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Gefitinib

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Gefitinib (ZD1839) is a novel targeted therapy that specifically inhibits the tyrosine kinase activity of the epidermal growth factor receptor (EGFR). This agent has shown potent activity in a number of tumour models, including non-small cell lung cancer (NSCLC) cell lines and xenografts. In contrast to monoclonal antibodies directed to the external epitope of the EGFR molecule, the level of EGFR expression does not seem to be directly correlated with the potency of gefitinib in preclinical models. Furthermore, gefitinib is readily absorbed orally and continuous administration is well tolerated.

NSCLC, one of the most common solid tumours, generally displays a high expression of EGFR. Recently, two large randomised phase II studies in patients with pretreated NSCLC have shown that gefitinib induces a response rate approaching 20% in patients receiving the agent as second-line therapy and approximately 10% in those pretreated with more lines of chemotherapy. In these studies it was also clear that patients who responded and several of those with stable disease had a significant improvement in disease-related symptoms.

As therapy of advanced NSCLC is mainly aimed at palliation, gefitinib appears to be a valuable addition to the present therapy armamentarium. Gefitinib should certainly be considered for patients who failed on platinum-based chemotherapy and docetaxel, as no other therapy is presently available for those patients. In second-line use, gefitinib certainly represents a significant challenge to docetaxel, in view of the far better toxicity profile, the ease of administration and possibly the higher potency. Randomised trials may be needed to properly assess differences between these two agents. Gefitinib as first-line therapy has been assessed in combination with two different chemotherapy regimens in two large randomised studies, results of which are expected shortly. Although no data are presently available, the use of gefitinib alone in first-line therapy in patients who are unfit to receive chemotherapy is not inconceivable.

In conclusion, gefitinib does appear to be a breakthrough in the treatment of advanced NSCLC. It is likely that its use will rapidly move from advanced late stage disease, to earlier and less advanced stages in the near future. ▲