Trastuzumab treatment beyond brain progression in HER2-positive metastatic breast cancer

We read with great interest the article by Park et al. [1] in which they suggested that trastuzumab treatment after the diagnosis of brain metastasis (BM) in HER2-positive breast cancer patients has prolonged survival compared with patients who never received or completed trastuzumab before the BM. In this study, median survival after BM was 13.6 months in patients who received trastuzumab after the diagnosis of BM and was significantly improved compared with those who received trastuzumab before BM. In addition, the median time to BM from the initial diagnosis of metastatic breast cancer was significantly longer in patients who received trastuzumab before BM compared with patients in the other two groups (19.0 versus 8.0 versus 7.0 months).

Although trastuzumab therapy is associated with increased response rate and survival in patients with HER2-positive breast cancer, the majority of patients who achieve an initial response to Herceptin-based regimens generally acquire resistance within 1 year [2]. Multiple mechanisms may be responsible for Herceptin resistance. One of the possible resistance mechanisms includes loss of PTEN activity [3]. Decreased levels of the PTEN phosphatase result in increased PI3K/Akt phosphorylation and signaling and block trastuzumab-mediated growth arrest of HER2-overexpressing breast cancer cells. The second is activation of insulin-like growth factor I receptor (IGF-1R) [4]. Increased expression of IGF-1R reduces trastuzumab-mediated growth arrest of HER2-overexpressing breast cancer cells. The other possible mechanisms include down-regulation of p27, increased circulating extracellular domain of the HER2 protein and increased expression of the membrane-associated glycoprotein MUC4 [5]. But the issue whether there is any benefit to continuing trastuzumab in patients who developed metastasis under the treatment of trastuzumab is unclear.

In presented study, the findings suggest that trastuzumab in patients with HER2-positive breast cancer is an effective treatment option. We think that acquired resistance to Herceptin developed during the therapy may cause the decreased survival after BM in patients who previously received trastuzumab and we believe that the results of the study should be investigated in larger patient series.

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