Fatigue is one of the most frequent complaints among BC survivors receiving RT. To explore whether biological processes underlying persistent fatigue can affect gene expression of blood cells, genome-wide expression analyses were performed on whole blood samples from BC survivors classified as chronic fatigued (CF) 2−6 years after diagnosis. Non-fatigued survivors served as controls. Several gene sets involved in plasma- and B cell pathways differed between the CF and the non-fatigued, suggesting that a dysregulation in these pathways is associated with CF and that a B cell mediated inflammatory process might underlie fatigue. The chronic fatigued also had a higher level of leucocytes, lymphocytes and neutrophils compared with the non-fatigued, thus further indicating that an activation of the immune system plays a role in the biology of CF in BC survivors.
With the above studies we hope to identify gene variants and gene expression profiles that predict long term adverse side effects of RT in BC patients that will shed light of the different mechanisms involved in order to develop preventive strategies.

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Society session (Mon, 21 Sep, 11:00−13:00)
SIOPE session

20 SIOPE Award

Multisystem Langerhans Cell Histiocytosis: progress in clinical management despite controversial biology

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More than a century after the first description of Langerhans cell histiocytosis (LCH), it is still an intriguing disease with a broad variety of presentation and enigmatic biology. Therefore, the management concepts over time have been changed according to the view on the nature of the disease process. At the beginning of the 20th century, LCH was believed to be of infectious or metabolic origin and starting with the unifying concept of "histiocytosis X" in 1953, it was considered a malignant disease. Hence, staging systems derived from other malignancies (e.g. lymphomas) were used. Some multi-institutional studies conducted in the USA between the 1950 s and 1970 s contributed to a better description of the disease variables and elaboration of treatment schedules. However, in the 1980 s, with the belief that LCH was a reactive rather than malignant process, the disease lost scientific interest and LCH fell into the category of "orphan diseases". Two prospective clinical trials in the early 1980 s (DAL-HX 83 and AIEOP-CNR-HX 83), both applying stratified systemic chemotherapy promptly after diagnosis, showed improvement in prognosis and reduced reactivation rates. These studies form the basis for the international trials (LCH-I, LCH-II, and LCH-III), conducted by the Histiocyte Society since the early 1990 s, after worldwide acceptance of uniform diagnostic criteria and disease stratification (single system (SS) vs multisystem (MS) LCH with/without risk organ (RO) involvement). The randomized LCH-I trial (1991–1995) compared vinblastine and etoposide in the treatment of patients with MS-LCH, and confirmed an equivalent efficacy of both drugs. Another important finding of LCH-I was that response to initial therapy is a reliable prognostic factor allowing for risk stratification and respectively tailored treatment intensity. The LCH-II trial (1996–2001) built upon the results of LCH-I, was a randomized phase-III trial for patients with risk MS-LCH (RO involvement: liver, spleen, haematopoetic system and/or lungs). In this study the effectiveness of 6 months therapy with the combination of oral prednisone, vinblastine and mercaptopurin, which has been established as a standard therapy for LCH, was compared to the same combination with the addition of etoposide. Overall, there was similar outcome in both therapy arms regarding early response, 5-year survival probability, disease reactivation frequency, and permanent consequences. Considering only risk patients the addition of etoposide showed significantly better results regarding speed of initial response and survival, thus, emphasizing the need of a more intensive approach in children with RO and resistant disease. In the LCH-III study (2001–2008) two randomized trials were incorporated. In the risk group the 12 months of steroids and vinblastine (standard arm) was compared to standard arm plus methotrexate, as an attempt for further improvement of survival and reactivation-free rate. The preliminary results of the LCH-III study do not show advantage of the addition of methotrexate. However, the overall survival of 85% at 2 years is the best result ever achieved in risk patients. In the low-risk group (no RO) the standard arm was randomly given for 6 or 12 months. The longer treatment arm showed a significant benefit in prevention of disease reactivation. Evolving knowledge of the disease biology will hopefully open new approaches for even more effective disease control in the near future.

Advocacy Session (Mon, 21 Sep, 13:30−15:00)
Informed cancer patients receive better treatment and care

21 INVITED

Surviving childhood cancers 'Informed cancer patients receive better treatment and care'

A. Brownsdon[1], C. Hails[1]. [1]*Independant, Cancer Survivorship, London, United Kingdom*

Rapid progress in the successful treatment of childhood cancers over the last 40 years has led to a new, ever expanding, cohort of childhood cancer survivors. For the authors, surviving childhood cancer has been an immensely positive opportunity and their experiences have led them both to pursue careers in healthcare. Whilst recognising that they are not unusual in this respect, the authors acknowledge that other survivors have not been so fortunate and may have suffered from late side effects of their treatments and/or encountered difficulties adjusting to a life that is no longer defined by cancer itself – whether this be at school, at work or in society.
Newly diagnosed patients can access information from a range of sources (including doctors and other healthcare professionals, the internet, cancer charities and other survivors) but the authors consider whether it is possible to truly be an 'informed cancer patient' when there is still so much that is unknown about the disease itself, treatments and their effects – both short-term and long-term.
They then focus on survivors as a source of information for patients, clinicians, and policy-makers, drawing on examples of a survivor mentoring programme, survivor representation on the British Childhood Cancer Survivor Study Steering Group and survivor representation on the Children and Young People's Workstream of the National Cancer Survivorship Initiative in the UK.
The authors share their experiences of being involved with the International Childhood Cancer Survivors' Network and how information is shared between patients, survivors, parents and clinicians globally. An international perspective has alerted them to the fact that they approach this subject from the privileged position of growing up in a country with a National Health Service and recognise that in many countries it is the family's economic circumstances that dictate the level of treatment and care the child receives, rather than their level of knowledge.
Finally, the authors discuss whether it should be the case that informed cancer patients receive better treatment and care. They conclude that all patients should be treated equally and receive the best available treatments based on clinical needs rather than on their access to information or financial circumstances.

22 INVITED

Talking with patients about expensive and unavailable new cancer drugs

L. Fallowfield[1]. [1]*University of Sussex, Oncology, Brighton East Sussex, United Kingdom*

Some very exciting developments have been made in the past decade which mean that more patients are being cured of cancer and/or living longer with meaningful remissions of their disease. The research community continue to make important discoveries that permit treatment to be tailored more precisely to an individual patient with these novel targeted therapies. Unfortunately many of these new treatments are extremely expensive and the healthcare budgets of most of the developed world are facing an impossible situation of having finite resources but infinite demands for the latest drugs. Arguments as to who should fund these ever expanding costs are heart-breaking for patients and their relatives who are desperate for access to the best available treatments. The media and popular press often fuel the debate in unhelpful ways by portraying benefits too optimistically. For healthcare professionals who practice in state-funded healthcare environments, sensitive discussions that should be happening about prognosis, supportive care and other end-of-life care

decisions increasingly get side-tracked by discussions about money. The current situation is uncomfortable for all and untenable in the future. In the UK the Department of Health commissioned a report by Michael Richards on recommendations as to how novel, unapproved but licensed drugs can be paid for within a National Health Service. In this talk some of those recommendations will be discussed together with illustrative DVD clips of an oncologists talking to patients about co-payments or top-up fees

23 INVITED

Getting your share of good care – an Eastern European perspective

V. Cursaru[1]. [1]*Multiple Myeloma Romania, Patients' Organisation, Bucharest, Romania*

Good care for myeloma patients should start with access to information. Yet, the acknowledged best practice in the Western European countries is not necessarily implemented by the emerging European countries such as Romania where cancer patients struggle sometimes to have friends and/or relatives translate foreign leaflets and brochures. When it comes to rare diseases such as multiple myeloma, with an incidence of about 3,000 in 22 million people, the situation is even worse.
In the Romanian hospitals for haematological diseases there are neither brochures nor leaflets on display. The Ministry of Health seems not to be concerned with this issue (invoking lack of resources) and what is even more difficult to understand, unlike in many other Western European countries, the Pharmaceutical industry has not done anything to overcome this situation.
Patients' empowerment, patients' rights do not exist as concepts.

24 INVITED

Silent no more: cancer patients as advocates

D. Schmitt[1]. [1]*Brustkrebs Deutschland, Scientific Board, Munich, Germany*

Perspective of life changes after the diagnosis of cancer patients being diagnosed with the deadly disease seek the most effective therapy and surgery as well as personalised aftercare. Without sufficient information patients have to rely on their doctor's decision to share the decision of the best cancer treatment and care with their doctors. Patients need easy to understand information and good communication skills.
Patient support organisations can empower cancer patients to take an active role in the decision making process regarding the right treatment option for them. Patient initiatives and support groups have come a long way. In the 1980ies they started getting involved with the patients rights and information supply of quality cancer care. Primary aim of cancer patients as advocates is to enable other patients to communicate with their doctors on one level and take part in the decision making of their therapy.
It is a paradigmen change for doctors, health services and politicians. They have to accept that patients today are starting to change their behaviour in terms of dealing with their disease. Adequately informed patients reach a better compliance of their medication and quality of life Patient groups support their members in taking responsibility for their disease free and overall survival.
It is essential that patients as advocates in order to receive better treatment and care raise their voices to fight inequalities in best quality cancer treatment in Europe. All cancer patients must have access to non-discriminating, multidisciplinary and innovative cancer therapies.

Special Session (Mon, 21 Sep, 14:00−15:00)
Bladder cancer in the elderly − issues on operation and choice of chemotherapy

25 INVITED

Surgery for bladder cancer in elderly patients: risk, benefit and selection of technique

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Purpose: To outline the indications for minimal-invasive (transurethral) tumour resection with or without additional radio- and chemotherapy and for more radical surgery with the necessary of a subsequent urinary diversion.
Source of data: Literature from sources such as Medline from the last seven years, recent guidelines (EAU, WHO) where the author actively contributed and personal data
Results: Recent data have shown that women are older than men at primary diagnosis of BC. Approximately 1/3 of patients present with muscle-invasive tumours out of which approximately 1/3 are already metastatic. No clear definition of an "elderly" patient exists for pelvic surgery. An age of $\geqslant$75 years (Karnofsky performance score 90–100%) or $\geqslant$70 years (KPS 80% or less) is proposed. Of those patients that succumb BC, 64 and 74% die within the first 2 and 4 years, resp. Regardless of quality of life patients who do not need an intestinal interposition for the urinary diversion after cystectomy but are required a narrow wet stoma for the rest of their life. According to an international survey the majority of elderly patients receive an ileal (abdominal) conduit, but in centres of excellence an orthotopic neobladder is offered in up to 1/3 of these patients.
Conclusions: The indications for a cystectomy in elderly patients (as defined above) are muscle invasive and symptomatic BC and a life expectancy of at least 5 years. Type of urinary diversion is dependent on tumour location and extent performance status and motivation. All patients who do not fall into the category outlined above, need extensive TURB with or without laser or other forms of interventional methods.

26 INVITED

Chemotherapy options in cisplatin-unfit patients with advanced urothelial cell cancer

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Findings of single-arm phase II and prospective randomized clinical trials involving patients with advanced urothelial cancers led to the conclusion that urothelial tumors are chemosensitive and that the treatment regimen should be a platinum- based combination. Through the 1990 s, the combination of methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) was the widely accepted treatment standard and proved to be superior in terms of prolonging life. Toxicities associated with this treatment, including diminished renal function, neutropenia and sepsis and mucositis tempered the use in the considerable group of patients who are comprised functionally (performance score (PS) <2) and have compromised renal function and other comorbid conditions. The gemcitabine/cisplatin (GC) regimen has been shown a valuable alternative chemotherapy option, providing identical response rates and survival, with the benefit of fewer side effects. Even in elderly patients (>75 years) GC is a feasible option, provided that patients are still basically healthy and have good renal function.
For individuals with a compromised renal function (creat clear 30−60 ml/min) a carboplatin-based combination (in lieu of cisplatin) is recommended, with dosing based on the estimated renal function of the individual patient. The single agent activity of carboplatin is 12%, which seems slightly inferior to that of cisplatin which was associated with an overall response rate of 17%. Carboplatin combination chemotherapy studies have produced median survival durations of 8−10 months, which again suggests a slightly inferiority against the 14−15 months obtained with MVAC and GC. Unfortunately carboplatin and cisplatin have never been directly compared in randomised trials that were sufficiently powered to test for superiority or non-inferiority. A confounding factor in interpreting the data from non-randomized studies is the proportion of patients with adverse prognostic factors for survival in phase II trials. The 2 predominant factors for survival following MVAC therapy are the presence of visceral disease in liver or bone and low PS (Bajorin risk groups 0, 1, or 2 factors present, corresponding with 0%, 11% and 33% 5year survival rates). Patients with no risk factors have a median survival of 18 months versus 4.4 months for those with the least favorable combination of adverse features present. Decreasing the proportion of patients with adverse prognostic factors in phase II trials will thus impact outcome and provide flattering results. In this light it is also difficult to interpret the non-randomized phase II data more recently obtained with platiunum-free combination chemotherapy, particularly taxanes with gemcitabine. Apart from myelotoxic effects these regimens seems to be well tolerated, but the true merit of these combinations can only be answered in randomized trials. The EORTC and Spanish Oncology Genitourinary Group have recently finished their randomized phaseII/III trial of gemcitabine/carboplatin (G/carbo) vs carboplatin/methotrexate/vinblastine (M-CAVI), in patients deemed unfit for cisplatin due to PS 2 and/or or impaired renal function (creat clear <60 ml/min). The randomized phase II part trial results have recently been presented (in press J Clin Oncol). Overall response rates were 42% for G/carbo and 30% for M-CAVI and severe acute toxicity (SAT) was manageable. Patients however, with both stratification parameters present (poor PS plus poor renal function), or poor PS plus visceral disease (Bajorin risk group 2) had a response rate of only 26% and 20% and a SAT rate of 26 and 25%, respectively. Carboplatin combinations are active in this group of cisplatin-unfit patients. However patients with multiple adverse prognostic factors are not likely to benefit from combination chemotherapy. Alternative treatment modalities should be sought for this subgroup of very poor risk patients.