Infusion of trastuzumab maintenance doses over 30 minutes

The humanized monoclonal antibody trastuzumab is licensed for both the adjuvant treatment of early breast cancer and the palliation of metastatic breast cancer [1]. In the UK, trastuzumab is usually administered on a three weekly schedule. According to the license, it is infused over a period of 90 min and the patient is observed for 4.5 h after the loading dose, and for 30 min after all subsequent maintenance infusions. Prolonged infusion times have been justified by the risk of infusion reactions, with 54% of patients having at least one symptom with their first infusion, usually pyrexia, headache or rigors [2]. Infusion reactions are much less common with maintenance doses, particularly when premedication with steroids or antihistamines is used, and severe reactions to infusions are very rare [2, 3]. On this basis, therefore, some
UK centres routinely administer maintenance doses of trastuzumab over 30 min, and this practice has become accepted in some clinical trials where infusion times can be reduced to 30 min if patients have not had a reaction to the loading dose [4].

In the Sussex Cancer Network, we have changed our practice to give patients maintenance trastuzumab infusions over 30 min, with a prospective audit to document infusion reactions. Patients were only permitted to receive 30-min infusions if they had not had a previous infusion reaction to trastuzumab or if they had had at most a grade 1 reaction (CTCAE v3.0) and had had at least four subsequent infusions with no reactions [5]. Premedications were according to local unit protocol.

The infusion reactions were observed over a 7-month period from September 2007 to April 2008. Over the audit period, 85 patients received 201 infusions of maintenance trastuzumab over 30 min. The median age of the patients was 55 (range 28–83) years. Fifty-four women (64%) were being treated in the adjuvant setting and 31 (36%) in the palliative settings. Twenty-nine (34%) of the patients received premedication (hydrocortisone 100 mg i.v. and chlorpheniramine 10 mg i.v.) and 56 (66%) received no premedication. The median number of cycles audited per patient was two (range 1–6).

Overall, three infusion reactions were observed, representing 1.5% (3 of 201) of infusions or 3.5% (3 of 85) of patients treated. Two of the infusion reactions were grade 1 and resolved spontaneously with no intervention. The third reaction was observed in a 57-year-old woman receiving her eighth cycle of adjuvant trastuzumab with premedication steroids and antihistamines. She developed throat tightening 60 min after the infusion with blood pressure and pulse measurements in normal range. Further hydrocortisone and chlorpheniramine were administered and the episode was resolved rapidly. This episode was designated grade 3, but on review was felt to be partly anxiety related and should be interpreted with caution.

In conclusion, the majority of women can safely tolerate 30-min infusions of trastuzumab. Infusion reactions are rare and can be managed as an outpatient. This change in practice has significant implications for patient convenience and capacity on chemotherapy units.

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doi:10.1093/annonc/mdn390
Published online 6 June 2008