that digital mammography and the addition of ultrasound in those with dense breasts will result in more earlier diagnosis. To address some of the issues of younger and older screening the UK has just started a randomised trial of women age 47−50 and 70−73. The results will not be available until at least 2020.
For women at increased risk of breast cancer it would seem sensible to start screening at a much younger age and, for those at very high risk, to offer MRI as a routine screening method. While more cancers will be detected there is yet to be any evidence that screening high risk women translates into a significant mortality reduction.

225 INVITED

EUSOMA Recommendations for the Management of Elderly Women With Breast Cancer

L. Biganzoli[1], C. Oakman[1], on behalf of Eusoma, European Society of Breast Cancer Specialists, Italy. [1]*Ospedale Misericordia e Dolce, Department of Oncology, Prato, Italy*

As the mean age of the global population increases, breast cancer in older women will be an increasingly common diagnosis encountered in clinical practice. Development of recommendations for management of older women with breast cancer is challenging due to limited robust clinical data in this remarkably heterogeneous population. The number of trials for older women is increasing, but is still low. Current practice is largely guided by data from limited retrospective subgroup analyses and by extrapolation of results for younger women. A multidisciplinary European Society of Breast Cancer Specialists (EUSOMA) taskforce was formed to review available evidence (published works and meeting abstracts) for the management of elderly women with breast cancer. This taskforce used the 2007 International Society of Geriatric Oncology (SIOG) guidelines as a starting point, updated them with new data and introduced new categories of geriatric evaluation and patient expectations.
There are important considerations for this cohort of women. A comprehensive geriatric assessment (CGA) may benefit some older women. There is strong evidence in the general population that CGA directed intervention improves survival and quality of life, and there is favorable evidence for CGA specifically in the cancer population. There are some geriatric domains (cognition, nutrition, co-morbidities, depression) which may be managed, with subsequent improvements in compliance, tolerability of therapy and survival.
Treatment should not be an age-based decision. Rather, decisions should be made taking into account individual patient's estimated absolute benefit, life expectancy, treatment tolerance, and preference. Under-treatment is well documented in older breast cancer patients however the evidence base for modified management strategies in elderly patients is poor. In a fit elderly patient, treatment decisions should be driven by disease biology and the same consideration should be given as to a young fit patient. In vulnerable or frail patients, treatment should be individualised.
Expectations of elderly patients may vary considerably in terms of disease outcomes and benefits from therapy, and must be considered. The patient should be fully informed of the alternatives of therapy. Physician and caregiver bias should not unduly influence the patient's decision. Special attention should be paid to cognitive status, depression, anxiety and social settings that can influence patient decisions.

226 INVITED

EUSOMA Recommendations for the Management of Young Women

Abstract not received

Society Session (Sun, 25 Sep, 16:45−18:15)
European Association for Cancer Research (EACR)

227 EACR Cancer Researcher Award

EACR Cancer Researcher Award: Cancer Epigenetics − From DNA Methylation to Non-coding RNAs

M. Esteller[1]. [1]*Bellvitge Biomedical Research Institute (IDIBELL), Cancer Epigenetics and Biology Program (PEBC), Barcelona, Spain*

Background: An altered pattern of epigenetic modifications is central to many common human diseases, including cancer. Many studies have explored the mosaic patterns of DNA methylation and histone modifications in cancer cells on a gene-by-gene basis, among them the seminal finding of transcriptional silencing of tumour suppressor genes by CpG island promoter hypermethylation. Epigenetic gene inactivation in transformed cells involves many "belts of silencing".
Materials and Methods: We are in the process of completing the molecular dissection of the entire epigenetic machinery involved in methylation-associated silencing, such as DNA methyltransferases, methyl-CpG binding domain proteins, histone deacetylases, histone methyltransferases, histone demethylases and Polycomb proteins.
Results: The first indications are also starting to emerge about how the combination of cellular selection and targeted pathways leads to abnormal DNA methylation. In addition to classical tumour-suppressor and DNA repair genes, epigenetic gene silencing includes microRNAs with growth inhibitory functions.
Conclusions: Recent technological advances are now enabling cancer epigenetics to be studied genome-wide. It is time to "upgrade" cancer epigenetics research and put together an ambitious plan to tackle the many unanswered questions in this field using genomics approaches to unravel the epigenome.

228 INVITED

From Genes to Cancer Therapies

A. Ullrich[1]. [1]*Max-Planck Institute for Biochemistry, Department of Molecular Biology, Martinsried, Germany*

Cancer represents a disease prototype that is connected to defects in the cellular signaling network that controls proliferation, motility, invasivity, survival and recognition by the immune surveillance system. We obtained the first insights into the genetic basis of cancer in the early 1980ies by comparing the sequences of retroviral oncogenes of animal origin with human proto-oncogenes that encoded components of the cellular signal transduction network. Currently the spectrum of known genetic alterations in cancer cells includes mutations in a variety of genes leading to structural and functional dysfunctions in cellular signal transmission and – definition as well as over − or under-expression of positive or negative signal regulatory proteins respectively.
For the past years we have investigated various aspects of signaling systems in tumour cells in order to identify critical switch points in the patho-physiological process that results in malignancy. These efforts aim at the selective blockade of abnormal, disease-promoting signaling mechanisms by monoclonal antibodies, or small molecule kinase inhibitors. This strategic approach began with the cloning of the EGF receptor cDNA and the related receptor HER-2/neu and translated the animal oncogene concept into target-directed therapy of human cancer. This work yielded the first specific oncogene target-based, FDA-approved (1998) therapeutic agent, "Herceptin", for the treatment of metastatic breast cancer. Earlier and subsequent "target-driven drug development" efforts that employed various genomic analysis strategies led to the cancer therapies that are based on EGFR, HER3, FGFR4, Axl/Ufo and Flk-1/VEGFR2 as critical signaling elements in tumour progression. The latter served, in cooperation with SUGEN Inc./Pharmacia/Pfizer, as basis for the development of SU11248. The drug discovery process that led to SU11248 represents a prototypical example for the adaptation of cancer therapeutics from highly specific to multi-targeted drugs. In 2006 the FDA approved SU11248/SUTENT/Sunitinib for the treatment of Gleevec-resistant GIST and Renal Cell Carcinoma (Pfizer) and the European Agency EMEA followed suit. Current research efforts aim at the elucidation of the mechanistic relevance of the Sunitinib target profile which may aid in the prediction of patient response to this multi-specific cancer therapeutic. While all novel cancer therapies target genetic alterations in tumour tissues innovative strategies are aimed at investigating the contribution of germ line determinants of the patient to disease progression and therapy response. One example is the common polymorphism at codon position 388 in the human FGFR4 gene of which the Arg388 allele represents a target for the development of individual genotype -dependent cancer therapy development. Current findings and their consequences for patient-specific cancer therapy will be discussed.

229 INVITED

Tumour Suppressor Networks: Lessons From p53

M. Oren[1], Y. Aylon[1], E. Shema[1], G. Fuchs[1]. [1]*Weizmann Institute of Science, Department of Biological Radiation, Rehovot, Israel*

Inactivation of tumour suppressors is a major driver of cancer progression. Like all key regulatory molecules, tumour suppressors do not act in isolation, but rather are part of intricate protein networks. Often, the network design includes multiple proteins that regulate negatively a pivotal tumour suppressor and, when overexpressed, will register as oncogenes, as well as proteins that sustain the activity of that pivotal tumour suppressor; the latter proteins will often register as tumour suppressors in their own right, since their inactivation may incapacitate the network. Furthermore, seemingly distinct tumour suppressor networks often cross-talk with each other: in some cases, this crosstalk serves to reinforce cancer-inhibitory

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