Progress in Anti-cancer Chemotherapy

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Preface

This is the fourth volume of our series Progress in Anti-cancer Therapy. For the past four years we have taken the challenge to select each year, some of the most interesting topics on the wide field of oncology. As usual, this volume continues the tradition and covers five cancers (breast, prostate, bladder, lymphoma and ovarian), the role of HIV and HTLV in cancer, as well as some developmental pharmacology and behavioral issues.

This year, we have particularly focused our attention on one of the most common (although rarely addressed) cancer accounting for more than 315,000 newly diagnosed cases and 41,000 cancer-related deaths annually (Landis SH *et al.*, 1999) : prostate cancer.

Five chapters address some of the issues concerning this disease. The chapter by Schroder describes the hopes and pitfalls of early detection of prostate cancer. It reviews the literature on screening studies that have been performed both in the US and in Europe. These studies suggest that cancer mortality could be reduced by screening for prostate cancer, mostly through PSA testing. However, the effectiveness of early detection still needs to be definitely confirmed and ongoing randomized studies are described, the results of which will probably help the medical community determine the worth of PSA-based screening for prostate cancer. On the same hand, the paper from von Eschenbach is reviewing the clinical problems that are related this disease.

One of the reasons why prostate cancer is so difficult to study is the high prevalence of "minimal disease" cases where it is hard to determine the real potential for further progression and metastasis that may significantly shorten the life of these (usually) aged patients. This question is addressed by Fidler *et al.*, in their chapter dealing with the molecular diagnosis to predict the metastatic potential of prostate cancer. The authors describe the different steps that are necessary for a cancer cell to metastasize, and the molecular events related to these steps. They show the results of an interesting multitest procedure that seems to predict the life-threatening potential of a given prostate cancer.

In their chapter, Wood *et al.* focus on the heterogeneity of prostate cancer and describe those events that, at the molecular and genomic level, condition the virulence of some cases. These two chapters present an excellent overview of current knowledge on the mechanisms of prostate cancer metastases.

Labrie provides a chapter on Combined Androgen Blockade in prostate cancer. He describes the progress made during the last 20 years in order to evalua-

te the activity and the indication of the different hormonal manipulations on the treatment of prostate cancer. His review of the available data leaves little room for doubt regarding the fact that combined androgen blockade is the most active available therapeutic approach to prostate cancer and its dissection of the reasons why acceptance of this concept has been so slow is of great interest.

In a related field, Moore's contribution to this volume is of particular interest. with the Taxanes as well as Gemcitabine entering the armamentarium of drugs against bladder cancer, the review of all reported trials in order to update our practices, is timely.

Three chapters address breast cancer. Hudis, very similarly, describes how new drugs should be integrated in the treatment of metastatic breast cancer. What is the role of Paclitaxel or Docetaxel, the possibility to combine them sequentially or simultaneously with other, more classical compounds, the benefit one might expect, as well as the specific toxicities are topics of particular daily interest.

Fisher summarizes conceptual advances on our therapeutic approach to non-metastatic breast cancer and the paradigm shifts that led us to our current management strategies. This is well complemented by the chapter by Namer *et al.*, which, more specifically, addresses the issues of adjuvant therapy in premenopausal women.

Ozols presents an excellent review of current knowledge and perspectives on the treatment of ovarian cancer. It is also very important to read the chapter written by Cascinelli *et al.* which describes the state of the art regarding the use of sentinel node biopsy in melanoma patients.

On the same hand, an exhaustive overview has been made by Pinto *et al.* on the emerging new drugs for the treatment of human lymphomas.

The chapters of Pharmacology focus this year, on four issues : the role of non-steroidal anti-inflammatory drugs in cancer, a debated topic well covered by one of its pioneers, Israel, and the new anti-cancer drugs under development, based on new and more specific targets. Indeed, the chapter by Dancey *et al.*, describes with a lot of detail, the most recent discovery of target-directed or rational drug design. Whether or not these drugs, aimed at inhibiting or activating key pathways important in the progression or propagation of cancer cells, will bring soon, to the bedside more active agents than those obtained through the systematic screening of chemical or natural compounds, is still questionable. However, the hope they provide is great, at the level of the task of objectively evaluating these new agents in the clinic. Finally, Pinto is reviewing the nature and efficacy of the new drugs that are available in the treatment of lymphomas, and, in another chapter, Pekarsky and Croce are analyzing the role of FHIT in human cancer.

In a different matter, Cleghorn *et al.* (from R. Gallo's team) reviews the role and the mechanisms by which HIV and HTLV are involved in cancer. Tubiana is making a significant contribution to the debate on smoking and its complications in the field of cancer.

And finally, the two last chapters, one from Jarrousse on sexuality and cancer, and one from Spiegel on the role of the mind in Cancer, are interesting contributions to questions related to behavioral sciences. These topics need,

most probably, to be addressed more often as they are seldom taught to our young colleagues furthermore these issues are very often of some concerns to our patients.

We hope that you will find this volume as interesting as you found the previous three volumes, and that this annual series brings you useful information for your practice.

David Khayat
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December 13th, 1999