The European School of Oncology gratefully acknowledges sponsorship for the Task Force received from Sterling Winthrop.
P. Workman (Ed.)


With 33 Figures and 10 Tables
Foreword

The European School of Oncology came into existence to respond to a need for information, education and training in the field of the diagnosis and treatment of cancer. There are two main reasons why such an initiative was considered necessary. Firstly, the teaching of oncology requires a rigorously multidisciplinary approach which is difficult for the Universities to put into practice since their system is mainly disciplinary orientated. Secondly, the rate of technological development that impinges on the diagnosis and treatment of cancer has been so rapid that it is not an easy task for medical faculties to adapt their curricula flexibly.

With its residential courses for organ pathologies and the seminars on new techniques (laser, monoclonal antibodies, imaging techniques etc.) or on the principal therapeutic controversies (conservative or mutilating surgery, primary or adjuvant chemotherapy, radiotherapy alone or integrated), it is the ambition of the European School of Oncology to fill a cultural and scientific gap and, thereby, create a bridge between the University and Industry and between these two and daily medical practice.

One of the more recent initiatives of ESO has been the institution of permanent study groups, also called task forces, where a limited number of leading experts are invited to meet once a year with the aim of defining the state of the art and possibly reaching a consensus on future developments in specific fields of oncology.

The ESO Monograph series was designed with the specific purpose of disseminating the results of these study group meetings, and providing concise and updated reviews of the topic discussed.

It was decided to keep the layout relatively simple, in order to restrict the costs and make the monographs available in the shortest possible time, thus overcoming a common problem in medical literature: that of the material being outdated even before publication.

Umberto Veronesi
Chairman Scientific Committee
European School of Oncology
Dedication

This volume is dedicated to two of our fellow soldiers in the war against cancer who were themselves lost to the disease in 1993: the French medical oncologist Michel Clavel, who was an active early clinical trialist and a great supporter of cancer pharmacology, and the American pharmaceutical company scientist Gerald Grindey, who was an insightful advocate of experimental chemotherapy and rational drug development. The editor also acknowledges the influence of two others who departed in 1993: the clinician, biologist and philosopher Lewis Thomas and the musician Frank Zappa.
# Contents

Introduction  P. Workman ................................................................. 1

Experimental Models to Investigate Novel Anticancer Drugs  M. D’Incalci ................................................................. 5

Principles in the Design of DNA-Interactive Molecules  S. Neidle ................................................................. 11

Discovery of Improved Platinum Analogues  K. R. Harrap ................................................................. 23

Pharmacological Intervention with Signal Transduction  G. Powis ................................................................. 39

Discovery and Design of Inhibitors of Oncogenic Tyrosine Kinases  P. Workman, V. G. Brunton and D. J. Robins .................................................. 55

Apoptosis and Cancer Therapy  W. Bursch ................................................................. 71

Engineering Antibodies for Targeted Cancer Therapy  R. E. Hawkins ................................................................. 87