

**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 statistically 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

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#### 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

erythema (PPE) and grade 2 diarrhoea. From the 57 patients without DPD deficiency, eight (14%) experienced grade 3 toxicities, which involved PPE (50%), nausea (25%) and diarrhoea (25%). No patient required hospital admission.

**Conclusion:** Our analysis validates our previous findings and demonstrates that prospective DPYD genotyping can predict severe toxicity with capecitabine. Patients carrying a genetic variant can receive capecitabine at a reduced dose without complications. Implementing routine prospective DPYD testing in clinical practice would not only benefit patient care but also reduce admission costs.

#### References

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#### Fertility Outcomes in Breast Cancer Survivors: Experience from a Tertiary Breast Cancer Centre within South-East London

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**Purpose:** Nearly 20% of women diagnosed with breast cancer are of reproductive age. Although the importance of offering fertility preservation to these women has been emphasised in the literature [1], knowledge of their fertility intentions and consequent outcomes is sparse.

**Methods:** Between July 2011 and December 2013 we conducted a prospective questionnaire-based observational study in female cancer survivors up to 42 years of age (inclusive), who had been treated for early breast cancer at Guy's and St Thomas' NHS Foundation Trust. The questionnaire was devised by a multidisciplinary team and contained 19 questions covering different aspects of menstrual and reproductive history.

**Results:** In total, 175 women completed the questionnaire at a median time of 6 years from the time of diagnosis (range 1–21 years). Their median age at the time of diagnosis was 37 (range 24–42) years and at the time of the survey was 43 (range 30–55) years. At the time of the survey, 42% had completed their family, 41% reported they would like to have children and 4% did not wish to have children. Twenty-seven respondents had actively tried to conceive; of those, 13 had had a live birth. There were also 12 unintended pregnancies; most of these were terminated (58%), with only three live births. In women under 50 years, 74 women were not using any contraception even though they did not wish to conceive.

**Conclusion:** A significant proportion of breast cancer survivors of a reproductive age wished to conceive and of those who actively tried, 48% were successful. Interestingly, there were 12 unintended pregnancies, with a 58% termination rate. Among those who did not wish to conceive, only 33% reported using contraception. This highlights the need for healthcare professionals to provide long-term contraceptive advice to women who do not wish to conceive.

#### Reference

- [1] Waks AG, Patridge AH. Fertility preservation in patients with breast cancer: necessity, methods, and safety. *J Natl Compr Canc Netw* 2016;14(3):355–63.

#### Experience of Next-generation Somatic Mutation Testing in Advanced Breast Cancer at Guy's Cancer Centre

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**Purpose:** FoundationOne is a next-generation sequencing assay testing for genomic alternations in 315 cancer-related genes. Through funding from Guy's and St Thomas' Charity, a number of patients with refractory

metastatic breast cancer were tested in the hope of identifying potential therapeutic agents.

**Methods:** Patients with metastatic breast cancer who had FoundationOne testing were identified through the phase 1 unit and outcomes evaluated.

**Results:** Nine patients had FoundationOne testing. The median age was 42 years (range 33–50). Two were metastatic on presentation. For the remainder, the median time to distant metastasis was 3.5 years (1–16) and the median time from metastasis to FoundationOne testing was 6 years (2–8). Seven patients were ER-positive, HER2-negative, one was ER-positive, HER2-positive and the other ER-negative, HER2-negative at diagnosis. Four subsequently had the metastatic site biopsied and in no cases did receptor status change. The median number of lines of systemic treatment for metastatic disease prior to FoundationOne testing was six (one to 10). Two patients had insufficient samples for testing. For the remaining seven the median number of genomic alternations identified was four (four to seven) of which five patients had potentially actionable alterations. Common genomic alternations identified were PIK3CA ( $n = 4$ ), GATA3 ( $n = 3$ ), TP53 ( $n = 2$ ), ERBB2 (L841V, V777L in one) and MYC amplification ( $n = 2$ ). The potentially actionable genomic alternations were: PIK3CA, CCND1, MDM4, MYC, MRE11A, ERBB2. Two have started treatment: everolimus for PIK3CA alteration, herceptin for ERBB2 mutation with partial response, the remainder are being seen by or are awaiting appointments with the clinical trials team.

**Conclusion:** All five patients with actionable somatic genomic alternations had ER-positive disease with a long history of response to numerous lines of therapy, suggesting this group may be the most appropriate to perform next-generation sequencing on. The one patient with chemoresistant triple-negative breast cancer had no actionable mutations identified.

#### Introduction of Hepatitis B, Hepatitis C and HIV Screening for Patients Undergoing Chemotherapy in a District General Hospital in London: Uptake and Outcomes

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**Purpose:** Viral hepatitis can cause significant morbidity and mortality in patients receiving chemotherapy. London cancer guidelines recommend universal pretreatment screening for hepatitis B (HBV) and hepatitis C (HCV). HIV-infected patients are at higher risk of developing AIDS-defining and non-AIDS-defining cancers. HIV testing for all oncology patients has been recommended. Studies reveal up to 30% of breast cancer patients may have undiagnosed diabetes [1]. Oncology patients with diabetes have an increased risk of complications: chemotherapy toxicities, steroid-induced hyperglycaemia and sepsis.

**Methods:** We implemented screening for HBV, HCV and HIV infection for patients starting chemotherapy in September 2017. In March 2018, diabetes screening was included. Uptake was defined as those screened for HBV surface antigen and core antibody, HCV antibody, HIV antibody/p24 antigen and HbA1c. Screening guidelines were developed and data collection was repeated in April–July 2018. Between data collection, findings were presented to our oncology department with hepatology teaching.

**Results:** In total, 133 patients started chemotherapy from September to December 2017, of which 69% ( $n = 92$ ) had virology screening. Of these, 14% ( $n = 13$ ) had previous HBV infection (core positive, sAg negative), one of which was already diagnosed. One patient was diagnosed with chronic HBV infection. Patients were started on lamivudine or monitored. From April to July 2018, 94% ( $n = 102$ ) patients had virology screening; 92% ( $n = 103$ ) were screened for diabetes. Five patients had previous HBV infection. There were no new HIV diagnoses in either cohort; one patient with cleared HCV infection was detected in each cohort. Five per cent ( $n = 6$ ) were diagnosed with diabetes from screening, 15% ( $n = 17$ ) had known diabetes. Patients were referred to a diabetes specialist nurse or general practitioner. One patient was admitted with steroid-induced hyperglycaemia.

**Conclusion:** Our cohort shows a significant rate of previous hepatitis B infection at risk of reactivation, requiring monitoring throughout chemotherapy treatment, and patients with diabetes at risk of complications. Screening has improved detection and management of hepatitis and diabetes in patients undergoing immunosuppression.