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Trastuzumab in metastatic breast cancer after complete remission: an expensive commitment for an entire life?

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Metastatic breast cancer has consistently been considered an incurable disease. However, targeted treatment against the human epidermal growth factor receptor 2 (HER2) significantly improves survival in patients with metastatic HER2-positive breast cancer, and some patients can respond with prolonged complete remissions. Maintenance treatment with trastuzumab until progression of disease remains the standard after response to first-line chemotherapy and an anti-HER2 agent. The optimal duration of trastuzumab for patients achieving complete response is still a matter of debate. The most significant limiting factor for the use of trastuzumab is cardiac toxicity, although in studies of trastuzumab treatment beyond progression, cardiac events are uncommon and mostly asymptomatic[1]. In a few cases in the literature in which patients, contrary to recommendation, decided to stop anti-HER2 treatment after achieving complete response of liver metastases, the patients did not relapse[2].

In September 2003, a 36-year-old patient was referred to our unit by a nearby centre, where, 1 year earlier, she had been diagnosed with primary metastatic breast cancer (lobular) with multiple liver metastases (T4NxM1, estrogen receptor–positive, progesterone receptor–negative, Mib-1 45%, HER2-positive). She had been treated with docetaxel, epirubicin, and gemcitabine plus trastuzumab for 6 months with better than 80% remission of the liver metastases and better than 50% reduction of the right breast mass. Subsequently, she underwent quadrantectomy and adjuvant radiotherapy. After that, she also received an intrahepatic arterial infusion of floxuridine for 2 weeks. Maintenance trastuzumab was restarted after surgery. Letrozole and a luteinizing hormone–releasing hormone analog had been started in June 2003.

Immediately before being referred to us, the patient underwent computed tomography and positron-emission tomography imaging that showed the complete disappearance of her liver disease. Today, she is still taking trastuzumab and hormonal treatment (14 years since diagnosis). Computed tomography imaging still shows no evidence of disease, and no signs of cardiac toxicity are evident (left ventricular ejection fraction > 60%).

Now and then, our team has had passionate internal discussions about whether this patient should stop trastuzumab, but given that no cardiotoxicity is present and she is still strongly willing to continue the treatment, we keep going. How much of our patient's present situation (long disease-free survival) is due to trastuzumab and how much to the strong chemotherapy and hormonal therapy she has experienced?

Some authors[2] raise questions about belief in the unavoidability of recurrence of metastatic breast cancer, specifically in the liver. Those questions open up the unprecedented possibility of a cure-like state in exceptional cases. Therefore, should we, given the high cost of trastuzumab, keep a patient who might possibly already be cured on trastuzumab treatment for the rest of her life? How long is enough[3]?

Some studies identified predictive biomarkers that might provide a clue for choosing patients who will benefit most from long-term trastuzumab maintenance after a complete response to first-line combined therapy[4]. On the other hand, some other studies were unable to identify any parameters useful in predicting long-term outcome[5]. Maybe a randomized clinical trial comparing trastuzumab maintenance with follow-up alone after a complete response to first-line therapy is truly needed, although the number of patients would be small and the option of stopping trastuzumab might not be attractive to at least some patients.

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We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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