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Fortunato Ciardiello is Professor of Medical Oncology and Director of Dipartimento Medico-Chirurgico di Internistica Clinica e Sperimentale, Seconda Università degli Studi di Napoli in Naples, Italy. He received his MD degree, his specialty training in Medical Oncology, and his PhD degree in Molecular Biology and Pathology from the University of Naples, Italy. Following this, he trained in cancer research for almost 5 years at the National Cancer Institute, National Institutes of Health, Bethesda, MD, USA. He received the G Venosta Award from the Italian Foundation for Cancer Research (FIRC) in November 2000 for research on novel therapeutic strategies in cancer. His research interests include the role of growth factors and their specific receptors in neoplastic transformation in addition to the development of novel therapeutic strategies targeting growth factor receptor signaling. He has published over 200 original research articles within these specific areas of interest and is an active member of several international scientific societies, including the European Society of Medical Oncology (ESMO), the American Association of Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO). He is currently member of the Executive Board and Treasurer of ESMO. He also serves on the editorial boards of *Clinical Cancer Research*, *Annals of Oncology*, *Current Cancer Therapy Reviews*, *International Journal of Oncology* and *Oncology Reports*.

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Foreword

EGFR inhibitors in cancer treatment

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Cancer cells may acquire the capacity for autonomous and dysregulated proliferation through the uncontrolled production of growth factors or through abnormal, enhanced expression of specific proteins (growth factor receptors) on the cell membranes to which growth factors selectively bind. This activates a series of intracellular signals that lead to the proliferation of cancer cells, induction of angiogenesis and metastasis. One important growth factor receptor involved in human cancer development and progression is the EGF receptor (EGFR), a cell membrane receptor with tyrosine kinase activity that plays a crucial role in the control of key cellular transduction pathways in both normal and cancer cells. EGFR is overexpressed in a variety of human tumors, including head and neck, breast, lung and colorectal cancers. Thus, it represents a relevant target for selective, molecularly targeted anticancer therapies.

The first anti-EGFR agents were developed in the 1980s. Two pharmacological approaches have been successful in inhibiting EGFR in cancer treatment: blocking monoclonal antibodies and small-molecule tyrosine kinase inhibitors. The first drugs that were developed were cetuximab, gefitinib and erlotinib that, with the addition of panitumumab, have been subsequently approved by regulatory agencies worldwide for the treatment of metastatic non-small-cell lung cancer, for colorectal cancer and for head and neck squamous cell carcinoma.

Despite the successful use of anti-EGFR therapies, approximately 10–20% of unselected patients respond to treatment, suggesting that there are several mechanisms of intrinsic or acquired resistance to this class of molecules, like somatic mutations in the *EGFR* gene, activation of downstream pathways through EGFR-independent mechanism or histologic transformation.

This has opened the research for specific biomarkers of efficacy or of resistance to be used to select patients to treat with anti-EGFR drugs for a truly personalized therapy. In this respect, two biomarkers have entered clinical practice: somatic activating EGFR mutations for selecting lung cancer patients to be treated with gefitinib or erlotinib; and somatic activating KRAS mutations to avoid treatment with cetuximab or panitumumab in colorectal cancer.

This book provides an overview of current knowledge on the use of EGFR inhibitors in cancer treatment, taking constant inspiration from the most recent advances coming from scientific literature in order to define evidence-based guidelines for the oncology community.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.