Response Rates to Newly Implemented Neoadjuvant TCHP Chemotherapy in the Dorset Cancer Network

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Purpose: The neoadjuvant chemotherapy regimen: docetaxel, carboplatin, trastuzumab and pertuzumab (TCHP) was first introduced to the Dorset Cancer Network (Royal Bournemouth County Hospital, Dorset County Hospital and Poole Hospital Foundation Trust) formulary in January 2017. The purpose of this audit was to assess the response to treatment and adherence to local guidelines.
Methods: All patients treated with neoadjuvant TCHP chemotherapy within the Dorset Cancer Network and who had undergone subsequent surgery with available histology results were included in this audit. Electronic notes including histology, radiology and breast multidisciplinary team reports were reviewed, together with the prescribing system, to ascertain information. Patients were excluded if they had not had surgery or had available histology at the time of the audit or were thought to have features on imaging that subsequently turned out to be metastatic disease.
Results: In total, 27 patients underwent TCHP chemotherapy with start dates from January 2017 until November 2017. 46.2% had a complete pathological response. Ductal carcinoma *in situ* was not included as residual invasive disease in keeping with other similar studies. All the patients were female with an average age of 53.4 years (30–74 years). All cancers were classified as invasive ductal carcinoma with 50% being ER-positive and 61.5% being node-positive. Tumour size varied from 10 to 90 mm. Fifty per cent of women managed six cycles at the full dose, with each cycle at the correct 3 weekly time intervals. Fifty-eight per cent of patients did not receive granulocyte colony-stimulating factor (GCSF) and of those who did, GCSF was usually started after a delay or infection.
Conclusion: The response rate seen within the Dorset Cancer Network is comparable with those from other centres and studies. A high percentage of patients required a dose reduction or delay in treatment. It is felt that GCSF should be introduced as a standard supportive medicine with the aim of maintaining dose intensity.

Adjuvant Bisphosphonates in Postmenopausal Women with Breast Cancer in Lanarkshire

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Purpose: According to EBCTCG meta-analysis, adjuvant bisphosphonates reduce the incidence of breast cancer mortality, bone recurrence and fractures [1]. The aim of our study was to review the prescribing practices of adjuvant bisphosphonate treatment in postmenopausal women with high-risk breast cancer.
Methods: Patients attending Lanarkshire oncology clinics between July and December 2017 were included in this retrospective analysis. We defined high risk as those who merited neoadjuvant or adjuvant chemotherapy from discussion at Lanarkshire Breast MDT. Data were collected on patient age, acceptance or refusal of treatment, timing in relation to radical surgery and reasons for delay in starting treatment.
Results: Among 80 patients (median age 66 years; range 46–97 years), 70 patients were offered treatment. Of these, 39 (56%) went on to receive it. Twenty-seven received oral ibandronic acid and 12 received intravenous zoledronic acid. All except one (38/39) patient received the drug in the adjuvant setting. The median duration of the interval from surgery to treatment initiation was 13 weeks (2–43 weeks). Treatment was delayed >8 weeks in 25/39 (64%). Reasons for delay were awaiting pretreatment dental assessment (13/25), awaiting completion of chemotherapy (10/25) and patient's indecision (2/25).
Thirty-one patients were offered but did not receive treatment. Among these, 27 declined and four were undecided and/or awaiting dental assessment prior to commencement.
Conclusion: Most women eligible for adjuvant bisphosphonates were offered the treatment. However, only 56% went on to receive it. Among those who received it, one-third of patients started treatment within an 8 week interval from surgery.

Reference

[1] Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials Early Breast Cancer Trialists' Collaborative Group. Lancet 2015;386(10001):1353–61.

Oncotype Dx in Node-negative Breast Cancer: Our Experience

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Purpose: This audit was conducted to review our practice for testing the gene signature, Oncotype Dx score, as per NICE guidelines, to risk stratify our breast cancer patients to choose the right advice regarding adjuvant chemotherapy. We also calculated the NHS Predict score for all of these patients. This is an online tool used conventionally to identify suitable candidates for chemotherapy. In our practice, all patients who have more than 3% improvement in survival with adjuvant chemotherapy on the NHS Predict tool are offered/recommended adjuvant chemotherapy.
Methods: Current NICE guidelines recommend Oncotype Dx testing for all chemotherapy eligible patients who undergo curative breast surgery and are node negative, hormone receptor positive and Her2neu negative. We reviewed all patients who were recommended to undergo Oncotype Dx testing between April 2016 and August 2017 for their recurrence score and subsequent adjuvant treatment. Demographic and clinicopathological features were also documented.
Results: Forty patients were identified in this cohort. All but one patient was node positive and another was found to be node mic positive. The average turnaround time for the Oncotype Dx result was 10 days, which was better than the overall UK result, as well as for central England and the London region, which was 12 days. A great majority of our patients were younger than 65 years (33 patients), whereas the rest (seven patients) were older than 65 years. Seventeen (42%) of these patients had grade 3 pathology and 22 were found to have grade 2 pathology, with only one having grade 1 pathology. Furthermore, 33 patients had a tumour dimension (T stage) <3 cm and seven had T stage measured as >3 cm. The online tool (NHS Predict) estimated that only three patients would have more than a 3% survival advantage with adjuvant chemotherapy. The Oncotype Dx recurrence score results showed that 22 patients had a recurrence score < 18 (low score), none of these patients received adjuvant chemotherapy. Ten patients had a recurrence score in the intermediate risk group (Oncotype DX recurrence score 18–30); records showed that two patients in this group received adjuvant chemotherapy. There were eight patients in the high-risk recurrence score group (>30); all of these eight patients received adjuvant chemotherapy.
Conclusion: In our experience, more patients (25% of total) were identified as suitable for adjuvant chemotherapy, as against based on the online NHS Predict estimation (7.5% showing survival advantage >3% with chemotherapy).

Real-world Factors Predicting Complete Pathological Response to Neoadjuvant Chemotherapy in Breast Cancer

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Purpose: Despite its widespread use, there is a lack of consensus as well as national guidelines as to who should be offered neoadjuvant chemotherapy (NACT) for locally advanced breast cancer. However, several factors associated with pathological complete response (pCR) have been identified in the published literature [1]. This study aims to evaluate whether these factors are predictive of pCR in the real world.
Methods: Patients undergoing NACT for breast cancer over a 2 year period from 1 January 2014 to 31 December 2015 were identified from the chemotherapy unit booking system. Data on clinical and pathological factors, including age, type and grade of tumour, oestrogen receptor and HER2 positivity, Ki67 proliferation index and final pathological response, were collected using electronic patient records, including histopathological and radiological reports.

Results: In total, 75 patients with 82 tumours were treated with NACT during the 2 year period. Of these, 31% of the tumours showed pCR. HER2 positivity ($P = 0.011$) and higher Ki67 proliferation index ($P = 0.044$) were significantly associated with pCR using Fisher's exact test and independent *t*-test, respectively. These findings were confirmed on logistic regression, which showed that the strongest predictor of pCR was HER2 positivity, with an odds ratio of 9.3 (95%CI 1.8–47.4), followed by Ki67 index (odds ratio 1.04, 95%CI 1.00–1.08, $P = 0.019$). The factors as a whole function well as a predictive model, as shown by a statically significant Omnibus Tests of Model Coefficients ($P = 0.045$).

Conclusion: Our study has shown that HER2 positivity and higher Ki67 proliferation index are predictive of pCR following NACT in locally advanced breast cancer, in keeping with previously reported findings in the published literature [1]. Although previously published studies have reported a significant association between negative oestrogen receptor status and pCR [1], this was not demonstrated in our study.

Reference

[1] Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Lancet Oncol 2018;19(1):27–39.

The Impact of the Addition of Pertuzumab to Neoadjuvant HER2 Targeting on Pathological Complete Response (pCR) Rates: Kent Oncology Centre (KOC) Experience

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Purpose: Neoadjuvant chemotherapy (NACT) with dual HER2 targeting improved pCR rates (ypT0ypN0) compared with herceptin plus chemotherapy in the TRYPHAENA and NeoSphere registration trials. Pertuzumab-containing regimens FEC-THP and TCHP were adopted at KOC following NICE approval (December 2016).

Methods: A retrospective case notes study of 126 (stage I–III) HER2-positive breast cancer patients receiving HER2-directed NACT at KOC was conducted. Single targeting treatment used FEC-TH. Dual targeting regimens were FEC-THP or TCHP. Patients were well matched for age, clinical stage and ER status.

Results: Overall, dual targeting increased pCR rates: 61% (dual) versus 29% (single). pCR rates were higher with dual targeting regardless of ER or nodal status. The highest pCR rate was seen among ER-negative patients receiving dual targeting treatment (76%). Among the 71 patients who received dual target regimens, 23 received FEC-THP and 48 TCHP. Nodal involvement was similar between the two regimens (52% versus 56% node positive, respectively). There were more ER-positive patients in the TCHP group (71% TCHP versus 35% FEC-THP). Overall, pCR rates were comparable (57% FEC-THP versus 63% TCHP). Fifty per cent of ER-positive patients achieved pCR, regardless of regimen. However, nearly all 14 ER-negative patients treated with TCHP achieved pCR (93%) compared with 60% in the FEC-THP group.

Conclusion: A substantial increase in pCR rates was observed with dual targeting, regardless of ER and nodal status, reproducing the registration trial data in real-world clinical practice. pCR rates were greatest in ER-negative patients, regardless of regimen. Ninety-three per cent of the ER-negative subset treated with TCHP achieved pCR.

Identifying and Managing the Barriers to Exercise During and Following Breast Cancer Treatment

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Purpose: Regular exercise has been shown to ameliorate many of the physical consequences of breast cancer treatment, including pain, fatigue and nausea [1]. Furthermore, a large meta-analysis demonstrated that higher physical activity was associated with reduced breast cancer-specific mortality as well as overall mortality [2]. It has been determined that only 37% of patients meet the recommended 150 min of moderate or 75 min of vigorous activity per week [3]. Given the benefits we wanted to promote regular exercise to our patients.

Methods: A qualitative survey was used to identify baseline knowledge of the evidence and to establish the barriers to exercise in a West London breast cancer clinic.

Results: Twenty-four patients were surveyed. Fifty per cent were over 50 years and two-thirds were receiving some form of treatment. All respondents indicated a desire to exercise more and the majority indicated that their exercise frequency had decreased post-diagnosis. The main barriers to exercise identified were fatigue (40%), pain (20%), difficulty accessing gyms/sports facilities (20%) and concerns about exercising while on treatment (10%). Half of those surveyed felt they lacked adequate information about exercising after being diagnosed and 60% were not aware of the health benefits in relation to breast cancer.

Conclusion: The main barriers established were a combination of perceived personal physical limitations, lack of knowledge of the benefit and lack of access to a programme. The information gained was used to promote access to existing resources and raise awareness in our clinics using verbal and written information, including a specially designed info-graphic leaflet created in collaboration with Maggie's Centre. This outlines the benefits of exercise and signposts to local support to address their personal exercise barriers and provide a suitable exercise programme. This leaflet is to be distributed to patients at diagnosis and again at entry into the Open Access Follow Up Clinic.

References

[1] Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM. Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. J Natl Cancer Inst 2012;104(11):815–40.
[2] Fong DY, Ho JW, Hui BP, Macfarlane DJ, Leung SS, Cerin E et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. Br Med J 2012;344:e70.
[3] Blanchard CM, Courneya KS, Stein K. Cancer survivors' adherence to lifestyle behavior recommendations and associations with health-related quality of life: results from the American Cancer Society's SCS-II. J Clin Oncol 2008;26:2198–220.

Pretreatment DPYD Genotyping Reduces the Risk of Capecitabine-associated Severe Toxicities: a Prospective Validation Study

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Purpose: Capecitabine is an oral fluoropyrimidine used for the treatment of metastatic breast cancer (m-BC) [1]. Its catabolism depends on the enzyme dihydropyrimidine dehydrogenase (DPD). Polymorphic variants in the DPYD gene are associated with partial or complete DPD activity and severe toxicities to fluoropyrimidine therapy [2]. Preliminary work previously carried out in our institution suggested that prospective DPYD genotyping is a cost-effective and predictive biomarker of capecitabine toxicity. The aim of this study was to validate these findings.

Methods: We reviewed medical records for consecutive patients with m-BC who underwent DPYD genotyping prior to commencing capecitabine in our institution between December 2014 and December 2017. Patients were tested for four DPYD sequence variants associated with reduced DPD activity. We collected data on patient demographics, presence of DPYD polymorphism and capecitabine-associated toxicities.

Results: Sixty-two patients underwent DPYD testing; average age 58 years (range 28–85). Five (8.4%) were found to carry DPYD genetic polymorphisms associated with reduced DPD activity. Of these, three received alternative chemotherapy, whereas two received dose-reduced capecitabine (50% of dose) without complications; one of these had the dose increased to 75% for cycle 2, resulting in grade 3 plantar-palmar