METASTASIS

LANDSCAPING BRAIN
METASTASIS THERAPY

Up to 50% of patients with metastatic HER2-positive breast cancer develop brain metastases and, although several treatment options are available, these are highly toxic. For patients with multiple central nervous system (CNS) lesions, whole brain radiotherapy (WBRT) is the standard of care. Then, if disease progresses, chemotherapy is used but it has limited effectiveness. Despite the fact that these tumours are HER2-positive, the HER2 antibody trastuzumab is not very effective either, as the drug does not cross the blood–brain barrier.

As new therapeutic options are urgently needed, Thomas Bachelot and colleagues aimed to investigate a different treatment strategy. “In 2007, the EGF105084 study was presented at the ASCO meeting by Nancy Lin,” explains Bachelot, “it showed that the combination of lapatinib (a small inhibitor of HER2 thought to be able to penetrate the blood–brain barrier) and capecitabine was able to control CNS progression after WBRT in a substantial number of patients.” The authors decided that enough rationale existed to test the combination therapy before WBRT in patients with HER2-positive breast cancer and brain metastases.

LANDSCAPE was designed as a single-arm, phase II, multicentre study to assess the activity of lapatinib and capecitabine in patients with HER2-positive breast cancer and previously untreated multiple brain metastases. Out of the 44 patients assessed, 29 patients had a partial response (66%) and nine patients (20%) had a volumetric reduction of $\geq 80\%$.

Nearly half of the patients had at least one grade 3 or grade 4 adverse event, and dose reductions of lapatinib and capecitabine were necessary in 36% and 58% of patients, respectively. Despite the presence of these toxic effects, “overall survival (17 months) compares favourably with published results with WBRT. The median time to WBRT in the study population was 8.3 months; therefore this strategy could help delaying the neurological toxicity associated with WBRT” claims Bachelot.

Although further evaluation is needed, combined lapatinib and capecitabine certainly seems a valid treatment option.

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Original article Bachelot T. et al. Lapatinib plus capecitabine in patients with previously untreated brain metastases from HER2-positive metastatic breast cancer (LANDSCAPE): a single-group phase 2 study. *Lancet Oncol.* doi:10.1016/S1470-2045(12)70432-1.