
CANCER STRATEGY

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Meeting Report

New challenges for oncology after the year 2000

1. International Oncological Meeting at Val Gardena, Italy

S Tanneberger¹ and F Pannuti¹

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The rapidly growing specialization of many fields of oncology causes a risk of losing the understanding of the cancer problem as a whole. No doubt this fact influences our ability to seek out the most effective strategies in the fight against cancer worldwide. However the majority of oncologists feel it is our common responsibility to ensure that we debate and scrutinize all current problems and arrangements together and, if necessary, replace them with models better suited to the new realities. This encouraged the Italian Associazione Nazionale Tumori (ANT) to organize at the beginning of the new millennium an unusual meeting focused not on cancer sites or specific technologies in oncology but on the main challenges for oncologists after 2000.

The first issue discussed was 'cancer in the rapidly aging population of the industrialized world', the second 'cancer in developing countries'. These two main topics were framed by a critical review on 'cancer prevention: illusions and hopes' and an outlook on 'cancer therapy in the future'. The idea of this unconventional meeting was kindly acknowledged by the patronage of the President of the Republic of Italy and the auspices of Italy's Ministry of Health and local authorities. The municipality of Ortisei, in the wonderful Val Gardena of Suedtirol, hosted the meeting. A great number of excellent scientists from nine countries and institutions of the international oncology responded positively to the invitation of the meeting presidents F Pannuti (Bologna), G Bonadonna (Milano) and G Robustelli della Cuna (Pavia). The WHO Cancer Unit, at this time still headed by Dr Sikora, kindly provided the Head of the Scientific Programme Committee, Professor S Tanneberger, with valuable advice.

1. Cancer prevention: illusions and hopes

Moderators: G Bonadonna (Milano) and F Pannuti (Bologna)

As Koroltchouk (WHO) pointed out, much is known about the causes of cancer. There is, however, an enormous gap between what is effectively applied to populations everywhere in a country and this knowledge base. WHO predicts that dramatic increases in life expectancy, combined with profound changes in lifestyle, will lead to global epidemics of cancer after 2000. Tanneberger

(Bologna) warned against an eventual new cancer risk factor in the western lifestyle. Available data arouse suspicion that an increase in maternal age over 30, as is noted more and more in industrialized countries, could be associated with a low but certain cancer risk for children born from these mothers.

The discussion on cancer prevention was introduced with a bitter evaluation by Maltoni (Bologna). He showed that cancer may be partly combated and controlled by acting on the only modifiable factor: the diffusion in the environment of exogenous, mostly man-made, carcinogenic agents. However, as he commented, the strategy is now absolutely inadequate to meet its goals: the cause of this is mostly attributable to cultural shortcomings and to sophisticated and deliberate pollution of information by economic and political interests through which many deleterious practices go on undeterred. Current research programmes, as he judged, are qualitatively and quantitatively inadequate. Measures for preventive control are reduced to minimalist, sectorial rules, which are the result of compromise and lobbying, and which require long time-scales which generally coincide with industrial marketing processes. In contrast, information to the public on these specific topics is almost non-existent and is substituted by well-organized campaigns insinuating that the solution to cancer will prove to be like some 'magic pill'. Maltoni concluded that research on cancer requires a thorough cultural revision and radical change in the new millennium.

Indeed, there wasn't any convincing evidence that we are closer to the discovery of any 'magic pill' against cancer. Soffritti (Bologna) commented that much of the information available on chemoprevention of cancer is unsound, being the product of inadequate studies or from hypotheses based more on paper-work of general basic knowledge than on targeted clinical research based upon end-points. He proposed a critical reappraisal and rethinking of all current programmes of chemoprevention, looking for a more scientifically grounded strategy after 2000.

The participants of the meeting agreed that there are many experimental and epidemiological data supporting the use of tamoxifen as a chemopreventive. Available results were presented by Bonanni (Milan) who discussed data from his own institute's trial, the Royal Marsden trial and the NSABP P-1 trial. Comparing the varying

preliminary results among these three studies, he concluded that the efficacy of tamoxifen varies, depending upon population type and the nature of risk and that further results are clearly needed. His conclusion certainly supports the approval of tamoxifen for breast cancer prevention in subjects at increased risk by FDA. But it lessened the actual optimism with respect to the rapid introduction of other antiestrogens as chemopreventive agents for breast cancer.

Tanneberger (Bologna) defined the field of immunoprevention as a totally underestimated part of chemoprevention. He hypothesised that the immune system is the best target for early intervention during the long latency period of carcinogenesis. It is a biological mechanism whose 'natural function' is to eliminate 'minimal erroneous' cells that regularly appear during cell multiplication. Immunotherapy for cancer has no strong rational basis. But it may well be that, for effective cancer prevention, we need to do nothing more than enhance this existing mechanism of cellular homeostasis. Therefore, as Tanneberger pointed out, immunoprevention of cancer poses one of the great challenges to both scientists and the pharmaceutical industry after 2000.

2. Fighting cancer in countries with limited resources: needs, hopes and projects

Moderators: C Sessa (Bellinzona), A Mazzoni (Bologna) and V Koroltchouk (WHO)

As shown by Pisani (IACR) the most recent estimates suggest a total of 8.1 million new cancer cases per year worldwide, divided almost equally between developed and developing countries. At the same time, there were 5.2 million cancer deaths, with about 2.85 million (55% of the total) occurring in developing countries. From 1985–1997 cancer deaths increased from 6% to 24% of total deaths in developing countries. These estimates confirm earlier findings that cancer is currently emerging as a major killer in the developing world. Discussing the reasons for this situation, Koroltchouk (WHO) pointed out that this increase in cancer mortality is due to the desirable risk in the average age of the population, strongly augmented by growing risk factors. In many instances there is clear evidence that increasing cancer mortality is related to socio-economic factors of poverty and ethnic discrimination. Higher smoking rates are associated with psychological conditions such as hostility, overcrowding and low social support, accompanied by aggressive marketing by the transnational tobacco industry.

The meeting showed that this situation will rapidly deteriorate due to the collapse of cancer control in many parts of the ex-socialist part of the world. Kerenji (Novy Sad) described how the circumstances in Yugoslavia have constantly worsened since 1990, influencing all aspects of life, including health care and prevention. The resources, diagnostics and the quality of care dropped drastically. Poverty, industrial collapse, and unemployment place Yugoslavia in the group of underdeveloped countries. Additionally, having lived close to war-affected regions over the last nine years, the people of Yugoslavia have been increasingly neglecting their health. Air, water and soil pollution in Yugoslavia, and the Balkans in general,

contributes to increased cancer incidence. This was illustrated by Secen (Novy Sad), describing the lung cancer situation. In the part of Vojvodina, lung cancer has increased from 1988–1998 by 37.6%. By the year 2004 another increase of 16.7% is to be expected. In parallel, the operability of lung cancer patients in Vojvodina has decreased from 25% (up to 1990) to only 12% (at present).

Participants agreed that this poses an enormous ethical challenge. Mazzoni (Bologna) reminded people of the Universal Declaration of Human Rights dating back to 1948, concluding that we are shamefully far from this declaration looking at the present situation in developing countries which actually never do develop.

One of the approaches for supporting developing countries in health care is transferring and adapting well-proven care models to their specific conditions. Two examples were presented at the meeting: a programme against cervical cancer in Nicaragua (Sessa, Bellinzona) and the ANT Hospital-at-Home in Albania (Pannuti, Bologna). With relatively low investments, high working efficiency was achieved in both cases where it was learned that war and political conflicts are the greatest risk against progress in the fight against cancer in the Third World.

However, in spite of such encouraging initiatives, the socioeconomical drama of many parts of our rich world cannot be overlooked at the end of this century (Padre Toschi, Bologna). About a quarter of the world's population lives in dire poverty and in many regions it is increasing. At present 870 million people are illiterate and over 120 million people worldwide are officially unemployed. But as Tanneberger (Bologna) pointed out, this depressing situation is not much reflected by the mass media in the industrialized world and even less in medical literature. Until July 1999, MEDLINE registered 183,514 publications on cancer chemotherapy, just 4242 on taxol and taxol-derivatives. However, only 848 papers on cancer in the developing countries were published. In an observational study he invited participants to his lectures on cancer in developing countries to compile a questionnaire on Third World problems. 53% were responders (51% MDs, 20% PhDs, 6% nurses, 4% technicians and 19% other professionals). 59% had never experienced any information on cancer in the Third World during the last five years and 92% believed that more information would be necessary. 47% evaluated cancer in developing countries as a global problem and 35% as an important one. 96% felt responsible not only for their own patients but also for all suffering from cancer in the world. In order to achieve progress, 83% called for further engagement of European oncologists. 35% of the subjects believed that the solution to the problem should be made by WHO and other international organisations but 57% believed that it is a duty for all of us.

Tanneberger's message to this session was unanimously supported by the participants. Any earthquake or flood is much more reported in the mass media than the fact that one-third of the world's population is living life-long in conditions much worse than those of any earthquake victim. No doubt the victims of such events need our help. But it is necessary to evaluate the world more for global suffering from life-long poverty and not only episodically for temporary suffering from any emergency situation. Unfortunately, oncologists cannot do much against the

main reason for global suffering, which is the use of enormous world resources for military purposes instead of fighting against poverty. However, oncologists can do something. Medical journals with the highest citation indices should include more information on cancer in the Third World. Cancer research funding bodies should have separate budgets to finance applied research in the Third World (Fehre, Essen). All cancer societies in the industrialised world should organize committees for cancer in developing countries elaborating plans of action. Last but not least, medical schools should include lectures on Third World oncology in their education programmes.

3. Cancer in an aging world

Moderators: G Robustelli della Cuna (Pavia) and F De Conno (Milan)

Rapid population aging is the most significant change in our world in the 21st century. As demonstrated by Buiatti (Florence) in Europe, the number of 65+ subjects will increase between 1990 and 2010 from 14.0% to 16.5%, which means 18 million people more in this age group. After 2000, an average of 70% of all cancers will occur in patients who are older than 65 years of age. For prostate cancer, the percentage will be 80% and for colon cancer 74% (Paladini, Bologna; Camaggi, Bologna).

All this means that we need a 'new oncology' better suited to meet the needs of the 'frail' elderly (Cucinotta, Bologna). This starts with the further use of modern technologies for the characterisation of the individual biology of the tumor before treatment (Grigioni, Bologna) as the basis for a more individual treatment tailored to the multi-morbidity of most patients (Zamagni, Bologna). Moreover, it includes a setting up of sanitary structures with specific functions to avoid discomfort for older patients deriving from insufficient models of organisation (Paladini, Bologna).

A higher age in patients can never be a reason to reduce efforts in assisting them adequately. Robustelli della Cuna's message for oncological treatment after the year 2000 was simple. (a) Always, whenever possible, older patients should receive optimal therapeutic approaches, tailored to the extent of disease and organ functions. (b) Treatment should be designed to meet physiopathological conditions, not based on chronological age alone. (c) There is an urgent need to develop treatment protocols for the elderly with the specific aim to achieve both cancer control and psychosocial integrity.

Psychosocial integrity often can be realised best by home care. Terminal care at home is certainly what many patients want. On the other hand, home care becomes more and more difficult due to the decreasing capability of many families to do so. Therefore, a profound discussion on this topic was included in the meeting programme.

4. End-of-life home care

Moderators: V Ventafridda (Milano) and A Martoni (Bologna)

As underlined by Ventafridda (Milano) in his introductory remarks, assistance at home is one of the main

elements in any programme for palliative care and for the majority of terminal patients the preferred place to die is the home. In this connection the critical review of Andrysek (Prague) on hospices will reduce enthusiasm regarding the hospice approach. He pointed out that hospices, in spite of their indisputable advantages, are seriously limited for the following disadvantages: (a) only a small proportion of citizens agree to stay in a hospice. Predominantly religious persons are coping with the unambiguous function of the hospice. (b) Hospices are mostly separate buildings outside hospitals without continuous supervision of an oncologist. Therefore, unjustified admission of individuals who have still a chance for palliative therapy with improvement of quality of life and/or prolonged survival cannot be excluded. (c) Patients are relatively separated from their families and their usual environment where most of them wish to spend the rest of their lives. (d) Hospices are expensive facilities serving only a small portion of the population.

How can we provide a majority of patients with end-of-life home care? What home care technologies do we have? What costs qualify home care? Is home care available for all who need it? Many of these questions were discussed by the following speakers.

De Conno and Saita (Milan) criticised that, in Italy, access to palliative care services is scarce and unevenly distributed throughout the country. The home care programme of the National Cancer Institute of Milan started in 1980 with the support of a private non-profit foundation in order to provide hospice-like care to advanced cancer patients. The programme works in collaboration with a number of similar units. About 2000 patients each year enter the home care programme. In the Milan area the percentage of home deaths for patients followed by the palliative care unit is stable at 85%. This result is achieved by preparing patients and their families to accept with serenity the inevitable event of death. In March 1997 a supplementary electronic diagnostic and telecommunication service was made available through the centre, following up to four palliative care patients at any time. Participants have installed in their homes a telephone-based, interactive, computerised video-communication system that transmits information in real time from the home to the centre and vice versa.

GP-based home care services were presented by Andrysek (Prague) and Diemer (Greifswald). Both train GPs in their given territories and provide them with consultation. In certain cases, the GP can also delegate his responsibilities to the service team of specialists. Diemer reported 2150 contacts with more than 210 patients, optimizing the pain therapy. In 46% of the patients, an increase of opioid dosages could solve the problem, in 16% a step up in the WHO ladder was necessary.

Available estimates made on the costs per course for specific cancer sites and for in-patient or out-patient settings are favouring therapy at home as being less costly and with advantages for the patient's quality of life. Hospital-at-home is the home care approach with the highest degree of coordination and the most comprehensive service. Tanneberger (Bologna) reported on costs for the ANT hospital-at-home for 802 advanced cancer patients treated in the period 1992-1998. He calculated a mean value of \$38.76 a day per patient. Hospital-at-

home chemotherapy costs were an average of 26% less than in hospital while non-chemotherapy, palliative care was a significant 65% lower at home *vs* in-hospital care. However, as he pointed out, this will never be a magic solution for public health systems in crisis. Moreover, the expansion of home care must be accompanied by two elements. Adequate financial support has to be organized for families. Otherwise, home care means an unfair transfer of care costs from the state's health care budget to the family's pocket. Secondly, it has to be accompanied by a corresponding reduction in the number of hospital or institutional beds. Otherwise, there is no cost reduction for the health care system of the state as a whole. While the economic advantage of home care is certainly important, Tanneberger stressed that better quality and dignity of life should be the main argument supporting the idea of home care.

However, in spite of encouraging experiences presented at the meeting, participants supported the critical conclusions of De Conno and Saita (Milano). Today, the focus is on active medicine and on prolonging the lives of patients. If professionals in oncology want to find a solution to the problem of advanced and terminal cancer, it is essential that economic resources be reallocated more equitably between active and palliative medicine. Only with greater attention to palliative care is there a chance that disease and death can be free of pain and grief and patients can be allowed to die with their loved ones near them, free of fear and more serenely. This is the objective for 2000 and this could be the gift of oncologists to the twenty-first century.

5. The Bologna Eubiosie Programme: a project for life

An approach to overcome the great challenges of oncology in the next century was presented by Pannuti (Bologna) reporting in his opening lecture on the Bologna Eubiosia project. His impassioned appeal for dignity of life was introduced by a critical look backward. At the end of this century we are looking back to 2000 years of human engagement to control human suffering. However, many hopes are not fulfilled. The moral, social and medical objectives defined within the great religious and philosophical concepts have not been achieved. More than 20% of the world's population is permanently suffering from hunger, pain and anxiety caused by poverty, war or diseases just like cancer. However, human suffering is not an essential part of human life. Suffering is frequently man-made and should be banished by man's intelligence and power.

The Associazione Nazionale Tumori (ANT) follows a very simple concept called EUBIOSIA, in contrast with the idea of euthanasia. The concept has four cornerstones: (a) Eubiosia is a basic human right for all, (b) the language of Eubiosia is the example, (c) we can always do something against suffering, (d) everybody is welcome to support the concept, independently of religious or political positions.

Initiated by Pannuti, in 1978 ANT started a programme of medical, social and free-of-charge home assistance for terminal cancer patients. After 20 years, this programme

is now supported by 250,000–300,000 members and sympathizers. At present it is carried on by a professional staff of 88 medical doctors and 47 nurses. The staff is working in 15 Hospitals-at-Home operating in all parts of Italy, assuring daily about 2000 terminal cancer patients their dignity of life (Farabegoli, Bologna). Only 12% of the annual budget of 6,080,262 EURO is covered by the Italian sanitary service, the remaining is being covered by private donations, derived from the enormous activity of thousands of fund-raising volunteers. The Eubiosia project is considered as a contribution to worldwide anti-cancer activities. This is an example of what can be achieved in fighting human suffering. The Eubiosia programme, supported by political, religious and private bodies, independent from their political colour, seems to be a reasonable approach to the moral aims of our civilisation as defined 2000 years ago but not as yet achieved.

6. Cancer therapy in the next century

Moderators: G Paolucci (Bologna) and Tanneberger (Bologna).

Certainly some progress in cancer treatment is obvious, as demonstrated by Possinger (Berlin) for breast cancer, Martoni (Bologna) for ovarian cancer and Lukas (Innsbruck) with radiotherapy. However, speakers in this session, in general, could not present convincing evidence that the available 'news' in cancer treatment, including gene therapy (Lollini, Bologna), indeed influences cancer mortality significantly. Altogether the session produced more scepticism than optimism (Klebingat, Greifswald; Rossi, Cesena; Rizzoli, Parma). Speakers discussed numerous open questions existing for a long time but obviously not answered until now after thousands of clinical trials performed in the last decades in clinical oncology.

Robustelli della Cuna quite correctly described the situation with his message for the year 2000. He defined a series of still open questions concerning adjuvant and neoadjuvant cancer chemotherapy in operable breast cancer: (a) should everyone get adjuvant chemotherapy? (b) what's the role of anthracycline containing regimens? (c) what are the benefits of dose-intensification? (d) what's the role of high-dose chemotherapy plus hematopoietic rescue in high-risk patients? (e) who should get taxanes? He concluded that, even though very promising results have been achieved by many research groups, primary chemotherapy has not yet been translated into definitive guidelines for the practising oncologist. Even HDCT for solid tumors still remains a field of clinical investigation after 2000. As Lelli (San Giovanni Rotondo) pointed out, that should only be used in the context of clinical trials. Only presently ongoing randomized studies will prove if 'more is better'.

Recommendations for more effective care models were presented by Lukas (Innsbruck) and Paolucci (Bologna). Their message for the year 2000 was that the treatment of cancer patients is becoming more and more individualized and multidisciplinary. Onco-conferences concerning the treatment of each single patient have to be organized

in every institution before the start of the treatment in order to choose the best available multidisciplinary approach for the individual cancer patient. This demand is not new but obviously the diffusion of such a concept in routine oncology is still limited. Moreover, the reduction in resources allocated by public financing health care and research greatly affects oncology, with the danger of shutting down the most effective organisational and scientific strategies. As pointed out by Paolucci (Bologna) loss of quality in pediatric oncology is avoided only thanks to the strong support of local parent associations which have contributed in setting up entire departments and laboratories, purchasing and maintaining indispen-

sable equipment and setting up contracts and scholarships for staff members.

In conclusion the message for 2000 of this session was, first, to use in the most rational and economic way what is already available. This concerns both specific treatment modalities and well-known oncological principles as multidisciplinary and concentration of oncological treatment in the hands of well-experience specialists treating adequate numbers of cases. Research should follow new rational ideas rather than copy the ideas of others, and should never follow fashion and the marketing interests of drug producers.