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