signals in a synergistic way, while in other cases one tumour suppressor network may actually back up for the dysfunction of another.
These principles are well illustrated by investigation of the p53 pathway. A major tumour suppressor and arguably the most frequent target of driver mutations in human cancer, p53 is the hub of a wide array of signals. The immediate p53 network contains tumour suppressors such as Arf and oncogenes such as Mdm2 and Mdmx. In addition, however, p53 communicates extensively with the pRb tumour suppressor pathway, as documented by many studies. We will focus primarily on the crosstalk between p53 and the Hippo tumour suppressor pathway, and particularly on the role of the Lats2 tumour suppressor, a major component of that pathway, in relaying oncogenic stress signals to p53 and mediating the apoptotic elimination of cancer-prone cells. In addition, we will address the link between the putative tumour suppressor RNF20 and p53.

Society Session (Sun, 25 Sep, 16:45−18:15)
Flims Alumni Club (FAC)

230 FAC Achievement Award

The Delicate Balance Between Clinic, Research and Education in Your Career in Oncology

Abstract not received

231 INVITED

How to Submit a Good Application?

P. Therasse[1]. [1]*GlaxoSmithKline Biologicals, Clinical Development, Rixensart, Belgium*

The joint ECCO − AACR − EORTC − ESMO Workshop on 'Methods in Clinical Cancer Research' organized yearly in Flims since 1999 provides a great opportunity for young clinicians to discuss and learn from a selected myriad of experts from various fields of oncology clinical research. Thanks to the financial support of oncology professional organizations access to the workshop is for free for those candidates whose applications have been selected by the workshop chairpersons. This selection is based on pre-defined criteria assessed by expert reviewers looking at each application individually and providing ranking and comments for each applicants. There is usually much more applicants than seats available on the workshop and the selection can be hard hence the need for criteria's that can help differentiating applications. These includes the profile of the applicant, his (clinical research) career development perspectives, his accomplishment so far, the support of his/her supervisor, the quality and feasibility of the proposed research project and how convincingly this can be embedded into the motivation letter introducing the applicant. These criteria's do no weight equally in the assessment and of course are exposed to subjective variation in their implementation by different experts. However, benchmarking the applications against some principles that are going to be presented provides some good predictive value of the chance of success of the applicants. Of course this is not robust science since the quality of an application will always depend of the quality of the other applications which by default cannot be predicted. But more than 900 clinicians will already tell you. . . this is really worth trying!

232 INVITED

Design and Conduct of a Successful Clinical Trial

Abstract not received

233 INVITED

How to Write and Review a Good Article?

M. Hutka[1]. [1]*Royal Marsden Hospital − NHS Trust, Department of Medicine, London, United Kingdom*

Publishing a paper is an accepted form of communicating important findings to the oncology community and of adding to the existing knowledge. The main focus is on originality and impact on current practice when both writing and reviewing a manuscript. The key elements are scientific reliability and appropriate study design with respect to the research question, its clear definition and appropriate answer.
The goals of peer review are to assist the editors in forming a decision concerning publication of a manuscript and to provide constructive feedback to authors in order to enhance the quality of the final written product. The important points to consider when reviewing a manuscript are appropriateness of the overall study design, adequate description of methods, patients, inclusion and exclusion criteria and a clear outcome measure. Randomised clinical trials, systematic reviews, observational studies and health economics studies have specific reporting guidelines and those must be adhered to. A review should assess whether the results of the study answer the research question and if results are discussed in light of previous evidence. The interpretation and conclusions need to be sufficiently derived from and focused on acquired data. The reviewer needs to assess whether the study was conducted according to ethical principles. The references should include relevant, uptodate papers.

Society Session (Sun, 25 Sep, 16:45−18:15)
European Association of Nuclear Medicine (EANM)

234 INVITED

Molecular Imaging in Radiation Oncology

V. Gregoire[1]. [1]*UCL Clinique Universitaires St. Luc, Department of Radiation Oncology, Brussels, Belgium*

The use of Molecular imaging in radiotherapy has becoming increasingly popular over the years. . . ! Molecular imaging can be used either as a predictive factor for tumour response, as an aid for treatment planning, or as a tool to evaluate modifications in organ function after treatment. The use of PET in general, and of FDG-PET in particular, for radiotherapy planning purposes has really taken a increasing importance up to a point that more and more radiation oncologists believe that adequate target volume selection and delineation cannot be performed adequately anymore without the use of FDG-PET! But what are the evidences supporting the use of FDG-PET in the treatment planning process?
When introducing a new imaging modality (e.g. FDG-PET), the question is thus whether the new comer is more sensitive and/or specific than what one were used to use (e.g. CT), and consequently how could it modify the planning processes. For example, if an additional lymph node is visualized with a new imaging modality known to be more specific than the standard modality, it might be legitimate to enlarge -if necessary- the target volume(s) beyond what would have been done using a standard procedure to include this new node; conversely, if fewer nodes are visualized with a new imaging modality known to be more sensitive than the standard modality, it might be legitimate to decrease the target volume(s) below what would have been done using a standard procedure.
Another use of FDG-PET in the radiotherapy planning process is the delineation of the primary tumour GTV. For the primary tumour, the benefit of FDG-PET in the radiotherapy planning process should be evaluated more in term of 3D delineation and demarcation of the tumour volume from peri-tumoral inflammation, edema or atelectasis (for lung primary). In this respect, comprehensive studies have been already reported for lung, brain and head and neck tumours. Studies are ongoing for other locations such as esophageal and rectal tumours.
Last, in the framework of target volume delineation, molecular imaging needs to be validated for its ability to depict spatial and temporal variation in tumour physiology (e.g. metabolism, proliferation, hypoxia), leading to a novel paradigm in radiation dose prescription. The so-called "dose-painting" approach refers to an intentionally created dose heterogeneity aiming at tailoring the dose prescription to variation in tumour physiology.

235 INVITED

Molecular Imaging for Response Monitoring in Esophageal Cancer

F. Lordick[1]. [1]*Klinikum Braunschweig, 3rd Medical Department, Braunschweig, Germany*

Metabolic imaging and early response assessment by positron emission tomography (PET) are gaining importance in guiding treatment of localized and metastatic esophago-gastric cancer. The most consistent results have been obtained during neoadjuvant treatment of adenocarcinoma of the esophagus and the esophago-gastric junction (AEG). It was demonstrated that PET is highly accurate for identifying non-responding and responding tumours within 2 weeks after the initiation of neoadjuvant chemotherapy when a quantitative threshold for metabolic response is used [Weber WA et al. JCO 2001; Ott K et al. JCO 2006]. In consecutive phase II studies the metabolic activity, defined by the standardized uptake (SUV) of 18-FDG before and during chemotherapy, was measured. Significant decreases of the SUV after only two weeks of induction chemotherapy were observed. A drop of $\geqslant$35% measured 2 weeks after the start of chemotherapy revealed as the most accurate cut-off to predict response after a full-course of preoperative chemotherapy lasting for 12 weeks. It was further noticed that the metabolic response to induction chemotherapy revealed as an independent prognostic factor in locally advanced AEG. This suggests that PET can be used to tailor treatment according to the

chemosensitivity of tumours. The concept was realized in the MUNICON-1 and -2 trials [Lordick F et al. Lancet Oncol 2007; Lordick et al. ASCO-GI 2011]. These trials prospectively confirmed that responders to induction chemotherapy can be identified by early metabolic imaging using FDG-PET. Continued neoadjuvant chemotherapy in the responding population resulted in a favourable outcome: The median overall survival was not reached in metabolic responders as compared to 26 months and 18 months in metabolical non-responders in MUNICON-1 and -2, respectively. MUNICON-1 showed that chemotherapy can be discontinued at an early stage in metabolic non-responders, thereby saving time and reducing side-effects and costs. Compared to previous studies one could delineate that the outcome of metabolic non-responders was at least not compromised by the early discontinuation of chemotherapy. MUNICON-2 showed that the addition of neoadjuvant radiation therapy in metabolic non-responders does not lead to an evident improvement of the poor prognosis, thus showing that early metabolic non-response indicates a dismal tumour biology.
Based on these results, the integration of FDG-PET can be recommended for further clinical studies. Important questions need to be addressed: Does metabolic non-response to induction chemotherapy stand for a definite unfavourable outcome or can further treatment modifications lead to improved response rates and outcome? Do patients with early metabolic non-response benefit from surgery? At this stage we feel that surgery offers a considerable amount of local control, at least, and is therefore indicated as the treatment of choice in metabolic non-responders. However, non-surgical local treatment, like chemoradiation, might offer the same magnitude of local control and clinical benefit in metabolic non-responders. These questions should be addressed in future randomized trials.

236 INVITED

Molecular Imaging for Personalised Treatment of Malignant Lymphoma

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Malignant lymphomas comprise a heterogeneous group of malignancies, including both indolent and highly aggressive diseases, and localised and disseminated disease presentations. Lymphomas are generally sensitive to therapy, and the goal of therapy is cure or very long-term disease control. High cure rates and long-term survival mean that patients, frequently young at diagnosis, are subject to the serious long-term of chemotherapy and radiotherapy, and the resulting excess morbidity and mortality is substantial. Management of malignant lymphoma is thus a balance between cure and toxicity, between over-treatment and under-treatment. The right treatment for the individual patient is an individualised treatment. With no access to highly accurate pre-treatment predictive markers, an individualised treatment should be tailored to the individual patient's risk and treatment response.
Molecular imaging, and in particular FDG-PET/CT, has become a cornerstone imaging procedure in most malignant lymphomas. The very high diagnostic accuracy at staging provides better pre-treatment assessment of disease extent and a better basis for accurate definition of highly conformal radiation therapy volumes. FDG-PET is the most powerful predictor of treatment response and prognosis in aggressive lymphomas, and the metabolic response assessment is possible very early during therapy, as opposed to response assessment by conventional imaging procedures. An early *in-vivo* treatment sensitivity test, rather than a late structural response assessment, makes it possible to adjust the individual patient's therapy according to the early treatment response. FDG-PET/CT is a key determinant of treatment response according to the revised international response criteria for aggressive lymphoma, due to a very high negative predictive value of post-therapy FDG-PET.
Other PET tracers than FDG have a potential role in the management of lymphoma, and they will be discussed briefly in this presentation, as well as the role of FDG-PET/CT in other clinical settings, such as follow-up/routine surveillance and the management of relapsed lymphoma. The presentation will also provide an overview of ongoing clinical trials investigating the role of PET-response adapted lymphoma therapy.

Society Session (Sun, 25 Sep, 16:45–18:15)
European Association of Neuro-Oncology (EANO)

237 INVITED

How to Improve the Extent of Surgery With Better Neurological Function Preservation

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Surgical removal of intrisinc cerebral neoplasms requires the combined efforts of a multidisclipinary team of neurosurgeon, neuroradiologist, neuropsychologist, neurophysiologist, and neurooncologists that all together contribute in the definition of the location, extension, and extent of functional involvement that a specific lesion has induced in a particular patient. Each tumour has induced particular and specific changes of the functional network, that varies among patients. This requires that each treatment plan should be tailored to the tumour and to the patient. When this is reached, surgery should be accomplished according to functional and anatomical boundaries, and has to aim to the maximal resection with the maximal patient functional preservation. This can be reached at the time of the initial surgery, depending on the functional organization of the brain, or may require additional surgeries, eventually intermingled with adjuvant treatments. The use of so called brain mapping techniques extend surgical indications, improve extent of resection with greater oncological impact, minimization of morbidity and increase in quality of life. To achieve the goal of a satisfactory tumour resection associated with the full preservation of the patients abilities, a series of neuropsychological, neurophysiological, neuroradiological and intraoperative investigations have to be performed. In this talk, we will describe the rationale, the indications and the modality for performing a safe and rewarding surgical removal of low grade gliomas by using these techniques, as well as the functional and oncological results.

238 INVITED

Quality of Life and Cognitive Function Monitoring

Abstract not received

239 INVITED

Stem Cells in Brain Tumours – Where Are We Going?

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Cancer stem cells (CSCs) are the rare population of undifferentiated tumorigenic cells that are responsible for tumour initiation, mainteinance and spreading. The existence of CSCs might explain why tumours are resistant to conventional therapies, which typically target the rapidly proliferating tumour cells but spare the slow dividing tumour stem cell population. Moreover, these cells seem to be intrinsically more resistant to apoptosis inducing stimuli. Indeed, resistance of brain tumours to current therapies may be related to the presence of CSCs, as shown by several studies that examined their role in the development of resistance to radiation and chemotherapy.
Hence, the discovery of CSCs has profound implications for the development of more effective treatments, since the selective targeting of these cells might lead to the eradication of the tumour. Different strategies towards CSC targeting are being investigated. One of such approach is forcing these cells to differentiate, rendering them vulnerable to therapy. Likewise, targeted therapies able to hinder the CSC survival machinery might prove to be higly effective. The main challenge towards this direction, however, remains the need for a full molecular characterization of CSCs. We are currently characterizing at different levels, including genome-wide expression of mRNA, microRNA and proteome profiling, CSCs from glioblastoma. Such extensive characterization may provide key information on the relavant pathways to be targeted for successfull therapies.
Novel CSC targeted therapy strategies in brain tumours might also arise from the recent demonstration that a significant portion of the vascular endothelium in glioblastoma derives from CSCs. Most importantly, the functional relavance of the CSC-derived endothelial vessels was established by the selective targeting of endothelial cells generated by CSCs in mouse xenografts, which resulted in tumour reduction and degeneration.
In conclusion, although the identification of CSCs is relatively recenbt, this research area appears extremely promising as it may significantly contribute to the rational design of new therapeutic approaches for brain cancer.