Florida CHAPTER

Trastuzumab

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CANCER BACKGROUND

Trastuzumab is a humanized monoclonal antibody that targets human epidermal growth factor receptor 2 (HER2). HER2 receptor kinase is overexpressed in about 15-20% of breast cancers and has dramatically improved the prognosis of women with HER2-positive breast cancer.

ADVERSE EFFECTS

In initial studies, either symptomatic heart failure or asymptomatic cardiac dysfunction developed in an alarming 27% of patients who received trastuzumab with traditional chemotherapy (doxorubicin and cyclophosphamide). In addition, trastuzumab if given with anthracyclines, is to be administered sequentially after treatment with other therapies, the presumption being that concomitant treatment would result in synergistic cardiotoxicity. Subsequent trials and clinical experience with trastuzumab showed a lower incidence of cardiomyopathy, perhaps in part owing to closer cardiac monitoring and recognition of cardiac toxicity.

In breast-cancer trials, the incidence of symptomatic heart failure in trastuzumab-treated patients was 2 to 4%, and the incidence of cardiac dysfunction was 3 to 19 percent.

Basic studies showed a critical, unexpected role for HER2 in cardiac biologic features, which suggested on-target toxicity. There was a synergistic cardio-toxicity with anthracyclines.

The major concern is treatment of Trastuzumab after Anthracyclines:

The incorporation of noninvasive cardiac monitoring into clinical practice in patients with breast cancer has allowed the recognition of subclinical cardiac dysfunction, including:

- Systolic dysfunction without heart-failure symptoms in many patients exposed to anthracyclines prior to starting trastuzumab.
- Nearly 8% of the patients in one breast-cancer trial were found to have cardiac dysfunction immediately after anthracycline therapy but before treatment with trastuzumab.
- Studies have suggested that the initiation of standard heart-failure medications was associated with at least partial recovery of cardiac function after treatment with anthracyclines.
- In the case of trastuzumab, most patients in whom cardiomyopathy developed have improvement in their symptoms or cardiac function, although approximately one third of the patients have some degree of persistent cardiac dysfunction.

RECOMMENDATIONS

All patients are required to have monitoring of cardiac function (every three months) during trastuzumab treatment. 2-D echocardiography, 3-D, and global longitudinal strain (GLS) are recommended. GLS may detect subclinical LV dysfunction before a drop in LVEF becomes evident. Use of biomarkers (troponin) may also help screening for early cardio-toxicity. Use of beta blockers and or/ACE, as cardio-protective strategies for high risk patients, is under further investigation. An important unanswered question is the long-term clinical sequelae of such subclinical cardiomyopathies. In 2016, the survivorship guidelines of the National Comprehensive Cancer Network emphasized early recognition and prevention of heart failure in patients who had received anthracyclines. They also advised that high-risk survivors should undergo a thorough clinical screening for heart failure within 1 year after completion of anthracycline therapy.

DATA TO SUPPORT

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INDICATIONS

Mainly used for HER2 positive breast cancer but recently Herceptin has been approved for gastric cancer, ovarian cancer (serous), HER2 positive colon cancer, but used much less because HER2 positivity is rare in these cancers.

ONCOLOGY COMMENTS

Oncologists recognize that the use of trastuzumab with anthracyclines can increase cardiotoxicity as defined earlier and are therefore decreasing the use of anthracyclines. With decreasing use of anthracyclines for HER2-positive breast cancer, the degree of cardiac dysfunction associated with trastuzumab is much less than that reported in earlier studies, in which all the patients were also treated with anthracycline-based chemotherapy. In a recent clinical trial involving 406 patients for early stage breast HER2 positive breast cancer who were treated with only paclitaxel and trastuzumab, clinical heart failure developed in only 2 patients (0.5%) and substantial systolic dysfunction in 13 (3.2%).