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.

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EUSOMA Recommendations for the Management of Elderly Women With Breast Cancer

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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.

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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

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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.

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From Genes to Cancer Therapies

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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.

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Tumour Suppressor Networks: Lessons From p53

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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