

EDITORIAL

Long-term Adjuvant Tamoxifen Therapy and Decreases in Contralateral Breast Cancer

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Tamoxifen revolutionized personalized medicine as the first targeted therapy proven to save lives in cancer.¹ The paradigm change proposed to block the breast tumor estrogen receptor (ER), apply long-term adjuvant therapy to block estrogen-stimulated recurrences,^{1,2} and apply the potential of

tamoxifen to prevent breast cancer.³ These strategic recommendations were translated, during the past 3 decades, to clinical care.⁴ A meta-analysis⁵ of randomized clinical trials revealed that the strategic use of long-term adjuvant tamoxifen therapy is the key to therapeutic success. In addition, we now know that treating metastatic breast cancer (MBC) is only palliative at the end of life, but the same medicine saves lives if applied as long-term adjuvant therapy. Nevertheless, the question has to be asked whether the results would be the same outside the clinical trials process.

The report in this issue of *JAMA Oncology* by Gierach and coworkers⁶ is reassuring because all the rules derived, until now, from randomized clinical trial overview analyses hold true.⁶ The authors⁶ performed a retrospective cohort study of contralateral breast cancer (CBC) in a population of 7541 patients from the records at Kaiser Permanente Northwest and Colorado from 1990 to 2008 and followed up through 2011. The median range of observation was 6.3 years, and 248 patients were identified to have developed CBC. Both tamoxifen and aromatase inhibitors reduced CBC, and longer adjuvant therapy proved to be more beneficial than shorter therapy. The authors⁶ estimate that 4 or more years of adjuvant tamoxifen therapy will prevent 3 CBCs per 100 women by 10 years after first diagnosis of ER-positive breast cancer. The authors⁶ stress that patients with breast cancer who are undergoing long-term adjuvant endocrine therapy should be encouraged to complete the full course. Indeed, this conclusion is even more important because in the future adjuvant endocrine therapy will last for 10 years.^{7,8} However, the challenge is adherence. Simply stated, no medicine, no benefit. A previous report⁹ calculates the number of deaths caused by nonadherence with adjuvant tamoxifen therapy. Low adherence results in early recurrence, increased medical costs, and a much worse quality of life.⁹

Gierach and coworkers⁶ report the persistence of the protective effects of adjuvant tamoxifen after treatment stops on CBC risk and that this effect is dependent on the duration of tamoxifen therapy. The authors⁶ cite a Danish study¹⁰ that found that current users of tamoxifen had a reduced risk of CBC,¹⁰ but former use of tamoxifen had no effect on CBC. Importantly,

the adjuvant therapy used was only for a short period (median, 1-2.5 years).¹⁰ Persistence of the protective effects of tamoxifen using 5 years of treatment in high-risk populations is noted in the National Surgical Adjuvant Breast and Bowel Project trial¹¹ to reduce the risk of primary breast cancer in high-risk women. These data¹¹ are supported by the 96-month follow-up of the International Breast Cancer Intervention Study trial and the 20-year follow-up of the Royal Marsden Breast Cancer Prevention trial.¹² The rule is clear: long-term treatment with tamoxifen (5 years) produces a sustained beneficial effect in preventing breast cancer, whereas short-term therapy does not.

This clinical reality now presents the medical community with a paradox. Tamoxifen is a competitive inhibitor of estrogen action at the tumor ER. However, long-term adjuvant tamoxifen therapy^{1,2} must be continuous because failure of tamoxifen to block the tumor ER will result in recurrence. However, this laboratory strategy³ was not predictive for 5 years of adjuvant therapy. Patients survive without the benefit of tamoxifen blocking the ER to prevent recurrence. Herein lies the paradox. Tamoxifen is not cytotoxic, so where does the cytotoxicity of long-term tamoxifen therapy come from to protect patients after 5 years of adjuvant tamoxifen therapy?

The answer comes from laboratory research on the evolution of acquired resistance to tamoxifen.^{13,14} Investigation of ER-positive breast tumors transplanted into tamoxifen-treated ovariectomized athymic mice results in the development of acquired resistance to tamoxifen within 1 to 2 years.¹² Uniquely, breast tumors develop because of tamoxifen treatment not despite tamoxifen treatment, and tumors use tamoxifen or estrogen to maintain tumor growth.^{15,17} This biological knowledge is the scientific foundation for using an aromatase inhibitor (to prevent the postmenopausal patient from synthesizing estrogen) or fulvestrant (which destroys the tumor ER as a pure antiestrogen) as second-line therapies for MBC in which tamoxifen treatment has not worked. Antiestrogenic therapy is the strategy of choice because estrogen stimulates tamoxifen-resistant tumor growth.

Additional transplantation of ER-positive breast tumors with early acquired resistance to tamoxifen into tamoxifen-treated athymic mice for up to 5 years replicates the clinical strategy of 5 years of adjuvant therapy.¹¹ Tamoxifen-stimulated growth continues, but paradoxically physiologic estrogen has a significant antitumor effect.¹¹ Estrogen is cytotoxic, and tumors disappear completely. Yao and coworkers¹⁶ proposed 2 clinical applications: (i) physiologic estrogen to treat MBC af-

Long Term Tamoxifen Treatment For Breast Cancer

Jerome F. Strauss, Robert L. Barbieri



Long Term Tamoxifen Treatment For Breast Cancer:

Long-term Tamoxifen Treatment for Breast Cancer Virgil Craig Jordan, 1994 During the past twenty years tamoxifen has become the most widely prescribed and most successful drug used in the treatment of breast cancer In this volume editor V Craig Jordan provides articles that trace the development pharmacology and clinical research surrounding this drug which by the year 2000 could be used to treat as many as one million women annually Drawing from research conducted by specialists in the United States the United Kingdom and Italy the series of articles describes the clinical testing of tamoxifen highlighting the benefits Studies show that tamoxifen lowers cholesterol and can potentially protect women against osteoporosis and fatal coronary heart disease Equally important is a discussion of side effects and possible drug interactions and how these issues relate to patient concerns An investigation of the development of a new class of drugs for use after tamoxifen fails provides valuable insight into future treatments as the contributors consider possible resistance to tamoxifen This volume provides invaluable information for physicians and surgeons who care for patients with breast cancer and for women interested in exploring this therapeutic dimension **Tamoxifen and Breast Cancer** Michael W.

DeGregorio, Valerie J. Wiebe, 1999-01-01 A discussion of the diagnosis of breast cancer and the risks benefits and limitations of treatment alternatives particularly tamoxifen This edition contains information on developments in the use of tamoxifen especially in the results of the Breast Cancer Prevention Trial **Journal of the National Cancer Institute** ,2005

Treatment of the Postmenopausal Woman Rogerio A. Lobo, 2007-06-05 For anyone who treats postmenopausal women this latest edition of Rogerio Lobo s classic work combines the best from two well known references Menopause and the second edition of *Treatment of the Postmenopausal Woman* By adding significant discussions of the basic science behind menopause it is possible to objectively assess the clinical value and limitations of current approaches to treatment and provide a basis and rationale for strategies that will result in better individualized and specialized care Not only does the third edition discuss diagnosis and treatment of menopause but it covers biological anatomical physiological pathobiological and pharmacological aspects as well bringing together in one source all of the information needed to understand and treat postmenopausal conditions Over 50% new material representing the vast amount of information available since the Women s Health Initiative WHI clinical trials were completed making this the most up to date reference on postmenopausal women Includes several new sections on comparisons between clinical trials and observational data urology and pelvic support Each section is preceded by a preface to put the area into context with many chapters having suggested treatment regimens

Tamoxifen Tales V. Craig Jordan, 2022-01-12 *Tamoxifen Tales* Suggestions for Scientific Survival presents a case study describing the academic journey of teams behind major advances in medical sciences highlighting lessons learned that are applicable to the next generation of scientists This book provides a manual on the successful mentoring of young scientists including stories describing how training experience shaped careers to become leaders in academia and the pharmaceutical

industry The book documents Professor V Craig Jordan s 50 year career in medical sciences that led to the discovery and development of Selective Estrogen Receptor Modulators SERMs which became the standard of women s healthcare around the world Additionally it illustrates the versatility of a scientist with a commitment to serving societies This important resource will be a useful and interesting book for established medical scientists research mentors and advanced students wanting to chart a successful and impactful research career Highlights lessons learned from the journey behind discovery science that are applicable to the scientific journey of the next generation of scientists Provides a manual on the successful mentoring of young scientists to become leaders in academia and the pharmaceutical industry Examines cancer treatment based on a personal determination to challenge at the frontiers of the science and to relate to personal life experience Includes references for further research reading

Biological and Hormonal Therapies of Cancer Kenneth A. Foon, Hyman B. Muss, 1998-01-31 This volume *Biological and Hormonal Therapies of Cancer* which is part of the series *Cancer Treatment and Research* presents selected new information concerning biologic and hormonal therapy of cancer We have attempted to provide the reader with topics of major interest in a timely fashion There is renewed interest in biologic therapy of cancer Two chapters review the role of interferon in the hematologic malignancies and in solid tumors Vaccine therapies have come to the forefront of cancer therapy recently and two chapters approach different strategies of vaccine therapies one reviews the cellular vaccine therapies and another the anti idotype approach The hormonal therapy chapters focus on current uses of endocrine therapy in endometrial breast and prostate cancer In addition hormonal strategies for the prevention of breast cancer and endometrial cancer including exciting information relating to phytochemicals are presented The effects of tamoxifen on endometrium is a topic of major interest and is discussed in detail Finally there is a chapter on estrogen receptor expression and regulation in human breast cancer These chapters are all written by experts in the field and contain timely and relevant information of interest to laboratory and clinical scientists and practitioners alike Biologic and endocrine therapies represent major areas of cancer research interest The advent of newer biologic therapies including new antibody targeted treatments and the use of biologics as tumor modulators to enhance the effects of other treatment regimens is an exploding avenue of research

Drug Therapy in Nursing Diane S. Aschenbrenner, Samantha J. Venable, 2009 This text presents a totally nursing focused framework for teaching and learning nursing pharmacology and places the patient at the center of all drug administration decisions and considerations The book presents core drug knowledge using prototypes of different drug classes and emphasizes core patient variables that influence the patient s response to therapy This thoroughly updated Third Edition covers newly approved drugs has separate chapters on drugs affecting fungal and viral infections and includes more pathophysiology information FDA Black Box warnings have been added to the discussion of each prototype when applicable and safety alerts have been added to emphasize prevention of common medication errors A companion Website offers student and instructor ancillaries including NCLEX style questions pathophysiology animations medication

administration videos and dosage calculation quizzes *Cumulated Index Medicus* ,1999 *Holland-Frei Cancer Medicine* 8 James F. Holland,2010 *Holland Frei Cancer Medicine* serves as a quick reference to current information on an extensive list of cancers including breast lung thyroid colorectal ovarian prostate and gastric cancer to name but a few Presented as an accessible pocket sized handbook the chapters are organized in an outline format offering only the most essential information on the etiology staging including TNM staging and treatment for each cancer type Individual chapters are devoted to the molecular biology of cancer cancer prevention cancer screening the mechanisms of chemotherapy and diagnostic imaging in cancer Additionally each chapter lists all the major phase III clinical trials and therefore serves as an excellent reference of the major randomized controlled trials for each cancer reported to date Specific chapters are also dedicated to the discussion of oncologic emergencies pain and palliation and prescription complications At the conclusion of the book a glossary of oncologic terms and chemotherapeutic drug programs a table of common cancer incidences and an overview of the mechanisms common uses and related toxicities of various anti cancer agents are featured In addition performance status tables mathematical formulas and a listing of common biomedical cancer web sites are highlighted **Clinical Ocular Toxicology E-Book** Frederick T. Fraunfelder,Frederick W. Fraunfelder,Wiley A. Chambers,2008-06-12 Written by international authorities in ocular toxicology including the Founder of The National Registry of Drug Induced Side Effects and its current Director this essential resource provides the clinically relevant information you need to effectively diagnose and manage herbal chemical and drug related ocular problems Comprehensive coverage of all drugs generic and trade drug names primary uses ocular and systemic side effects and clinical significance make this book like its best selling predecessor *Drug Induced Ocular Side Effects* the ideal reference for quick on the spot consultation Leaders in the field provide need to know information on all aspects of ocular toxicology all in one concise reference Data from the National Registry of Drug Induced Ocular Side Effects Casey Eye Institute Portland OR and the World Health Organization Uppsala Sweden help you recognize and avoid drug induced ocular side effects A highly templated format makes retrieval of essential knowledge quick and easy A wealth of full color photographs provide vivid visual diagnostic guidance The latest information on approved medications helps you stay up to date and provide state of the art care Extensive coverage of principles of therapy ocular drug delivery methods to evaluate drug induced visual side effects and the role of electrophysiology and psychophysics gives you the knowledge you need to manage any challenge in ocular toxicology Authoritative guidance on ocular drugs and their use in pregnancy helps you safely manage the unique needs of these patients The inclusion of the WHO classification system helps you determine whether a particular side effect is certain probable or likely to occur **Meyler's Side Effects of Drugs** Jeffrey K. Aronson,2015-10-15 *Meyler s Side Effects of Drugs* The International Encyclopedia of Adverse Drug Reactions and Interactions Sixteenth Edition Seven Volume Set builds on the success of the 15 previous editions providing an extensively reorganized and expanded resource that now comprises more than 1 500 individual drug articles with the most

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Comprehensive Geriatric Oncology Lodovico Balducci,Gary H. Lyman,William B. Ershler,Martine Extermann,2004-03-01 Published in 2004 This new edition of Comprehensive Geriatric Oncology still offers an exhaustive review of the biology of cancer and aging of the epidemiologic trends in the country and in the world and of the clinical trials that concern cancer prevention and cancer treatment in the elderly

Cancer Chemotherapy and Biotherapy Bruce A. Chabner,Dan L. Longo,2011-12-07 Updated to include the newest drugs and those currently in development this Fifth Edition is a comprehensive reference on the preclinical and clinical pharmacology of anticancer agents Organized by drug class the book provides the latest information on all drugs and biological agents their mechanisms of action interactions with other agents toxicities side effects and mechanisms of resistance The authors explain the rationale for use of drugs in specific schedules and combinations and offer guidelines for dose adjustment in particular situations This edition s introduction includes timely information on general strategies for drug usage the science of drug discovery and development economic and regulatory aspects of cancer drug development and principles of pharmacokinetics Eight new chapters have been added and more than twenty have been significantly revised A companion website includes the fully searchable text and an image bank

Yen and Jaffe's Reproductive Endocrinology Jerome Frank Strauss,Robert L. Barbieri,2009-01-01 Thoroughly revised and now enhanced with color artwork this new edition offers the latest information on the diagnosis and management of reproductive endocrine disorders As an Expert Consult title it includes convenient online access to the complete text of the book along with all of the images and references linked to Medline

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Yen & Jaffe's Reproductive Endocrinology Jerome F. Strauss, III MD, PhD, Robert L. Barbieri, MD, 2013-09-13 Yen Jaffe's Reproductive Endocrinology helps you successfully diagnose and manage the spectrum of female and male reproductive system diseases from impaired fertility infertility and recurrent pregnancy loss through problems of sexual development puberty menstrual disturbances fibroids endometriosis and reproductive aging This trusted endocrinology reference book is ideal for fellows endocrinologists or as a quick reference when making daily diagnostic and therapeutic decisions It is just the resource you need to offer your patients the best possible reproductive care This new edition helps the reader to stay on top of recent developments It is a must for subspecialists in reproductive medicine and a valuable source of information in the library of any department and clinical unit involved in reproductive medicine Reviewed by Acta Obstetricia et Gynecologica Scandinavica February 2015 It is a must for subspecialists in reproductive medicine and a valuable source of information in the library of any department and clinical unit involved in reproductive medicine Reviewed by Acta Obstetricia et Gynecologica Scandinavica March 2015 Get unmatched guidance you can trust such as fresh insights into today's field and future advances through the knowledge gleaned from worldwide fertility experts in reproductive medicine Further your study of Reproductive Endocrinology with a list of suggested readings at the end of each chapter Conveniently access the fully searchable text and view all of the images online at Expert Consult Apply the latest reproductive endocrinology advances in basic and clinical science including molecular cellular and genetic concepts and grasp their relevance to pathophysiology diagnosis and therapy Maximize fertility in women and men undergoing chemotherapy and other cancer treatments and counsel patients on environmental factors affecting reproduction Stay on top of recent developments including the impact of obesity on fertility ovarian tissue banking cryopreservation pre implantation genetic diagnosis ovulation induction and risks and treatments for steroid hormone responsive cancers View basic anatomic

structures endocrine processes and cell function and dysfunction with absolute clarity through full color illustrations and new images throughout Confidently perform procedures through expanded coverage of reproductive and infertility surgery and online videos demonstrating key techniques **Speroff's Clinical Gynecologic Endocrinology and Infertility** Hugh S. Taylor,Lubna Pal,Emre Seli,2025-09-16 For more than 50 years Speroff s Clinical Gynecologic Endocrinology and Infertility has been one of the world s most widely read and respected gynecology texts with its authoritative coverage of physiology clinical endocrinology contraception and infertility The fully revised 10th Edition edited by Drs Hugh Taylor Lubna Pal and Emre Seli continues the tradition of excellence offering a complete explanation of the female endocrine system and practical guidance for evaluation and treatment of common disorders This classic text remains indispensable for students residents and clinicians working in reproductive endocrinology and infertility bringing readers up to date with recent advances that have occurred in this fast changing field **Drug Resistance in Oncology** S. Bernal,1997-08-21 This timely new reference integrates the latest clinical results and laboratory studies on the resistance of specific cancers to chemotherapeutic drugs covering drug resistance in lung breast ovary and colon cancer as well as hematological malignancies **Cardiotoxicity of Non-Cardiovascular Drugs** Giorgio Minotti,2010-03-25 Some drugs which are not aimed at treating heart disease have nevertheless been found to have profound effects on heart muscle Cardiotoxicity is one of the major forms of toxicity seen in drugs and it accounts for most drug recalls and delays experienced in regulatory approvals In recent years a number of non cardiac blockbuster drugs such as terfenadine have been withdrawn from major markets because of cardiotoxicity concerns while other drugs have either been withdrawn prior to marketing or required labelling changes that significantly restricted their use In Cardiotoxicity of Non Cardiovascular Drugs international experts describe the molecular mechanisms and clinical read outs of cardiac events induced by a broad variety of noncardiovascular drugs Particular emphasis is paid to the preclinical screening of drug cardiotoxicity Topics include metabolic targets of cardiotoxicity regulatory aspects translating molecular mechanisms into clinical trials structure activity relationships in arrhythmias by antihistamines and psychoactive drugs cardiovascular toxicity of antitumor drugs cardiovascular toxicities of non steroidal anti inflammatory drugs cardiovascular toxicities of antiretroviral therapies Cardiotoxicity of Non Cardiovascular Drugs is an essential guide to this important area of drug development It will find a place on the bookshelves of researchers regulators and students in medicinal chemistry drug development pharmacology pharmacy and cardiovascular disease

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