

---

Recent Results  
in Cancer Research 53

---

Fortschritte der Krebsforschung  
Progrès dans les recherches sur le cancer

---

# Recent Results in Cancer Research

---

# 53

Fortschritte der Krebstorschung  
Progrès dans les recherches sur le cancer

*Edited by*

V. G. Allfrey, New York • M. Allgöwer, Basel  
K. H. Bauer, Heidelberg • I. Berenblum, Rehovoth  
F. Bergel, Jersey • J. Bernard, Paris • W. Bernhard,  
Villejuif • N. N. Blokhin, Moskva • H. E. Bock,  
Tübingen • W. Braun, New Brunswick • P. Bucalossi,  
Milano • A. V. Chaklin, Moskva • M. Chorazy,  
Gliwice • G. J. Cunningham, Richmond  
G. Della Porta, Milano • P. Denoix, Villejuif  
R. Dulbecco, La Jolla • H. Eagle, New York • R. Eker,  
Oslo • R. A. Good, New York • P. Grabar, Paris  
H. Hamperl, Bonn • R. J. C. Harris, Salisbury  
E. Hecker, Heidelberg • R. Herbenval, Nancy  
J. Higginson, Lyon • W. C. Hueper, Fort Myers  
H. Isliker, Lausanne • J. Kieler, København  
G. Klein, Stockholm • H. Koprowski, Philadelphia  
L. G. Koss, New York • G. Martz, Zürich  
G. Mathé, Villejuif • O. Mühlbock, Amsterdam  
W. Nakahara, Tokyo • L. J. Old, New York  
V. R. Potter, Madison • A. B. Sabin, Rehovoth  
L. Sachs, Rehovoth • E. A. Saxén, Helsinki  
C. G. Schmidt, Essen • S. Spiegelman, New York  
W. Szybalski, Madison • H. Tagnon, Bruxelles  
R. M. Taylor, Toronto • A. Tissières, Genève  
E. Uehlinger, Zürich • R. W. Wissler, Chicago

*Editor in Chief: P. Rentnick, Genève*

Revised and enlarged edition of:

MATHÉ et KENIS: La Chimiothérapie des Cancers, 3<sup>e</sup> édition

Copyright © 1973, 1975 by

Expansion Scientifique Française, Paris

ALBERT CLARYSSE, MD, FACP, Chief, Division of Cancer  
Chemotherapy, Sint Janshospitaal, Bruges, Belgium,  
and Former Assistant Professor of Medicine, University  
of Utah School of Medicine, Salt Lake City, U.S.A.

YVON KENIS, MD, Division of Cancer Chemotherapy,  
Institut Jules Bordet, Brussels, Belgium

GEORGES MATHÉ, MD, Professor of Oncology, University  
of Paris Sud; Institut de Cancérologie et d'Immunogénétique,  
Hopital Paul Brousse; Division of Hematology,  
Institut Gustave Roussy, Villejuif, France

*Sponsored by the Swiss League against Cancer*

ISBN 3-540-07573-9 Springer-Verlag Berlin · Heidelberg · New York

ISBN 0-387-07573-9 Springer-Verlag New York · Heidelberg · Berlin

Library of Congress Cataloging in Publication Data. Clarysse, A. 1936— Cancer chemotherapy. (Recent results in cancer research; v. 53.) Rev. and enl. translation of the 3d ed. of La chimiothérapie des cancers; by G. Mathé and Y. Kenis. Includes bibliographical references and index. 1. Cancer — Chemotherapy. 2. Antineoplastic agents. I. Kenis, Yvon, joint author. II. Mathé, Georges, 1922— joint author. III. Mathé, Georges, 1922— La chimiothérapie des cancers. IV. Title. V. Series. [DNLM: 1. Antineoplastic agents — Therapeutic use. 2. Neoplasms — Drug therapy. W1 RE106P v. 53/QZ267 C614c.] RC261.R35 vol. 53 [RC271.C5] 616.9'94'008s [616.9'94'061] 75-43554.

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically those of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying machine or similar means, and storage in data banks. Unter § 54 of the German Copyright Law where copies are made for other than private use, a fee is payable to the publisher, the amount of the fee to be determined by agreement with the publisher.

© by Springer-Verlag Berlin · Heidelberg 1976.

Printed in Germany.

The use of registered names, trademarks, etc. in the publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Typesetting, printing and binding:

Konrad Triltsch, Graphischer Betrieb, 87 Würzburg, Germany.

A. Clarysse Y. Kenis G. Mathé

# Cancer Chemotherapy

Its Role in the Treatment Strategy of  
Hematologic Malignancies and Solid Tumors

With 154 Figures



Springer-Verlag  
Berlin Heidelberg New York 1976

## Introduction

This book is addressed primarily to the practicing oncologist and hematologist and to others who may not be able personally to scan the plethora of papers discussing the use of cytotoxic agents in the treatment of cancer. In addition, anyone in any way concerned with the problem of cancer or its treatment — be he internist, surgeon, radiotherapist, family physician, basic researcher, or pharmacologist — will find some useful information here. We especially wish physicians who may see cancer patients in their practice to be informed about the progress being made in the management of advanced cancer, particularly the indications for therapy and the results. Our greatest concern is that every patient should receive the best therapy currently available.

This text is the first English edition of *La chimiothérapie des cancers* by G. Mathé. The two earlier editions have been completely revised, enlarged, and updated. Some of the authors have worked on both sides of the Atlantic, so that European and American points of view have been integrated, hopefully to advantage.

The first part outlines the basic principles of cancer chemotherapy. Certain aspects of cellular and molecular biology, and of tumor cell characteristics and kinetics are reviewed because they are necessary to an understanding of the mechanisms of action of cytotoxic drugs. The reader is given the experimental data on which current chemotherapy protocols are based and shown how they are applied to the clinical situation. In view of the importance of organized cooperative trials, several chapters describe the different phases of preclinical and clinical trials and the practical aspects of treatment with cytotoxic agents.

A considerable portion of this review has been devoted to a discussion of general principles because they constitute the rationale upon which current and future chemotherapeutic protocols are based. As our understanding of these principles increases, it is no longer enough to hand out cookbook-type recipes for cancer chemotherapy.

On several occasions we have, for sake of clarity, made statements on issues that are still under debate; for example, the classification of cytotoxic agents according to their effect on the cell cycle.

The second part of the book deals with the treatment of various hematologic malignancies and solid tumors. All through this textbook, we discuss chemotherapy in the context of the overall treatment strategy, the aim of which is to cure the patient. A cure requires that all cancer cells be killed. The strategy includes four treatment modalities, each of which may play a specific role in the achievement of a cure, according to the stage of the disease at which the patient presents for treatment.

For each disease entity we have reviewed the effectiveness of the various conventional and experimental cytotoxic agents, used singly and in various combinations. The reader will appreciate that such information can only be relative. Most of it is based on data obtained by a number of authors, using different schedules and different criteria to evaluate response, and treating different patient populations, often in trials that are not comparable. When a particular regimen is clearly superior, we have indicated this. The authors do not claim to be without some personal bias, but every effort has been made to consider different opinions. Special recommendations are based on treatment schedules for which adequate data have been published. At the Institut de Cancérologie et d'Immunogénétique and at the Institut Gustave Roussy we are investigating protocols that exploit the phenomena of cell synchronization, recruitment, and potentiation. We hope by these means to improve existing regimens, but we must wait until we have sufficient data to justify their use.

The reader may sometimes have the impression that not much in the way of conclusions can be drawn from the results listed in various tables. Unfortunately, this is all too true. This vagueness serves to stress the necessity for controlled trials and organized studies to obtain answers to specific questions.

The need for more uniformity in terminology, staging classifications and procedures, criteria for evaluating responses, and methods for reporting results is also repeatedly emphasized. Without uniformity in such matters, the institutions and treatment groups cannot be compared.

We constantly stress the need for a concerted effort in the management of cancer patients: at the time of diagnosis and at various stages in the course of the illness, a case should be discussed by a surgeon, a radiotherapist, a chemotherapist and nowadays an immunotherapist. We anticipate that in the years to come a significant effort will be made to employ systematic chemotherapy and immunotherapy to supplement surgery or radiotherapy in apparently localized disease. If the results of treating residual disease by systematic chemotherapy have so far been of questionable value, this may be because it was carried out under suboptimal conditions. The next decade should confirm whether adjuvant therapy of good quality is capable of improving the overall cure rate of one in three cancer patients. The cooperative approach is usually practicable only in centers or clinics that specialize in the treatment of cancer, but it in no way excludes the participation of the

family doctor. On the contrary, he becomes an integral part of a team that takes care of his patient from diagnosis until death, if not cure.

This work is based on the observations of many dedicated and competent researchers and clinicians. Some important contributions may well have escaped our attention and hence fail to appear in this text. We also realize the temporary value of a work of this nature. Chemotherapy is a rapidly changing discipline and many recommendations made today may no longer be valid a couple of years from now.

We have tried to keep the contents updated as much as possible during the time-consuming process of publication. Complementary data can be found in G. Mathé:

Cancer Active Immunotherapy, Immunoprophylaxis and Immunorestitution. Springer-Verlag, 1976. Readers are urgent to check the original articles for the correctness of dosage schedules, modes of administration, toxicity and special precautions.

#### *Acknowledgements*

We wish to thank JENNIFER TOVEY, MARIE-ANNE BONNAMY and NICOLE VRIZ for secretarial assistance. The reading of the manuscript by Dr. LOUIS BALIZET enabled us to cut out some of the errors in the English language. We are also indebted to the contributors to former French editions of this text and to the publishers, Springer-Verlag.

A. CLARYSSE, Y. KENIS, G. MATHÉ

## Contents

### *Chapter 1. The History of Cancer Chemotherapy 1*

### *Chapter 2. Basic Cell Biology 4*

- A. The Normal Cell 4
  - 1. The Cell Structure 4
  - 2. Molecular Biology 6
    - (i) Structure of Nucleic Acids 6
    - (ii) Function of Nucleic Acids 10
    - (iii) Synthesis of Nucleic Acids 13
  - 3. Cell Division 15
- B. The Cancer Cell 22
  - 1. Biochemical Characteristics 23
  - 2. Surface Properties 24
  - 3. Chromosome Constitution 24
  - 4. Tumor Cell Kinetics 24

### *Chapter 3. Classification of Chemotherapeutic Agents According to their Mechanisms of Action 36*

- A. Drugs Interfering with Biosynthesis of DNA, RNA, and Proteins 36
  - 1. Folic Acid Analogs 37
  - 2. Purine Analogs 41
  - 3. Pyrimidine Analogs 41
  - 4. Other Agents with Similar Action 43
- B. Inhibitors of Protein Synthesis 45
- C. Drugs Interfering with Replication, Transcription, and Translation 46
  - 1. Alkylating Agents 46



- (i) Bischloroethylamines 47
- (ii) Ethylene-Imines 50
- (iii) Sulfonic Esters 50
- (iv) Other Agents with Alkylating Action 51
- 2. Agents Interfering with Transcription 53
- 3. Agents Interfering with Translation 56
- D. Agents with Radiomimetic Effect 56
- E. Agents Interfering with the Mitotic Spindle 57
- F. Other Cytotoxic Agents 58

#### *Chapter 4. Hormonal Agents Used in the Treatment of Cancer 84*

- A. Steroid Hormones 84
  - 1. Corticosteroids 85
  - 2. Androgens 87
  - 3. Estrogens 89
  - 4. Progestational Agents 90
- B. Thyroid Hormones 91
- C. Other Substances with Hormonal Activity 92

#### *Chapter 5. Classification of Chemotherapeutic Agents According to their Effect on the Cell Cycle 101*

- A. Classification into Phase- and Cycle-Dependent Agents 101
- B. Practical Applications of this Classification 105

#### *Chapter 6. General Principles of Cancer Chemotherapy. Experimental Data 112*

- A. Principles Learned from Single-Agent Therapy 112
- B. Cell Kinetics and Growth Characteristics 116
- C. Differential Cell Kill 117
- D. Tissue Selectivity 121
- E. Methods to Augment Cell Kill Above that of Single-Agent Therapy 122
- F. The Problem of Drug Resistance 125

*Chapter 7. Application of the Basic Principles of  
Chemotherapy to Human Malignancies 130*

- A. Tumor Selectivity 130
- B. Tissue Selectivity: Toxicity 135
- C. Cell Kinetics and Growth Characteristics of the Tumor  
to be Treated 142
- D. Methods to Augment Cell Kill 144

*Chapter 8. Preclinical and Clinical Evaluation  
of Chemotherapeutic Agents 164*

- A. Classification of Studies According to Objectives 164
  - 1. Toxicologic and/or Tolerance Studies 164
  - 2. Screening Studies 164
  - 3. Pharmacodynamic Research 164
  - 4. Pharmacokinetic Research 164
  - 5. Operational Research 165
  - 6. Strategic Research 166
- B. Phased Clinical Trials 167
  - 1. Phase-I Trials 167
  - 2. Phase-II Trials 168
  - 3. Phase-III Trials 170
  - 4. Phase-IV Trials 171

*Chapter 9. Achievements and Failures of Cancer  
Chemotherapy 173*

- A. Results of Current Chemotherapy 173
- B. Progress at the Experimental and Clinical Levels 173
- C. Causes of Failure of Chemotherapy 176

*Chapter 10. Practical Aspects of the Treatment  
of Cancer with Chemotherapy 179*

- A. Work-Up of Patient Prior to Chemotherapy 179
- B. Who Should Treat the Cancer Patient? 181
- C. Factors that Influence the Selection of Therapy 184
- D. Objectives of Chemotherapy 184
- E. When Should Chemotherapy be Used? 185
- F. Treatment Protocol: Recording Tumor Response and  
Toxicity 185

- G. Duration of Therapy: Indications for a Change in Therapy 190
- H. Final Evaluation of Therapy 192

### *Chapter 11. Management of Complications in the Course of Malignant Disease 201*

- A. Infections 201
- B. Bleeding 204
- C. Anemia 205
- D. Hypercalcemia 205
- E. Hyperuricemia 206
- F. Malignant Effusions 208
- G. Intracranial Hypertension 212
- H. Spinal Cord Compression 213
- I. Superior Vena Cava Obstruction 213
- K. Emotional Problems of Cancer Patients 214

### *Chapter 12. Local and Regional Chemotherapy 222*

- A. Local Applications and Instillations 222
- B. Intra-Arterial Chemotherapy: Perfusion and Infusion 223

### *Chapter 13. Strategy of Cancer Treatment 230*

- A. The Role of Each of the Four Treatment Modalities in the Treatment of Cancer 230
- B. Cancer Treatment Strategy for Disseminated Tumors 235
- C. Cancer Treatment Strategy for Localized Tumors, not Curable by Surgery and/or Radiotherapy 235
- D. Cancer Treatment Strategy for Localized Tumors, Curable by Surgery or Radiotherapy 238

### *Chapter 14. Acute Lymphoid Leukemia 250*

- A. Chemotherapy 251
  - 1. Induction of Remission 251
  - 2. Maintenance Therapy 253
- B. Strategy 261
  - 1. Immunotherapy 261
    - (i) Experimental Data 261
    - (ii) Clinical Trials 262

- 2. Surgery and Radiotherapy 271
- C. Discussion 271

### *Chapter 15. Acute Myeloid Leukemia 279*

- A. Chemotherapy 280
  - 1. Induction of Remission 280
  - 2. Maintenance Therapy 288
- B. Strategy 294
  - 1. Immunotherapy 294
  - 2. Bone Marrow Transplantation 294

### *Chapter 16. Chronic Myeloid Leukemia 302*

- A. Chemotherapy 303
  - 1. Remission Induction with Busulfan 303
  - 2. Maintenance Therapy with Busulfan 303
  - 3. Other Agents Effective in CML 303
- B. Strategy 306
  - Surgery and Radiotherapy 306
- C. Treatment of Acute Blastic Transformation 306
- D. Discussion 309

### *Chapter 17. Polycythemia Vera (Vaquez-Osler) and Myelosclerosis with Myeloid Metaplasia 313*

#### *Polycythemia Vera 313*

- A. Chemotherapy 313
- B. Strategy 314
  - 1. Phlebotomy 314
  - 2. Myelosuppressive Therapy 315

#### *Myelosclerosis with Myeloid Metaplasia 315*

Strategy 315

### *Chapter 18. Chronic Lymphoid Leukemia 318*

- A. Chemotherapy 319
  - 1. Remission Induction 319
  - 2. Maintenance Therapy 320
- B. Strategy 320
  - 1. Radiotherapy and Radioactive Isotopes 320
  - 2. Antilymphocyte Serum and Lymphocytaphoresis 321
  - 3. Indications for Therapy 321
  - 4. Treatment of Refractory Cases and Complications 322

*Chapter 19. Multiple Myeloma and Primary Macroglobulinemia (Waldenström)* 326

*Multiple Myeloma* 326

- A. Supportive Therapy 328
- B. Chemotherapy 329
  - 1. Single Agents 329
  - 2. Combinations 330
- C. Strategy 331
  - Radiotherapy and Surgery 331

*Primary Macroglobulinemia (Waldenström)* 332

- A. Strategy 332
  - Plasmaphoresis and Chemotherapy 332

*Chapter 20. Hodgkin's Disease* 336

- A. Chemotherapy 339
  - 1. Single Agents 339
  - 2. Combinations 341
    - (i) Remission Induction 341
    - (ii) Maintenance Therapy 344
- B. Strategy 345
  - 1. Surgery 345
  - 2. Radiotherapy 345
  - 3. Combined Chemotherapy-Radiotherapy 346
  - 4. Immunotherapy 346
  - 5. Treatment Plan for Stages I and II 346
  - 6. Treatment Plan for Stage III 348
  - 7. Treatment Plan for Stage IV 350

*Chapter 21. Non-Hodgkin Lymphomas (Lymphosarcoma, Reticulosarcoma)* 358

- A. Chemotherapy 360
  - 1. Single Agents 360
  - 2. Combinations 362
- B. Strategy 363
  - 1. Surgery 363
  - 2. Radiotherapy 363
  - 3. Adjuvant Chemotherapy and Immunotherapy 369
  - 4. Treatment Plan for Localized NHL 369
  - 5. Treatment Plan for Disseminated NHL 369

*Burkitt's Tumor* 369

- A. Chemotherapy 370
- B. Strategy 371
  - 1. Surgery 371
  - 2. Radiotherapy 371

3. Immunotherapy 371
4. Discussion 371

### *Mycosis Fungoides* 371

- A. Strategy 373
  1. Topical Therapy and Radiotherapy 373
  2. Chemotherapy 373

### *Histiocytosis-X* 374

- A. Strategy 374
  1. Localized Histiocytosis-X 374
  2. Disseminated Histiocytosis-X 374

## *Chapter 22. Skin Cancer and Malignant Melanoma* 383

### *Skin Cancer* 383

- A. Strategy 383
  1. Localized Skin Cancer 383
  2. Advanced Skin Cancer 383

### *Malignant Melanoma* 384

- A. Chemotherapy 385
  1. Single-Agent Chemotherapy 385
  2. Combinations 386
  3. Intra-Arterial Chemotherapy 387
- B. Strategy 387
  1. Localized Malignant Melanoma 387
    - (i) Surgery 387
    - (ii) Radiotherapy 389
    - (iii) Adjuvant Therapy 389
  2. Advanced Malignant Melanoma 389

## *Chapter 23. Head and Neck Cancer* 395

- A. Chemotherapy 396
  1. Single-Agent Chemotherapy 396
  2. Combinations 398
  3. Intra-Arterial Chemotherapy 398
- B. Strategy 400
  1. Localized Head and Neck Cancer 400
    - (i) Surgery and Radiotherapy 400
    - (ii) Chemotherapy-Radiotherapy with or without Surgery 400
    - (iii) Adjuvant Chemotherapy and Immunotherapy 400
  2. Advanced Head and Neck Cancer 401

*Chapter 24. Lung Cancer* 405

- A. Chemotherapy 406
  - 1. Single-Agent Chemotherapy 406
  - 2. Combinations 409
- B. Strategy 413
  - 1. Localized Lung Cancer 413
    - (i) Surgery 413
    - (ii) Radiotherapy 413
    - (iii) Adjuvant Chemotherapy and Immunotherapy 413
    - (iv) Combined Chemotherapy-Radiotherapy 415
  - 2. Disseminated Disease 415
  - 3. Discussion 417

*Chapter 25. Gastrointestinal Cancer* 424

- A. Cancer of the Esophagus 424
  - 1. Chemotherapy 424
  - 2. Strategy 424
    - (i) Localized Esophageal Carcinoma 425
    - (ii) Advanced Esophageal Carcinoma 425
- B. Cancer of the Stomach 425
  - 1. Chemotherapy 425
    - (i) Single-Agent Chemotherapy 425
    - (ii) Combinations 425
  - 2. Strategy 427
    - (i) Localized Stomach Cancer 427
    - (ii) Adjuvant Chemotherapy 427
    - (iii) Advanced Stomach Cancer 427
- C. Cancer of the Colon and Rectum 427
  - 1. Chemotherapy 427
    - (i) Single-Agent Chemotherapy 427
    - (ii) Combinations 430
  - 2. Strategy 430
    - (i) Localized Cancer of Colon and Rectum 430
    - (ii) Adjuvant Chemotherapy 430
    - (iii) Advanced Cancer of Colon and Rectum 431
- D. Cancer of the Pancreas 431
  - 1. Chemotherapy 432
  - 2. Strategy 432
- E. Primary Liver Cancer 432
  - 1. Chemotherapy 433
  - 2. Strategy 433

*Chapter 26. Breast Cancer* 439

*Cancer of the Female Breast* 439

- A. Hormone Therapy 439
  - 1. Estrogens 442
  - 2. Androgens 444
  - 3. Progestational Agents 445
  - 4. Corticosteroids and Other Agents 446
- B. Chemotherapy 446
  - 1. Single-Agent Chemotherapy 446
  - 2. Combinations 448
- C. Strategy 452
  - 1. Localized Breast Cancer 452
    - (i) Surgery and Radiotherapy 452
    - (ii) Adjuvant Chemotherapy 453
    - (iii) Prophylactic Versus Therapeutic Castration 456
  - 2. Disseminated Breast Cancer 457
    - (i) Hormone Therapy Versus Chemotherapy 457
    - (ii) Hormone Therapy in Premenopausal Women 458
    - (iii) Hormone Therapy in Postmenopausal Women 459

*Cancer of the Male Breast* 460

- A. Strategy 460
  - 1. Localized Breast Cancer 460
  - 2. Recurrent and Disseminated Disease 460

*Chapter 27. Gynecologic Cancer and Trophoblastic Disease* 471

- A. Cancer of the Ovary 471
  - 1. Chemotherapy 472
    - (i) Single-Agent Chemotherapy 472
    - (ii) Combinations 474
  - 2. Strategy 475
    - (i) Stage-I Ovarian Carcinoma 475
    - (ii) Stage-II Ovarian Carcinoma 476
    - (iii) Stage-III Ovarian Carcinoma 476
    - (iv) Stage-IV Ovarian Carcinoma 476
- B. Cancer of the Endometrium 477
  - 1. Hormone Therapy 477
  - 2. Chemotherapy 479
  - 3. Strategy 479
- C. Cancer of the Cervix 479
  - 1. Chemotherapy 481
  - 2. Strategy 481
- D. Gynecologic Sarcomas 482
  - 1. Chemotherapy 482



- E. Trophoblastic Disease 483
  - 1. Chemotherapy 484
  - 2. Strategy 485
    - (i) Molar Pregnancy and Nonmetastatic Trophoblastic Disease 485
    - (ii) Metastatic Trophoblastic Disease 486
    - (iii) Immunotherapy 486

## *Chapter 28. Testicular Cancers 492*

- A. Chemotherapy 493
  - 1. Single-Agent Chemotherapy 493
  - 2. Combinations 494
- B. Strategy 497
  - 1. Seminoma 497
    - (i) Early Stages (I and II) 497
    - (ii) Advanced Stage (III) 497
  - 2. Nonseminomatous Germinal-Cell Tumors 497
    - (i) Early Stages (I, II) 497
    - (ii) Advanced Stage (III) 498

## *Chapter 29. Prostate, Renal and Bladder Cancer 501*

### *Prostate Cancer 501*

- A. Hormone Therapy 501
- B. Chemotherapy 504
- C. Strategy 505

### *Renal Carcinoma 505*

- A. Chemotherapy 507
- B. Hormone Therapy 507
- C. Strategy 508
  - 1. Localized Renal Adenocarcinoma 508
  - 2. Locally Advanced and Disseminated Renal Carcinoma 509

### *Bladder Cancer 509*

- A. Chemotherapy 510
  - 1. Systemic Chemotherapy 510
  - 2. Topical Chemotherapy 510
- B. Strategy 511
  - 1. Early, Superficial Tumors (Stage 0, A) 511
  - 2. Lesions Invading the Muscle Wall 511
  - 3. Locally Advanced and Disseminated Bladder Carcinoma 512