology A
National Cancer Institute - Aviano (PN) Italy

The occurrence of CNS involvement at diagnosis of DLBCL is a very rare event. However, up to 5% of patients experience a relapse or progression during the course of the disease with a dismal outcome. The impact of both intrathecal and/or systemic prophylaxis is still a matter of discussion. The introduction of rituximab in the treatment of patients with DLBCL has significantly reduced the rate of CNS progression. However, patients with a significant higher risk of. Progression and particular sites involvement (i.e. testis, paranasal sinus, Breast, paraspinal massese) should receive prophylaxis as part of treatment. The new strategies in terms of drugs and route of administration will be discussed.

Modern approach to HIV related lymphomas

Michele Spina, MD
Co-director Division of Medical Oncology A
National Cancer Institute – Aviano - Italy

Patients infected with human immunodeficiency virus (HIV) are at greater risk of developing non-Hodgkin's lymphoma than the general population, and aggressive B-cell lymphoma has become one of the most common of the initial AIDS-defining illnesses. In the recent years new prognostic factors and new approaches to the treatment of patients with AIDS-related lymphoma (ARL) have been tested. Since highly active antiretroviral therapy (HAART) became available, the survival of many ARL patients has become comparable to that of HIV-negative patients. This is partly due to the decrease in the incidence of opportunistic infections and improved prognosis. Both developments can also be attributed to new treatment strategies for ARL, such as the use of effective infusional regimens, Rituximab combinations and high-dose therapy with autologous stem-cell transplantation for relapsed disease. However, unresolved issues persist, like the optimal therapy for patients with Burkitt's ARL or central nervous system involvement.

The role of high-dose therapy (HDT) followed by autologous stem-cell transplantation (ASCT) in the treatment of multiple myeloma (MM) continues to evolve in the novel agent era.

Michele Cavo

The choice of induction therapy has moved from conventional chemotherapy to newer regimens incorporating the immunomodulatory derivatives (IMiDs) thalidomide or lenalidomide, and the proteasome inhibitor bortezomib. These drugs combine well with traditional therapies and with one another to form various doublet, triplet and quadruplet regimens. Up-front use of these induction treatments, in particular bortezomib-based triplet regimens, has affected unprecedented rates of complete response that rival those previously seen with conventional chemotherapy and subsequent ASCT.

Autotransplantation applied after novel-agent-based induction regimens provides further improvement in the depth of response, a gain which translates into extended progression-free survival (PFS) and, potentially, overall survival (OS). High activity shown by IMiDs and bortezomib before ASCT has recently led to their use as consolidation and maintenance therapies after autotransplantation. Novel agent-based consolidation and maintenance therapies have further improved PFS and OS. Novel agents and ASCT are complementary treatment strategies for MM.

Allogeneic Stem Cell Transplantation in Multiple Myeloma in the era of novel drugs

Nicolaus Kröger, Hamburg, Germany

Compared with other treatment modalities in multiple myeloma, allogeneic stem cell transplantation induces the highest rate of clinical complete and molecular remission], and it can induce long-term freedom from disease in about 30–40 % of the cases. Despite the recent improvement in performing allogeneic stem cell procedure, it is still the treatment modality with the highest treatment-related morbidity and mortality. Both morbidity and mortality are related to organ toxicity induced by the conditioning regimen and to immunological complications after transplantation such as graft-versus-host disease and infectious diseases. Evidence of a strong immunologically mediated anti-myeloma effect came from donor-lymphocyte infusions given to patients who relapsed after allogeneic stem cell transplantation. Response rate (CR / PR) up to 67 % can be achieved but only in a minority of patients these remissions are durable. Since the toxicity of the conditioning regimen prior to allogeneic stem cell transplantation contributes to treatment-related morbidity and mortality, a strategy to reduce treatment-related mortality by reducing the toxicity of the conditioning regimen by either toxicity- or dose-reduced regimens has been investigated. The most commonly used regimens in myeloma are either a very-low-intensity approach using 2 Gy total-body irradiation (TBI) with or without fludarabine, or melphalan at an intermediate dose of 100–160 mg/m² in combination with fludarabine. To maintain the efficacy of intensive chemotherapy, the concept of autologous-allogeneic-tandem transplantation was introduced. In this treatment concept, high-dose chemotherapy and adoptive immunotherapy by immunocompetent donor-T-cells were splitted within an interval of two to three months in order to lower toxicity and treatment-related mortality but maintain high-dose chemotherapy as well as the immunomediated graft-versus-myeloma effect. However randomized trials according HLA-identical sibling donor availability showed different results. The randomized French IFM99 protocol used after a cytoreductive autograft (melphalan 200 mg/m²) a dose reduced conditioning consisting of busulfan (4 mg/kg BW) in combination with fludarabine and anti-thymocyte-globulin (12.5 mg/kg Thymoglobulin®) and compared this approach to a second autologous transplantation in high risk patients defined by deletion 13q14 and high β 2-microglobulin. This randomized study did not show any significant difference in event-free and overall survival between the auto-allo- and the tandem-auto-arm. The Italian study group compared 54 patients with multiple myeloma who received auto-allo-tandem transplantation from HLA-identical sibling and compared the results with 54 patients who receive tandem-autologous stem cell transplantation within the same time period. They reported a higher CR rate (54 % vs. 26 %) and an improved progression-free (75 % vs. 41 %, $p < 0.001$) and overall survival (84 % vs. 62 %, $p = 0.006$) for patients who received an allograft.

The EBMT NMAM 2000 compare autologous-allogeneic (reduced-intensity conditioning) vs. single or tandem autologous transplantation with a progression-free survival at 60 months of 35 % for autologous-allogeneic transplantation compared to 18 % ($p = 0.001$) for autologous transplantation, and an overall survival of 65 % compared to 57 % ($p = 0.005$) in favor of autologous-allogeneic transplantation. The aforementioned study did only include HLA-identical siblings as stem cell donor. Other large prospective randomized studies comparing tandem-autologous transplantation with auto-allo transplantation such as Bone Marrow Transplant Clinical Trial Network (BMT/CTN) have completed accrual (EBMT-trial NMAM2000) and first results with a relative short follow-up did not show superiority of allogeneic stem cell transplantation.

The major issue for further improvement of immunologically based strategies post-allo-transplant lies in the separation of the graft-versus-myeloma effect from the graft-versus-host reaction, which would allow a more specific tumor-targeting without or lesser risk of GvHD. Potential candidates for a more specific T-cell response myeloma specific antigens or other cellular compounds such as NK cells or immunomodulating drugs such as bortezomib or thalidomide/lenalidomide.

National Speakers - Oral Presentations

THE DIAGNOSTIC UTILITY OF BONE MARROW BIOPSIES PERFORMED FOR THE INVESTIGATION OF FEVER AND/OR CYTOPENIAS IN HIV-INFECTED ADULTS AT GROOTE SCHUUR HOSPITAL, WESTERN CAPE, SOUTH AFRICA

W A van Schalkwyk, J Opie, N Novitzky

Department of Haematology, Groote Schuur Hospital and National Health Laboratory Service, University of Cape Town.

Introduction: A bone marrow biopsy is frequently requested in the work-up of patients with human immunodeficiency virus (HIV) infection who present with fever and/or cytopenias in the search for opportunistic infections and malignancies.

Methods: This is a retrospective review of the results of consecutive bone marrow biopsies performed at our institution over a three-year period on HIV-positive patients for the investigation of fever and/or cytopenias. Clinical data, haematological parameters, morphological features, Ziehl-Neelsen staining and microbiological culture results were analysed. The aim of the study was to determine the diagnostic yield of this investigation.

Results: Sixty-three males and 84 female patients were included for analysis. The bone marrow biopsy gave a high diagnostic yield of 47% (70 patients) and a unique diagnosis in 33% (49 patients). Immune thrombocytopenic purpura and disseminated mycobacterial infections were the most common unique diagnoses made (each 14%, respectively), followed by malignancies (4%). In this cohort, four cases of primary bone marrow involvement by Hodgkin lymphoma and one case of involvement by non-Hodgkin lymphoma were diagnosed.

Conclusion: In our study group, a bone marrow biopsy was a useful investigation with a high diagnostic yield.

DEMOGRAPHICS AND CLINICAL PRESENTATION OF ADULT HODGKIN LYMPHOMA AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

F B Fazel¹, M Patel¹, V Philip¹, A Lakha¹

¹Division of Clinical Haematology, Department of Internal Medicine, Chris Hani Baragwanath Academic Hospital; Faculty of Health Sciences, University of the Witwatersrand

Introduction: Hodgkin lymphoma is a lymphoproliferative disorder that was first described by Thomas Hodgkin and Samuel Wilks in the first half of the nineteenth century. It is characterised by painless lymphadenopathy, usually in the cervical region. There are clear differences in the demographics and clinical presentation of Hodgkin Lymphoma between developed and developing countries. The main aim of this study was to document these characteristics in a developing sub-Saharan African population, and to compare the findings with findings elsewhere in Africa and the world.

Methods and patients: This was a retrospective review of all adult patients with a confirmed histological diagnosis of Hodgkin Lymphoma, presenting at Chris Hani Baragwanath Academic Hospital during the period January 1990 to December 2004. Data was recorded on an EXCEL spreadsheet and analysed in Stata. A p-value of less than 0.05 was considered to be of statistical significance.

Results: 163 patients were seen over the fifteen year period (January 1990 – December 2004). The median age at presentation was 29yrs (range 13-87yrs). There was no clear second peak in incidence in older patients. There were 93 males and 70 females with a M:F ratio of 1.3:1. 23% of patients were HIV positive. 78% of patients had one or more B symptoms. 69% of patients had advanced stage disease at presentation. Nodular sclerosis Hodgkin Lymphoma was the main histological subtype in younger, HIV negative patients. Mixed cellularity Hodgkin Lymphoma was the commonest subtype seen in older patients and the HIV positive population. 63% of patients had a complete response to first line therapy, 18% had a partial response, 2% had stable disease and 17% had progressive disease. Patients who were older, who had advanced stage disease and who were HIV positive all had significantly poorer survival outcomes

Conclusion: Hodgkin Lymphoma in adults at Chris Hani Baragwanath Academic Hospital displays characteristics typical of a developing nation, such as the absence of a bi-modal age distribution, more B symptoms and more advanced stage disease at presentation. However, the predominance of the nodular sclerosis histological subtype in the younger, HIV negative population tends to mimic the pattern of developed nations. Increasing HIV seropositivity appears to be an emerging trend. 75% of patients assessed for treatment response were alive at 63 months. The large number of patients lost to follow-up precludes accurate assessment of overall survival, as well as documentation of long term complications of therapy in a significant number of patients.

HIV ASSOCIATED HODGKIN'S LYMPHOMA : 2004 – 2009, A GROOTE SCHUUR HOSPITAL EXPERIENCE

N Vawda, Z Mohamed, Department of Radiation Oncology, Groote Schuur Hospital

N Novitzky, Department of Haematology, Groote Schuur Hospital

Background: This audit aims to examine the demographic and disease profiles as well as the treatment outcome of all patients with Hodgkin's lymphoma treated at Groote Schuur Hospital over a 5 year period. **Methods:** The medical records of 125 patients with Hodgkin's lymphoma who received treatment from 2004 until 2009 were reviewed. There was sufficient clinical information to analyse the data of 113 patients of whom 78% (88) were HIV negative and 22% (25) were HIV positive. The results of the 25 HIV positive patients were then analysed. **Results:** There was a single peak in the 30-39 age group with males and females being equally represented. With regards to racial demographics, 88% of patients were of the Black race, followed by Mixed Race (8%) then White Race (4%). Nodular Sclerosis, Mixed Cellularity and Unspecified were equally represented (32%). Advanced disease was present in 76% of patients and of these, 89% had IPS scores between 3 -7. Bone marrow involvement was present in 45% of patients at diagnosis. The median CD4 count was 154. At the time of diagnosis HAART had been instituted in 40 % of patients. The mean duration of antiretroviral therapy prior to diagnosis was 16.7 months (range, 1 – 36). Pulmonary Tuberculosis was diagnosed in 32% of patients. The treatment modality comprised chemotherapy alone in 72 % of patients and a combination of chemotherapy and radiotherapy in 8% of patients. 20% of patients demised prior to any therapy. OS rates at 2 and 5 years, with a median follow up of 21.1 months for surviving patients, was 48% and 45% respectively. **Conclusion:** The majority of patients presented with advanced disease. This is reflected by the 20% of patients who demised prior to therapy and the poor overall survival in the remainder of patients. HIV related co-infections and low rate of HAART therapy are possible contributors to these results.

A RETROSPECTIVE REVIEW OF 46 HIV-POSITIVE PATIENTS WITH PLASMABLASTIC LYMPHOMA SEEN AT GROOTE SCHUUR HOSPITAL, CAPE TOWN FROM 2004-2012

Z Mohamed, Department of Radiation Oncology, Groote Schuur Hospital

N Novitzky, Department of Haematology, Groote Schuur Hospital

Introduction: Plasmablastic lymphoma (PBL) is an aggressive subtype of B-cell Non Hodgkin lymphoma that has become a frequently seen AIDS-related lymphoma in South Africa. There is currently no standard of care for treatment of this disease.

Patients and Methods: 46 HIV-positive patients with PBL were seen at Groote Schuur hospital from August 2004 until August 2012. A retrospective review of the patient charts was performed to obtain demographic and clinical information. Survival analysis and statistical examination of potential prognostic factors was performed

Results: Data from 25 male and 21 female patients with a median age of 35 years (22-57) were reviewed. The majority of patients were black (78%), 20% were mixed race and there was 1 white patient. The commonest stage at presentation was Ann Arbor stage 4 (50%), with 33% having stage 1 disease. Extranodal involvement occurred in 44 out of 46 patients with 50% having 1 and 45% having more than 1 extranodal site. At presentation median LDH was 708iu (310-20000) and median CD4 count was 115 x10⁶cells/l (23-484). ARVs had been commenced within 3 months of, or at lymphoma diagnosis, in 66% of patients. CHOP was administered to all patients with 57% completing 4 or more cycles of chemotherapy. Intrathecal chemotherapy was administered to 10 patients (22%). Nearly half of the patients (47%) received radiotherapy, 50% for palliation and 50% as involved-field radiotherapy after CR. Complete or good partial response to treatment was seen in 23 patients (50%) of whom 8 (35%) relapsed. Median overall survival for uncensored patients was 1000 days (2.7 years). At the end of the analysis 27 patients had died (59%), 12 (26%) were still alive and the survival status of 7 patients was not known. Univariate and multivariate analysis was performed looking at demographic, clinical and treatment-related factors. There were no significant associated factors for death.

Conclusions: Plasmablastic lymphoma occurs with late HIV infection. There was a 50% response rate to CHOP chemotherapy but the relapse rate is very high and late relapse was commonly seen. The survival curve did not exhibit any plateau and no prognostic indicators were identified in this study. A more aggressive yet cost-effective approach is required for this AIDS-related malignancy.

MULTIPLE MYELOMA AND HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION: A COMPARISON OF HIV-INFECTED AND HIV-NEGATIVE PATIENTS

V J Louw¹, J J B de Groot², J E Raubenheimer³, M J Webb¹

Departments: 1Division of Clinical Haematology, Department of Internal Medicine, 2Department of Haematology, VU University Medical Center, Amsterdam, The Netherlands, 3Department of Biostatistics, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa

Introduction and aim: No large studies providing data on multiple myeloma (MM) in HIV-infected patients have been reported in the literature. The aim of this study was to compare the features of HIV-infected and HIV-negative MM patients at first presentation.

Methodology: This was a single-centre, retrospective, descriptive cohort study comparing the demographic and clinical features of 16 HIV-infected patients to 73 HIV-negative patients at first presentation with multiple myeloma (MM) between January 1, 2004 and December 31, 2011. Results: HIV-infected patients generally presented at a younger age with a male predominance. The diagnosis of HIV was mostly newly made and patients presented with relatively high CD4 counts. HIV patients presented at a similar stage of disease, but with more plasmacytomas, while an absence of bone marrow plasmacytosis was common. The HIV-infected patients had less renal involvement, and except for the lower prevalence of osteolytic lesions in the HIV-infected group, the bone involvement was found to be similar in both groups. All HIV-infected patients presented with paraproteins of the IgG type, which might imply a relationship between MM and an IgG response to HIV antigens.

Conclusion: A number of notable differences were found in this study which comprises the largest series of patients with HIV-related myeloma in the world at present. Some of the findings were novel and indicate that there may be a connection between the development of multiple myeloma and HIV.

Clinical Debates

Clinical Debate 1:

In patients with Lymphoma, should ARVs be started early during chemotherapy or at the end of the Lymphoma treatment?

Dr J Thomson
Dr M du Toit

Clinical Debate 2:

Second generation TKIs have now been registered as first line therapy in CML. However, with the advent of imatinib generics it is not worth changing...

Dr D Moodley
Dr N Sewpersad

CPD Information

Continuing Professional Development (CPD)

We urge delegates to wear their name badges at all times. CPD points are awarded at a rate of 1 point per hour. Discovery Health will facilitate the CPD/CME process at the conference. Please collect your bar-coded tag from the registration desk on your first day of the conference if it is not included in your conference name badge. The Discovery staff will scan your bar coded tag outside the main entrance of the lecture room at the start of each session daily.

The data is logged on the website www.mycpd.co.za and delegates will receive unique access codes to access the website, review their points and print out CPD certificates within 7-10 working days after the conference closes.

No points will be awarded retrospectively.

Please switch off your cell phones during sessions.

Acknowledgments

The success of this meeting belongs to many dedicated colleagues and friends. Firstly, our thanks go to all the local participants who shared with us their academic interests. We are equally grateful to our international guests, for coming to South Africa and sharing their research with us. In addition, we wish to acknowledge the financial and logistical support given by all our partners in the Pharma industry and particularly our main sponsors Roche, Janssen, Fresenius Medical Care, Key Oncologics, Sanofi-Aventis, Novartis, CIPLA Medpro, AMGEN, Viking Medical & Surgical, National Bioproducts Institute, The Scientific Group, Haemotec, MSD, Tema Medical and Discovery Health. We are thankful to Discovery Health for managing the CPD for this conference. Lastly, we thank Charne Millett-Clay from Scatterlings and particularly Coleen Fredericks for the administrative and organisational support given and to all of you for your continuing support.

Best wishes

Nicolas Novitzky and Nazeer Alli for SACHaS

Welcome Address

Dear Friends and colleagues,

You may have seen that this year the format of two popular meetings of the SA Clinical Haematology Society and the SA Stem Cell Transplantation Society have merged "in tandem", the one following the other. Due to time pressures in an academically busy calendar and a response to overall funding pressures, we have tested the concept of a single meeting joining forces among Haematologists with interest in general Haematology and those with a focus on stem cell transplantation. The initial impression is that having the two meetings together seems valuable. We will analyse the outcome of the meeting based on feedback that the delegates will provide. Please take a few minutes to fill in the form that will be distributed at the conference, making your opinions count.

We have local and international speakers who will review topics of great interest in the management of patients with HIV and blood disorders. In this regard, on Thursday 24 October, we have put together a program that focuses on the biology, management of HIV as well as some discussions on topics on the treatment of lymphomas. Friday afternoon and Saturday will be dedicated to discussing topics on stem cell transplantation and transplant immunology. We are thus grateful that Professors Michele Spina, Michele Cavo, Nicolaus Kröger, Jakob Passweg and Dr Peter Donnelly who have travelled from Europe to be with us and share their clinical experience and research work. Please feel free to interact with them informally and participate during question time so that we all get the maximum benefit from their visit. Last, but not least, have an enjoyable few days in Johannesburg and an academically fulfilling meeting.

Kind regards,

Nicolas Novitzky

Organizational and Administrative Support

ORGANIZING COMMITTEE:

SOUTH AFRICAN STEM CELL TRANSPLANTATION SOCIETY CONFERENCE (SASCeTS):

Prof Nicolas Novitzky	Nicolas.Novitzky@uct.ac.za
Dr Jackie Thomson	jthomson@oncology-sa.co.za
Dr Devan Moodley	shun@iafrica.com
Dr Mike du Toit	jmgdutoit@mweb.co.za
Dr David Reynders	david.reynders@up.ac.za

CONFERENCE SECRETARIAT:

Scatterlings Conference & Events

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Activity Programme

STEM CELL TRANSPLANTATION SYMPOSIUM

Friday 25 October 2013

Time	Speaker	Topic	Chair person
13.00 – 13.05	Prof Nicolas Novitzky	Welcome address	
13:05 – 13:50	Prof Jakob Passweg	The EBMT activity Survey, trends in the use of Stem Cell Transplantation	Prof Nicolas Novitzky
13:50 – 14:30	Prof Peter Donnelly	Diagnostic pitfalls of invasive fungal infections: from bench to bedside and back.	
14:30 – 15:15	Dr A McDonald: allogeneic Dr J Singh: autologous	Debate: <i>In the era of rituximab patients with recurrent follicular lymphoma should be offered allogeneic / autologous stem cell transplantation.</i>	
15:15 – 15:45	Tea		
15:45 – 16:30	Prof Nicolaus Kröger	Mismatch unrelated Stem Cell Transplantation.	Dr Jackie Thomson
17:00 – 18:00	AGM		

Activity Programme *(continued)*

Saturday 26 October 2013

Time	Speaker	Topic	Chair person
08:05 – 08:00	Prof Nicolaus Kröger	New trends in allogeneic SCT for MDS and myelofibrosis.	Dr Andrew McDonald
08:50 – 09:35	Prof Peter Donnelly	Help and harm of treatment prophylaxis and empirical antifungal therapy.	
09:35 – 10:00	Tea		
10:00 – 11:30	Dr A McDonald (1) Dr J Thomson Prof N Novitzky (1) Dr A McDonald (2) Prof N Novitzky (2) Sr Malebo Mogomotsi [Poster]	<i>Proffered Papers 2</i>	Dr Mike du Toit
11:30 – 12:15	Prof Jakob Passweg	Adoptive Immunotherapy using NK cells.	
12:15 – 13:15	Lunch		
13:15 – 14:00	Prof Peter Donnelly	Care pathways for managing invasive fungal disease.	Dr Devan Moodley
14:00 – 14:45	Prof Jakob Passweg	Pathophysiology and Treatment of GvHD.	
14:45 – 15:15	Tea		
15:15 – 16:00	Dr Nitien Naran	Origins and Ethics (α - Ω)	
16:00 – 16:15	Closure		

Nurses Forum Programme

Nurses Conference

25th October 2013

08h00 to 08h05	Welcome	B. Lass
08h05 to 08h30	Workshop on Side Effects	B. Lass
08h30 to 09h00	Leucodepletion	H. Birns
09h00 to 09h45	Genetic Typing	Dr. Catherine Worlsey
09h45 to 10h15	Tea	
10h15 to 11h00	Transplant Patient	Les Phillips
11h00 to 11h15	Bone Marrow Ceremony	Nurses Presentation
11h15 to 12h00	Cancer Alliance	Lauren Pretorius
12h00 to 12h15	The effect of working in Isolation	Nurses Presentation
12h15 to 13h15	Lunch	
13h15 to 13h50	Pain Control	Christa Du Toit
13h50 to 14h30	Doctor's Lecture	Prof Peter Donnelly
14h30 to 15h00	Stress to Wellness	Samantha Guercio
15h00 to 15h15	Wrap Up for the day	B. Lass
15h15 to 15h45	Tea	
15h45 to 16h30	Doctor's Lecture	Prof. Nicolaus Kroger

International Speakers

Prof. Dr. med. Jakob R. Passweg, M.S.

born June 21, 1959, Biel-Bienne, Switzerland

Family children married to: Marianne Schnegg Passweg M.D.
Jonas Raphaël, born August 30th 1996
Lea Pauline, born January 20th 2000

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Education/ Diplomas

1978 Graduated High School (Matura), Dt. Gymnasium, Biel
1984 Graduated, Medical School, University of Berne, Switzerland
1987 Dissertation, University of Berne
1994 Swiss Board Certification (FMH) Internal Medicine and Hematology
1996 Master of Science, Epidemiology, Medical College of Wisconsin, USA

Postgraduate Training

1985 Institute for Clinical Pharmacology, University of Berne, CH (Prof. R. Preisig, MD Thesis)
1985 Editorial assistant, pharma-kritik drug letter (Dr. E Gysling)
1986 Residency Internal Medicine, Ziegler City Hospital Berne (Prof. R Hoigné)
1987 Residency Geriatrics, Basel University Hospital (Prof. H.B.Stähelin)
1988 Residency Internal Medicine Kantonsspital Bruderholz (Prof. H.Kummer)
1990 Residency Internal Medicine Basel University Hospital (Prof. W. Stauffacher)
1991 Fellowship Nephrology, Basel University Hospital (Prof. G. Thiel)
1990 Fellowship Hematology, Basel Univ Hospital (Proff. B. Speck, A.Gratwohl, A. Tichelli)
1994 Clinical and Research Fellow, International Bone Marrow Transplant Registry, Health Policy Institute, Medical College of Wisconsin (Prof. MM Horowitz) and Bone Marrow Transplant Program MCW (Prof. W. Burns)

Academic position

1995 Visiting Assistant Professor, Health Policy Institute, Medical College of Wisconsin, USA
2001 Venia docendi, University of Basel, Medizinische Fakultät, Innere Medizin
2005 Professeur ordinaire, Faculté de Médecine, Université de Genève
2011 Ordinarius Hämatologie, Medizinische Fakultät, Universität Basel

Clinical Position

96-02 Attending physician (Oberarzt), Hematology Division; Basel University Hospital
02-05 Leitender Arzt, Hematology Division; Basel University Hospital
05-10 Chair, Hematology Division, Hôpitaux Universitaires de Genève
Professor of Hematology, Geneva University

Current Position

2011 Chair, Hematology Division, Basel University Hospital
Professor of Hematology, Basel University

International Speakers *(continued)*

Dr Peter Donnelly

Dr Peter Donnelly is Coordinator of Studies in Supportive Care of the Department of Haematology and is a member of the Nijmegen Institute for Infection, Inflammation and Immunity, Nijmegen, The Netherlands. He is Chair of the Infectious Disease Group of the European Organisation for Research and Treatment of Cancer (EORTC), General Secretary to the International Society for Human and Animal Mycology (ISHAM), chair of the ISHAM Working Group – European Aspergillus PCR Initiative (EAPCRI), and a member of the European Group for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party. He is also a Fellow of the Royal College of Pathology.



Dr Donnelly graduated with a Bachelor of Science at the University of Glasgow in 1974, earning his PhD on the topic of 'Viridans streptococci and allogeneic bone marrow transplant' in 1993. After working in Microbiology Technician posts at Gartnavel General Hospital, Glasgow, UK, and as Senior Scientific Officer at Hammersmith Hospital, London, he moved to the Medical Microbiology department of the University Hospital Nijmegen in 1987 and finally became a staff member of the Department of Haematology.

His current research interests are the epidemiology, diagnosis and management of invasive fungal diseases, mucosal barrier injury, and infection and infectious complications of the neutropenic patient. Dr Donnelly is author of over 200 research papers and reviews and 15 book chapters. He is also Senior Editor of the Journal Antimicrobial Chemotherapy, section editor of the International Journal of Infectious Diseases, and regular reviewer for top peer-reviewed journals including the Lancet and Clinical Infectious Diseases.

International Speakers *(continued)*

Nicolaus Martin Kröger

Professor
 Medical Director
 Dept of Stem Cell Transplantation
 University Hospital Hamburg-Eppendorf/ Germany



EDUCATION AND TRAINING

Institution And Location

Year Conferred Field Of Study

Degree

(If Applicable)

University Hospital Hamburg-Eppendorf, Hamburg, Germany	MD	1982-1988	Medicine
MD Anderson Hospital, Houston/TX, USA	Research	1988	Hematology
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Internal Medicine	1994	Internal Medicine
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Hematology / Oncology	1996	Board Certified
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Assistant Medical Director, BMT	since 1997	
University Hospital Hamburg-Eppendorf, Hamburg, Germany	Medical Director	Since 2011	

RESEARCH AND PROFESSIONAL EXPERIENCE

1988	MD Anderson Hospital, Houston / TX, USA
1988 – 1992	Internal Medicine, Israelite Hospital, Hamburg, Germany
1993 – 1996	Dept. of Hematology and Oncology, University Hospital Hamburg-Eppendorf, Germany
1995	Exam of the European Society of Medical Oncology (ESMO)
1997-2010	Assistant Medical Director, Bone Marrow Transplantation, University Hospital Hamburg-Eppendorf, Hamburg, Germany
1999	Scientific Secretary of the 25th annual EBMT meeting
2006 -2011	Chair of the MDS subcommittee of the European Group for Blood and Marrow Transplantation (EBMT)
Since 2011:	Medical Director, Bone Marrow Transplantation, University Hospital Hamburg-Eppendorf, Hamburg, Germany
Since 2012	Chair of the Chronic Malignancies Working Party of EBMT
2013	Organizing Committee of the 2. NCI Workshop Relapse after Stem Cell Transplantation, Bethesda, USA

Memberships

- European Society of Medical Oncology
- American Society of Clinical Oncology
- European Group for Blood and Marrow Transplantation
- American Society of Hematology
- MDS Foundation: Center of Excellence
- International Working Group Myelofibrosis Research and Treatment (IWG-MRT)
- International Myeloma Working Group (IMWG)

Honors

2010	Award Hamburger Cancer Society
2005	Poster-Award: 3rd International Congress on Myeloproliferative Diseases. Washington / DC, USA
2005	Award Werner-Otto-Foundation for Medical Research
2003	Center of Excellence: International MDS Foundation
2002	Poster-Award: International Symposium Transplantation in Hematology and Oncology

Publications: more than 300 publications in peer reviewed journals

International Speaker Abstracts

Diagnostic pitfalls and invasive fungal disease: from bench to bedside and back

J Peter Donnelly BSc PhD FRCPath, Department of Haematology, Radboudumc, Nijmegen, The Netherlands

Much has been written about the diagnosis of invasive fungal infections and disease in recent years mostly about how difficult it is to diagnose invasive fungal disease early enough to make a difference. Yet there have been significant progress since the publication of the EORTC/MSG consensus definitions of invasive fungal disease (de Pauw et al *Clin Infect Dis* 2008; **46**: 1813-21). We are fortunate to be better aware of who gets invasive fungal disease and when, we have better means of imaging internal organs especially the lungs thanks to the CT scan and we no longer have to rely entirely on culture and microscopy to detect fungi but can turn to antigen tests and even nucleic acid detection directly from blood. We even have 3 classes of antifungal drugs to choose from compared with only a single class 25 years ago. Yet why then are so few of us taking full advantage of it? Why has the gap between the bench and bedside not yet been bridged? Some physicians rely on the CT scan to alert them to the possibility of apulmonary fungal disease. Others screen twice weekly for galactomannan and if detected then order a CT scan. There are also reports appearing on combined screening tests with beta-d-glucan and PCR. However there are also concerns about the impact of antifungal prophylaxis on the performance of screening tests. The bronchoalveolar lavage (BAL) has also moved centre stage as these specimens allow antigens such as galactomannan and fungal nucleic acid to be detected. Yet there are no standards for obtaining a BAL nor for handling the fluid in the laboratory. This presentation will set out to explore this extensively with a view to offering remedies that are realistic and reliable. The different parts of the journey from the bedside to the bench will be explored in terms of which specimens should be ordered and when. What then happens at the bench will be discussed not only in terms of the tests themselves but also their relative performance and what the results mean. The end result will be set against the backdrop of guidelines from different groups so as to distil the data into useful information.

Help and harm of antifungal prophylaxis and treatment

J Peter Donnelly BSc PhD FRCPath, Department of Haematology, Radboudumc, Nijmegen, The Netherlands

We all know the adage “prevention is better than cure”. This holds true for invasive fungal diseases as with other illnesses. If we can prevent colonisation from becoming infection and, in turn, infection from progressing to disease, we would be sparing our patients from considerably morbidity and more would survive. That, at least, is the conviction that motivates us to attempt to prevent infection in the first place. As moulds invariably originate from the local environment be it air or water, the first step is to protect the patient from spores by supplying filtered air and perhaps water as well. However patients are seldom admitted for the entire duration of their treatment and spend various times at home placing them at risk of inhaling fungal spores again. Many centres now adopt a bridging approach in which patients assumed to be at risk for invasive mould diseases are given prophylaxis inside and outside of hospitals to prevent infection and disease. Azole antifungal drugs are most often used as they can be given orally and for long periods apparently without harm. However none of the drugs available is perfect. Fluconazole has the ideal properties of a drug being almost completely absorbed and result in exposure that is directly related to the dose. However the drug is not active against moulds so its use is limited to preventing *Candida* infections. The triazoles, itraconazole and posaconazole share similar spectra of activity in vitro but neither are tolerated particularly well in their present forms resulting in erratic absorption and variable compliance. Moreover neither is licensed for first-line treatment of invasive aspergillosis. By contrast, voriconazole is, but has only been tested to a limited extent for its efficacy as prophylaxis. These drugs also can be associated with side effects making compliance even more difficult, To combat this many centres give an echinocandin as these are well tolerated though none has been shown to be effective as first line treatment of invasive mould diseases and all need to be given parenterally. Amphotericin B then remains the only option but like the echinocandins cannot be given effectively by mouth requiring patients to be admitted at least for the infusion. The question then remains should prophylaxis be given since no drug is perfect and, if so to whom and when? This aspect will be explored more fully to help provide an answer that is reasonable and useful in practice.

Care pathways for managing invasive fungal disease

J Peter Donnelly BSc PhD FRCPath, Department of Haematology, Radboudumc, Nijmegen, The Netherlands

Effective management of invasive fungal diseases can no longer be achieved at the bedside by a lone physician. Diagnosis requires the efforts of a multidisciplinary team comprising nurses, radiologists, pharmacists, microbiologists and others besides the physician who takes care of the patient. The patient also has a role. This all presents a challenge to the health care professionals as they must decide whether to continue with a loose arrangement or to attempt to make their involvement explicit by establish a care pathway in which the responsibilities and task are clearly set out making the whole process amenable to audit. This motivating a group of experts from different fields to develop care pathways for patients typically considered at risk for invasive fungal disease, those being treated for haematological malignancies and recipients of an allogeneic haematopoietic stem cell transplant. In essence two different care pathways were identified – a diagnostic driven approach leading to direct antifungal therapy and an alternative approach that relied on giving these drugs empirically. Each of these approaches was linked to whether or not the patient was protected from fungal infection or not. The support for each of these was based on the available evidence which was far from conclusive. Never the less adoption, of this approach should aid better management, lead to better use of laboratory services and help in the stewardship of antifungal drugs. A large multicentre trial is currently running under the auspices of the Infectious Diseases Group of the EORTC which should help decide which of these approaches, if any, is better and help guide future strategies for managing invasive fungal diseases in vulnerable patients.

Stem Cell Transplantation in MDS as MPN

Nicolaus Kröger

Despite improvement in treatment of MDS and the approval of novel drugs such as hypomethylating agents, the treatment strategy with the highest curative potential remains allogeneic stem cell transplantation. The numbers of allogeneic stem cell transplants are rapidly increasing in Europe. While in 2001 620 patients with MDS have been transplanted, the number increased to 1636 in 2010. This increase is due to transplantation of elderly patients (>50 years) and to an increase of matched unrelated donors.

Allogeneic haematopoietic stem cell transplantation is the treatment of choice for patients with advanced stage MDS who have a suitable donor. Patients with less advanced stage of MDS such as RA or RARS may benefit as well from allogeneic stem cell transplantation with long-term disease-free survival of more than 50 %. The outcome after allogeneic stem cell transplantation has improved progressively in the last years due to a continuous reduction in non-relapse mortality. Reduced intensity conditioning (RIC) regimens have extended the use of allogeneic stem cell transplantation to elderly patients up to the age of 70 years, but its role in the treatment of MDS patients remains to be determined. Currently relapse has become the major cause of treatment failure. Cytogenetic abnormalities and number of blasts at time of transplantation are the major risk factors for relapse. Several questions remain to be solved by prospective studies such as the impact of pre-transplant chemotherapy in RAEB/RAEB-t patients or the comparison between reduced intensity and standard myeloablative conditioning. Since age is no longer a limiting factor, comorbidity indices needed to be considered in new studies. New trials of allogeneic SCT will incorporate new agents such as demethylating agents or histone-deacetylase-inhibitors either as induction to reduce blast count prior to transplantation or as a post-transplant strategy to prevent relapse.

Hematopoietic stem cell transplantation offers a curative therapy for patients with myelofibrosis. Due to toxicity, allografting following myeloablative regimens is mainly applicable to young patients. With the introduction of dose-reduced conditioning using busulfan or melphalan with fludarabin, transplantation became tolerable also in older patients. Implementation of antithymocyte globuline in the conditioning resulted in an effective graft versus host disease prevention and an increased use of alternative donors. Through the discovery of new disease specific mutations, close monitoring of residual disease became feasible in many patients and the outcome of post-transplant strategies improved. Still challenging is achieving of new transplant-derived models to estimate risk status and possible outcome in every individual patient and help in therapy decision and determine optimal timing of stem cell transplantation. Such a tool may optimally include not only clinico-morphological characteristics but also other potentially relevant factors such as cytogenetics and novel molecular markers. Since the introduction of JAK inhibitors in the treatment of Myelofibrosis a careful selection of patient for allogeneic stem cell transplantation has to be done. Furthermore, JAK inhibitors offer new possibilities to improve constitutional symptoms and spleen size before transplantation, which may result in a lower therapy related morbidity and mortality.

Minimal Residual Disease Following Allogeneic Hematopoietic Stem Cell Transplantation

Nicolaus Kröger

University Hospital Hamburg-Eppendorf, Hamburg, Germany

Relapse has become the leading cause of death following allogeneic hematopoietic stem cell transplantation (HSCT). Despite improved understanding of the biology that underlies the graft-versus-leukemia/tumor (GVT) effect the relapse rate did not decrease over the past 20 years. In general, prognosis is poor for patients who relapsed to an allograft since effective treatment options are limited. Minimal residual disease (MRD), in the setting of allogeneic hematopoietic stem cell transplantation (alloHSCT), poses several interesting questions and complex challenges. The relevance of these questions and challenges is personified by the relationship between MRD and the risk of relapse, which is primary cause of treatment failure and death after alloHSCT. The clinical relation of post-transplant MRD with relapse was recognized early with development of cytogenetic and molecular techniques of detection. The clinical relevance of MRD has been further recognized with the increased use of non-myeloablative and reduced-intensity conditioning regimens, with which relapse is even a greater clinical problem.

Despite the clear association of MRD with relapse, the clinical relevance of MRD in the AlloHSCT setting remains to be determined. First and foremost, the definition of MRD needs to be defined for each disease, and needs to be distinguished from what we currently refer to as “remission” or “relapse”. The detection of persistent disease post-transplant by immunophenotypic measures has significantly different implications for patients with acute lymphocytic leukemia (ALL) as compared to someone with persistent chronic lymphocytic leukemia (CLL). Similarly the molecular detection of a cytogenetic abnormality in the post-transplant is markedly different for a patient transplanted with CML as compared to a patient with acute myeloid leukemia (AML). Second, when and how often we should be using available techniques for a specific disease remains to be defined. This not only applies to the post-transplant setting but also to the pre-transplant setting, where multiple studies have demonstrated the prognostic significance of MRD prior to conditioning. As the majority of relapses occur within the first six months after transplant, it is important to determine the frequency of monitoring for recurrent disease within this post-transplant period. If we can determine when and how often, the next question is what tests should we performing and are those tests adequately sensitive, specific, reproducible, practical and economical. There is sufficient evidence that detection of MRD provides prognostic information. However, does this information result in clinical decisions, relative to choice of conditioning regimen or stem cell product relative to detection of pre-transplant MRD or intervention (e.g. withdrawal of immune suppression or donor lymphocyte infusion) that result in improved outcomes? These remain essential questions for which there are relatively limited data and recommendations with the possible exceptions of CML and ALL, and even with these diseases, there remains a need for further investigation.

National Speakers - Oral Presentations

CHARACTERIZATION OF BONE MARROW HARVESTS PERFORMED AT ALBERTS CELLULAR THERAPY

A McDonald, J Thomson, D Brittain, T Gerdener, C Wissing, D Reynders

Alberts Cellular Therapy, Pretoria

Bone marrow harvests for stem cell transplantation are uncommonly performed in South Africa. We report on the indications, adequacy of harvests and outcomes of transplants performed using this stem cell modality performed from 1 January 2011 to 31 August 2013.

The indications for marrow harvest at ACT are: i) Paediatric donors (n=10), ii) Donor preference (n=0), iii) Recipients with Idiopathic Myelofibrosis (n=1), iv) Other reasons(n=1) and v) Autologous donors with inadequate PBSC mobilisation for whom plerixafor was not available (n=7).

Bone marrow harvests were collected by 2 operators via bilateral punctures at the posterior superior iliac spine, to a maximum volume of 15-20ml/kg donor weight. Harvests were collected in a standard Fenwal BM harvest collection set. BM harvests were processed in the allogeneic setting to remove RBC in the case of ABO incompatibility, and to volume reduce and remove RBC in large volume autologous harvests prior to cryopreservation. Neutrophil engraftment was defined as the first day of count $>0.5 \times 10^9/l$ of 3 successive counts, and platelets as the first day $>20 \times 10^9/l$ of 3 successive counts in the absence of platelet transfusions.

In the paediatric allogeneic setting, mean collection volume was 630.9ml (SD 354.5), with a mean TNC/kg of $4.8 \times 10^6/kg$ (SD 2.4). 2 harvests were processed to reduce RBC volume. Neutrophil engraftment occurred at 18.6 days (SD 8.4) and platelet engraftment at 30 days (SD 21.2)

In the autologous setting, mean collection volume 1069ml (SD 475.1), with a mean TNC/kg of $2.88 \times 10^6/kg$ (SD1.27). The bone marrow harvests were infused together with previously harvested PBSC. Neutrophil engraftment occurred at 14.7days (SD2.9) and platelet engraftment at 57 days (SD32.6)

In the adult allogeneic setting, only 2 harvests were performed. One harvest was performed for a second transplant from a sibling following graft rejection (TV 1091ml with TNC $5.7 \times 10^6/kg$) and one Myelofibrosis (TV 1100ml with TNC $5.28 \times 10^6/kg$). The first engrafted neutrophils on D28, but demised prior to platelet engraftment; the second is well post transplant with neutrophil engraftment at D10 and platelets at D12.

Conclusion: Bone marrow harvest remains a valuable practice to harvest stem cells in appropriate situations.

OUTCOMES ANALYSIS OF STEM CELL TRANSPLANTATION AT ALBERTS CELLULAR THERAPY (ACT) DURING 2006-2012

J Thomson, D Brittain, A McDonald, D Reynders and T Gerdener

Alberts Cellular Therapy, Pretoria

Introduction: In order to evaluate the clinical outcome of the transplant program at ACT we performed outcomes analysis of all transplant procedures performed.

Methods and Patients: The audit period was June 2006 to December 2012. The key clinical indicators evaluated were: Engraftment period, Overall Survival (OS) by Kaplan Meier, Non Relapse Mortality (NRM) and Graft vs. Host Disease Gr II - IV (GVHD) probability.

Four hundred and ninety seven (497) patients were transplanted during this period, 245 autologous transplants, 166 matched related donor (MRD) transplants and 114 matched unrelated donor transplants. The most common disease for the autologous was myeloma, and for the allogeneic was acute leukaemia and myelodysplastic syndromes. Most patients $>90\%$ received a myeloablative conditioning regimen. GVHD prophylaxis was given with Campath ex vivo, followed by tacrolimus till day plus 60.

Results:

Auto: 245 patients received autografts, the days to neutrophil engraftment were 11.66 days range (8-16), the NRM at one year was 3%, at 2 years was 3% and at 3 years remained 3%. The Kaplan Meier survival at one year was 87%, at 2 years was 74%, 5 years was 65% for all autografts. The 5 years the OS was 70% for the patients transplanted for lymphoma.

MRD: 166 patients received MRD allografts, the days to neutrophil engraftment were 14 days range (9-16), the NRM at one year was 18%, at 2 years was 20% and at 3 years remained 20%. The OS at one year was 70%, at 2 years was 65%, 5 years was 55% for all MRD allografts. For the acute leukaemia patients in first CR the 5 years the Kaplan Meier survival was 68%. The probability of GVHD Gr II - IV at 2 years was 22%.

MUD: 116 patients received MUD allografts, the days to neutrophil engraftment were 14 days range (10-18), the NRM at one year was 22%, at 2 years was 30% and at 3 years remained 30%. The OS at one year was 55%, at 2 years was 45%, 5 years was 40% for all MUD allografts. The NRM is statistically higher for the MUD allografts compared to the MRD allografts ($p < 0.009$). When two cohorts were matched for disease stage, donor sex and time to transplant, no statistical significance ($p < 0.09$) were found in NRM, indicating that advanced disease status and time to transplant may be the major contributing factors to the inferior survival and not the use of a MUD donor. The probability of GVHD Gr II - IV at 2 years was 15%.

Conclusion:

Seven years of data were analysed to evaluate the success of the transplant program at ACT. The outcome analysis revealed that the clinical indicators are within range of the international reference standards. We concluded that although the results were acceptable, improvement of the MUD allografts can be achieved by shortening the time to transplant and by transplanting earlier disease stages. However the availability of matched unrelated donors makes this difficult; due to our small local donor registry and limited funding for international donors.

ALLOGENEIC STEM CELL TRANSPLANTATION FOR LYMPHOPROLIFERATIVE MALIGNANCIES WITH T-CELL DEPLETED GRAFTS

N Novitzky^{1,2}, V Thomas¹, D Pillay, C du Toit¹ and Z Mohamed³

1 The University of Cape Town Leukaemia Unit and the

2 Department of Haematology, Groote Schuur Hospital, Observatory.

3 Department of Radiation Oncology, Groote Schuur Hospital, Observatory, Cape Town, South Africa.

Introduction: Despite the common use of monoclonal antibodies in the management of NHL, the long term prognosis of patients with lymphoproliferative disorders remains unsatisfactory. Allogeneic stem cell transplantation can be curative, but patients receiving standard dose conditioning are reported to have substantial morbidity and mortality from graft vs host disease (GvHD), while in aggressive malignancies, reduced intensity conditioning schedules may result in higher rates of disease recurrence.

Methods: Patients with advanced low grade lymphoma, transformed B-cell malignancy, and non CD30+ T-cell lymphomas still responsive to chemotherapy who had an HLA identical donor were offered stem cell grafts. Conditioning was with ablative doses of either combination chemotherapy or total body radiotherapy (12Gy). Stem cell grafts from HLA identical donors (Siblings n= 65) were harvested from the peripheral blood, by apheresis following mobilisation with cytokines (PBPC). GvHD prophylaxis was by ex vivo depletion of lymphocytes from the graft with CAMPATH-1 G or H antibodies. Patients received post-transplant cyclosporine until day 90.

Results: Seventy-two chemotherapy responsive patients with non-Hodgkin's lymphoma (low grade: 22, transformed: 21, and T-cell: 29) received stem cell grafts. Median age was 46 (range 18-59) years and 25 were female. Conditioning was with chemotherapy in 42 and TBI based in the rest. The median CFU-GM and CD34+ cells infused were $23.6 \times 10^4/\text{kg}$ and $4.7 \times 10^6/\text{kg}$, respectively. All patients engrafted but twenty one patients died. Twelve patients were lost to follow up or died of unrelated causes (MVA) and were censored at last visit. Five patients (7%) died within 100 days of transplantation mainly of infection. One year TRM was 14%. Nine patients developed GvHD and except for 2 who survive, died of infections. Twelve died of disease recurrence including one of secondary PTLD EBV+ unresponsive lymphoma. At a median of 2474 (45-7258) days 70% survive and 68% remain disease free. There was no significant difference in survival among the 3 histological groups. Univariate analysis showed that donor female gender and GvHD were significant adverse factors for survival. Cox regression analysis confirmed that GvHD independently affected survival.

Conclusions: By reducing the incidence and severity of GvHD, patients can tolerate myeloablative doses of chemotherapy satisfactorily. This has resulted in acceptable treatment related mortality and adequate protection from disease recurrence.

National Speakers - Oral Presentations *(continued)*

INTRODUCTION OF A MODIFIED DOSE WEIGHT CALCULATION FOR HIGH DOSE CHEMOTHERAPY

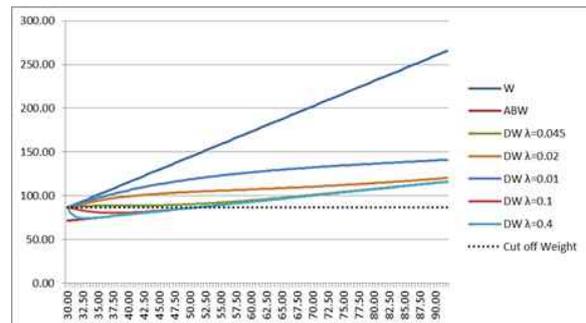
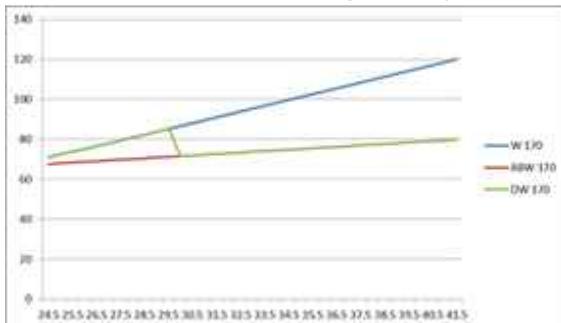
A McDonald

Alberts Cellular Therapy, Pretoria

Due to inferior outcomes in obese patients with malignancy, ASCO 2012 guidelines now recommend chemotherapy dosing based on actual body weight, with dose reductions for patients experiencing severe side-effects¹. However, high dose chemotherapy (particularly myelo-ablative preconditioning regimens) is typically given only once, and the side-effects may be irreversible or fatal. Some chemotherapy package inserts give formulas for dosing based on ideal body weight. At ACT, an IBW referenced to a BMI of 23 was chosen (work by prior authors indicates that standard IBW formulas are inaccurate²). For patients with a BMI under 30 (underweight, normal weight and overweight), dosing (per kg or BSA) is based on actual body weight. For patients with a BMI over 30 (all obese categories), dosing is based on Adjusted Ideal Body Weight (AIBW) = Ideal Body Weight (IBW) + 0.25 (Actual body weight-IBW). However, at the threshold BMI, there is an average 18% drop in dosing weight, with potential for undertreatment and higher relapse rates.

????????????????30?1002 is used, with the decay factor lambda ensuring asymptotic approach to AIBW without significant threshold drop. Lambda = 0.045 appears to best model a curve without significant increase or decrease in AIBW.

This formula is now in use for dosing of obese patients at ACT.



References:

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2. Shah B, Sucher K, Hollenbeck CB. Comparison of Ideal Body Weight Equations and Published Height-Weight Tables with Body Mass Index Tables for Healthy Adults in the United States. *Nutrition in Clinical Practice* 2006 21:312-319

CHARACTERIZATION OF THE VARIABLES AFFECTING EFFICACY OF IMMUNODEPLETION EX VIVO (CAMPATH IN THE BAG) OF PBPC GRAFTS BY ALEMTUZUMAB

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Introduction: We have previously shown that ex vivo immunodepletion with alemtuzumab leads to 2 - 3 log depletion of T cells, with highest cell kill in the presence of complement. It remains unclear what the fate of any excess alemtuzumab is in the stem cell transfer bag. In vivo Campath 1H has long survival which leads to on-going depletion of thymic emigrants post transplantation. The aim of the study was to determine if the antibody is consumed by cells from the supernatant and determine optimal cell / antibody concentration of the transplant product.

Methods: PBPC from six normal allogeneic stem cell donors harvested by apheresis were first quantitated and the cellular content defined by flowcytometry. Mononuclear cells were then incubated with incremental concentrations of alemtuzumab (0.00001, 0.0001, 0.001 and 0.01 mg/mL) for 30 min at 20°C. Cells were enumerated and analysed by flowcytometry before

National Speakers - Oral Presentations *(continued)*

and after exposure to alemtuzumab. In a second step and to determine presence of unbound anti CD52, the supernatant of the cell dose responses were stored at -80°C until analysis using ELISA assay. Mononuclear cells had been suspended at 1, 5 and 10×10^6 cells/mL in IMDM in the presence of 10% fresh AB serum and of 0.001 mg/mL alemtuzumab in cell number dose response studies. Controls without cells, serum or alemtuzumab were included with each run. Optical densities of log values of the working concentrations of alemtuzumab were plotted on a graph and a standard curve was drawn from the control samples.

Results: Incremental concentrations of alemtuzumab led to a significant (2 log) reduction in the CD3, CD4 and CD8 populations which plateaued at 0.001 mg/mL. Addition of complement led to a further significant reduction in the CD4 cells. The maximum CD4 (3 log) and CD8 (2 log) cell death was obtained at 10×10^6 cells/mL. Supernatant of incremental number of cells analysed by ELISA showed significant reduction in the residual concentration of alemtuzumab at the two higher cell numbers, suggesting that ex vivo alemtuzumab is depleted by cells and the free concentration drops below the level of detection at 5×10^6 cells/mL.

Conclusions: Alemtuzumab depletes all cells expressing the CD52 antigen and has higher activity on CD3, CD8 and particularly on CD4 cells, which are reduced in excess of 2 logs. From this study, we were able to derive that the optimal cell kill in the graft without detectable free alemtuzumab in the supernatant can be achieved with 1 mg of antibody per 100 mL containing 10×10^9 cells and active complement (AB serum).

National Speakers - Poster Presentations

REPORT COMPARING TWO MOBILIZATION STRATEGIES FOR PERIPHERAL BLOOD STEM CELL HARVEST IN A HIV POSITIVE PLASMABLASTIC LYMPHOMA PATIENT PLANNED FOR HIGH DOSE CHEMO-RADIATION THERAPY AS CONDITIONING FOR AUTOLOGOUS STEM CELL TRANSPLANT AT ACT

M Mogomotsi, C Wissing, A Prinsloo, A McDonald, J Thomson & D Brittain

Alberts Cellular Therapy at Pretoria

Introduction: Collection of an adequate number of haemopoetic stem cell can be difficult in patient with Lymphoma and who are infected with Human Immunodeficiency Virus. Several studies have described HIV infection as a risk factor for poor mobilization ref. This report compares the results of two mobilization strategies of peripheral blood stem cell in a patient with plasmablastic lymphoma and HIV infection at our practice.

Patient and method: The following variables were collected from the patient; previous chemotherapy treatment and outcomes; clinical features; as well as mobilization strategies viz. a) Chemotherapy + G-CSF + Plerixafor and b) Chemotherapy + G-CSF. The standard mobilization protocol at our practice is to start G-CSF on day 5 of cycle 3 or 4 of the salvage chemotherapy and harvest stem cells when the peripheral blood CD34 count rises above $10 \times 10^6/\text{l}$ (ideally over $30 \times 10^6/\text{l}$). During the first mobilization (standard therapy) he failed to mobilize stem cells to the peripheral blood and his PB CD34 count peaked at $1 \times 10^6/\text{L}$. The harvest was abandoned on day 12 when despite recovery of his WCC ($9.4 \times 10^9/\text{l}$). He was given a 10 week break and then was mobilized with a plerixafor and G-CSF regimen. We evaluated CD34 (+) counts and WBC counts and differential from the night of the first plerixafor injection and 8 hours after plerixafor injection. After the first dose his peripheral blood CD34 count was $17 \times 10^6/\text{L}$ and he was harvested immediately. He achieved a harvest of $2.47 \times 10^6/\text{kg}$ and proceeded to ASCT 4 weeks later.

Conclusions: This case study indicates that patients who are at high risk to fail mobilization due to HIV infection may be effectively mobilized by Plerixafor.

Clinical Debates

Clinical Debate:

In the era of rituximab patients with recurrent follicular lymphoma should be offered allogeneic / autologous stem cell transplantation.

Dr A McDonald: allogeneic

Dr J Singh: autologous

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Acknowledgments

The success of this meeting belongs to many dedicated colleagues and friends. Firstly, our thanks go to all the local participants who shared with us their academic interests. We are equally grateful to our international guests, for coming to South Africa and sharing their research with us. In addition, we wish to acknowledge the financial and logistical support given by all our partners in the Pharma industry and particularly our main sponsors Roche, Janssen, Fresenius Medical Care, Key Oncologics, Sanofi-Aventis, Novartis, CIPLA Medpro, AMGEN, Viking Medical & Surgical, National Bioproducts Institute, The Scientific Group, Haemotec, MSD, Tema Medical and Discovery Health. We are thankful to Discovery Health for managing the CPD for this conference. Lastly, we thank Charne Millett-Clay from Scatterlings and particularly Coleen Fredericks for the administrative and organisational support given and to all of you for your continuing support.

Best wishes

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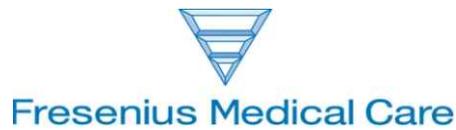


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