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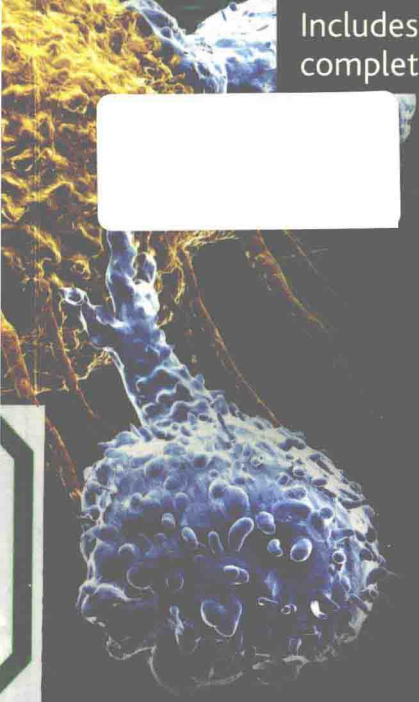

Handbook of Targeted Cancer Therapy

Daniel D. Karp
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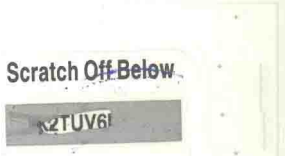

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Preface

The exponential growth of oncology drug development and personalized/targeted therapy in the recent years has presented a challenge to even the most experienced cancer researchers. Many of us struggle to keep up with the hundreds of clinical trials conducted each year. To help with this challenge, we present here a concise handbook intended to make the results of clinical trials of targeted cancer treatments more easily accessible to cancer researchers and clinicians.

As medical oncologists in a large phase I clinical trials unit at a major cancer center, we have had the privilege of observing oncology drug development from a unique perspective. We work at the intersection between exciting preclinical discoveries and the clinical realities of first-in-human clinical trials. This book was conceived with a broad audience in mind. It is our hope that this book will find use among academic oncologists, community oncologists, lab scientists, pharmacists, nurses, residents, clinical fellows, midlevel providers, postdoctoral fellows, and the numerous other staff who are essential for clinical and translational cancer research. Indeed, some motivated patients or family members may even find this book helpful in their quest to identify the most promising cancer treatments available.

We approach this book primarily from the viewpoint of clinician investigators. We have focused on agents for which clinical data are available, either published or publicly presented at a national meeting. We did not have the space in this work to mention the many clinical trials for which results were not yet available at the time these pages were sent to press, and we apologize in advance to anyone who is surprised or offended to discover that their favorite agent was not included. Furthermore, we expect that by the time this work is available for purchase, results of ongoing clinical trials will have become available and could significantly

alter various aspects of the therapeutic landscape. In recognition of this limitation, the companion electronic version of this book will be updated regularly.

Importantly, this collection is a handbook, not a textbook. Our goal was to create a publication that was small enough to comfortably fit into a lab coat pocket so that it may be easily accessible for reference in the clinic. To our knowledge, there is not another book available with the scope of this work in such a concise format. Please note that the color-coded format is designed to produce an intuitive organizational framework. For example, in the illustrations in Section 3, red is used for loss-of-function alterations and green for gain-of-function alterations. In Section 4, FDA-approved drugs are in green, whereas those in late-phase development are in orange. To conserve pages, the references have been abbreviated in the print book but appear in full form in the companion electronic book.

The book is divided into four core sections. (1) Targets by Organ Site: This section contains the "secret sauce" of our publication. Organized by tumor type and molecular target, this section provides a concise description of clinical experience with various targeted agents, in an easy-to-read table format. Each organ site includes tabular information on common molecular alterations observed and targeted therapies that have shown efficacy. (2) Carcinogenesis from the Perspective of Targeted Therapy: Although our book does not have a traditional textbook format, we include this section as a primer for cancer researchers. We have built on Hanahan and Weinberg's Hallmarks of Cancer, which we consider to be a seminal work. As clinicians, we have added our own clinical flavor to their observations. (3) Molecular Targets and Pathways: If the medication section describes the many different vehicles on the cancer-treatment highway, then this section is a map of the road each vehicle travels. The numerous cellular pathways involved in cancer survival and proliferation are arranged functionally, with emphasis on actionable molecular targets. Understanding each of these pathways gives context and rationale for modern cancer drug development. (4) Targeted Therapy Agents: We describe more than 140 drugs in this section. For the sake of conciseness, we have chosen the most immediately relevant information that most clinicians and researchers would want to

know. Mechanism of action, dosing schedule, FDA-approval and/or clinical trial investigations, and common toxicities are listed for each agent.

For historical context, we are mindful that effective systemic treatments for cancer were first introduced less than 70 years ago. In spite of the gains in recent years, there is still much need for improvement. Success in drug development is still typically measured in months, not years, of life extended. It is our hope that, in addition to its use in the clinic, this book will facilitate new discoveries that result in better treatments for our patients.

Daniel D. Karp
Gerald S. Falchook

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We would like to acknowledge and thank the many people who made this book possible. In particular, we would like to express our appreciation to the dedicated coauthors of each individual subsection. We are truly grateful for their willingness to share their knowledge and insights within the pages of this compilation. Johnique Atkins deserves unique credit for the countless hours she has devoted and the numerous responsibilities she has taken on, and we are fully convinced that this book would never have materialized without her central role. We would like to extend special recognition to Dr. Razelle Kurzrock, who has been our colleague, friend, and mentor, and who is responsible for inspiring the success of many of the coauthors who contributed to this book. In addition, Dr. Waun Ki Hong and Dr. John Mendelsohn, two internationally recognized and distinguished leaders, were the original architects of personalized cancer medicine at our institution, and their work has had a broad and deep impact on the entire cancer community. We would also like to thank many individuals who have inspired and supported us in so many ways, including Dr. Ron DePinho and the senior MD Anderson leadership, Dr. Funda Meric-Bernstam, and Kathryn Carnes; and, at Wolters Kluwer Health, Emilie Moyer, Julie Goolsby, Lisa McAllister, Marian Bellus, and our dear, recently departed colleague Jonathan Pine. We are extremely appreciative of our spouses and families, who have always been so supportive but who have been especially understanding and encouraging during this project.

Above all, we would like to thank our brave patients and their supportive families, to whom this book is dedicated.

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