

NEOADJUVANT CHEMOTHERAPY FOR HER2+ BREAST CANCER

TRIAL SUMMARY: Promising pathologic complete response

Gupta N, Giblin E, Leagre C, et al. Pertuzumab and trastuzumab in combination with weekly paclitaxel delivers high pCR rates with favourable toxicity profile in neoadjuvant treatment of HER2-positive breast cancer. San Antonio Breast Cancer Symposium, December 6-10, 2016. Abstract P5-16-12.

This trial evaluated the efficacy and safety of a combination of pertuzumab (P) and trastuzumab (T) with weekly paclitaxel (PAC) given in a neoadjuvant fashion in HER2+ patients. The trial included women with tumour size >2 cm or lymph node (LN)-positive or inflammatory breast cancer with HER2 positivity by immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH). The treatment regimen was pertuzumab on day 1 at a loading dose of 840 mg, followed by 420 mg every 3 weeks, T on day 1 at a 8 mg/kg loading dose, followed by 6 mg/kg every 3 weeks, and PAC on days 1 and 8 at a dose of 80 mg/m². Six cycles

were given at 3-week intervals. T was continued for a total of 1 year. Adjuvant radiation and hormonal treatments were given as per the National Comprehensive Cancer Network (NCCN) guidelines. Data on pathologic complete response (pCR) rate and safety profile were collected. Left ventricular ejection fraction (LVEF) was measured at baseline and every 6 weeks during neoadjuvant treatment.

Results: A total of 31 women were treated from March 2014 to January 2016. Median age was 43 years. Two patients had T1 disease, 23 had T2, 5 had T3 and 1 patient had inflammatory breast cancer; 16 patients had LN involvement. Receptor profile was ER+/PR+ in 22 patients; ER+/PR- in 2 patients; and ER-/PR- in 7. All patients were able to complete the planned 6 cycles; 13 achieved pCR (41.9%). Five out of 7 ER-/PR- patients (71.4%) showed pCR. Grade 3/4 adverse events included neutropenia (9.6%), diarrhea (3.2%) and neuropathy (6.4%). There were no cases of febrile neutropenia, and 1 patient had an LVEF drop of more than 10% from baseline to less than 50%

IN BRIEF

Already known

- Pertuzumab and trastuzumab with chemotherapy is the standard of care for the neoadjuvant treatment of locally advanced/inflammatory HER2+ breast cancer.
- Neutropenia and diarrhea are associated with commonly-used chemotherapies.

What this study showed

- The combination of pertuzumab, trastuzumab and paclitaxel achieved pathological complete response in 41.9% of patients with fewer adverse events than seen with chemotherapy.

Next steps

- This small study (31 patients) indicates the value of exploring the possibility of this combination for patients with HER2+ breast cancer.

COMMENTARY: HER2 is overexpressed or amplified in 20% of breast carcinomas, and confers a more aggressive behaviour with poor clinical outcome. A combination of P and T with chemotherapy is the standard of care for the neoadjuvant treatment of locally advanced/inflammatory HER2+ breast cancer. Neutropenia and diarrhea are the 2 common adverse events observed with the commonly used chemotherapy regimens. This trial showed that a combination of P, T and PAC yields impressive pCR rates with minimal side effects compared to the commonly used chemotherapy regimens. This combination could be explored for the benefit of patients with HER2+ breast cancer.

References

1. Pernas S. Neoadjuvant therapy of early stage human epidermal growth factor receptor 2 positive breast cancer: latest evidence and clinical implications. *Ther Adv Med Oncol.* 2014;6(5):210-221.