Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors: Evolving Role in the Treatment of Solid Tumors

Peggy Krozely, RN, BSN

Inhibitors of epidermal growth factor receptor tyrosine kinase (EGFR-TK) activity have shown promise as novel anticancer agents in a variety of common solid tumors. In preclinical studies and phase I trials, tumor responses to EGFR-TK inhibitors (EGFR-TKIs), such as gefitinib (Iressa®), AstraZeneca Pharmaceuticals LP, Wilmington, DE) and erlotinib (Tarceva™, OSI Pharmaceuticals, Melville, NY, and Genentech, Inc., South San Francisco, CA) were observed in heavily pretreated patients with advanced non-small cell lung cancer (NSCLC), head and neck cancer, breast cancer, colorectal cancer, and other solid tumors. Subsequent phase II studies resulted in tumor responses, disease stabilization, symptom improvement, and improved quality of life in patients with advanced NSCLC who had received prior platinum-based chemotherapy or platinum and docetaxel chemotherapies. Side effects related to treatment with EGFR-TKIs were generally mild, reversible, and noncumulative. Severity and frequency of drug-related adverse events were related directly to dose. The potential role of EGFR-TKIs in treating other solid tumors currently is being studied. Furthermore, research is being conducted to explore the potential use of EGFR-TKIs in novel combinations with chemotherapy, radiation therapy, endocrine therapy, and other molecular targeted therapies.

Key Words: carcinoma, non-small-cell lung; receptor, epidermal growth factor

Targeting Epidermal Growth Factor Receptors

EGFR-TK plays a pivotal role in the development of many of the most common solid tumors (Dy & Adjei, 2002; Prenzel, Fischer, Streit, Hart, & Ullrich, 2001; Raymond et al., 2000). EGFR, also known as ErbB1 or HER1, is present in most cell types, with the exception of hematopoietic cells. Under normal circumstances, EGFR-TK signaling is controlled strictly. In tumor cells, however, normal regulations that limit EGFR-TK enzyme activity and the subsequent transduction of growth signals are lost. A variety of tumor cell responses results from aberrantly activated EGFR-TK, including stimulation of cell growth, promotion of cell motility, alteration of adhesion and invasiveness, prolongation of cell survival, and stimulation of angiogenesis (Herbst & Shin, 2001; Raymond et al., 2000). Many of the most common solid tumors (Dy & Adjei, 2002; Prenzel, Fischer, Streit, Hart, & Ullrich, 2001; Raymond et al., 2000) demonstrate overexpression of EGFR, including stimulation of cell

Submitted August 2003. Accepted for publication October 8, 2003. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society.) Peggy Krozely, RN, BSN, has served as a consultant to AstraZeneca, manufacturer of Iressa® (gefitinib), which is mentioned in this article.

Digital Object Identifier: 10.1188/04.CJON.163-168