

## Feature Articles

# Joint NCI-EORTC Consensus Meeting on Neoplasia in the Elderly

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THIS MEETING was organised with the following aims:

To review the natural history, treatment methods and results of treatment in patients aged more than 70 years in USA and Europe.

To update results of prospective ongoing trials in patients aged more than 70 years in USA and Europe.

To make plans for cooperative studies within the European Community aiming at a better diagnostic and therapeutic approach to tumours in the elderly.

### OUTCOMES

The meeting was concluded with a discussion from which the following agreements could be obtained.

#### *Dimension of the problem*

The size of the problem of cancer in the elderly was recognised by all participants in the meeting. Predictions for the year 2000 are that approximately 60-70% of all cancers will occur in persons aged 65 years or older, in developed countries. This formed the basis for the consensus that "neoplasia in the elderly is an oncological time bomb". The problem cannot be dismissed because of a presumed "slower growth" of tumours in the elderly. There is no good evidence that cancer in the elderly has, as many still believe, a less aggressive course than in younger patients.

#### *Referral of elderly patients*

Some participants were of the opinion that the elderly (over 70 years old) are not receiving the same standard of specialised

oncological care as younger patients. This assumption needs validation. Referral of older patients with cancer to specialised cancer centres or at least to certified clinical oncologists (surgical oncologists, radiotherapists, medical oncologists) may occur in less than 50% of elderly patients with cancer. The reason for reluctance to refer patients has been ascribed to the pessimism regarding the results of cancer treatment in the elderly. There are at present few comprehensive data on referral patterns for elderly cancer patients. Some cancer registries, such as those in Sweden or Switzerland, could give this kind of information. However, these registries are not representative of the population of Europe and the USA. The International Cancer Exchange Data Patient System (ICEDPS), whose data base now includes clinical information on more than 200 000 cancer cases in Europe and the USA, can be a possible mechanism for comparative studies. Two suggestions have been made for increasing the referral of elderly patients to specialised cancer centers and cancer specialists. The first is to include older members of the population in programs of public education about cancer. The second is to run properly designed protocols for the elderly.

#### *Retrospective studies*

Although the meeting was designed to review the natural history of cancer and its treatment in patients aged more than 70 years in the USA and in Europe, few data were available. Retrospective studies from the literature suffer from several drawbacks: (a) patient selection (b) lack of appropriate collection and recording of diagnostic and laboratory data, side-effects and results of treatment in the aged and (c) absence of studies conducted according to appropriate therapeutic protocols, designed to study results of treatment in elderly patients. In general, available studies mostly include the elderly as part of a general population which has been treated according to the same protocol. In particular, the difficulty of retrospective assessment of dose intensity was underlined.

#### *Patient selection*

Chronological age should not be regarded as an endpoint for decisions on therapy. Physiological status was felt to be much more relevant. Thus frailty rather than age should be regarded as the primary constraint in the use of cancer therapy. It was clear that even for patients referred to specialised cancer centres, it is often not possible to articulate reasons for excluding a patient from a therapeutic protocol. At the meeting, there was

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an agreement that the reasons for excluding patients from therapeutic protocols should be clearly stated in clinical charts.

### *Prospective studies*

The results of prospective studies presented during the meeting only related to non-Hodgkin lymphomas, acute myelogenous leukaemia and breast carcinoma. Recommendations were made that the possibility of entering therapeutic protocols should be offered to elderly patients, since this is accompanied usually by superior care to therapy of protocol. Protocols for prospective controlled randomised trials should not be restricted by age. Protocol development requires knowledge on indications for and complications of surgery and radiotherapy in the elderly. New protocols utilising cancer chemotherapy could be reduced more safely by facing doses on pharmacokinetic monitoring, since new relatively simple methods have been devised for estimating the area under the curve based on limited numbers of plasma samples [1, 2].

In particular, the following alternative options could be used in protocol design: (1) the same treatment protocol used in young adults should be adopted for elderly, unless there are specific contraindications; (2) the modification of the existing protocols should be based on considerations on the pharmacokinetics and specific side-effects of some antitumour drugs in the elderly, particularly toxicity to kidney, heart and central nervous system; (3) studies should be conducted with specifically designed protocols, in particular for medical and surgical treatment in patients intolerant to standard treatment.

The participation and compliance of elderly patients in controlled trials need monitoring to the same degree as in trials of younger subjects. The clinical data on diagnostic approaches, response to treatment, toxicity and evaluability rates of elderly patients should be also collected.

As the elderly are more likely to accept a medical opinion without question, it is particularly important to assure that alternative options for treatment are fully explained to them and to their relatives. The opinion of the patient should be obtained so that therapeutic interventions take into account his or her desires.

### *Assessment of the somatic and mental status*

As there is a critical balance between the quality of life and intensity of treatment, prospective trials in the elderly must include an assessment of the quality of life before, during and after treatment. Diagnostic and therapeutic approaches can then take into account not only standard medical parameters but also the quality of life. In Europe instruments used to judge the quality of life may be those prepared by the EORTC. In the USA "companion protocols" for the assessment of quality of life are already available.

It was felt, nevertheless, that to describe the degree of fitness of elderly patients with cancer before initiating therapy, traditional oncological parameters, such as performance status according to Karnofsky and the ECOG scale, are not sufficient. Biological age of older patients is different from the chronological age, and perhaps can be best assessed by organ function test and neuropsychiatric evaluation. However, in addition to pathophysiological parameters, attention should be paid to the importance of behavioral and socioeconomic features that influence the choice of treatment, compliance and access to supportive care.

Surgical oncologists present at the meeting described a "fitness" scale for patients undergoing surgery, as used by the anaesthetists, that could be also used for cancer patients undergoing surgery. A similar methodology could also be used for patients to be treated with cancer chemotherapy. This scale should take into account daily activity, possible cognitive impairments, social and economic conditions, and access to cancer centres. It was generally agreed that behavioral and psychological assessment could be accomplished in geriatric cancer patients. The use of a validated scale, such as the Rapid Disability Rating Scale 2 of Linn [3] and of the Short Portable Mental Status Questionnaire (SPMSQ) of Pfeiffer [4] was discussed. If such a new means of selecting patients is proposed, its validity could be submitted to clinical trials testing by comparing the new scale versus standard criteria for study entry such as the Karnofsky performance status. Kidney and liver function test and cardiovascular parameters should be collected separately.

### *Early diagnosis of cancer in the elderly*

Early diagnosis of cancer was as important in the elderly as in younger persons. It was appreciated that compliance with recommendations for mammographic screening was poor. A number of factors, including possible cognitive impairment, seclusion, infirmity, other diseases, cost and distance from facilities reduce the possibility that early diagnosis and screening may be sought by elderly patients (e.g. cervical carcinoma, breast carcinoma). For this reason specific plans should address the special problems of elderly people.

### *Future prospects*

As new procedures of limited surgery became available (e.g. quadrantectomy, colonoscopic exfulguration, laparoscopic surgery) they could be offered to selected elderly patients, as alternatives to standard extensive surgical procedures. In cancer chemotherapy, the safety of intensive treatment can be enhanced by pharmacokinetically guided anticancer drug administration, with specific interventions to reduce bone marrow toxicity (CSFs), renal toxicity (hydration and diuresis), and cardiotoxicity (ICRF-187 with anthracyclines), as well as in the administration of regimens specifically devised for the elderly.

### *Conclusions*

Whenever possible elderly patients should receive maximal curative treatment on accepted protocols.

Adjustment to protocols should be based on physiological considerations, not age alone.

Protocols that accommodate to the specific psychosocial problems of the elderly, as well as their physical impairments, should be designed and adopted.

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