available at www.sciencedirect.com

ScienceDirect

ELSEVIER

Speakers' Abstracts

Session 1. Cancer Prevention and Health Politics: Economical and other Controversies

S1
Modern cancer drugs – will they be affordable in the future?

T. Szucs*. *Zurich, Switzerland*

Abstract not available at time of printing.

S2
Optimal allocation of cancer directed financial resources – tensions between primary prevention, early detection, and treatment

B.E. Hillner*. *Virginia Commonwealth University, Richmond, VA, USA*

In most countries, the allocation of financial resources for cancer prevention, early detection, and treatment come from different non-related 'silos'. In many low-income countries, primary prevention benefits have the greatest economic return since the cancer benefits are intertwined with other major health conditions. Examples include cervical papilloma virus vaccine (cervical cancer and HIV), hepatitis B control via vaccine or improved sanitation (hepatoma and cirrhosis), and tobacco control (lung and other cancers and coronary disease). In most affluent countries, beneficial cancer viral associated vaccines are (wisely) widely available if not optimally utilized. Tobacco control via taxation and social engineering (e.g. bans in workplaces and restaurants) have been beneficial across the relative affluence spectrum. The magnitude of the additional cancer burden and costs from the failure of primary prevention due to the increasing frequency and severity of obesity is still evolving. In 2009, the American debate about 'health care reform' and early detection guidelines exploded into a political firestorm. At a minimum, this debate fostered a recognition that the current early detection methods have recently minimally improved, that over-diagnosis, unneeded procedures and anxiety need to be more forthrightly acknowledged. The last 20 years in high-income countries, there has been an explosion in demand and the costs of cancer drug (or biologic) therapy, a similar growth in some forms of radiation, yet minimal change in surgical costs for primary disease control. Cancer drugs are now the world leader (over cardiac) of any class of medications. While three have been true blockbusters (trastuzumab, imatinib, rituximab), essentially all drugs introduced in this period have strained budgets or are simply unaffordable. During the next decade, the growth in genomic profiling and biologic imaging using PET may or may not lead to more selective and/or shorter courses of therapy in both the adjuvant or advanced setting. Genomic profiling may dramatically decline in costs especially if SNP profiles prove valuable. Thus, more targeted use based on genomic or metabolic profiling, as well as more explicit consensus and expertise in palliative care may help to 'bend' the current unrelenting cancer care cost curve yet expand benefits.

S3
Lessons learned from prevention programs: expectations, observations and possible considerations

F. Porzsolt*. *Clinical Economics, University of Ulm, Ulm, Germany*

It is mandatory to compare cost and consequences of health care services if public support is requested. This will apply to all health care services. As the demand for prevention will always exceed the available resources we have to identify and implement effective & efficient prevention programs. For identification we need appropriate criteria but the right criteria can be selected only if we realize that our expectations from prevention programs are higher than what is observed. New considerations may, therefore, be necessary to make progress with our prevention programs. The expectations of different partners of the health care system are different. Healthy and ill citizens expect the maintenance of health from prevention programs while politicians and health care professionals expect additional advantages. Interactions between these expectations complicate their understanding. The risk of ineffectiveness is higher and the conduct of valid studies is more difficult in 1′ than 2′ or 3′ prevention. Examples will be presented. The reduction of breast cancer incidence by behavioral changes is suggested but could not yet be confirmed in clinical trials. The recommendations of the US Prevention Services Task Force had to be adapted recently (regular breast cancer screening only in the age of 50, screening only every other year, neither encouraging nor teaching breast self examination and no mammography beyond 75. Consequently, we should differentiate structural markers (such as histology and size of a lesion) from functional markers (such as quality of life and survival). Mixing these markers may lead to inadequate disease management. Self-limiting disease (SLD) may exist frequently in some types of cancer. SLD might be likely when screening brings about a discrepancy between incidence and mortality. A simple approach is to compare statistics in countries with high and low screening rates. These theoretical considerations will lead to practical recommendations. Molecular screening should not be used in the healthy population as true positive cases cannot be differentiated from true positive SLD and false positive cases. The molecular profile of patients with early cancer should be correlated with the clinical course and treatment. Multivariate statistics will identify the impact of tumor biology and treatment on the clinical course. It should be mandatory for doctors who offer breast cancer screening to report risk factors to the national data base. This information ought to be available also for women who refuse mammography. The information is essential for a correct interpretation of mammography data. It can

1359-6349/ $ – see front matter

be concluded that priorities have to be set, expectations have to be supported by reliable data, interpretations that are not considered are the true risks of prevention, well-supported theoretical considerations are the cut diamonds of prevention, and practical considerations will unfold from a good theory.

Session 2. Cancer Prevention: The Scientific Base

S4
Genetics in cancer prevention

J. Garber*. *Dana-Farber Cancer Institute, Boston MA, USA*

Genetics has enabled us to identify individuals at remarkably high risk of specific cancers. Some of this information can be used to distinguish individuals with high cancer risk who can consider cancer risk-reducing interventions too invasive for the rest of the population, including prophylactic surgical removal of organs at risk, and intensified surveillance to direct resection of premalignant lesions. Genetic information can also identify individuals who do not share the increased risk with relatives, and can avoid invasive measures. Epidemiologic data can identify specific exposures that can modify inherited cancer risk. Examples would include the earlier age at onset of lung cancers among Li Fraumeni (p53 mutation) family members who smoke cigarettes, and the reduction in breast cancer risk among BRCA1/2 family members who exercise. One issue is whether the biology of tumors that develop in the setting of inherited susceptibility is different from that of the sporadic cancers of that organ, so that targeted mechanisms of risk reduction cannot be generalized to the larger population. Alternatively, if inherited cancers are more accelerated versions of malignant development along the standard pathway, then study of genetic risk populations should lead to faster development of risk reduction interventions. Examples will be discussed.

S5
Biomarkers for early detection and as surrogate endpoints in cancer prevention trials: issues and opportunities

B. Dunn*. *Basic Prevention Science Research Group, Bethesda, MD, USA*

In order to improve the early detection and diagnosis of cancer, give more accurate prognoses, stratify individuals by risk, predict response to treatment, and help the transition of basic research into clinical application, biomarkers are needed that accurately represent or predict clinical outcomes. To be useful in trials for chemopreventive agent development, biomarkers must be subject to modulation, easy to obtain and quantify, and have biological meaning, ideally representing steps in well-understood carcinogenic pathways. Though difficult to validate fully, wisely chosen biomarkers in early-phase trials can inform the prioritization of large-scale, long-term trials that measure clinical outcomes. When well-designed, smaller trials using biomarkers as surrogate endpoints should promote faster decisions regarding which targeted preventive agents to pursue, promising greater progress in the personalization of medicine. Biomarkers could become useful in distinguishing indolent from aggressive forms of ductal carcinoma in situ as well as localized invasive breast and prostate cancer, lesions that are often overtreated. Chemopreventive strategies that reduce the progression of early forms of pre-malignancy can benefit patients not only by reducing their risk of cancer and death from cancer but by reducing their need for invasive interventions. Genomic and proteomic methods offer the possibility of revealing new potential markers, especially for diseases whose biology is complex or not well understood. Panels of markers may be used to accommodate the molecular heterogeneity of cancers. Biomarkers in phase 2 prevention trials of combinations of chemopreventive drugs have been used to demonstrate synergistic action of multiple agents, allowing use of lower doses, with less toxicity, a critical feature of interventions intended for cancer prevention.

S6
Targeting polyamines and inflammation for cancer prevention

E.W. Gerner*. *The University of Arizona, Arizona Cancer Center, Tucson, Arizona 85724-5024, USA*

Increased polyamine synthesis and inflammation have long been associated with intraepithelial neoplasia, which are risk factors for cancer development in humans (Gerner and Meyskens, Clinical Cancer Research 15: 758–61, 2009). Both experimental and clinical studies suggest that polyamines may be involved in inflammatory processes in several tissues. Genetic epidemiology results indicate that a single nucleotide polymorphism influencing the expression of a polyamine biosynthetic gene is associated with risk of colon and prostate cancers. This genetic variant is also predictive of response to aspirin as a colon adenoma preventive agent. A prospective, randomized, placebo-controlled clinical trial of difluoromethylornithine (DFMO), a selective inhibitor of polyamine synthesis, showed that the one year treatment duration reduced prostate volume and serum prostate-specific antigen (PSA) doubling time in men with a family history of prostate cancer (Simoneau et al Cancer Epidemiology, Biomarkers and Prevention 17: 292–9, 2008). This trial also provided anecdotal evidence for suppression of prostate cancer progression. A second, randomized, placebo-controlled clinical trial of DFMO in combination with sulindac, a nonsteroidal anti-inflammatory drug in patients with prior colon polyps found that the three-year treatment was associated with a 70% reduction of all, and over a 90% reduction of advanced and/or multiple metachronous colon adenomas (Meyskens et al Cancer Prevention Research 1: 32–38, 2008). Treatment-associated toxicities were rare and associated with pre-treatment clinical and genetic risk factors. This latter proof-of-principle trial indicates that targeting polyamine synthesis and inflammation can be an effective strategy for reducing risk factors, such as colon adenomas, that are closely associated with the development of colon cancers in humans. This strategy may be applicable for reduction of risk factors for other human cancers.

S7
Thinking about the role (largely ignored) of heavy metals in cancer prevention: chromium and melanoma as a case in point

F. Meyskens*. *Orange, CA, USA*

Abstract not available at time of printing.

Session 3. Infection and Cancer Prevention: Hepatitis and *H. pylori*

S8
Hepatitis B virus and cancer prevention

M. Chang*. *Department of Pediatrics, and Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan*

Chronic infection of a virus of bacteria may closely relate to carcinogenesis. Chronic Hepatitis B virus (HBV) infection can cause liver inflammation, injury and regeneration (chronic hepatitis, liver cirrhosis), and lead to hepatocellular carcinoma (HCC). HBV is the world most common etiologic