be discussed, based on findings from individual trials and systematic reviews.
3. Overview of the applications of PROMs in daily oncology practice to support and improve individual patient care.

The presentation will briefly describe technical aspects of real-time data collection (such as the use of touch-screen computers, mobile devices and web-based data collection). The main focus will be on the impact of PROMs on process of care (doctor-patient communication, decision-making) and on patient well-being and satisfaction with care. The experience of using PROMs during cancer chemotherapy in Leeds Cancer Centre, Leeds, UK will be presented.

Scientific Symposium (Tue, 22 Sep, 09:00−11:00) **Role of PET imaging**

95 INVITED

New PET-Tracers for imaging pathophysiology and response

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Metabolic imaging with PET and PET/CT using F-18 fluordesoxyglucose is now a routine tool in clinical practice for therapy response evaluation, viability assessment of posttherapeutic residual masses, restaging and potentially staging in Hodgkin's disease and Non-Hodgkin's lymphoma. Beyond imaging glucose metabolism, important molecular and cellular targets and pathophysiological important pathways can be addressed: these include amino acid transport/protein synthesis for imaging multiple myeloma with radiolabelled amino acids such as C-11 methionine, proliferation with F-18 fluorothymidine angiogenesis with radiolabelled RGD-peptides, apoptosis with F-18 labelled anexin-V, membrane turnover with F-11/F-18 choline, tumour receptors and antigens with CD20, CD33, CD45 or CD66 radiolabelled monoclonal antibodies. Advanced pharmacokinetic modelling improved cellular targeting significantly and is available for more efficient therapeutic targeting when antibodies are labelled with therapeutic radionuclides. Intense preclinical research is focussed on development of measuring tumour cell tracking, imaging of tumour stem cells, cell signalling and gene expression with appropriate probes and reporter gene approaches. Multimodality imaging with PET/CT, SPECT/CT, PET/MR both in small animal and clinical/preclinical settings will close the gap between traditional anatomical based morphological and molecular imaging based functional imaging approaches.

96 INVITED

PET imaging of non-Hodgkin lymphoma: defining methodologies for early prediction of response

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Achieving a complete response to first-line therapy is an important goal in managing patients with aggressive lymphomas such as diffuse large B-cell lymphoma (DLBCL), as long-term outcome is greatly improved compared with those patients with residual disease. ^{18}F- Fluorodeoxyglucose positron emission tomography (FDG-PET) is emerging as a powerful technique for the assessment of response in patients with DLBCL and also appears to be a valuable predictor of long-term outcome. A number of studies have shown that patients who have a negative PET scan (during the induction phase or after several cycles of induction chemotherapy) have a significantly better event-free survival (EFS) than those who have an abnormal PET scan. This suggests that it may be possible to use FDG-PET to identify poor responders during the course of induction therapy and modify their treatment accordingly. This approach is being investigated in an ongoing GELA (Groupe d'Etude des Lymphomes de l'Adulte) study (07−3B Study). Patients under the age of 60 years of age and with an age adjusted-IPI score of 2–3 were randomized to receive four cycles of either R-ACVBP14 + intrathecal methotrexate (MTX it) + G-CSF (group A) or R-CHOP14 + MTX it + G-CSF (group B). PET assessments are performed at baseline and after the second and fourth cycle of therapy. Further treatment is then given according to response, as assessed by PET. Patients from either treatment group who are PET positive after the fourth cycle of treatment leave the study to receive salvage therapy. Those who are PET negative after both the second and fourth cycle of treatment continue to receive induction therapy (group A: MTX iv, R-ifosfamide-vepeside, cytarabine; group B: 4 cycles of R-CHOP14 + G-CSF), while those who are PET positive after the second cycle but PET negative after the fourth cycle receive more intense, consolidation therapy − MTX iv followed by Z-BEAM (^{90}Y-ibritumomab tiuxetan plus BEAM) with autologous stem cell support. Indeed, for patients who are PET positive at the end of induction therapy, consolidation therapy involving ^{90}Y-ibritumomab tiuxetan may be an appropriate option. The results of this study should help determine the value of using PET assessment during the course of induction therapy to modify the course of treatment and also the role of ^{90}Y-ibritumomab tiuxetan as consolidation therapy in poor risk patients with DLBCL.

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97 INVITED

Role of FDG-PET and PET/CT in treatment planning of other haematological tumours

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FDG-PET has been extensively investigated in Hodgkin lymphoma, whereas less data are available in myeloma and leukemias.
Hodgkin lymphoma (HL): Initial staging determines the treatment plan. PET detects more disease sites than conventional imaging methods. However, there are methodological problems, in particular the lack of a valid reference test. Nevertheless, PET is today considered part of the routine staging of HL. In published series PET changed disease stage in 10−40% of cases, more often upstaging than downstaging patients, leading to changes in treatment strategy in about half. Whether these changes will lead to improvement in outcome is still unknown.
Early response evaluation with PET after 1−2 cycles of ABVD is highly predictive of outcome, but whether treatment should be modified on this basis is not known. Moreover, the predictive value of an early PET may be lower with more intensive regimens like BEACOPP. Randomized trials are testing if treatment reduction in PET negative and treatment intensification in PET positive patients can improve outcome. Despite the lack of randomized evidence, treatment intensification in patients with a positive PET-scan after 4 cycles of therapy has become a widespread practice.
Radiotherapy in HL has changed dramatically. The old treatment strategy maximized the use of radical radiotherapy, and extensive treatment fields were used. In the modern era, radiotherapy is part of a combined modality treatment, and smaller volumes and doses are employed. In most situations the volume for radiotherapy is only the initial (pre-chemotherapy), macroscopically involved tissue volume in early stage disease, and residual masses after chemotherapy in advanced disease. This has led to dramatic reductions in the normal tissues being irradiated, and equally dramatic reductions in the risk of serious long-term complications. One major problem with more and more conformal radiotherapy is the need to define the target volume very precisely to avoid geographical misses. Image guidance is essential. PET is increasingly being incorporated in the planning process, and changes treatment fields in about 1/3 of early stage patients. To be able to use combined PET and CT for the planning of

radiotherapy, the PET data must be spatially co-registered to the planning CT data set. Therefore, the PET images must be acquired with the patient in the treatment position, on a flat couch top, with immobilization devices, and using markers at skin positions visible in the image. For this purpose, combined PET/CT scanners with increased bore size and flat-bed inserts are preferable. The initial lymphoma volume on the pre-chemotherapy PET/CT-scan must be contoured on the planning CT-scan done after chemotherapy, and image fusion may be employed to allow pre- and post-chemotherapy images to be combined.

Myeloma: MRI is superior to PET in the assessment of bone marrow involvement, whereas PET/CT is superior for the detection of extramedullary disease. Hence, they may supplement each other in the evaluation of the extent of disease. This is particularly important for the differentiation between solitary plasmocytoma, which may be curable by local radiotherapy, and multiple myeloma, where systemic treatment is indicated and radiotherapy is only palliative.

Leukemias: Only very few publications exist, but PET may be of value in detecting extramedullary infiltrates guiding treatment both in the primary and the recurrent situation.

98 INVITED

Role of PET in clinical trials of novel therapies in haematology

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FDG-PET/CT scans have been clearly demonstrated to be the most sensitive and specific imaging modality currently available for patients with lymphoma. Nevertheless, the extensive published literature provides little guidance as to the optimal use of this technology. Although widely applied for staging, assessment during and following treatment and for posttreatment surveillance, data prospectively validating PET in those settings are limited. Moreover, PET results may be confounded by issues such as variation in interpretation among readers, necessitating the requirement for central review in clinical trials. The positive predictive value is relatively low as a result of a large number of false positives related to timing of the scans, the regimen being used, infection, sarcoidosis, inflammation, and others. In 2007, the International Harmonisation Project standardized interpretation of PET scans and provided recommendations for the use of PET in clinical trials (Cheson, et al J Clin Oncol 25;579–586, 2008). For patients with routinely FDG-avid, curable histologies (e.g. diffuse large B-cell lymphoma (DLBCL) and Hodgkin's lymphoma (HL), PET scans should be done prior to and following therapy. However, for other histologies, PET scans should only be considered if complete remission is a primary study endpoint and the scan was positive prior to therapy. Post-treatment surveillance PET/CT scans are not cost-effective and should not be routinely performed.

Numerous studies demonstrate that a PET scan performed after one or more cycles of therapy is a better predictor of outcome than standard prognostic scoring systems; however, whether altering treatment on the basis of that information improves outcome remains a critical clinical question. Thus, numerous risk-adapted treatment strategies are under investigation to reduce the amount of unnecessary therapy for patients with favorable disease, and to improve the outcome for poor-risk patients. In North America, protocols are accruing patients with limited stage, bulky, or advanced stage HL who are being treated with standard doses of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) and further treatment determined by the results of a PET scan after two cycles of therapy. Similar trials are ongoing in Europe. Early interim PET scans are also being evaluated as a surrogate endpoint for expediting evaluation of new agents. For example, in the CALGB Lymphoma Committee, patients with previously untreated follicular lymphoma undergo a PET/CT scan following one cycle of a biological doublet and the results correlated with outcome.

Thus, at present, in clinical practice PET should be reserved primarily for the pre- and post-treatment evaluation of the curable, FDG-avid lymphomas. Application of this technology to other settings must first be prospectively validated. It is the goal of current and planned clinical trials to better establish the role of PET/CT in the management of patients with lymphoma leading to improved outcome.

Scientific Symposium (Tue, 22 Sep, 09:00−11:00)
Recent breakthroughs and future directions

99 INVITED

SIOP brain tumour trials

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Brain tumours are the leading cause of solid tumours in paediactrics and a major cause of cancer related-death during childhood. They represent a specific challenge for increasing cure rates while decreasing the morbidity related to the diseases and to the treatments. The SIOP-Europe brain tumour committee conducts collaborative projects in all the main subtypes of paediatric brain tumours (low and high grade glioma, medulloblastoma/primitive neuro-ectodermal tumours, ependymoma, intra-cranial germ cell tumours, craniopharyngioma, atypical teratoid rhabdoid tumours) as well as studies upon quality of survival.

The recently closed SIOP- Europe Brain tumour committee studies will be presented, as well as the ongoing studies and the current projects.

We will insist upon:

- the upper age limit which makes some studies opened not only for children and adolescents but also for young adults, especially for medulloblastoma and intra-cranial germ cell tumours
- the introduction of selected biological parameters that may help to therapeutic stratification in some childhood brain tumour subtypes

100 INVITED

Improving outcomes in Wilms tumour: an update from the SIOP Renal Tumours Study Group

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With current approaches to risk stratification, approximately 15% of children with Wilms tumour eventually die of their disease while half are exposed to treatments that carry a significant risk of late sequelae. The philosophy of improving treatment is therefore changing emphasis from improving overall survival to maximising relapse free survival while minimising risks of late effects for an individual patient, i.e "cure at least cost". This is particularly important for the young children affected by Wilms tumour (median age 3 yrs), who are more susceptible to permanent long term side effects that may only become apparent years after treatment has ended.

The current trial of the SIOP Renal Tumours Study Group, SIOP WT 2001, continues the philosophy of reducing treatment intensity for the majority, with a randomised question about the need for doxorubicin in the post-operative chemotherapy for stage II and III, intermediate risk histology Wilms tumours. This randomisation is expected to close to recruitment at the end of 2009. The answer to the trial question will require long term follow up to fully assess the balance of risks of removing a potentially cardiotoxic drug from front line therapy.

This trial has also introduced a new 'high risk' category based on the histological response of the blastemal component of Wilms tumour to pre-operative chemotherapy. Preliminary analysis of the outcome of this subgroup, which represents ~8% of all Wilms tumours, shows that EFS for localised disease is improved by intensifying chemotherapy to the 'high risk' stratum. However, when metastatic at diagnosis, outcomes are as bad as for diffuse anaplastic tumours, with EFS of ~30%, despite intensive chemotherapy with a 4 drug regimen.

Future strategies involve better definition of the molecular characteristics of 'blastemal type' Wilms tumour and assessment of prognostic biomarkers, including those currently used by the Children's Oncology Group (allele loss on chromosomes 1p and 16q) for risk stratification. These associated biological studies should complement histological risk stratification and identify practical markers of resistant blastema to simplify diagnosis of this entity, which is currently very time consuming for pathologists. Recent analyses by genomic profiling have shown an association of copy number changes in *MYCN* with the SIOP 'high risk' Wilms tumour categories. Gain of *MYCN* is emerging as a finding in several other childhood cancers