Results: Fifteen patients were identified. Nine patients had ductal carcinoma, the remaining were mixed. Six had grade 3 tumours, the remaining were grade 2. Nine were ER-positive. The median tumour size was 26 mm at diagnosis. Twelve had pertuzumab and trastuzumab with FEC-T (FEC-T PH) and three with docetaxel and carboplatin (TC-PH). Six were currently receiving chemotherapy or awaiting surgery and one patient died due to coexisting morbidity. There was no cardiac toxicity. Three patients relapsed (20%). The median time between first administration of treatment and relapse was 7.5 months. Radiologically, eight patients had a partial response and five had a complete response (pCR). Eight had undergone histological review of their surgical specimens. ER-positive patients had a pCR of 75% (3), whereas ER-negative patients had a 25% (1) rate. TC-PH was more successful than FEC-T (FEC-T PH) (100 and 33.33%, respectively).
Conclusion: Pertuzumab and trastuzumab has been successfully delivered to patients and is associated with radiological and pathological responses. TC-PH seems to be more effective than FEC-T PH. Further evaluation will take place on a larger cohort.

A National Retrospective Multicentre Audit of Long-term Trastuzumab Use in Metastatic Breast Cancer: Breast Cancer Trainees Research Collaborative Group (BCTRCG)

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Purpose: Approximately 25–30% of breast cancers overexpress HER2, previously associated with higher risk of relapse and worse prognosis [1,2]. The addition of anti-HER2 targeted agents has improved the prognosis for metastatic HER2-positive patients [3]. Current NICE guidance is to continue trastuzumab until evidence of extracranial disease progression [4]; in some this may be many years. Long-term trastuzumab is not without impact on quality of life, risk of cardiotoxicity and cost. There is a clear indication for a need to gain more information on long-term trastuzumab use to inform future practice.
Methods: This project proposal was presented at the inaugural meeting of the BCTRCG in May 2018 and subsequently adopted as a BCTRCG research project. A project steering group, run by trainees with oversight by clinical clinicians, has been set up and key tasks have been allocated. A literature search has been performed and feasibility data have been collected from local trusts to estimate patient numbers.
Results: The project protocol has been written; this includes both a current practice questionnaire and a national retrospective audit, for patients who have undergone a minimum of 2 years of trastuzumab for metastatic breast cancer without disease progression. The current practice questionnaire will obtain an overview of trastuzumab prescribing practice throughout the UK and highlight variations. The audit will focus on overall and progression-free survival, evidence of cardiotoxicity, previous and current systemic anticancer treatments and indications for discontinuing trastuzumab.
Conclusion: This national retrospective audit and current practice questionnaire will provide a large quantity of data on treatment and outcomes of HER2-positive metastatic breast cancer in the UK. This will allow an in-depth analysis and a platform for future research. The audit and questionnaire will be piloted locally, with data capture on an electronic database. We aim to start national recruitment in the first half of 2019.
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Variation in the Delivery of Breast Boosts in Adjuvant Radiotherapy Across the UK

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Purpose: Breast tumour bed boosts are used as an adjunct to standard adjuvant radiotherapy for a proportion of patients (a recent RCR consensus document states this includes all patients with invasive breast cancer who are less than 50 years old, and to be considered if over 50 years with higher risk pathological features [1]). The benefits of tumour bed boosts were demonstrated in EORTC Boost, with a reduced rate of local recurrence [2]. There is no universally accepted dose and fractionation for breast boosts, and with the move towards intensity-modulated radiotherapy in some centres, simultaneous integrated boost (SIB) use may well increase pending the results of IMPORT HIGH. We set out to gain information about different practice for breast boosts across the UK.
Methods: A survey was sent to the heads of radiotherapy physics in all centres in the UK, to assess fractionation schedules of boosts and frequency of SIB versus sequential tumour bed boost. An option for free text commentary was included.
Results: In total, 23 centres replied to the survey, all of which give tumour bed boosts to high-risk patients. Two centres are using SIB, with the remainder using sequential boosts. Fractionation schedules were varied, with six different sequential fractionations used, ranging from 9 Gy/3 fractions to 16 Gy/8 fractions. Eight centres volunteered that they were in discussion or planning on implementing SIB. Both centres using SIB were giving 48 Gy to the tumour bed.
Conclusion: This survey demonstrates that practice is variable throughout the UK. The RCR consensus statement had no 100% consensus on any one fractionation [1]. A move towards SIB is occurring or being considered in a number of centres, and standardisation of fractionation may occur as a result. We recommend more work is carried out to establish clear recommendations, including indication, suggested dose and fractionation to standardise treatment, and we await IMPORT HIGH results to help guide this.
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Prevention of Everolimus-related Stomatitis: a Retrospective and Prospective Study

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Purpose: In 2017, the SWISH trial reported that prophylactic dexamethasone mouthwash was effective in preventing everolimus-associated stomatitis [1,2]. In December 2017, the Royal Marsden Hospital (RMH) breast unit changed from aspirin mucilage (AM) prophylaxis alone to AM + steroid-based mouthwash (AM+S) using betamethasone soluble tablets, due to the high cost of dexamethasone mouthwash.
Methods: Data were collected for patients receiving everolimus between August 2016 and August 2017 for the AM group and from December 2017 to May 2018 for the AM+S group. Chi-squared test was used to determine whether the rate of toxicities differed between the two groups.
Results: In total, 54 patients received AM and 23 patients received AM+S during the study period. The median starting dose of everolimus in both

groups was 5 mg. 35/54 AM patients (64.8%) developed stomatitis of any grade (CTCAE grade 1 27.8%; grade 2 20.4%; grade 3 11.1%) compared with 13/23 AM+S patients (56.5%) (CTCAE grade 1 30.4%; grade 2 17.4%; grade 3 8.6%); $P = 0.49$. There was no difference between the frequency of grade 2–3 stomatitis between the AM group (31.5%) and the AM+S group (26.1%); $P = 0.67$. Stomatitis was an early toxicity in both groups, occurring during cycle 1 in almost 70% of patients in the AM group and the AM+S group. Everolimus was discontinued due to stomatitis in 12% of patients in both groups.

Conclusion: The addition of a betamethasone mouthwash did not reduce the rate of everolimus-related stomatitis. The rate of grade 2–3 stomatitis was significantly higher in our study (26.1%) than reported in the SWISH clinical trial with the dexamethasone mouthwash (2%). This audit highlights the significant challenges that still exist with administering everolimus in the real-life clinical setting.

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A Real-world Analysis of the Treatment of HER2+ Metastatic Breast Cancer (mBC) Beyond First-line HER2-directed Therapies

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Purpose: The treatment of HER2+ mBC is clinically challenging and treatment algorithms continue to be updated based on clinical trial outcomes. Challenges to treatment sequencing include prior exposure to HER2-directed therapies, including exposure in the neoadjuvant/adjuvant setting. We interrogated our Sussex Cancer Network mBC dataset to determine real-world patterns in HER2+ disease responses.

Methods: Clinical coding was used to identify patients treated by the breast oncology team for HER2+ mBC between 2014 and 2017. Clinical notes, radiology and chemotherapy e-prescribing records were used to collect histopathological, treatment and survival data.

Results: In total, 86 patients were treated for HER2+ mBC, of which 34.8% ($n = 30$) presented with *de novo* HER2+ mBC. In the first-line setting, 79% of patients ($n = 68$) received HER2-directed therapies, of which 51% ($n = 35$) received docetaxel/trastuzumab/pertuzumab, 38% ($n = 26$) received other cytotoxic agents, i.e. paclitaxel, capecitabine, vinorelbine, and the remaining 11% ($n = 8$) received endocrine treatment in combination with HER2-targeted therapies. Patients received a median of 2.5 lines (1–8) of treatment. Sixty per cent ($n = 52$) received second-line therapies on progression, of which chemotherapy in combination with HER2-directed therapies (57.6%, $n = 30$) and endocrine-only (21%, $n = 11$) were the most commonly used treatment modalities. The median overall survival for this HER2+ patient group was 34 months. Survival analysis indicates that continuity of systemic therapy correlates with median overall survival, i.e. one line (15.5 months, $n = 31$), two to three lines (26.7 months, $n = 33$) and more than three lines (38.8 months, $n = 20$). Interestingly, a difference in median overall survival was observed between patients with *de novo* mBC (44.4 months, $n = 30$) when compared with patients previously treated for early breast cancer (19.5 months, $n = 56$), suggesting that disease recurrences following exposure to trastuzumab may be associated with poorer outcomes influenced by alternate pathways of resistance.

Conclusion: This analysis indicates that continuing beyond three lines of treatment may be beneficial to overall survival, while contributing to the argument that treatment plans for HER2+ mBC need to be individualised, factoring in the timeline of previous exposure to HER2-targeted therapies. Predictive biomarkers could play a role in predetermining resistance/response and aid in rationalising treatment plans. Our onward analysis will assess the influence of the hormone receptor status in the treatment responses of HER2+ mBC.

Prospective Observational Study in Patients with Metastatic Breast Cancer Involving the Central Nervous System (PRIMROSE)

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Purpose: Central nervous system (CNS) involvement from breast cancer is an increasing clinical problem and is associated with a poor prognosis. Incidence of CNS metastasis and response to treatment varies by breast cancer subtype and no breast cancer-specific CNS metastasis guidelines currently exist to help guide management. Treatment options include surgery, stereotactic and whole brain radiotherapy, systemic and intrathecal therapies. There is a need to understand how current treatment paradigms affect CNS metastasis outcomes across subtypes, and generate data to inform future practice guidelines.

Methods: This prospective, multicentre observational study aims to register patients diagnosed with CNS involvement secondary to breast cancer throughout the UK and will collect data relating to the primary breast cancer and extracranial metastatic disease, presentation and diagnosis of CNS metastasis and CNS-directed treatment outcomes. The primary outcome is measurement of overall survival from the time of diagnosis of CNS metastasis. Secondary outcomes include prevalence of brain metastasis by subtype and progression-free survival (local/brain relapse versus relapse at other sites) following therapy. Inclusion criteria are female or male patients with breast cancer of any subtype, with histologically or radiologically confirmed breast cancer involving the CNS or diagnosis of a paraneoplastic syndrome. This is a trainee-led study involving specialist registrars training in medical oncology, clinical oncology, pathology and neurosurgery. Study sites cover major cancer centres and peripheral centres throughout the UK. The study will be registered at individual sites according to local trust policy. Subjects will be identified via breast cancer clinical teams, acute oncology services, neuroradiologists, neurosurgical multidisciplinary teams and radiotherapy referrals. Data will be recorded and stored on a centralised data system, RedCap, in compliance with ICH-GCP. Data collection will start early 2019 and the first database lock for evaluation of number and data spread will be carried out after 8 months.

Results: N/A (study in progress).

Conclusion: N/A (study in progress).

Role of Primary Chemotherapy in Women with Biopsy-proven Lymph Node-positive Breast Cancer

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Purpose: Women with lymph node-positive early breast cancer who achieve a good response to primary chemotherapy could potentially avoid axillary node clearance (ANC) and proceed to sentinel lymph node biopsy (SLNB) [1]. This would reduce the risk of significant lymphoedema. We have previously reported response rates in the axilla following primary chemotherapy in our population [2]. We now report on 30 patients who had a marker clip inserted in the lymph node prior to primary chemotherapy. At the time of breast surgery, patients either underwent ANC or SLNB with at least three lymph nodes removed, including the marker clip, to enable accurate assessment of response.

Methods: This was a retrospective single-centre study. We examined the records of all patients, through the Guy's Breast Cancer Database and chemotherapy prescribing system, who had node-positive breast cancer, marker coil in the axilla and primary chemotherapy from October 2016 to October 2017.

Results: We identified 30 patients with lymph node-positive disease, who had primary chemotherapy. At the time of surgery, 7/30 had a pathological complete response (pCR) in the axillary lymph node. Of these, 5/7 patients