

in the development of pancreatic ductal adenocarcinoma (Guerra et al., Cancer Cell, 2007).

We have used the same targeting strategy to generate mice carrying an endogenous H-ras oncogene. As recently reported in humans suffering from Costello syndrome, germ line expression of H-RasV12, unlike that of K-RasV12, is tolerated during embryonic development. Moreover, these mice do not develop overt tumor formation at least for nine months. These observations indicate that H-Ras and K-Ras oncoproteins have significantly different properties in vivo.

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INVITED

Biological roles of PI 3-kinase isoforms

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The PI 3-kinase pathway has been implicated in a wide variety of physiological responses, and is considered as a therapeutic target amongst other in cancer and inflammation. Mammals have 8 distinct isoforms of PI3K, and global inhibition of all isoforms of PI3K is toxic in vivo. Therapeutic intervention with the PI3K pathway will therefore most likely have to be centered on specific (subsets of) PI3K isoforms. However, identifying the indications that will provide the best opportunity for isoform-selective PI3K inhibitors is the subject of intense debate. Indeed, it has turned to be particularly difficult to gain insight into the physiological roles of PI3K isoforms by classical mouse gene targeting/knock-out approaches. We have pioneered the use of so-called 'kinase knockin' mice in which we have created germline inactivating mutations in the ATP-binding site of PI 3-kinase isoforms. This strategy more faithfully mimics pharmacological inhibitors than the classical knock-out approaches, and has allowed us to uncover isoform-selective roles of several isoforms of PI3K and begin validation of these PI3Ks as therapeutic targets. An overview of these efforts will be presented.

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INVITED

Preclinical and clinical studies

G.B. Mills. USA

Abstract not received.

Symposium (Tue, 25 Sep, 14:45–16:50) Issues in geriatric oncology

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INVITED

The right treatment for elderly with cancer is not easy to determine: a research strategy

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Background: Never ending discussions on the right oncological treatment of, especially frail, elderly with cancer; obvious reasons being a limited but often varying, life expectancy, vulnerability, complicating presence of co-morbidity, increase in age flattening above 80 years and social reasons like being cared for at home, transportation. Quality of life matters a lot when your time is relatively short. Communication problems are large. One could argue that the right treatment hardly exists: there is either over- or undertreatment.

Materials: Data from the population-based Eindhoven Cancer Registry that comprise co-morbidity and SES and various studies on prevalence, effects on stage and treatment policy and outcome; literature on research strategy and a forthcoming special issue on Cancer management in the Elderly of the European Journal of Cancer based on an ESO course in april 2007.

Results: Prevalence of serious co-morbidity is substantial in elderly (less than one third being without overt serious co-morbidity, with sometimes small, sometimes large effects on life expectancy, but necessitating medical and organizational adaptations in care supply. Medical care in the (very) elderly is in fact individualized, as patients become more unique medically and socially, thus hampering traditional clinical research e.g. by means of RCT's. The annual number of specific (with respect to pattern of co-morbidity) older patients per hospital is usually rather small, which points to regional collaboration. Geriatricians with extensive knowledge of oncological treatments are usually scarce.

Conclusions: Prospective (and also retrospective, if suitable) research should be population-based, thus exhibiting the broad spectre of disease

and health status. Collaborations of large numbers of hospitals is necessary in order to have adequate numbers in subgroups. When the standard oncological treatment risks to be overtreatment, the study should rather focus on complications, side effects that determine QL. When, more or less deliberately, undertreatment is administered (less lymphnode sampling and/or adjuvant treatment) studies are necessary of recurrence rates and metastasis, and of QL at short and longer term. One could argue to learn more from at short term less risky undertreatment than from (the oncologically right?) overtreatment. Results should be more expressed in numbers needed to treat, stage, etc to avoid one (extra) recurrence, or side effect or complication.

With respect to care development, practical steps should be taken to develop or cut care paths (in the jungle of) the hospital that take account with co-morbidity management and address communication problems.

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INVITED

Comorbidity assessment and the influence of comorbidity on toxicity and choice of treatment

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One characteristic of ageing is an increased prevalence of comorbidity. In western countries, 35% of people aged 65–79 reports at least two diseases, this ratio increases up to 70% at age 80 and older.

Comorbidity may affect the accuracy of cancer screening or diagnosis. It can also influence both treatment and prognosis of cancer itself. Then, comorbidity requires careful assessment before planning cancer treatment. Various scales are available to measure it, with the capacity for predicting, for instance, the risk for hospitalization or death. Concomitant morbid conditions may be more difficult to treat, adding complexity in terms of competing risks; potentially incompatible therapies; burden or costs of therapies that patient can not tolerate, and synergistic likelihood of adverse outcomes, including disability and death. In many cases, geriatricians should help oncologists to define the hierarchy of patient diseases, including cancer and prioritize those requiring immediate treatments.

On the other hand, a common comorbidity in elderly patients such as diabetes mellitus has been suspected to worsen cancer outcomes. Obesity appears also to affect the prognosis of prostate cancer or breast cancer. Conversely hypothyroidism seems to be associated with a lesser incidence of breast cancer.

Furthermore, multiple concomitant diseases frequently lead to polypharmacy, increasing the likelihood of drug interaction with chemotherapy agents or supportive treatment. In fact, inappropriate medication use is frequent in older people taking at least 5 medications.

The management of elderly cancer patients should take into account not only the impact of cancer treatment on comorbidity and the effect of comorbidity in delivering cancer treatment, but also the impact of comorbidity on the behavior of the cancer in the elderly patients.

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INVITED

The essentials of geriatric oncology studies: do's and don'ts

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What is a geriatric oncology study? This is not a study of elderly patients defined as aged above 65, but it should be a study that takes into account principles of geriatric assessment. It should ideally include patients representative of all "elderly categories". This means including frail patients, because of age alone or because of biological limitations. Study endpoints may vary, from relapse-free survival to overall survival, as in many settings death from other causes may become a predominant issue, while patients value relapse-free time. Geriatric oncology studies need also to overcome the perceived "impossibility" that prevails in many settings. Well informed elderly patients and their caregivers will never refuse a well conceived study. There is a need to define standardized geriatric assessment tools to collect information in cancer patients. Once ongoing studies will have provided further information, an effort to coordinate cooperative groups should be done, so that all use a common tool, which will be a means to compare studies. This is similar to the easier but long process which lead to the adoption of performance status as a key element of all studies in oncology. The SIOG (International Society for Geriatric Oncology) Task Force on Geriatric assessment suggested that some of the data analyzed should be: checking whether screening tools correctly identify patients (i.e., too well, too ill); validating inclusion/exclusion categories; developing a scoring algorithm to identify target groups, identifying the best candidates for a specific intervention. b) defining the patient's status: prospective data about the importance of hemoglobin levels, albumin levels, creatinine clearance and drug interactions are needed. Studies should evaluate these determinants prospectively in order to define for which drugs such data are important in the choice of the treatment. c) definition of the disease:

this will follow the same pattern as in younger patients and one awaits confirmatory studies which will prove or not that complex and expensive methodologies are superior to adequately quality controlled evaluations of endocrine-responsiveness or (over)expression of targets (like HER-2) in breast cancer. Drug dose adaptations will need to follow established guidelines, and care about potentially severe interactions in patients who receive many drugs is needed. The SIOG has many working groups that have published about these matters and some of these data will be highlighted.

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INVITED

Optimizing geriatric oncology care: the EONS programme

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Cancer is largely a disease of elderly people with 60% of new cancers and over 70% of cancer deaths occurring in patients over 65 years and older in Europe. It is anticipated that the number of malignancies affecting this age group will continue to rise as the demographics of our society ages. Given the rising number of older adults in Europe the management of cancer in older people will be an increasingly common aspect of oncology practice. Inadequacies in the care and treatment received by older people with cancer as opposed to their younger counterparts has been well documented. This situation reflects the ageism within society generally but is particularly concerning within cancer care given the age of the majority of our patients. Despite the significant population of older people with cancer, there is limited opportunity for cancer care clinicians to access specialised education in relation to care of the older adult or engage in optimal multidisciplinary working with all relevant professionals. In recognition of these challenges EONS developed a core curriculum for Cancer in Older People (EONS 2006) which is the first comprehensive curriculum in this field in Europe for nurses. It provides a model for an integrated education programme for geriatric oncology that, if widely implemented, could substantially improve the supportive care of older adults with cancer.

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INVITED

Ethics and the elderly: do we know what they want?

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Background: cancer is primarily a disease of senior adults with >60% of new diagnosis and >70% of cancer related death occurring in person 65+ years. Due to the aging of the population worldwide the increase in cancer mortality is being observed in developing countries. Many barriers to adequate management of senior adults with cancer still exist. Efforts we dedicate to research, care, and education in geriatric oncology are limited.

Results: Medical, psychological, social, economical, political and cultural factors contribute to the aging process in a interdependent manner. Competence and sensitivity to interface individual patient's request are increasingly required to the geriatric oncologist. To better understand older patients attitudes toward cancer care we need to consider the social and the cultural meanings of aging. Different cultures, societies and even health care systems recognize a different "value" to the older persons and this may collide with the crude medical data. Western societies tend to attribute value to persons based on a productive evaluation. Therefore elderly have less value because no longer productive. Other cultures, i.e. Far Eastern culture recognize a strong moral role to the elderly thus even physically and economically limited, thus they have reasons for living.

In western countries senior adults are less actively involved in the society and also their role within the family may change, reducing social interactions and increasing time at home alone. Gender differences in such behaviours are well known. In particular differences in the need for friendship and emotional support are prominent.

A second important aspect of cultural implications of aging is to rely in their family or more often in some member of the family, the informal care giver, and to delegate to them medical decisions.

We conducted a study in 622 elderly cancer patient undergoing chemotherapy to analyze by a structured interview, the patient/informal care giver and physician relationship and the type of information regarding cancer diagnosis and prognosis discussed with the patient.

We found that 32.8% of our patients received only limited information on their disease. Years of education, age, stage of disease and living with the spouse were strongly related with the chance to have more information. 86.5% of the patients reported to have the strongest support in facing the cancer experience in a family member. 45.5% prefer to discuss medical issue in the presence of a family member.

Conclusions: awareness of special needs of the older population and ability to negotiate cultural issues are now playing an important role in the clinical management of elderly cancer patient. Geriatric oncologists must familiarize with ethical and cultural issues as well as they are trained in physiological and psychological changes related to the aging process.

Symposium (Tue, 25 Sep, 14:45–16:45)

Primary brain tumours – molecular targets and clinical applications

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INVITED

Malignant glioma: molecular pathways, mechanisms of disease and resistance to chemoradiotherapy

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As part of a comprehensive translational research effort accompanying the randomized clinical trial EORTC26981/NCIC CE.3 we determined profiles of gene expression (Affymetrix HG-U133 Plus 2.0) and genomic copy number aberrations (aCGH, BAC array) of glioblastoma tissues obtained from patients enrolled. This trial established a survival benefit for glioblastoma patients, who received concomitant and adjuvant temozolomide to standard radiotherapy (Stupp et al., 2005). However, benefit from the addition of TMZ was basically confined to patients, whose tumors had an epigenetically inactivated MGMT gene (Hegi et al., 2005). In order to identify other resistance factors and new therapeutic targets we combined unsupervised and supervised analysis of the gene expression profiles. Correlated gene sets identified by CTWC (Coupled Two Way Clustering) were investigated for their association with survival of patients treated