EBMT (UK) NAP Group 38th Meeting

York, June 17th, 2010

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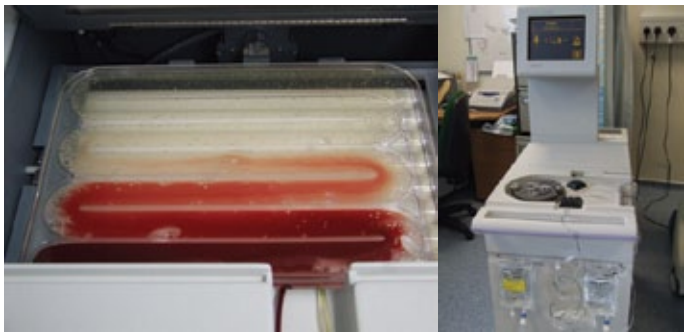

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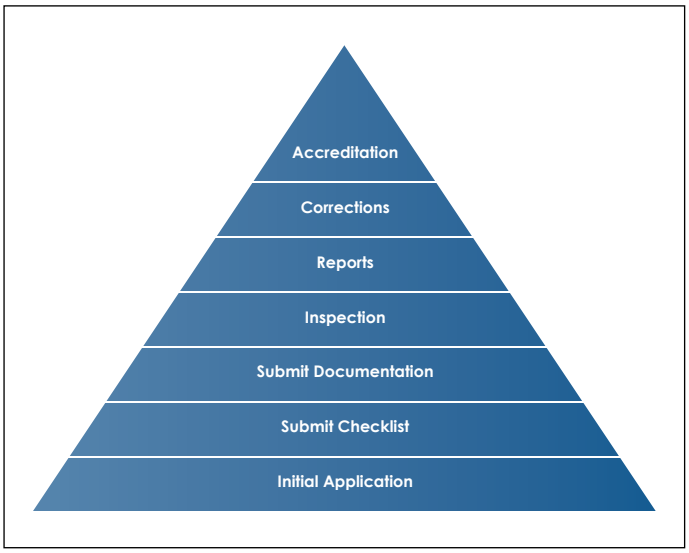

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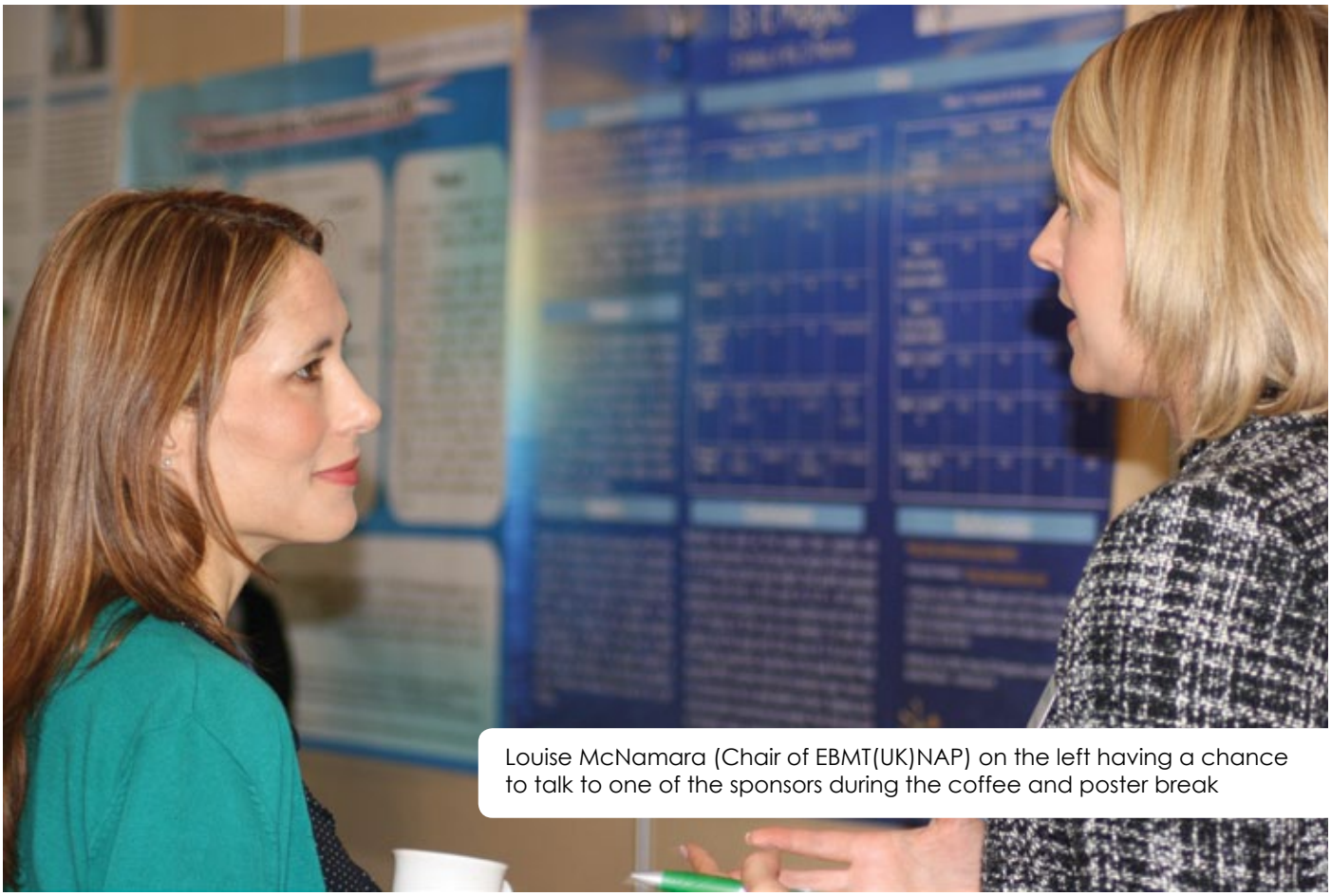
Introduction:
EBMT (UK) NAP Group 38th Meeting

The 38th EBMT (UK) NAP meeting, chaired by Louise McNamara, took place on 17th June in York, and offered an exciting and diverse programme including an educational session on graft versus host disease (GVHD), presentations of case reports and new research, and an update on structural changes and opportunities taking place within clinical practice and the EBMT. Several scientific posters presented at the 2010 EBMT Annual Congress were also available for viewing and discussion.



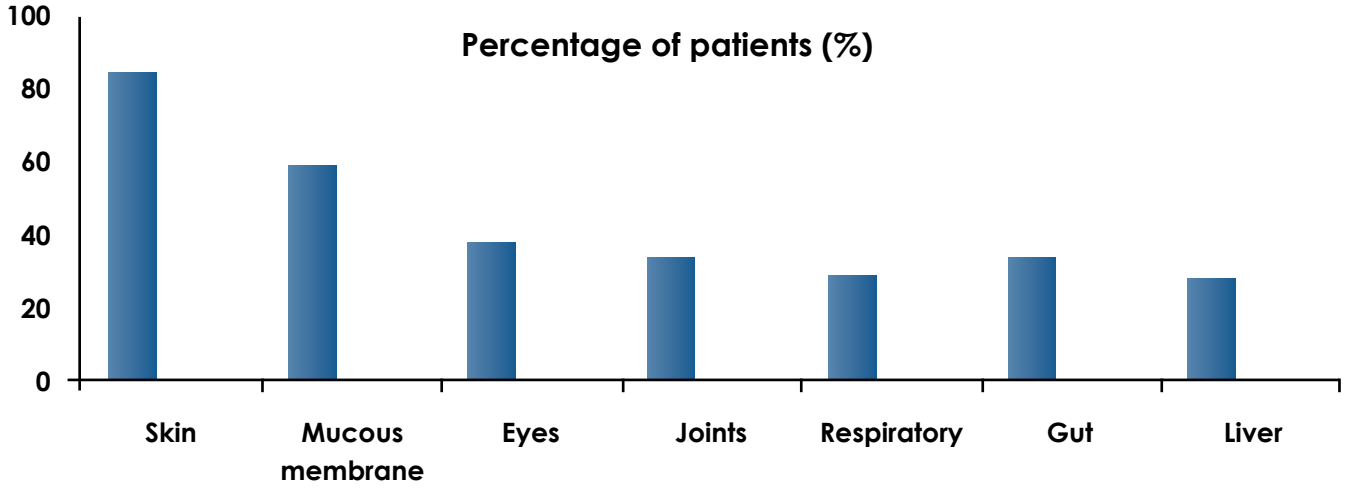
Louise McNamara (Chair of EBMT(UK)NAP) on the left having a chance to talk to one of the sponsors during the coffee and poster break

Overview of GVHD

Dr Peter Taylor

Consultant Haematologist, Rotherham

GVHD, which occurs after allogeneic stem-cell transplantation (ASCT), is usually reasonably well controlled in the majority of patients. However, in some patients it can become a life-threatening event. The improvements seen in acute GVHD (aGVHD) have not translated to chronic GVHD (cGVHD), which has an incidence of around 30-60% and is the primary cause of transplant mortality.[1] Systemic infection is one of the most common causes of death in these patients.[2] cGVHD can affects multiple sites, including the skin, mucosa, eye, joints, respiratory system, gastrointestinal tract and liver.



Skin lesions, which are the most commonly presenting feature of cGVHD, are red to violet and typically first appear on the palms of the hands, soles of the feet, cheeks, neck, ears and upper trunk. They can progress to involve the whole body. In severe cases, bullae may be observed, and vesicles may form. cGVHD can lead to lichenoid skin lesions or sclerodermatous thickening of the skin, which sometimes causes contractures and limits joint mobility. In addition to skin involvement, atrophy of the oral mucosa can often occur, associated with erythema, and lichenoid lesions of the buccal and labial mucosae.

Our current understanding of the biology of cGVHD is unclear, but it is believed that inappropriate recognition of host self-antigens may occur. cGVHD is a syndrome that mimics autoimmune disease. Donor T-cells play an important role in its development, but humoral immunity is also implicated.

A number of strategies have been investigated for the prevention of cGVHD, including prolonged cyclosporin, T cell depletion, intravenous immunoglobulin and campath. However, none of these have resulted in satisfactory outcomes. Extracorporeal photopheresis (ECP), which is a very specialised service, has also been used as a treatment for steroid-refractory acute and cGVHD. It is available in only a few centres across the UK and has been used in the Department of Clinical Haematology at Rotherham General Hospital since 1994.

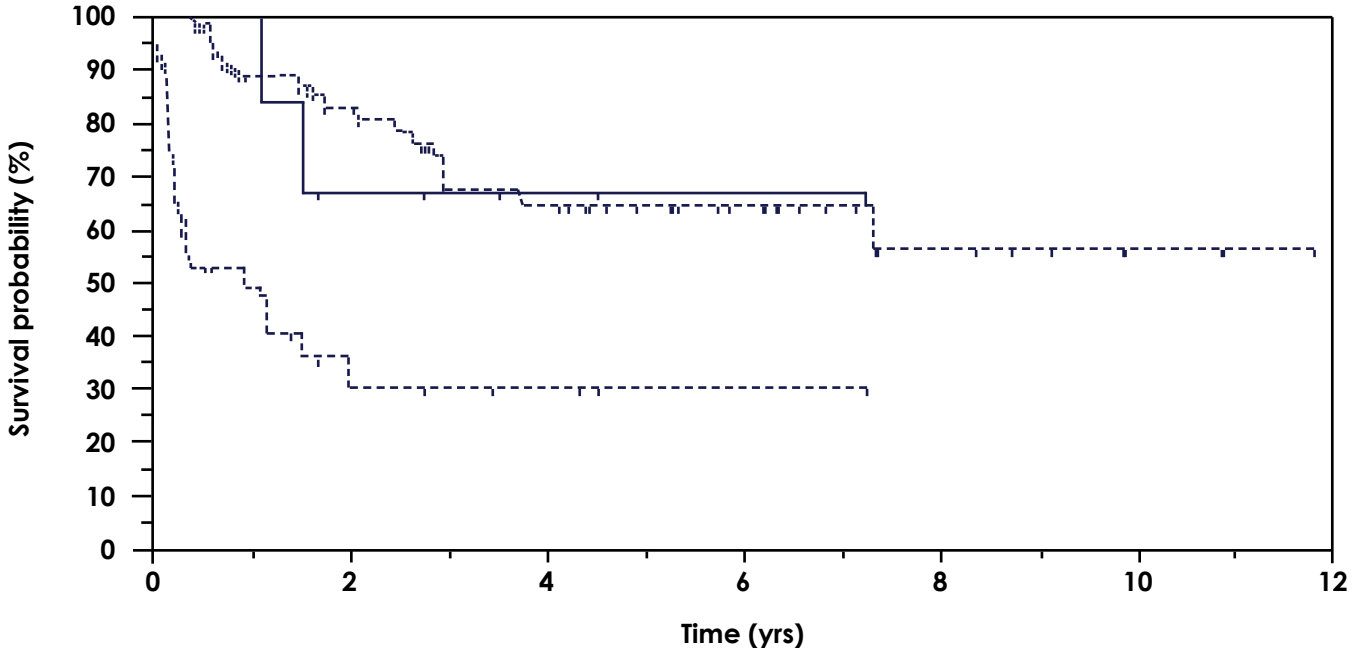
Extracorporeal photopheresis (ECP)

The mechanism of action of ECP is not well understood. The main direct effects of ECP on treated circulating T cells are thought to include apoptosis.[3] However, this by itself does not explain the efficacy,

as only a small proportion of pathogenic T cells are treated during the ECP process. It has been proposed that the immune system could be involved by downmodulating the pathogenic T-lymphocyte reactivity. *In vivo* production of immunosuppressive cytokines by macrophages or monocytes, following ingestion of apoptotic cells, has been suggested as a general immune effect of ECP.[4] Apoptotic cell engagement has been reported to induce several changes and functional activities in the engulfing antigen-presenting cell. These antigen-presenting cells decrease production of proinflammatory cytokines, increase production of anti-inflammatory cytokines, lower the ability to stimulate T-cell response, delete CD8 T effector cells and induce regulatory T cells. Any and all of these mechanisms could explain the noted effect in cGVHD. However, it is still unclear which one or ones are truly responsible.

The first reported case of ECP used to treat cGVHD was published in 1994.[5] In 2006, ECP was retrospectively evaluated in 71 patients with severe cGVHD.[6] The response rate was 61%, with best responses observed in the skin, liver, oral mucosa and eye. There was a trend toward a higher response rate in *de novo* cGVHD in these patients (76%). At 6 months, 69% of patients who were alive continued to have a sustained response and the cumulative incidence of steroid discontinuation at 1 year was 22%. The overall survival from initiation of therapy was 53% at 1 year. Response to ECP and platelet count at initiation of therapy were the strongest predictors of nonrelapse mortality. The safety and efficacy of ECP for 12 to 24 weeks together with standard therapy has also been compared with standard therapy alone in patients with cutaneous manifestations of cGVHD that could not be adequately controlled by corticosteroid treatment.[7] The primary efficacy end point was a blinded quantitative comparison of percentage change from baseline in Total Skin Score (TSS) of 10 body regions at week 12. The median percentage improvement in TSS at week 12 was 14.5% for the ECP arm and 8.5% for the control arm (p= 0.48). The proportion of patients who had at least a 50% reduction in steroid dose and at least a 25% decrease from baseline in TSS was 8.3% in the ECP arm at week 12 and 0% in the control arm (p = 0.04). In another study to assess the improvement of skin cGVHD in steroid refractory patients, ECP treatment resulted in a skin score response in 56% and 72% of patients at 3 and 6 months, respectively. The skin score improved with time. Regardless of the time to response, a survival advantage is seen in all patients who respond to therapy.[8]

Survival in cGvHD dependent upon response to ECP



The improvements in net health outcome reported by studies of ECP for treatment-refractory, extensive cGVHD are achievable outside the investigational setting. In the UK there are several centres with experience using the approved device to treat patients with refractory GVHD and providing supportive care and symptom management for these patients.

However, eligibility for treatment is restricted to patients with biopsy-confirmed cGVHD that is extensive, presenting as cutaneously, mucosally or hepatically, and which is intolerant or refractory to steroid treatment.[9]

There have been more than 500,000 ECP treatments since it began,[10] with evidence of long-term clinical response rates[8,11] that improve the outcomes in the treatment of cGVHD patients.

Investigating topical therapy for vaginal GvHD : A case report

Angie Leather

Stem Cell Transplant Coordinator, The Christie , Manchester

Although vaginal GVHD can occur in female patients after transplantation, it is often under-recognised or ignored. There are few effective treatment options for these patients, yet it continues to have a major impact on personal relationships and patient well-being. Patients often find it difficult to raise and discuss the issue with their healthcare practitioner, highlighting the need to identify patients with vaginal involvement and to offer appropriate treatment and support.

The role of complimentary therapy was investigated in a young women who developed vaginal GVHD after treatment for acute lymphocytic leukaemia (ALL). The patient had experienced a prolonged period of pain and discomfort and found it difficult to impossible to have normal sexual relationships with her partner. The usual supportive care with hormone replacement, dilation and lubrication brought little relief and she was referred for surgery for adhesions and strictures. However, there was little improvement. It was decided to try an alternative therapy using cocoa butter based essential oil pessaries. These were prescribed for use 6 days a week for 3 out of every 4 weeks. The treatment was well tolerated, with only initial tingling reported. The patient began to feel psychologically better and found she was able to use longer and wider dilators. Her comfort score improved steadily over 11 weeks of observation and she was eventually able to reduce the number of pessaries to one per week and resumed normal sexual relations.

As a result of the success of this treatment other patients have been identified in the practice with similar problems and two have begun treatment with this alternative therapy. It is hoped that an open-label Phase II trial will begin shortly.

Feedback from Main EBMT 2010 and ELF Fellowship Project

Gemma White

Senior Staff Nurse, GSTT and ELF fellowship winner 2009

Gemma White, who won the Elimination of Leukaemia Fund (ELF) Fellowship, reported her experiences from the 2010 EBMT Annual Congress in Vienna and presented details of her service development project, which she is carrying out as part of her fellowship. The project, which is focussing on apheresis, is the development of an educational pack for newly qualified nurses and a competency pack for initial and annual assessments. These packs will prove very useful in support current clinical practice.

Joint Patient and Professionals Session: Social difficulties – research, practice and patient care

Emma Podmore

Research Assistant, Psychosocial Oncology and Clinical Practice Research Group, St James Institute of Oncology, Leeds

Social difficulties, such as work or financial worries, can have a significant impact on the recovery process in patients with cancer, which is turn can result in an increase in complex interventions and burden of disease for both the patient and the NHS. However, identification of social difficulties in routine practice is limited.

The recognition of its impact has resulted in the initiation of an assessment programme at the Psychosocial Oncology and Clinical Practice Research Group (POG) in Leeds. This programme has included the development, testing and utilisation of an assessment tool called the SDI-21 that can be used easily via a touch screen computer. The tool, which consists of 21 questions relating to social function, was psychometrically tested and 16 questions were assigned to the main assessment (SDI-16), with five assigned to a subset of questions. Within the SDI-16, a score of 10 or more, and a high score in the subset questions was indicative of social difficulties that could impact on patient recovery.

Two pilot studies are underway to assess standard care versus provision of information and implementation of the SDI, respectively. The outcomes of both studies will be used to assess the SDI as part of a complex intervention. It is hoped that the utilisation of the SDI will increase patient awareness of and access to services, and detection of social difficulties, as well as improvement in staff awareness and communication so that patients can resolve their social difficulties and improve well-being.

It is recognised that the use of this tool in clinical practice could increase referrals and workload as a result of identifying patients with significant social difficulties. As a result, an information pack has been developed for patients to address common problems.

Get your abstract accepted to main EBMT – behind the scenes and top tips

Mairead NiChonghaile
Chair of Scientific Committee, Main EBMT Nurses' Group

The 2011 EBMT Annual Congress will take place in Paris and it's time to start thinking about abstracts for submission. The deadline for abstract submission is November 24th.

Annually, around 150-160 abstracts are submitted by nurses to EBMT and it is hoped that this number can continue to increase. Abstract can be submitted for poster or oral presentation and, in next year's programme, there will be space for 55 oral presentations by nurses. In the overall programme, there will be eight educational sessions, four workshops (three English and one French) and five plenary sessions.

Although abstracts can be used to present work from research projects, they can also communicate interesting case studies or address and answer important issues experienced in clinical practice. Any research work should be completed and the results need to be included in the submitted abstract. Submitters should also ensure that they address topics relevant to haematological cancer treatment and should use terminology that is appropriate for a European audience, e.g. guidelines or currency.

The presentation of your work at the EBMT is a great experience and allows you to communicate your work and clinical expertise to a wider audience. There is also the added incentive of two prizes for best abstract/poster and best abstract/oral presentation.

If you feel you have something to contribute to innovation in cancer care, which is relevant to nursing, impactful and thought provoking, then EBMT looks forward to receiving your abstract in the next few months.

What's in a name? Practice development matron

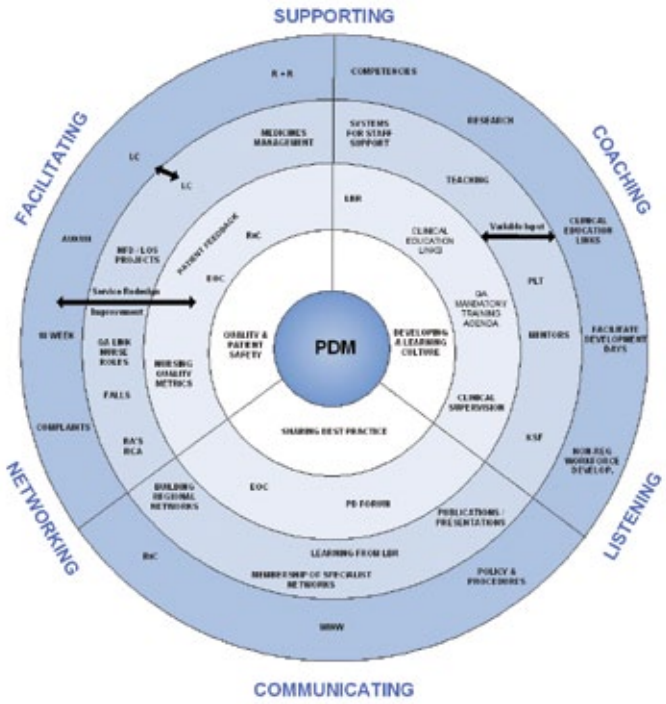
Lisa Furlonger

Practice Development Matron, Nottingham University Hospital

Practice development is a continuous process of developing person-centred cultures, enabled by facilitators who authentically engage with individuals and teams to blend personal qualities and creative imagination with practice skills and practice wisdom. The learning that occurs brings about transformations of individual and team practices. This is sustained by embedding both processes and outcomes in corporate strategy.[12]

With the merger of two Primary Care Trusts, Nottingham University Hospital (NUH) wanted to ensure that practice development was maintained and so created the position of Practice Development Matron or PDM to facilitate the process. In NUH there are now 29 PDMs who are responsible for coaching, networking, listening and facilitating so that a learning culture is maintained, best practice is implemented and patient safety and quality of care is achieved.

These goals are included in the essence of care (EOC), launched in 2001, which uses best practice evidence to structure a patient-focused approach to care. It provides a process for sharing and comparing practices, enabling the development of action plans to remedy practice that is identified as needing improvement. It also stresses the need for good practice to be shared to make sure that improvements are passed on and poor practice is identified.



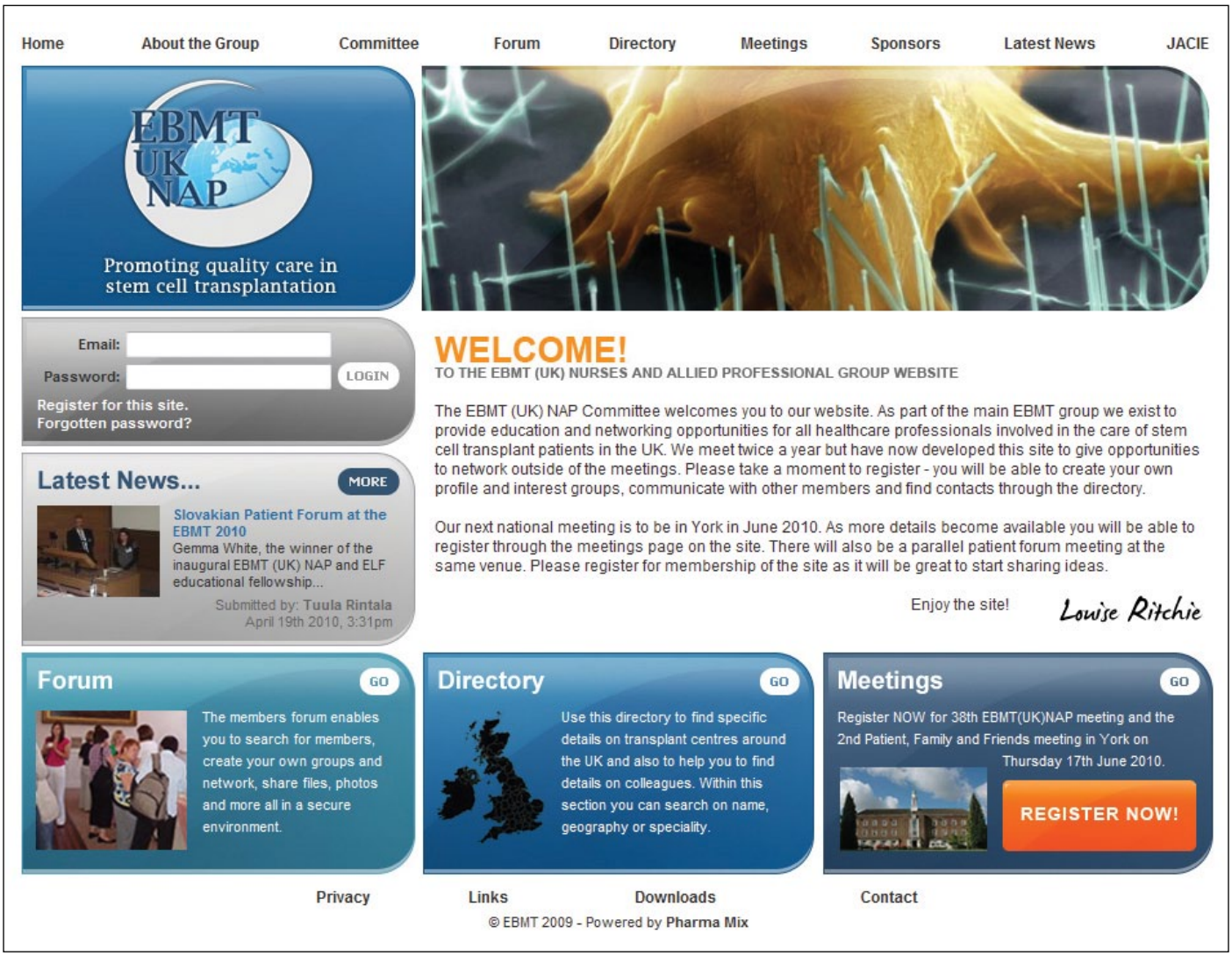
Patient safety is a big aspect of the role of the PDM, and involves validation, documentation, infection control, safer medication practices, as well as service improvement projects and training and development programmes. PDMs also play a key role at directorate team meetings and on Trust groups and committees, often deputising for the clinical lead.

This new rewarding and challenging role ensures the uniform induction, preceptorship and clinical supervision across all areas of healthcare.

Tutorial session: a new EBMT (UK) NAP website for nurses, building professional networks and fostering professional exchange

Debbie Lancaster
Pharma-Mix

EBMT website homepage



The EBMT (UK) has a new and exciting website which provides useful information on upcoming meetings and enables users to network, develop forums and exchange ideas. Developed by Pharma-Mix for the EBMT (UK) NAP, it is designed for easy use and navigation.

Go to **www.ebmt.co.uk** and register for an opportunity to meet colleagues with similar interests and to share your clinical experiences.

If you would like more information on how to use the website, contact Debbie Lancaster at Pharma-Mix: **Debbie.lancaster@pharma-mix.com**

Hope for poor stem cell mobilisers? Our experience with Plerixafor

Janet Baker

Senior Staff Nurse, RMH, London and EBMT (UK) NAP scholarship winner 2010

Poor mobilisation of stem cells is a significant problem for some patients, with risk increasing with increasing age, diagnosis of non-Hodgkin's lymphoma (NHL) versus Hodgkin's lymphoma (HL), degree of active disease, number and type of prior treatments and low platelet counts.

ASCT is the standard of care for eligible patients with multiple myeloma or lymphoma. However, patients must collect a minimum of $2x10^6$ CD34+ cells/kg for lymphoma and $4x10^6$ for multiple myeloma and germ cell tumours during apheresis to proceed with high dose chemotherapy and ASCT.

Plerixafor is a first in class CXCR4 antagonist that mobilises stem cells from bone marrow, increasing their number in peripheral blood. It blocks the chemokine receptor 4 (CXCR4) found on stem cells, preventing binding between CXCR4 and its ligand, stromal cell derived factor-1 (SDF-1a) in the bone marrow.

Phase III trials have demonstrated its efficacy in combination with granulocyte colony-stimulating factor (G-CSF) versus G-CSF alone in patients with NHL[13] and multiple myeloma.[14]

It was first used at the Royal Marsden Hospital (RMH) on a compassionate use basis prior to licensing in July 2009. A retrospective analysis of this compassionate use in 22 patients was carried out to ascertain if the outcomes reflected those seen in clinical trials. Two thirds of the patients (n=14) had multiple myeloma, with the remainder diagnosed with NHL (n=5), HL (n=2) and germ cell tumour (n=1). Over half of the patients had three or more prior therapies and all had at least one failed mobilisation.

It is known that Plerixafor activity peaks at 6-11 hours after administration and G-CSF treatment results in peak CD34+ cells 1-4 hours post dose. Therefore, in these patients, apheresis was commenced 10 hours after Plerixafor and 1 hour after G-CSF administration.

Protocol	
Days	
1,2,3	Patient receives G-CSF 10mcg/kg subcutaneously at 9am
3	Patient admitted to hospital Plerixafor administered 240 mcg/kg subcutaneously at 12 midnight
4	G-CSF at 9am Apheresis initiated by 10am Await CD34+ bag yield result If target dose not reached, patient kept in hospital and above process repeated for up to 2-3 consecutive days

Of the 22 patients treated, 13 achieved target, with a mean CD34+ yield of $2\text{-}3x10^6$ cells/kg. One patient failed to mobilise. A total of 16 patients required two rounds of apheresis and 15 went on to stem cell transplantation, with grafting consistent with conventionally mobilised patients. These results are comparable to that found in the Phase III clinical study, where 70.3% of patients achieved $\geq 6x10^6$ CD34+ cells/kg in 4 or less apheresis days, together with successful engraftment.[14]

Since licensing, Plerixafor has been given to six patients and all have collected enough stem cells for transplantation.

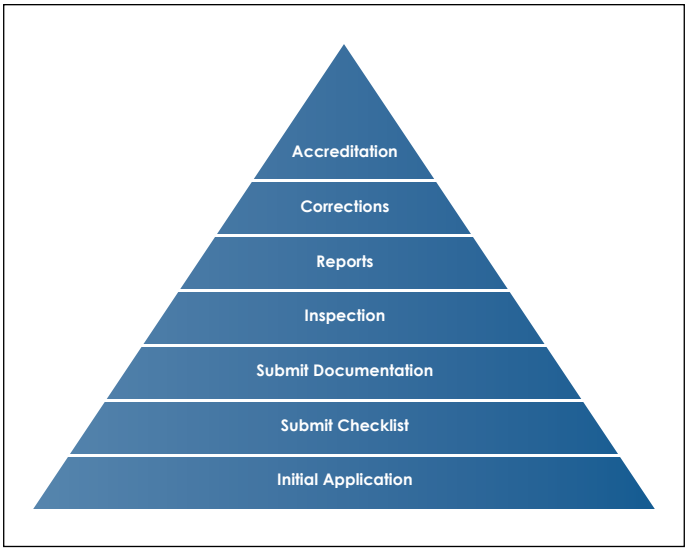
JACIE inspectors: the nursing perspective

Tuula Rintala and Louise McNamara

EBMT (UK) NAP committee

The Joint Accreditation committee of ISHAGE (JACIE) was established in 1999 with the aim of creating a standardised system of accreditation across Europe for stem cell transplantation (SCT). The accreditation process requires specific standard for each area of SCT, from clinical management, through stem cell collection to processing, with around 200 standards per facility.

JACIE process



There is an increasing need for more inspectors, and nurses can play a key role not only in the preparation for inspection but also as part of the inspection team. The latest edition of the standards has recognised the expertise of apheresis nurses, who can now be Collection Facility Directors and apply to be Collection Facility Inspectors.

Training and acting as a JACIE inspector is a fulfilling experience. An annual one-day course takes place in Athens every June, which is followed by a multiple choice-based exam. Once qualified, inspectors attend one inspection as an observer before carrying out their first inspection.

Being an inspector requires commitment and can be initially daunting. However, it can also be fulfilling and enhances career development. Inspectors are expected to carry out about one inspection per year, on a voluntary basis, which takes 1-2 days plus another 1-2 days to write the report.

The addition of nurses to the JACIE inspection process will help to raise the profile of nursing in SCT and enable nurses to play a more active role in this multidisciplinary, international team. As part of the team, they can help shape and interpret standards, as well as develop insight into the regulatory, quality aspects of SCT.

2nd EBMT(UK)NAP Patient, Family and Friends Forum

The Patient, Family and Friends forum take a break over lunch

The second forum of this exciting initiative took place as a parallel meeting to the nurse main meeting. The day is an informal opportunity for patients and carers to understand more about stem cell transplantation and have an opportunity to share and learn from each other and healthcare professionals involved in treatment.

Date of next meeting

The 39th meeting of the EBMT(UK)NAP Group and 3rd Patient , Family and Friends Forum will be 11th November 2011 in Cheltenham.

Registration will be via the website at:

www.ebmt.co.uk

The nurses meeting is open to all nurses and allied professionals with an interest in stem cell transplantation across the UK.

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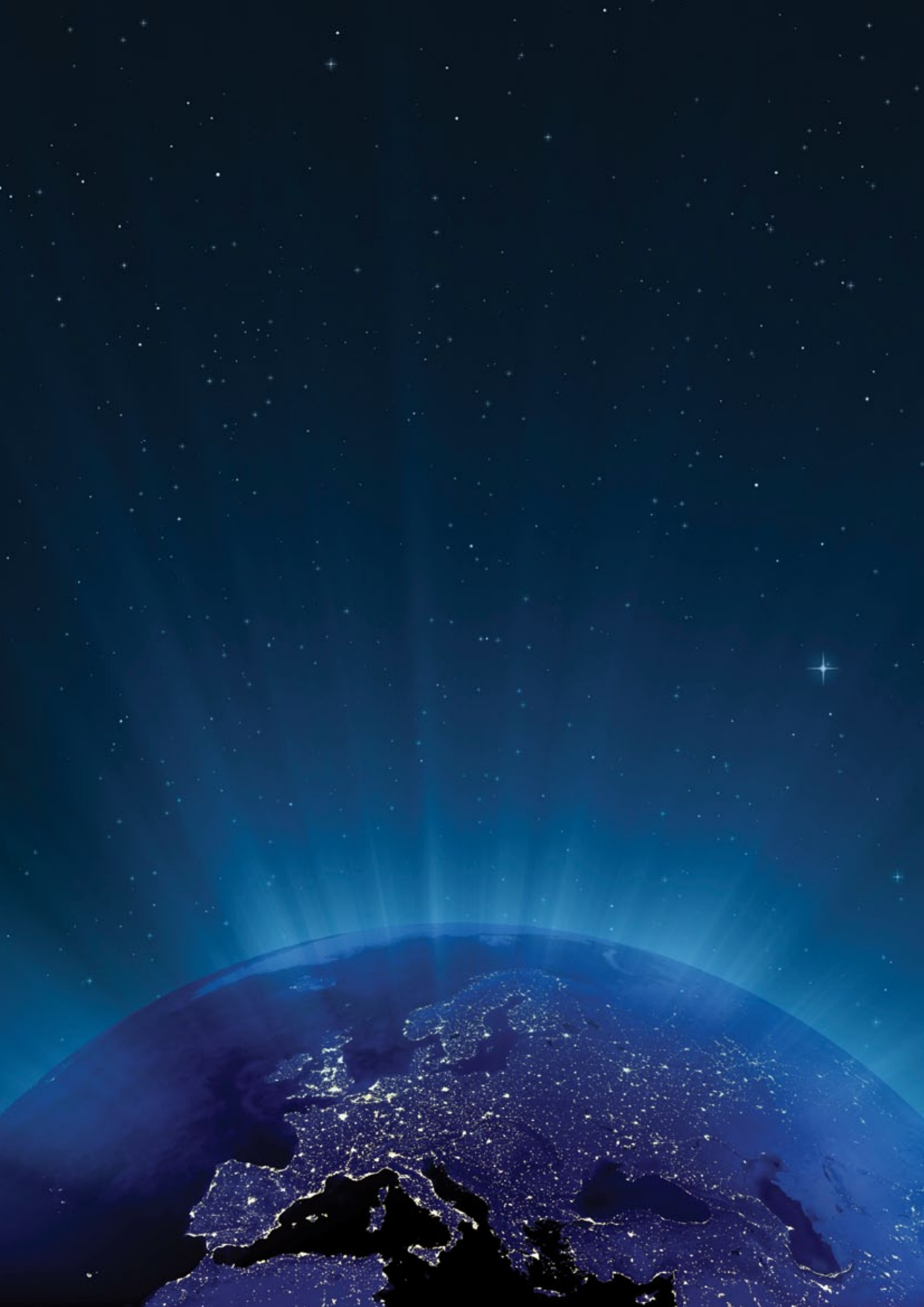
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