

An Analysis of the Use of Neo-adjuvant Chemotherapy with Trastuzumab for Patients with HER-2 Positive Breast Cancer

Authors: Dr Ik Shin Chin, Canada Cherry, Dr Racha Kussaibati
Birmingham Heartlands Hospital, Birmingham

Introduction

- Use of anti-HER-2 therapy with chemotherapy in the neo-adjuvant setting improves the pathological complete response (pCR) rate. (1)
- pCR has been shown to be a good indicator of prognosis. (2)
- The proportion of patients achieving pCR with the addition of neo-adjuvant Trastuzumab is 22.6-65.2%. (3,4)
- Dual anti-Her-2 therapy is now recommended with neo-adjuvant chemotherapy for HER-2 positive tumours at high risk of recurrence (5)

Aims

- To determine the pCR rate in HER-2 positive patients who have received neo-adjuvant chemotherapy and Trastuzumab
- To identify tumour characteristics of the patient group
- To establish the proportion of patients who had breast conserving surgery
- To determine the percentage of patients who developed recurrence or metastases

Methods

- A list of eligible patients were collected from pharmacy records
- Data was collected retrospectively for all patients treated with neo-adjuvant chemotherapy and Trastuzumab between January 2011 and January 2016 using the hospital's electronic records.

Results

- A total of 18 patients had HER-2 positive invasive ductal carcinoma
- All patients received neo-adjuvant chemotherapy with Fluorouracil, Epirubicin and Cyclophosphamide followed by Docetaxel and Trastuzumab.
- HER-2 status was determined using immunohistochemistry (IHC) in 88.9% and Fluorescence in situ hybridisation (FISH) was done to confirm in 11.1% when the IHC score was equivocal
- One patient did not complete treatment due to idiopathic thrombocytopenia purport (ITP), subsequently did not achieve a pathological response and received adjuvant chemotherapy. No other patients received adjuvant chemotherapy.
- 16 (89%) patients had a pathological response and among them, 10 (56%) achieved pCR
- Among those who had pCR, 50% were hormonal receptor negative, 70% had grade 3 tumours and positive lymph nodes.
- 11 (61%) patients showed radiological response to treatment.
- 8 (44%) patients had breast conserving surgery and 10 (56%) underwent mastectomy
- All patients received adjuvant Trastuzumab.
- The final nodal status of the tumours post surgery as are Figure 2.
- 33% had positive lymph nodes as opposed to 72% at baseline.
- One patient had a >10% drop in left ventricular ejection fraction and Trastuzumab was suspended temporarily before rechallenging later on. This patient developed breast recurrence three years after diagnosis.
- Two patients developed metastatic disease after two and three years after their original diagnosis.
- All patients were alive at analysis.

Figure 1. Complete Pathological Response

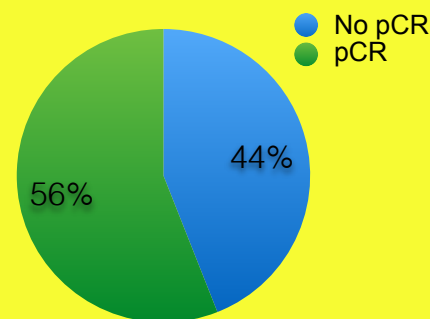


Figure 2. Final Nodal Status

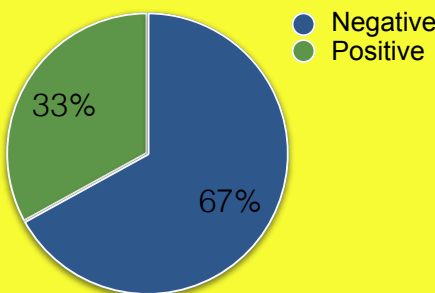


Table 1. Tumour Characteristics of Study Population

Characteristics	No. of patients (%)
Grade of tumour	
Grade 2	9 (50%)
Grade 3	9 (50%)
Hormone receptor status	
Positive	12 (67%)
Negative	6 (33%)
HER-2 status	
Positive	18 (100%)
Negative	0 (0%)
Lymph nodes status	
Positive	13 (72%)
Negative	5 (28%)

Discussion and Recommendations

- The rate of pCR to neo-adjuvant chemotherapy and Trastuzumab achieved at our unit is comparable with other studies.
- A considerable number of patient were able to achieve breast preservation as a result of their response to neo-adjuvant treatment.
- Patients with more aggressive tumours appeared to achieve a better response, however a larger sample size is needed to further strengthen this association.
- pCR rates in the NeoSphere trial are 29% for Trastuzumab plus Docetaxel and 45.8% for Pertuzumab, Trastuzumab and Docetaxel. (6)
- NCCN and ESMO guidelines now recommend using neoadjuvant Pertuzumab plus Trastuzumab in selected high risk cases with the approval of NICE and our unit have now implemented this. (5-8)

References

1. Rastogi P et al. Preoperative Chemotherapy: Updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. J Clin Oncol 26:778-785 2008
2. Wolmark N et al. Preoperative Chemotherapy in Patients with Operable Breast Cancer: Nine-Year Results From National Surgical Adjuvant Breast and Bowel Project B-18. J Natl Cancer Inst Monogr 2001;30:96-102
3. Sevcikova K et al. Neoadjuvant Treatment in Patients with HER2-positive Breast Cancer. ISRN Oncol. 2013; 2013: 362467
4. Untch M et al. Pathological complete response after neoadjuvant chemotherapy and trastuzumab treatment predicts survival and detects a patient subgroup at high need for improvement of anti-HER2 therapy. Three year median follow up data of the TECHNO trial. J Clin Oncol. 2011;29(25):3351-3357.
5. NICE TA424. Pertuzumab for the neoadjuvant treatment of HER-2 positive breast cancer 2016 [cited 10 June 16]. Available at <https://www.nice.org.uk/guidance/ta424>
6. Gianni L et al. Efficacy and safety of neoadjuvant pertuzumab and Trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. The Lancet Oncology 2012;13 (1):25-32
7. National Comprehensive Cancer Network. Breast Cancer, NCCN Evidence Blocks. Version 2. 2016
8. Senkus E et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2015;26 (5)