



Adjuvant Herceptin Therapy in HER-2 positive Early-Stage Breast Cancer

Introduction

According to the most recent data from the Centers for Disease Control and Prevention, breast cancer is the most common cancer in women in the United States, and the second leading cause of cancer deaths. Overexpression of the human epidermal growth factor receptor type 2 (HER2) which is encoded by the ERBB2 gene occurs in approximately 15 to 20% of invasive breast cancers, and is associated with a less favorable prognosis. However, targeted therapies have emerged which have markedly improved the prognosis for this subtype of breast cancer. Patients are selected for this targeted therapy based on detection of the predictive biomarker (HER2) detected by immunohistochemistry on tumor tissue, with follow up by fluorescence in situ hybridization in selected cases.

Trastuzumab (Herceptin; Genentech, South San Francisco, CA), is a monoclonal antibody that targets HER2. Several large clinical trials studying over 8,000 women with Stage II or Stage III HER2-positive breast cancers have shown that when Herceptin is given in conjunction with conventional chemotherapy, the risk of breast cancer recurrence is decreased by approximately 50%, with a significant improvement in overall survival.

The benefit of Herceptin in patients with Stage I HER2-positive breast cancer is less clear cut. This review of cases was undertaken to look at the use of adjuvant Herceptin therapy in Stage I breast cancer patients at Portsmouth Regional Hospital.

Background - Clinical Trials for Stage II and Above

Results from two important clinical trials, HERA and PHARE, confirm that a one year course of Trastuzumab (Herceptin), is clearly effective in reducing the risk of recurrence in women diagnosed with HER2-positive early-stage breast cancer.

The Herceptin Adjuvant Trial (HERA) which started in 2001 included 5,090 women with early-stage HER2-positive breast cancer. After 1 year of follow-up, the study showed that women who received Herceptin following standard adjuvant chemotherapy had a 46% lower risk of recurrence compared to those who did not receive Herceptin. The trial also looked at the potential benefit of 2 years versus 1 year of adjuvant Herceptin, and found there to be no additional benefit gained from the longer course after 8 years of follow up.

The PHARE (Protocol for Herceptin as Adjuvant Therapy with Reduced Exposure) trial randomly assigned 3,380 women to receive either 6 months or 12 months of Herceptin following standard adjuvant chemotherapy. The median follow up was 42.5 months. The study showed that a one year treatment course with Herceptin is better at reducing the risk of recurrence than 6 months of Herceptin.

Background - Stage I Patients

The benefit of Herceptin in patients with Stage I HER2-positive tumors is less compelling. However in some cases the potential benefits of the treatment are sufficiently significant to recommend.

A recent paper titled "Adjuvant Paclitaxel and Herceptin for Node-Negative, HER2-Positive Breast Cancer" (APT Trial) published on January 8, 2015 in the *New England Journal of Medicine*, also supports the efficacy of Herceptin in the treatment of early stage HER-2 positive breast cancer. In this study, women with stage 1 HER2-positive breast cancer who received a combination of Paclitaxel chemotherapy and Herceptin following surgery were highly unlikely to have the cancer recur within three years. In fact, the study found that 98.7 percent of women treated with the combination after surgery were alive and free of invasive breast cancer three years after receiving treatment .

The current National Comprehensive Cancer Network (NCCN) guidelines recommend adjuvant chemotherapy with Herceptin to be offered to patients with HER2- positive tumors measuring more than 1 cm.in diameter. For tumors less than 1 cm, the current recommendation is to just consider adjuvant chemotherapy with Herceptin.

Stage I Breast Cancer Cases at PRH, 2010-2013

The purpose of our review of cases was to look at the use of adjuvant Herceptin therapy in Stage 1 breast cancer at Portsmouth Regional Hospital. The criteria for inclusion criteria were confirmed Stage 1 HER2-positive breast cancer with a first contact year between 2010-2013. We did a retrospective review of 17 charts. Four cases were excluded. Two cases were excluded because they were HER2 negative. One case was excluded due to a tumor size less than 0.5 cm. One case, the patient transferred care to an outside hospital.

Of the remaining 13 cases in the final review, 11 of these patients were offered adjuvant therapy with Herceptin and 9 patients went on to receive therapy while the other two declined treatment. Of the two patients not recommended for Herceptin, one patient was lost to follow up and the details of therapy and disease status are unknown. The other patient was not felt to be a candidate for additional treatment due to poor performance status.

The study revealed that the majority of patients (85%) at Portsmouth Regional Hospital with Stage 1 HER2+ breast cancer are offered adjuvant treatment with Herceptin as recommended by NCCN guidelines. This number is not expected to be 100% as not all patients are

appropriate for adjuvant therapy depending on medical comorbidities, overall life expectancy and patient preference.

Treatment with Herceptin alone has no data. Typically, women who go on Herceptin are also taking chemotherapy. 69.2% of our patients actually received the recommended Herceptin in combination with chemotherapy.

Fear of side effects may be a reason some patients decline Herceptin therapy. Although in early stage (curable) HER2-positive breast cancer, Herceptin-containing regimens can improve overall survival and disease-free progression, there is increased risk of heart failure and decline in left ventricular ejection fraction.

Implementing an effective system of communication and follow up with patients and their primary care providers is important when Herceptin therapy is declined to ensure that a fully informed decision is made. Timely counseling might encourage adherence to recommended treatment.

References

Adjuvant Paclitaxel and Herceptin for Node-Negative, HER2-Positive Breast Cancer

N Engl J Med 2015; 372:134-141 [January 8, 2015](#) DOI: 10.1056/NEJMoa1406281

Uptodate

PiVot X, Romieu G, Debled M et al 6 months versus 12 months of adjuvant Herceptin for HER-2 positive early Breast cancer (PHARE) *Lancet Oncology* 2013;14:741

Goldhirsch A, Gelber RD, Piccart-Gebhart MJ et al 2 years Vs 1 year of Adjuvant trastuzumab for HER-2 positive breast cancer (HERA) *Lancet* 2013;382:1021