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Gefitinib

A Viewpoint by Lesley Seymour

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In the final decades of the 20th century considerable progress was made in identifying and understanding signal transduction pathways relevant in the development and progression of human tumours; the next step was to develop therapeutics targeting these pathways. Significant advances have been made: a number of monoclonal antibodies are approved for use in diseases such as breast cancer and haematological malignancies, and the first of the small molecule inhibitors (imatinib mesylate) has become part of the standard of care for patients with chronic myelogenous leukaemia and gastrointestinal stromal tumours.

Despite these compelling successes, the agents currently approved for use are beneficial in a relatively small number of patients (e.g. those with unusual or rare diseases or with a high expression of specific factors such as Her-2). Data are rapidly emerging regarding agents affecting one of the most common targets, the epidermal growth factor receptor (EGFR), a receptor ubiquitously expressed in many human tumours.

Gefitinib is the most advanced in development of a number of new therapeutics (including cetuximab, erlotinib) which target EGFR. Small molecule inhibitors such as gefitinib have a convenient oral administration schedule and are not associated with hypersensitivity reactions seen with the parenteral monoclonal antibody inhibitors. Development of gefitinib has been focused and rapid, and phase II data confirm antitumour and palliative effects in a subset of patients with recurrent, relapsed non-small cell lung cancer (NSCLC). Perhaps most compellingly, symptom and quality of life improvement could be demonstrated in addition to a very tolerable safety profile and a convenient oral schedule. Phase III studies of gefitinib in combination with standard chemotherapy regimens have been completed, and results from these studies are eagerly awaited.

It seems possible that gefitinib will become part of the oncologists armamentarium, given the emerging evidence of clinical benefit. A number of key questions remain to be answered, such as the impact of single agent gefitinib on survival in NSCLC, the relevance of the immunocytochemical expression of EGFR in tumours, and the optimal timing of therapy (late versus early stage disease). With the promising phase II results reported to date, excitement in both the patient and research community has led to the design and initiation of numerous trials designed to answer many of these questions, including studies in the adjuvant setting in NSCLC. ▲