Drugs 2007; 67 (14): 2109-2110
0012-6667/07/0014-2109/$49.95/0

Lapatinib

A Viewpoint by Masakazu Toi

Faculty of Medicine, Kyoto University,
Kyoto, Japan

HER2-targeted therapy has been shown to improve prognosis and quality of life in breast cancer patients. Lapatinib is a dual kinase inhibitor that inhibits both epidermal growth factor receptor and human epidermal receptor (HER) 2, and selectively suppresses cell growth of HER2-overexpressing breast cancer cells. This experimental finding has been confirmed in several clinical trials and lapatinib has been developed as a treatment option for HER2-positive tumours.

A study comparing the efficacy of capecitabine plus lapatinib with capecitabine alone in HER2-overexpressing metastatic breast cancer patients demonstrated that the addition of lapatinib significantly increased overall response rates and extended the time to progression of disease. Although the mechanism of synergistic action of the two agents has not yet been characterised, combined therapy with lapatinib and capecitabine offers a novel treatment option for patients with HER2-positive breast cancer. A number of studies assessing the efficacy of lapatinib in combination with chemotherapeutics, such as taxanes, are being conducted in the metastatic breast cancer setting. In addition, global trials evaluating the efficacy of lapatinib in primary breast cancer patients will be initiated soon, where the effect of lapatinib monotherapy and that of lapatinib plus trastuzumab combination therapy will be tested in an adjuvant setting.

Lapatinib inhibits the tyrosine kinase activity of the HER receptors resulting in the termination of the downstream signalling. Recent *in vitro* results indicate that there is significant correlation between akt signalling and the anti-proliferative activity of lapatinib, which suggests that akt phosphorylation status may be a predictor of lapatinib activity. Often in human breast cancers, in addition to the overexpression of full-length HER2, a p95 truncated form of HER2 (p95HER2) is also overexpressed. Interestingly, tumours overexpressing p95HER2 are resistant to trastuzumab but responsive to lapatinib. Furthermore, in contrast to trastuzumab, lapatinib can pass through the blood-brain barrier and may reduce the risk of brain metastases. On the other hand, trastuzumab has an advantage over lapatinib in that it may elicit immune responses such as antibody-dependent cellular cytotoxicity. These data suggest that lapatinib and trastuzumab may work complimentarily or synergistically with each other. Future studies to tailor these two anti-HER2 therapies for the treatment of HER2-positive breast cancer are warranted. ▲