

Neratinib and capecitabine for breast cancer brain metastases



The results of a recent phase 2 trial have shown that combined treatment with neratinib and capecitabine is active in patients with refractory HER2-positive breast cancer who have brain metastases.

Between April 2014, and November, 2016, Rachel Freedman (Dana Farber Cancer Institute, Boston, MA, USA) and colleagues enrolled 49 patients with HER2-positive breast cancer and measurable CNS metastases with CNS progression after CNS-directed therapy in the study; those who had not previously been treated with lapatinib were assigned to cohort 3A (n=37) and those who had were assigned to cohort 3B (n=12). Both cohorts received 240 mg oral neratinib once per day without breaks, and capecitabine at 750 mg/m² twice per day for 14 days, followed by a 7-day break. All patients received treatment until tumour progression, unacceptable

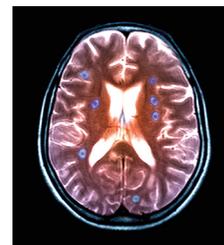
toxicity, or patient request or provider discretion. The primary endpoint was the proportion of patients achieving a CNS objective response and secondary endpoints included progression-free survival, overall survival, and toxicity.

18 (49%; 95% CI 32–66) of 37 patients in cohort 3A and four (33%; 10–65) of 12 patients in cohort 3B achieved an objective response. Median progression-free survival in cohort 3A was 5.5 months (range 0.8–18.8) and 3.1 months (0.7–14.6) in cohort 3B. Median overall survival was 13.3 months (range 2.2–27.6) in cohort 3A and 15.1 months (0.8–23.7) in cohort 3B. The most common grade 3 adverse event was diarrhoea (14 [29%] of 49 patients in both cohorts combined).

Freedman said "Brain metastasis from breast cancer is a challenging clinical problem and there are limited agents that have shown efficacy in

this setting. Combining neratinib and capecitabine for progressive brain metastases showed activity, with nearly half of patients having an objective response to therapy." Jacek Jassem (Medical University of Gdansk, Gdansk, Poland) said "This is another study showing an apparent activity of HER2 tyrosine kinase inhibitors (TKI) in combination with capecitabine in patients with HER2-positive breast cancer and brain metastases. An intriguing aspect of both studies is a spectacular effect of adding capecitabine to a HER2 TKI, given that the activity of both lapatinib and neratinib given alone is modest. This suggests that a combination of a HER2 TKI and capecitabine may be considered in lieu of whole brain radiotherapy, a development of high clinical relevance."

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