collaborative Interfant Study Group has been founded with the aim to improve survival of these patients by recruiting sufficient patients for prospective randomized trials, forming a platform allowing for integration of new targeted drugs, developing new prognostic factors and improving the understanding of the biologic background of the disease. The Interfant-99 study has been closed in 2006 providing results of 482 patients with an event-free survival (EFS) rate at 4 years of 47%. As major risk factors, MLL translocation, high leukocyte counts, age below 6 month, and response to prednisone could be determined. Within the trial, minimal residual disease could be established as additional relevant prognostic factor. A new protocol Interfant-06 has recently been opened investigating a more AML-oriented therapy for this patient cohort.
3–5% of children with ALL have a Philadelphia-chromosome positive (Ph+) disease with a poor prognosis and EFS rates of 25–30%. The tyrosine kinase inhibitor imatinib specifically inhibits proliferation of BCR/ABL positive leukemias. In the EsPhALL trial, imatinib is used on the basis of the ALL-BFM 2000 HR therapy in all Ph+ patients with high risk features, whereas it is randomized in good-risk patients. About 30 patients per year are recruited. The trial will provide the opportunity to assess in a prospective controlled manner the importance of imatinib in non-HR Ph+ patients.
Relapse it the most frequent adverse event in childhood ALL occurring in about 20% of patients. Within the I-BFM SG, common risk stratification on the basis of conventional risk factors and minimal residual disease has been established. A variety of interesting new compounds has been developed in recent years with targeted activity in ALL. The importance of these drugs needs to be prospectively evaluated in randomized phase III trials before being integrated into frontline therapies. The EuReALL 2010 trial is planned to include patients from nearly all relevant European study groups and some non European groups aiming at a recruitment rate of at least 200 patients per year. This will allow answering randomized questions in standard and high risk relapse ALL separately within 4 years.
In conclusion, the I-BFM SG is the most important European organisation for childhood ALL, and provides an ideal setting for planning and conducting clinical trials in rare subgroups of patients.

Advocacy Session (Tue, 22 Sep, 09:00–10:30)
The burden of cancer

105 INVITED

Recent trends in the burden of cancer in Europe: a combined approach of incidence, survival and mortality for 17 major cancer sites since the 1990 s

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An overview is presented of most recent trends in incidence of, mortality from cancer across Europe since the mid 1990 s thereby interpreting relative survival trends for patients with cancer from the Eurocare study. The fact that the prevalence of cancer (i.e. also comprising ex-cancer) is rising by 3–5% annually does not necessarily imply that the cancer problem is worsening, on the contrary. Given the downward trends in cancer mortality for most major cancer sities in most countries the reverse is rather happening. Thus the combined interpretation avoids the flaws of the separate view. Incidence and survival can be strongly biased by early detection and screening and mortality by other causes of death. Data were obtained in 2008 from cancer registries in 21 European countries on incidence, mortality and 5-year relative survival from the mid 1990 s to early 2000 for cancers of oral cavity and pharynx, oesophagus, stomach, colorectum, pancreas, larynx, lung, skin melanoma, breast, cervix, corpus uteri, ovary, prostate, testis, kidney, bladder, and Hodgkin's disease. Annual percentages of change in incidence and mortality were calculated. Survival trends were analyzed by calculating the relative difference in 5-year relative survival between 1990–94 and 2000–02 using data from the EUROCARE-project. Trends in incidence as measured by population-based cancer registries were generally favorable in the more prosperous countries from Northern and Western Europe, except for obesity, alcohol and UV-related cancers. Whereas incidence of and mortality from tobacco-related cancers decreased for males in Northern, Western and Southern Europe, they increased for both sexes in Central Europe and for females nearly everywhere. Survival rates generally improved, mostly due to better access to specialized diagnostics, staging and treatment. Marked effects of organised or large scale opportunistic screening became visible for breast and prostate cancer in the wealthier countries and possibly also for melanoma. After decades of rises & unfavourable trends, cancer prevention and management in Europe seems to be moving in the right direction, suggesting that the rising awareness during the 80's is paying off. Still, cancer prevention efforts have much to attain, especially in the domain of female smoking and the emerging obesity epidemic. Standards of care can potentially rise by efforts to regionalize, to be documented through cancer registries. Conclusion: a comprehensive approach remains needed to measuring epidemiologic progress against cancer. Lit refs: Cancer Control in Europe: state of the art. Eur J Cancer special issue 2008; 44:1345–89. Survival of Cancer patients in Europe, 1995–2002: the Eurocare 4 study. Eur J Cancer special issue 2009;45:6:901–1084.

106 INVITED

Economic burden of cancer on patients

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In the European Union, one new case of breast cancer is diagnosed every two minutes.
In particular, breast cancer, second after lung cancer, is the most common form of tumour in Europe. 35% of the 275.000 women diagnosed with breast cancer every year are under 55 years of age, and 12% of them are under 45. The high incidence of this type of tumour, together with the relatively young age of the patients, has a major impact not only on the social lives of the patients, but also on their employment and their economical situation now and in the future. With increasing prevalence of survivors it is impostant to shed light on problems facing these persons after diagnosis and treatment. The overall aim of this study was to evaluate the rehbilitation process following a breast cancer diagnosis for women at working age by examing factors related to type of socio-economic status, working condition, life/working satisfaction and their association with return to work.
The Swedish study was distributed as an electronic questionnaire and linked to homepages for several patient-organizations, newspapers and magazines and generally to all institutions connected to cancer. The study was announced threw articles in newsletters, advertisemnet in newspapers and press-release was also sent about this study. In the Swedish study it participated 714 persons and the majority was in the ages 20–60 years old. This gave us an excellent basis for the evaluation of the results.
The study was a part of an European Commission project "Promoting new measures for the protection of women workers with oncolocigal conditions by means of social dialogue and company-level collective bargaining", and gave us good possibilities to compare the results in the participating countries.
The study showed that the women strove to belong to the labour market, but the study also revealed how women's perceptions of the value of the employment changed. The quality of social support received from employers and co-workers differed between women who returned to work and those still sick-listed one-two year after breast cancer treatment. Work situation after breast cancer is still a critical issue, even though a high proportion of these women are able to return to any type of work.
The return to work for women with breast cancer can be part of the transition to a state of well-being, even if women may find that returning to labour market is not particularly easy, either in physical or psychological terms, due to the feelings of tiredness that they may not have had before, and which they try to conceal, and due to anxiety about oncological risk, which remains a constant factor.
The principal finding was that most of the studied women who were working before cancer returned to work after their active cancer treatments were completed. Type of treatment as well as work-related factors, life satisfaction and coping skills were associated with return to work.
The group of women who not return to work or those who change to part-time work have big changes in their economical situation as a burden of their cancer and one of the most important difficulties to overcome consists of the need to strike balance between working hours, medical treatment and the person's individual needs.

108 INVITED

Return to working life with/after cancer

S. Rozman[1]. [1]*Europa Donna European breast Cancer Coalition, Ljubljana, Slovenia*

The quality of life after cancer experience is becoming an increasingly important issue and return to work belongs in this topic. For most survivors, work is a financial and emotional necessity, to help them keep their self-esteem and social support, but work is also a source of stress and can adversely affect health. According to American authors, up to 65% of cancer survivors remain professionally active, but as much as 75% of cancer survivors have to change their working status due to the disease consequences. In Europe there are no data on how many cancer patients return to work and how easy they find it to do so.
Permanent consequences experienced by cancer survivors may be:
- physical consequences – loss of function and structure of organs

- consequences of aggressive treatments (amputations, contractures, burns, fatigue)
- consequences of stress and the psychological processes of adjustment to disability (PTSD, impairment of immune system, depression, anxiety, adjustment disorders)
- changes in life goals, values and priorities, expectations and prejudices
- social consequences that affect the family (impoverishment, divorce, diseases of other family members)
- social consequences in working environment: loss of employment or advancement at work, discrimination, mobbing, conflict with employers or doctors due to administrative pressures of insurance companies to lower workers' compensations.

The studies on return to work reveal that the severity of the disease and the impairment of function are usually the most important factor influencing the return to work, but other environmental and personal factors are important too. Factors influencing the return to work are:

- *demographical factors*: age, economic status, education
- *disease factors*: localization, status of disease at diagnosis, functional status after treatment, other diseases and handicaps
- *work factors*: adaptation of workplace, easier jobs, reduced strain and stress, reduced working hours, suitable transportation to work, can be decisive factors in retaining working ability
- *treatment factors*: quality of life factors should be considered at treatment planning. The accessibility of paid sick-leave and of vocational and medical rehabilitation in a multidisciplinary team also can make a lot of difference.

In many European countries employers still discriminate against the people who have had a cancer diagnosis. The European Employment Framework Directive, 2004, obliged EU member states to introduce legislation to outlaw unreasonable discrimination against people with disabilities. According to discrimination protection laws, employers are supposed to make a "reasonable accommodation" to adapt the working environment to the needs of people with disabilities, but this may not take into account the needs of people with cancer, as the definition of disability is sometimes not suited to the long term chronic illness. The way this legislation has been implemented across EU varies widely, and the differences are even greater in practice. There is room for improvement and a job for survivor advocates. Because millions of cancer survivors, more than ever before, are now working age adults, advocacy efforts should shift from expanding legal protection from cancer-based discrimination to providing resources to help survivors meet their individual employment related concerns. Changing laws is the first step, now minds have to be changed.

Advocacy Session (Tue, 22 Sep, 11:00−12:00)
From patient to partner: evolution of the patient's role in health care

109 INVITED

Why we need a patient voice in Europe

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For the last five years the involvement of patient organisations in the discussions and formulation of health and research policy and their healthcare has become increasingly important. At the European level, it is now a fact that politicians consider the voice of patients along that of other stakeholders as critical to their work in health policy.

As Co-chair of **MEPs against Cancer** (MAC) I have been on the frontline of working with patient groups and appreciated their contribution which has helped MAC members to convince the European Parliament and indeed Member States under the Slovenian EU Presidency to make the political commitment to invigorate the fight against cancer across the EU. The arguments put forward by an umbrella organisation such as the European Cancer Patient Coalition who, speaking with one voice for all cancer patients across the EU, convinced us that urgent action was needed to reduce the burden of cancer and tackle head-on the existing inequalities in prevalence and mortality across the EU. The spectre, predicted by WHO, of a looming cancer epidemic largely due to Europe's ageing population, provides us with the urgency to act now. The European Commission is set to embark on a **European Partnership – Action against Cancer** in autumn 2009. With one in three people developing cancer in their lifetime, this ambitious action programme involving key stakeholders and Member States in a concerted effort is a very timely measure.

From a politician's perspective listening to the patient's voice and working in partnership on effective cancer control is an imperative for Europe. Not only does the health and well-being of our citizens depend on it, it is also a tremendous economic, social and political challenge for our ageing societies, placing an ever increasing burden on our economy. We need a healthy population and workforce to sustain our economies. We have to be vigilant that in the time of an economic crisis we keep up effective investment in health services. I know I am joined by cancer patients when I say that we are all looking forward to the European Cancer Partnership to invest in Europe's future health by taking long-term, sustainable actions to tackle cancer. By investing more in prevention, screening and early diagnosis, by sharing our knowledge and expertise about best treatment and care, we have an opportunity to save many European citizens lives now and in the future.

Society session (Tue, 22 Sep, 09:00−11:00)
EACR session

111 INVITED

The complex genomic landscape of breast cancer

C. Caldas[1]. [1]*Cancer Research UK Cambridge Research Institute, Department of Oncology, Cambridge, United Kingdom*

The first generation molecular profiling studies of breast cancer have at most analysed few hundreds of samples each. We have now completed the analysis of 1000 breast cancer genomes using high-resolution SNP arrays, gene expression arrays and focused mutation analysis (including TP53). The pathology of the tumors was rigorously assessed and information on histological type, grade, size, lymph node metastasis and ER was available for all cases. This study is the largest ever done and reveals the molecular taxonomy of breast cancer is more complex than gleaned until now. A copy-number based classification of breast cancer shows there are new subtypes that have been previously missed. Copy number vs gene expression correlation has highlighted both copy-number dependent as well as copy-number independent chromosomal loci. New breast cancer oncogenes and tumor suppressor genes have been identified. The genomic landscape of breast cancer is therefore extremely complex and this has both biological and clinical implications.

112 INVITED

Cancer stem cell spotting: the example of breast cancer

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Tumor heterogeneity is a hallmark of cancer and it is responsible for tumor progression and resistance to therapy. According to Nowell's classical theory of clonal evolution tumor heterogeneity is caused by genetic instability and phenotypic drifting. Thus, tumors arise from a single "mutated" cell which upon subsequent additional alterations gives rise to more aggressive subpopulations within the original neoplastic clone. These cells may leave a large number of offspring by chance, or new mutations may provide a growth advantage over the other tumor cells. Waves of such clonal expansion and selection drive the process. Therefore, any cancer cell can potentially become invasive and cause metastasis. This stochastic model predicts that the evolution of cancer cells is influenced by intrinsic (e.g. signaling pathways) or extrinsic (e.g. microenvironment) factors. These influences are unpredictable or random and result in heterogeneity in the cell phenotype or in the tumor initiating capacity. A key tenet of this model is that all cells of the tumor are equally sensitive to such stochastic influences. Moreover, tumor initiating cells cannot be identified prospectively or enriched for by for sorting cells based on intrinsic characteristics.

Recently, our understanding of tumor heterogeneity has been expanded through "the hierarchy model" which predicts that cancers contain a minority population of tumor initiating cells or cancer stem cells (CSC) that resist treatment and give rise to the bulk of the more differentiated tumor cells. Thus, a tumor can be considered a hierarchy defined by a maturation process analogous to normal tissue homeostasis. Therefore heterogeneity arises as a consequence of the presence of biological distinct classes of cells with differing functional abilities and behavior within the hierarchy. As opposed to the stochastic model the hierarchy model predicts that tumor-initiating cells can be identified prospectively and purified from the bulk of non-tumorigenic population based on intrinsic characteristics. The fact that most epithelial cancers are composed of cells that retain at least some level of differentiation suggests that the cancer stem cell generates a linage restricted progeny with a finite life span which nevertheless constitute the majority of the tumor. It follows that the bulk of the tumor would die out without being replenished from the cancer stem cells. Other than that little is known about the function of differentiated cancer cells.

Evidence will be presented here for the existence of a stem cell hierarchy in the normal breast and in breast cancer.