UK Interdisciplinary Breast Cancer Symposium

Abstract Book

22nd - 23rd January 2024
ICC Birmingham

Contents

Plenary Lectures

Plenary Lecture: Clinical implications of late recurrence/dormancy (Cridlan Lecture)
Dan Hayes, University of Michigan, Ann Arbor, USA

Adjuvant systemic therapy (AST) has dramatically improved outcomes for patients with newly diagnosed breast cancer, and appropriate use of tumor biomarkers (TBs) has permitted judicious application of AST, identifying those who do not need it, and those for whom specific types of AST will not work. These TBs include estrogen receptor (ER), HER2, multi-gene expression genomic assays, and germline susceptibility assays.Adjuvant endocrine therapy (ET) has arguably been the most beneficial therapy in all of oncology in regards to lives saved, given the incidence of ER positive breast cancer and the potency of the treatment. However, although the benefits of adjuvant ET for positive breast in the first five year safter diagnosis are substantial, ER positive micrometastases can remain in dormancy and re-appear as metastases years or even decades after diagnosis, even in women who have taken ET for 5 years. One of the great challenges in modern oncology is to define which patients still have microscopic metastases, which of these is likely to remain in dormancy or more importantly escape from it, and what therapeutic approaches should be taken to prevent this circumstance.These issues will be discussed in the presentation

Plenary Lecture: Enhancing the targeting of breast cancer prevention
Jack Cuzick, Queen Mary's University, London, UK

Presentation details to follow…

Plenary Lecture: Treatment of ER+ HER2- metastatic breast cancer (The Mary-Jean Mitchell Green Foundation Lecture)
Stephen Johnston, Royal Marsden Hospital, London, UK

Presentation details to follow…

Plenary Lecture: Breast and axillary surgery after neoadjuvant chemotherapy – the USA perspective
Judy Boughey, Mayo Clinic, Rochester, USA

Neoadjuvant chemotherapy (NAC) is known to decrease the extent of disease in the breast and reduce the likelihood of nodal positivity and thus can increase rates of breast conservation and decrease need for axillary node dissection and its associated morbidities.

Several prospective clinical trials have assessed the false negative rate (FNR) of SLN after NAC for patients with clinically node positive disease at presentation and demonstrated FNRs ranging from 8 to 14%. Multiple ways to decrease the FNR of axillary surgery after NAC have been identified – including use of dual tracer mapping, resection of at least 2 SLNs, placing a marker in the biopsy-proven positive node and ensuring resection of that node at surgery (targetted axillary dissection) and use of IHC to evaluate for residual disease in the SLNs. Surgeons are incorporating SLN after NAC into their clinical practice for patients with a good response to NAC. How this has been implemented and changed practice patterns in the US will be discussed.

Consideration of axillary radiation in place of axillary dissection for patients with residual positive SLNs after NAC is currently being evaluated and slowly being adopted while data is awaited from prospective trials.

Further evolution of surgical management based on response to therapy is being evaluated in terms of exploring the role of omisison of breast surgery for patients with complete imaging response and omission of axillary surgery for patients with excellent response.

Plenary Lecture: Use of Ki67 and Oncotype prior to surgery to avoid chemotherapy (ADAPT programme)
Nadia Harbeck, LMU Breast Center, Munich, Germany

In HR+ HER2- early breast cancer, the question whether chemotherapy is needed in addition to endocrine therapy (ET) is key. In patients with < 3 involved lymph nodes (LN), gene expression assays (GEA) help to estimate risk of recurrence more accurately than clinic-pathological factors. In postmenopausal patients < 3LN, prospective clinical trials (e.g. TAILOR X, RxPONDER, MINDACT) have shown that chemotherapy can safely be omitted in low-risk tumors by GEA. However, in premenopausal patients < 3LN, uncertainty remains whether different GEA cut-offs are needed or whether N+ patients derive small benefit from chemotherapy even if low-risk by GEA.

The ADAPT program builds on the pioneering work from the POETIC trialists and their prior translational research and combines GEA and short preoperative ET. Endocrine response is defined as Ki67 of < 10% (surgical specimen) after 3-4 weeks of preoperative ET. In ADAPT (n=2290), patients with < 3 LN, endocrine responsive tumors and an Oncotype DX recurrence score < 25 were able to forgo chemotherapy and had excellent 5y dDFS of about 97%, independent of menopausal status. Thus, combining endocrine response assessment and GEA results leads to more patients being safely spared chemotherapy than using GEA alone. Optimal preoperative ET with an endocrine response probability of 70-80% consists of 2-4 weeks of AI in postmenopausal and 4 weeks of GnRH +AI in premenopausal patients. ADAPTcycle (n=1670 randomized) is evaluating whether chemotherapy can be replaced by CDK 4/6i + ET in intermediate risk patients according to GEA and endocrine response assessment.

Plenary Lecture: Pregnancy after breast cancer diagnosis
Olivia Pagani, International Breast Cancer Study Group (IBCSG), Faculty of Medicine University of Geneva & Faculty of Medicine University of Lugano, Switzerland

About 20% of women with breast cancer are diagnosed in their reproductive years and for many of these women, fertility and pregnancy are priority concerns. In western countries, many women get breast cancer before even having thought of their family planning: they are maybe aged 30 to 35 with no children and then breast cancer enters their life and their pregnancy desire can be blown up because they fear there is no time left.

In addition, most young women with early breast cancer have an estrogen receptor-positive disease and receive adjuvant endocrine treatment which may be prescribed for 5-10 years, preventing conception while on treatment.

The recently published results of the POSITIVE study showed that young women with early, low risk, breast cancer who paused their endocrine treatment to try to get pregnant were able to do so safely. The rates of breast cancer relapse were like in women who did not interrupt their treatment, and most were able to conceive and deliver healthy babies.

In addition, with a total of 365 babies born in the study, the rates of conception and childbirth were like or higher than rates in the general population.

Discussion on pregnancy desire and fertility preservation should therefore become part of the routine care of young patients with early disease.

Review of the year

Basic science/translational
Rob Clarke, University of Manchester, Manchester, UK

The review will cover several outstanding advances in basic and translational breast cancer research in 2023. Important advances in our understanding of the evolutionary histories of mutated cell clones in normal, precancerous and cancer tissues will be described. Multiomic investigation of a large cohort comparing primary and multiple metastatic breast tumours from the same patients will be presented. The bone colonization of cancer cells occurs in an environment that undergoes constant remodeling and a new study will be reviewed that provides mechanistic insights into how bone homeostasis and pathologic repair lead to the outgrowth of disseminated cancer cells. Finally, the immune landscape in invasive and lobular breast cancer have been compared and reveal differences in the macrophage populations that drive divergent microenvironments in ER+ breast cancer offering potential for novel immune therapies.

Update on the key developments in early breast cancer treatment in 2023
Cliona Kirwan, Wythenshaw Hospital, Manchester, UK

Updating on 4-5 of the most important developments in early breast cancer treatment in 2022, including systemic therapy, surgery andradiotherapy

Metastatic breast cancer
Iain MacPherson, University of Glasgow, Glasgow, UK

Presentation details to follow…

Session 1.1 - Tailoring surgery in early breast cancer

Mastectomy versus breast conservation plus radiotherapy
Jana de Boniface, Karolinska Institute/ Capio St. Göran's Hospital, Stockholm, Sweden

Randomised trials from the 1970s and 1980s have shown the oncological equivalence of breast-conserving surgery followed by whole-breast radiotherapy and simple mastectomy without radiotherapy. Large population-based data from a modern treatment era have however pointed out a survival benefit for those women with early breast cancer who undergo breast conservation. While epidemiological data have their inherent drawbacks in comparison with randomised trials, such findings have been repeatedly reported. Here, we will discuss one of the largest national populations yet studied and take into account socioeconomic aspects, surgical complication rates and pay special attention to specific age groups.

Surgery for multi-focal disease
Judy Boughey, Mayo Clinic, USA

Presentation details to follow…

Optimising oncoplastic breast surgery
Shelley Potter, Bristol Medical School, Bristol, UK

Oncoplastic breast conserving surgery (OPBCS) describes a range of procedures that combine excision of the breast cancer with plastic surgical techniques to reconstruct or reshape the breast. These procedures extend the boundaries of standard breast conservation by allowing larger volumes of tissue to be safely removed while achieving satisfactory cosmetic outcomes. Effective use of OPBCS may allow women to avoid the need for mastectomy with or without immediate breast reconstruction. This talk will present the current evidence for why we should optimise the use of OPBCS to benefit women with breast cancer and outline some of the multidisciplinary strategies by which this may be achieved.

Session 1.2 - Tumour cell dormancy

Modelling dormancy
Marco Montagner, University of Padua, Padua, Italy

How can we study disseminate cancer cells that we cannot even detect in patients? Disseminated dormant metastatic cells lie far below the radar of current diagnostic tools for many years and due to the asymptomatic nature of this invisible phase, isolation, and analysis of disseminated dormant cancer cells from clinically disease-free patients is ethically and technically unfeasible, except for the bone marrow. According to the available data, delayed metastasis is a combination of cell-intrinsic factors, such as the cancer subtype, and crosstalk between the cancer cell and the metastatic niche. For this reason, many laboratories developed in vitro models of the metastatic niche for different organs and different types of cancers, including breast cancer. Over the last decade, in parallel with the development of microfluidics and biofabrication, several in vitro models allowed to explore the contribution of different components of the metastatic niche, such as organ-specific cellular populations as well as physical (stiffness, 3D architecture) and biochemical (oxygenation, ECM composition and growth factors availability) cues. Together with microenvironmental factors, new cellular systems, transgenic mice, and biomarkers have been developed and characterized. Recently, we have developed a lung organotypic system that allowed us to identify new microenvironmental factors contributing to dormancy of disseminated breast cancer cells.

Regulation of dormancy by natural killer cells
Mohammed Bentires-Alj, University Hospital, Basel, Switzerland

Each year over 2.6 million new cases of breast cancer occur among women worldwide and 650,000 women die from this disease. In most cases, metastasis is the cause of death. Indeed, while 98% of patients survive 5 years or more after being diagnosed with a localized (confined to the primary site) breast cancer, this number drops to 15-25% if the cancer has metastasized to distant organs. Curing metastatic breast cancer clearly represents an unmet medical need.

Although progress has been made in broadly understanding breast tumor biology and progression to metastases, most of the relevant molecules and pathways remain undefined. The thread connecting the research in my lab is tumor heterogeneity. We assess mechanisms that influence normal and neoplastic breast stem cells, metastasis, and resistance to targeted therapies at the molecular, cellular, and whole organism levels considering both cell autonomous and noncell autonomous mechanisms. We have also developed a personalized breast cancer treatment program. Results of experiments using mouse models (e.g., transgenic mice, xenografts, patients-derived xenografts (PDX)), patient samples, and a variety of OMICs, cell biological and biochemical assays will presented.

The microenvironment regulates escape from dormancy
Clare Isacke, Institute of Cancer Research, London, UK

Patients with oestrogen receptor-positive (ER+) breast cancer are at risk of metastatic relapse for decades after primary tumour resection and treatment, a consequence of dormant disseminated tumour cells (DTCs) reawakening at secondary sites. We have used syngeneic ER+ mouse models in which DTCs display a dormant phenotype in young mice but accelerated metastatic outgrowth in an aged or fibrotic microenvironment. In young mice, low-level Pdgfc expression by ER+ DTCs is required for their maintenance in secondary sites but insufficient to support development of macrometastases. By contrast, the PDGF-CHigh environment of ageing or fibrotic lungs promotes DTC proliferation and further stromal activation. I will discuss our studies aimed at blocking DTC outgrowth using pharmacological inhibition and antibody-drug conjugates.

Session 1.3 - Targeting HER2 in metastatic breast cancer

HER2 +ve metastatic breast cancer: past, present and future
David Cameron, University of Edinburgh, Edinburgh, UK

Presentation details to follow…

Biological heterogeneity of HER2 +ve metastatic breast cancer: clinical implications
Maggie Cheang, Institute of Cancer Research, London, UK

Presentation details to follow…

What is HER2 low and what are the clinical implications?
Abeer Shaaban, Queen Elizabeth Hospital Birmingham and University of Birmingham, Birmingham, UK

Her2-low breast cancer refers to HER2 immunohistochemistry score of 1+ or 2+, ISH negative; currently classified as HER2 negative. The Destiny Breast-04 trial showed doubling of progression free survival using antibody drug conjugates (T-DXd) in patients with metastatic breast cancer with low levels of HER2 expression. The talk will review the definition, reliability of pathological categorisation, evolution of expression, choice of tumour samples to test and the prognosis of HER2-low breast cancer. Relevant guidelines including ASCO/CAP, ESMO Expert Consensus, RCPath and NICE guidance together with future directions will be discussed.

Session 1.4 - Living with and beyond breast cancer

Fear of cancer recurrence and progression: Early recognition, support and validation
Susanne Cruickshank, Royal Marsden Hospital, London, UK

Presentation details to follow…

Sexual Intimacy and breast cancer
Isabel White, Perci Health Ltd, London, UK

This session outlines the impact of sexual consequences of breast cancer and its treatment on people living with breast cancer in the UK today, 70% of whom are estimated to experience treatment-related sexual concerns. A 2019 UK survey of people with breast cancer and health care professionals (HCPs) found that most respondents had not had any discussion with HCPs about the potential impact of breast cancer treatment on their sexual lives either prior to (85%) or following (82%) the start of treatment.

This concurred with HCP findings, where only 22% of HCPs had routinely asked women about treatment-related sexual issues. 44% of women surveyed were offered no help with sexual concerns, despite 61% stating that a discussion with their specialist nurse would have been helpful. The main reasons given by HCPs for lack of discussion were limited clinic time, no local referral route, other clinical priorities, and a lack of knowledge.

We will discuss HCP and patient communication strategies to open sensitive conversations, without which the impact and range of difficulties remains hidden, and support needs unmet.

We will also touch on the development of digital innovations and self-management strategies that can enhance vaginal health and introduce behavioural strategies towards a graduated resumption of sexual intimacy.

Our aim is to highlight how the implementation of practice developments at both the individual and service delivery level can make a difference to the potential availability and quality of psychoeducation and specialist support needed to improve this important aspect of supportive cancer care.

The psychological and psychiatric sequelae of breast cancer
Asanga Fernando, St George's Hospital, London, UK

Presentation details to follow…

Session 2.1 - Genetic testing and optimising patient care

Optimising clinical and cost utility from genetic testing for breast cancer susceptibility
Clare Turnbull, Institute of Cancer Research, London, UK

I shall present new data on the frequency, cancer risks and clinical utility of testing for different breast cancer susceptibility genes. In this context, I shall consider how we might best utilise resource available for genetic testing to deliver maximal impact and minimal harms in regard of improving survival from interventions for cancer prevention and early detection.

The role of polygenic risk scores in preventing breast cancer
Gareth Evans, Manchester University NHS Foundation Trust, Manchester, UK

Polygenic Risk Scores (PRS) are a major component of accurate breast cancer risk prediction and have the potential to improve screening and prevention strategies. PRS combine the risk from Single nucleotide polymorphisms (SNPs) associated with breast cancer in Genome Wide Association Studies (GWAS) and explain over 30% of breast cancer heritability and currently more than that of known moderate and high risk genes such as BRCA1/2. When incorporated into risk models, the more personalised risk assessment derived from PRS, help identify women at higher risk of breast cancer development and enables the implementation of stratified screening and prevention approaches. We have examined the role of PRS within more well-established risk prediction models which incorporate known classic risk factors and I will discuss the interaction of PRS with these factors and their capacity to predict breast cancer subtypes. Before PRS can be implemented on a population-wide scale, there are several challenges that must be addressed. Perhaps the most pressing of these is the use of PRS in women of non-White European origin, where PRS have been shown to have attenuated risk prediction both in discrimination and calibration. I will discuss progress in developing and applying PRS in non-white European populations. PRS represent a significant advance in breast cancer risk prediction and their further development will undoubtedly enhance personalisation. For instance in BC-PREDICT study 77% of women identified as high risk who accessed a risk appointment went on to take preventive medication.

Supporting patient decision making
Claire Foster, University of Southampton, Southampton, UK

The focus of this talk is on supporting patient decision making. Information surrounding genetic risk and its implications is complex, changeable and has implications for the person undergoing genetic testing and those around them. Decisions regarding whether or not to have a genetic test and what to do with the information are highly personal. Such decisions have immediate and longer term consequences. For example, in terms of risk management decisions, who to tell and how to tell others. This talk will consider the complexity of decision making and ways in which people can be supported to take time to make decisions.

Session 2.2 - Can we move from risk-adapted to personalised breast radiotherapy?

Selecting radiotherapy for DCIS: clinico-pathological data or genomic assays?
Elinor Sawyer, Guy's and St Thomas NHS Foundation Trust & King's College London, London, UK

Presentation details to follow…

Partial breast radiotherapy for women with early breast cancer: 10-year outcomes from IMPORT LOW
Anna Kirby, The Royal Marsden Hospital NHS Foundation Trust and Institute of Cancer Research, London, UK

Presentation details to follow…

Genomic analysis of local recurrences following risk adapted breast radiotherapy in the IMPORT trials defines 'true recurrences' and 'new primaries'
Sara Lightowlers, University of Cambridge, Cambridge, UK

Presentation details to follow…

Session 2.3 - Health inequalities and ethnicity and effect on breast cancer outcomes?

Associations of ethnicity and breast cancer
Toral Gathani, University of Oxford, Oxford, UK

Presentation details to follow…

The health consequences of racism and xenophobia
Delan Devakumar, University College London, London, UK

Presentation details to follow…

Diversity and genetic ancestry effects in the cancer cohort of the UK 100,000 Genomes Project
Matt Silver, Genomics England, London, UK

The 100,000 Genomes Project was launched in 2013 by Genomics England in close partnership with the NHS. It aimed to study the potential benefits of whole genome sequencing for patients with cancer and rare diseases and to provide a resource for researchers. As part of an ongoing initiative to improve health equity in personalised patient care in England, we are reviewing the 100,000 Genomes Project for potential biases between groups with different ancestries.

The talk will provide results from our preliminary analysis of the impact of genetically-inferred ancestry on the prioritization of germline and somatic genetic variants in the cancer bioinformatics pipeline.

Session 3.1 - Personalised breast cancer screening: hype or hope?

Adapting imaging to risk and breast density – time to change
Fiona Gilbert, University of Cambridge, Cambridge, UK

Currently population screening is designed to offer mammography to women every two or three years irrespective of their risk of developing breast cancer, unless they are suspected or known to have genetic predisposition or a strong family history. For those without a genetic predisposition age is still the greatest risk but family history can play a big role as well as breast density. This information can be used to create a risk profile and a more targeted imaging strategy implemented. This is being explored in the WISDOM and MyPEBS trials where frequency of mammography is being varied according to risk.

Breast density can hide breast cancers and result in later stage or interval cancers being diagnosed with a worse prognosis. Breast density also poses an increased risk of developing cancer. BIRADS C & D densities are present in up to 40% of the population and this group have the highest rate of interval cancers. Supplemental imaging is advocated for these women with Whole breast ultrasound (ABUS), contrast mammography and MRI recommended for increased cancer detection. The UK BRAID trial (Breast Screening Risk Adapted Imaging for Density) is a randomized controlled trial comparing comparing each of these to standard 2D mammography. The size, type and grade of additional cancers that are found as well as interval cancer rates are being used to estimate the benefits of introducing supplemental imaging to breast screening. Other trials examining adapting imaging will be examined.

CanRisk: personalising breast cancer risk prediction for prevention and early detection
Antonis Antoniou, University of Cambridge, Cambridge, UK

Much more reliable and powerful breast cancer risk prediction can be achieved by combining data on all known genetic, lifestyle and hormonal risk factors for the disease. We have recently enabled multifactorial breast cancer risk-assessment through the BOADICEA model. This has been implemented in the CanRisk tool (www.canrisk.org) which allows healthcare professionals to obtain personalised cancer risks easily. The presentation will review the latest progress in BOADICEA/CanRisk development, the challenges in combining the effects of rare pathogenic variants in known susceptibility genes, polygenic risk scores, questionnaire-based risk factors, mammographic density, ethnicity and family history into multifactorial cancer risk prediction algorithms; and will review the efforts to assess the clinical validity of the predicted risks in large independent studies. The presentation will finally discuss ongoing efforts for the implementation of multifactorial cancer risk assessment in routine clinical practice for enabling cancer risk stratification and the better targeting of early detection and prevention approaches to those most likely to benefit.

Acceptability and impact of personalised breast screening for women invited and healthcare professionals
David French, University of Manchester, Manchester, UK

It is possible to accurately estimate breast cancer risk for women of screening age, and thereby provide tailored screening and prevention offers according to risk estimates. I will present a series of linked studies from a NIHR-funded programme that concerned the feasibility of incorporating this into the NHS Breast Screening Programme.

In 2019-2021, risk stratification via the BC-Predict system was offered by three screening services to 19,464 women in North West England, of whom 14,661 attended screening (60.7%). Only 2,429 women (12.5%) who were eligible took up the offer of BC-Predict. This figure was lower than expected, probably due to the effects of the COVID-19 pandemic. When personally approached, 137/263 (52.0%) of women took up this offer.

A nested questionnaire study found no changes in general anxiety or cancer-related worry for women offered BC-Predict. Thematic analyses of qualitative interviews revealed women were positive about BC-Predict, with only transient increases in worry reported by women who were at high risk. Interviews with healthcare professionals that had been involved with the implementation found that they were generally enthusiastic, with their concerns elicited before implementation not materializing.

An agenda-setting meeting with 74 clinicians, researchers and those with national policy decision-making or implementation roles identified a consensual view that risk-stratified screening is likely to happen eventually. Two major trials are underway (MyPeBS and WISDOM) to examine effectiveness of risk-stratified screening at

preventing later-stage (2+) breast cancers, which should report by 2026. It is now timely to develop plans to prepare for risk stratified screening.

Session 3.2 - Genomic assays in ER+ HER2- early breast cancer

Do genomic assays add information to conventional markers in early breast cancer
Oscar Rueda, University of Cambridge, Cambridge, UK

Treatment approaches for breast cancer are diverse and varied. Clinicians must balance risks and benefits when deciding treatments, and models have been developed to support this decision-making. Genomic risk scores (GRSs) may offer greater clinical value than standard clinicopathological models, but there is limited evidence as to whether these models perform better than the current clinical standard of care. We evaluate the utility of several genomic risk scores to predict 10-year survival in breast cancer patients using an independent dataset (METABRIC). We compare their performance to the well-established tool PREDICT in terms of discrimination, calibration and reclassification. We propose the incorporation of well-established clinical biomarkers into the design and development of genomic prognostic models and discuss two examples, one for predicting risk of relapse and another for prediction of response to neoadjuvant treatment.

Genomic assays for node positive disease, are they ready for routine care
Dan Hayes, University of Michigan, Ann Arbor, USA

Presentation details to follow…

Breast Cancer Index for late relapse and extended adjuvant endocrine therapy
Dan Rea, University of Birmingham, Birmingham, UK

Presentation details to follow…

Session 3.3 - UK Clinical Trials showcase

Mammographic surveillance in early breast cancer patients aged 50 years or over: results of the Mammo-50 non-inferiority trial of annual versus less frequent mammography
Andy Evans, Royal Derby Hospitals, Derby, UK

Presentation details to follow…

Surgical margins in breast conserving surgery (BCS) for ductal carcinoma in-situ (DCIS) and clinical outcomes: significant associations with increased recurrence and overall survival
John Robertson, University of Nottingham, Nottingham, UK

Presentation details to follow…

Trials in Progress updates:
HER2-RADiCAL
Iain Macpherson, University of Glasgow, Glasgow, UK

ATNEC
Amit Goyal, Royal Derby Hospitals, Derby, UK

EndoNET
Ramsey Cutress, University of Southampton, Southampton, UK

SMALL
Speaker TBC

PHOENIX
Speaker TBC

POETIC-A
Stephen Johnston, Royal Marsden Hospital, London, UK

Embedding routine data for enhanced evidence generation from cancer clinical trials
Peter Hall, University of Edinburgh, Edinburgh, UK

Presentation details to follow…

Session 4.1 - Locoregional aspects of neoadjuvant therapy

Optimising breast surgery after neoadjuvant therapy
Walter Weber, University Hospital Basel, Basel, Switzerland

Walter Weber will present data from the OPBC-OMA (TAD vs SLN for ypN0) and OPBC-ICARO studies (role of ALND in residual ITCs) that have been / will be presented at San Antonio in 22/23. He will also show some St Gallen 2023 voting on +/- ALND for residual nodal disease and TAXIS subproject results. The remaining time of his talk he will stress the point that breast surgery should be driven by response to neoadjuvant therapy.

Tailoring breast and axillary radiotherapy after neoadjuvant therapy
Charlotte Coles, University of Cambridge, Cambridge, UK

This presentation will address the current challenges and uncertainties in radiotherapy breast and axillary management after neo-adjuvant therapy. The published literature will be reviewed and presented, along with examples of consensus guidance. On-going research trials investigating this topic will be summarised.

Role of radiologists in planning loco-regional therapy after neoadjuvant therapy
Nisha Sharma, Leeds Teaching Hospital NHS Trust, Leeds, UK

Presentation details to follow…

Session 4.2 - Lifestyle and breast cancer

Considerations for designing a clinical trial to test a physical activity intervention in women with advanced breast cancer
Sam Smith, University of Leeds, Leeds, UK

Treatment advances in metastatic breast cancer (MBC) have improved survival across all disease sub-types. While this is good news for patients, it means there is a growing population of women who are living for longer with treatment-related side-effects. Physical activity (PA) could support symptom management, improve functional Quality of Life (fQOL) and extend survival in women with MBC. This talk will describe the considerations for studying physical activity in women with MBC, including a review of existing and ongoing trials, and patient and public involvement activities we have undertaken as part of a prospective programme of work with this population. An additional focus of this talk will be on the use of a novel methodological approach involving highly efficient complex factorial clinical trial designs to optimise multi-component interventions prior to definitive evaluation. It will describe the justification for this approach in the context of MBC, considerations for their design and delivery, and the added value of such an approach for patients, healthcare professionals and research scientists.

The case for exercise interventions in breast cancer patients
Anne May, University Medical Center Utrecht, Utrecht, The Netherlands

The evidence that exercise has positive effects on clinical and patients-reported outcomes of patients with breast cancer is increasing. More and more studies are appearing reporting positive results, e.g., regarding beneficial effects on cancer-related fatigue. This has led to recent publications of several international guidelines initiated by, for example, ASCO that all recommend being physically active during and after cancer treatment.
During the presentation, the guideline recommendations will be discussed. Also, results of several studies including patients with breast cancer; in the adjuvant and metastatic setting, will be presented. Finally, implications for exercise implementation in clinical practice will be given.

Preventing & Managing Breast Cancer with Weight Control–Opportunities & Challenges
Michelle Harvie, University of Manchester, Manchester, UK

Presentation details to follow…

Session 4.3 - Supporting health care professionals in the NHS

Why do healthcare professionals need support, and why is it important?
Sally Kum, Breast Cancer Now, London, UK

Presentation details to follow…

The power of collaboration – how patients can support their healthcare professionals
Karen Gannon, Patient advocate

Presentation details to follow…

Help is out there – how changing ways of working can alleviate pressure
3x case studies from:
Jo Beaumont, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
Caroline Leek, Fruitfly Collective, London, UK
Michaela Rossman, Breast Cancer Now, London, UK

Fruitfly Collective
A brief overview of the aims of Fruit Fly Collective, and why it was set up. Bringing evidence from children affected by parental cancer, parents diagnosed with cancer, and cancer healthcare professionals, to illustrate the importance of our work.

We will highlight the main areas of impact we have measured from the Parenting with Cancer project launched in 2023, providing examples of practical support we offer to both families and healthcare professionals, and an insight on ways our services can become embedded in the NHS.

How to take care of yourself
Jayne Ellis, EF Training

Presentation details to follow…

Chairs' discussion/summing up, followed by Q&A
Claire Ryan, Maidstone and Tunbridge Wells NHS Trust, Kent, UK
Sally Kum, Breast Cancer Now, London, UK

Presentation details to follow…

Session 5.1 - Lessons and opportunities from presurgical studies

Challenges for the surgeon from window of opportunity studies – lessons from the POETIC and POETIC A studies
John Robertson, University of Nottingham and University Hospitals of Derby & Burton, Derby, UK

Presentation details to follow…

Molecular and clinical lessons from the POETIC study
Mitch Dowsett, Royal Marsden Hospital, London, UK

Presentation details to follow…

Presurgical studies for guiding breast cancer risk reduction (or prevention)
Andrea DeCensi, Galliera Hospital, Genova, Italy

Presentation details to follow…

Session 5.2 - Triple negative metastatic breast cancer

Identifying and targeting DNA repair deficient forms of metastatic TNBC beyond PARPi in patients with gBRCA 1/2m and in non-gBRCA 1/2m breast cancer
Andrew Tutt, Institute of Cancer Research & King's College London, London, UK

Presentation details to follow…

Androgen associated triple negative metastatic breast cancer and effectiveness of targeting it
Hervé Bonnefoi, University of Bordeaux, Bordeaux, France, Bordeaux, France

Presentation details to follow…

'How to best improve first line metastatic TNBC therapy - What can we learn from the tumour microenvironment in those who have significant residual disease despite NACT + Pembro
Sheeba Irshad, King's College London, London, UK

Presentation details to follow…

Session 5.3 - Early Breast Cancer Trialists' Collaborative Group update

Forty years of the Early Breast Cancer Trialists' Collaborative Group

Robert Hills, University of Oxford, Oxford, UK

The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) was conceived in 1983, and based at the University of Oxford's Clinical Trial Service Unit. For forty years it has periodically sought up-to-date data on each individual woman in randomised trials of treatments for early breast cancer for meta-analysis, initially every five years, and more recently on a question-by-question basis. This worldwide collaboration involves over 1000 trialists from about 650 trials, giving a database of some two-thirds of a million women and 5.5 million woman-years of follow-up. It has demonstrated many moderate but real differences in long-term survival that were not reliably identified in the separate trials. Through a series of step-by-step improvements in local and systemic treatments, each producing only moderate mortality reductions, UK breast cancer mortality rates in middle age have more than halved since the 1980s.

Reliable assessment of the magnitudes of the benefits and risks of the various treatment options for early breast cancer is crucial to informed decision making. Estimates of the effects of treatment based on individual studies or, worse, observational data are often misleading, no matter what precautions are taken. Meta-analyses of individual patient data from all relevant randomised clinical trials provide the most reliable evidence on particular therapeutic questions. By looking at the totality of the randomised evidence, meta-analyses avoid the systematic errors that commonly arise in narrative reviews through selective citation of striking results, and provides the most precise estimates of treatment effects by including larger numbers of patients and events. This talk will discuss the history and methodology of EBCTCG, the contributions it has made to improving outcomes, and look forward to its fifth decade.

Importance and limitations of meta-analysis

David Dodwell, University of Oxford, Oxford, UK

Individual patient level meta-analysis, as conducted by EBCTCG, is generally recognised to provide the highest level of evidence to identify and quantify treatment effects. It is of particular value when treatment effects are small or modest in size as is the case for most treatments in early breast cancer.
EBCTCG meta-analyses rely on a number of attributes to provide this evidence. These include-

- Inclusivity – Attempts to obtain all randomised data, whether published or not, by ongoing systematic searching for relevant trials and EBCTCG's relationships with >1000 investigators and trials groups. This provides the greatest possible statistical power.
- Relevance – A clinically representative global steering committee to advise on important questions
- Statistical reliability – The use of validated and consistent tests
- Trust – 40 years of pedigree in producing highly cited, authoritative, often practice changing, outputs, which dominate international guidelines.

There are also potential downsides in IP-level meta-analysis.

- Obtaining individual patient data can be subject to data sharing and privacy concerns. Perceived commercial sensitivities can also limit access.
- Substantial time and resources are often required. It is common for a single individual patient level meta-analysis to take 5+ years.
- Endpoints that are robust and not subject to varying interpretation between studies (eg all-cause mortality) are easier to analyze than 'softer' endpoints (eg QL, toxicity and cosmesis).
- The time taken for individual trials to mature and provide data, and the time taken to conduct individual patient level meta-analysis can mean that there is a risk that definitive results become too dated to influence contemporary practice.

EBCTCG meta-analyses provide reliable evidence for treatment effects. The implementation of this evidence into care has played a substantial part in the marked improvements in outcomes, particularly mortality, from early breast cancer seen over the last 30 years.

Bringing molecular approaches to Early Breast Cancer Trialists' Collaborative Group
Roberto Salgado, University Hospital, Antwerp, Belgium

At present, in breast cancer, clinico-pathological risk stratification is mostly performed using a limited set of features such as tumour size and lymph node status. Very large adjuvant trials have illustrated the key problem with the current scheme - it does not stratify patients with sufficient granularity to permit optimal selection and this selection hence does not always reflect a clear understanding of the biological diversity of cancer at diagnosis. One of the most rapidly expanding areas of research at present is that focused on combining histopathology, genomics, and artificial intelligence. Several results in this area have identified genomic/transcriptomic features which in hindsight are associated with histological features. This area of research has the potential to significantly impact the management of breast cancer but is challenged by the lack of a robust framework for the validation and dissemination of research tools. Key to a potential solution is the establishment of a digital pathology platform linked with well-annotated patient information including long term outcomes collected using randomized clinical trials of for example the EBCTCG.

Session 5.4 - Young Investigator session

Crown-like structures are associated with changes in immune cell signatures in patients with primary invasive breast cancer
Theme: Preclinical research

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Background: Obesity can initiate, promote, and maintain systemic low-grade inflammation partly via metabolic reprogramming of macrophages that encircle adipocytes termed crown-like structures (CLS). This pro-inflammatory environment correlates to systemic metabolic dysfunction that may promote tumour immune evasion. We previously showed that CLS were strongly associated with poor clinical outcomes in patients with HER2+ breast cancer (BC). CLS, tumour-associated macrophages (TAM), and T-cells are diverse and heterogenous cell populations. Nevertheless, the association between CLS and the spatial distribution of TAM and T-cells in BC is still not clear.

Methods: We investigated the association between CLS and immune cell signatures in early BC in the BEGIN (Investigating outcomes from breast cancer: Correlating genetic, immunological, and nutritional predictors) cohort using multiplex immunohistochemistry (IHC) and targeted RNA sequencing. Primary tumours (n=134) were stained for the expression of macrophage and T-cell immune markers, and these were correlated to the presence of CLS. Border was defined as a field of view (FoV) that was located ≤ 1 mm from the adipose tissue-tumour interface and Core was defined as a FoV that was located >1.5 mm away from the adipose tissue-tumour interface into the tumour. 36 matched multiplexed tumours were selected for RNA-targeted analysis using the HTG EdgeSeq Precision Immuno-oncology panel. ImageJ (v1.52n) and Architect XD64 were used for digital pathology analysis. Bioinformatic and descriptive statistical techniques were applied using R language and STATA/IC (v15), respectively.

Results: CD163+ CLS were strongly associated with higher Body Mass, Fat Mass, and Fat Free Mass Indices (adjusted $p<0.05$). In the whole cohort, CD163+ CLS were associated with a higher density of CD68+CD163+CD16+ macrophages in the stromal border, whereas CD68+CD163+CD16+CD32+ macrophages was the predominant population in the stromal core (adjusted $p<0.05$). A higher CD8/CD4 ratio was observed at the stromal border in the CLS positive compared to CLS negative patients (adjusted $p<0.05$). There was a weak association between CLS and higher stromal PD1+ T-cell density (adjusted $p=0.11$) and strong evidence of association between CLS and higher stromal Foxp3+ regulatory T-cell density at the border (adjusted $p<0.05$). CLS were associated with higher density of SMA+ fibroblasts in the stromal core. In addition, high fibroblast density was positively correlated with Foxp3+ regulatory T-cells and CD163+ macrophages in the stroma in CLS patients suggesting that fibroblasts may be associated with an immunosuppressive environment.

Targeted RNA sequencing showed that gene sets that are associated with cell cycle progression were upregulated, whereas gene sets involved in the regulation of anticancer immune responses were downregulated in CLS patients that was consistent with the IHC findings.

Conclusions: CD163+ CLS were associated with inflammatory signatures at the border and an aggressive molecular phenotype in the core of the tumour that may promote tumour growth and immune suppression.

Developing and feasibility testing of an intervention to support women with adherence to adjuvant endocrine therapy and improve quality of life - the SWEET study
Theme: Living with BC/QoL/Patient perspective/Supportive care

Lucy Mcgeagh[1], Sarah-Jane Stewart[2], Joanna Slodkowska-Barabasz[1], Zoe Moon[2], Jo Brett[1], Lesley Turner[3], Jan Rose[3], Mary Wells[4], Linda Sharp[5], Eila Watson[1]
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Purpose & Background: Oestrogen receptor positive breast cancer (BC) patients are recommended adjuvant endocrine therapy (AET) for 5-10 years to reduce risk of recurrence. However, up to 50% do not take AET as prescribed. As part of the SWEET research programme we have co-designed and feasibility tested a supported self-management intervention to reduce poor AET adherence and improve quality-of-life (QoL) in women with BC (HT&Me). A full trial is now in set-up to assess effectiveness and cost-effectiveness.

Methods: Guided by the Medical Research Council framework for complex interventions, and adopting a person-based approach, design and development of HT&Me was evidence-based and theoretically underpinned. Literature reviews, behavioural analysis, and stakeholder involvement informed 'guiding principles' and an intervention logic model. Using co-design principles, working closely with our patient advisory group, a prototype intervention was developed and refined in optimisation studies with 35 women. A feasibility study then assessed acceptability of the intervention. 111 women, from 5 NHS sites participated. Women completed questionnaires at baseline and 8 weeks. Interviews with a subset of participating women and relevant health care professionals explored experiences of the intervention, acceptability of the recruitment processes and study logistics, and identified any changes needed prior to progression to an RCT.

Results: The HT&Me intervention provides tailored support to women prescribed AET. It consists of an initial and follow-up consultation with a trained Study Nurse, an animation, web-app and ongoing motivational 'nudge' messages. Content addresses perceptual and practical barriers to adherence, as well as providing information, support and behaviour change techniques to improve adherence and QoL. Iterative patient and health professional feedback informed final intervention content.

The feasibility study clearly demonstrated the acceptability of all elements of the intervention as well as the feasibility of conducting a large-scale trial. Women found the consultations helpful, valuing the supportive and detailed explanations around AET and discussion about perceptions and practicalities. Feedback on the web-app was excellent. Women particularly liked the animation, side effect diary, 'real life experiences of others', external links and 'My Personal Support'. It was very user friendly, clear and easy to navigate. Web analytics showed that women accessed multiple website sections, set reminders for taking AET and collecting prescriptions and set goals that were predominantly for increasing physical activity levels. Health Care Professionals saw the intervention as straightforward to deliver, with no additional clinical processes needed and believed it was easy to recruit. They felt that there is a huge unmet need for patients, and the SWEET intervention is addressing this.

Discussion and Implications: HT&Me has been systematically and rigorously developed to promote AET adherence and improve QoL. Feasibility findings have informed the development of a RCT of effectiveness and cost-effectiveness due to commence January 2024.

Spatial Transcriptomics Delineates Tumour Heterogeneity in NACT Triple-Negative Breast Cancer
Theme: Pathology

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Background: Triple-Negative Breast Cancer (TNBC) is a highly aggressive subtype of breast cancer, characterised by the lack of estrogen-receptor (ER), progesterone-receptor (PR) and human-epidermal-growth-factor-receptor-2 (HER2) expression. Only about 40% of TNBC patients achieve a pathological complete response (pCR) following neoadjuvant chemotherapy (NACT). Since molecular heterogeneity of TNBC may contribute to variable responses to NACT, we aimed to deconvolute TNBC's histological and spatial transcriptomics (ST) patterns.

Methods: 91 pre-treatment core needle biopsies (FFPE and fresh frozen) were collected from TNBC patients who received NACT, either as standard of care or as part of the ongoing FORCE (NCT03238144) clinical trial at Guy's Hospital, London, UK. Of these, 38 achieved pCR (Responder), 46 had residual disease (Non-Responder) whilst 7 patients are currently undergoing NACT ; 46 post-treatment surgical resections were collected from Non-Responders.

A representative tumour block was sectioned, H&E stained, imaged and annotated by a pathologist to select ST regions of interest (ROIs) and provide detailed histological characterization. These annotations were used to design a novel histological classifier that captures the tumour region, epithelial type and immune cell localization, population, distribution and number of each ROI, culminating in a unique 6-digit ROI classification code (Table 1).

Table 1: ROI Classification

Category	Class	Code
Tumour Region	Edge	1
	Center	2
	Isolated Foci	3
Epithelial Type	Invasive	1
	Normal	2
	Normal Adjacent	3
	Hyperplasia	4
	Atypia	5
	DCIS	6
	LCIS	7
	Lymphovascular Invasion	8
	Not Applicable	0
Immune Cell Localisation	Stroma	1
	Intra-tumoural	2
	Tumour Border	3
	Mixed	4
	Not Applicable	0
Immune Cell Population	T cells	1
	B cells	2
	Myeloid Cells	3
	Mixed	4
	Not Applicable	0
Immune Cell Distribution	Patchy	1
	Dispersed	2
	Not Applicable	0
Immune Cell Number	Few	1
	Moderate	2
	Extensive	3
	None	0
	ROI Classification Code	**111412**

ST profiling was performed with the nanoString GeoMx Digital Spatial ProfilerPanCK. Tissues were sectioned and stained with fluorescent antibodies against PanCK for tumour cells and CD45 for immune cells, which were used to select ROIs and illuminate transcriptomic profiles of the tumour and immune-enriched compartments, defined as PanCK+/CD45- and PanCK-/CD45+, respectively.

Data cleaning, quality control and batch correction was performed in R 4.3.1 using the limma, dplyr, EdgeR, GeoMx Tools, GeoMx Workflows and RUV4 packages. Spatial Experiment, SpatialDecon and GSVA packages were used to perform differential gene expression, immune cell deconvolution and gene set enrichment analysis (GSEA), respectively.

Results: To date, spatial transcriptomic profiling has been carried out on 120 TNBC samples from 82 patients (46 Non-Responders; 36 Responders), comprising a total of 3917 tumour or immune-cell enriched regions. Preliminary GSEA of the tumour compartments revealed that KEGG pathways involved in tissue adhesion are upregulated in

Non-Responders compared to Responders, whilst those involved in genomic integrity are suppressed. Unsupervised clustering of PanCK+ regions per patient identified clusters of tumour cells present in both pre- and post-NACT samples, suggesting potential chemo-resistant properties. Moreover, immune cell deconvolution of the CD45+ regions revealed spatially distinct patters of immune cell composition which we mapped to histological annotations identified using our ROI classifier.

Conclusions(s): To the best of our knowledge, this is the first study to perform large scale spatial transcriptomic profiling of TNBC before and after NACT. We designed a novel ROI classifier to spatially resolve transcriptomes of histological features, providing an in-depth characterization of the histo-genomics of TNBC.

Sleepwalking through evolution: a tale of epigenetic adaptation in dormant Breast Cancer
Theme: Metastatic breast cancer

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Patients diagnosed with Estrogen receptor positive breast cancer (ER+ BC) receive five or more years of adjuvant endocrine therapies (ETs). Adjuvant ETs delay relapse by targeting clinically undetectable micro-metastatic deposits, yet up to 50% of patients receiving ETs relapse at a constant rate over the course of decades after surgery. The mechanisms driving these clinical dynamics are largely unknown but likely involve dormancy. We developed two approaches to study the fate of dormant cells in long-term experiments. Firstly, we longitudinally profiled a rare cohort of patients treated with long-term neoadjuvant ETs until progression. This allowed us to dissect the contribution of genetic and transcriptional changes to tumour awakening. Next, we developed an unprecedented in vitro evolutionary study to systematically record adaptive strategies of individual lineages in unperturbed parallel experiments through several months. Collectively our data demonstrate that ETs induce a non-genetic cell state transition into dormancy in a stochastically selected subset of cancer cells via epigenetic reprogramming. Single lineages with divergent phenotypes awaken unpredictably and sequentially via epigenetic erosion in the absence of detectable genetic alterations. Targeting the dormant epigenome shows promising activity against adapting cancer cells. Overall, this study uncovers the contribution of epigenetic adaptation to the evolution of resistance to ETs with profound implications for breast cancer.

Cerenkov Luminescence Imaging and Flexible AutoRadiography – a first-in-human novel imaging study for intra-operative margin assessment in women undergoing breast-conserving surgery for cancer
Theme: Surgery

Aaditya Sinha[1,2], Hannah Jeffery[1,2], Zhane Peterson[1,2], Belul Shifa[1,2], Patriek Jurrius[1], Sarah Allen[1,2], Eugene Lee[2], Mohammed Azmat[2], Rachel Barrass[2], Vas Karydakis[2], Elina Shaari[2], Mangesh Thorat[2], Hisham Hamed[2], Georgina Bitsakou[2], Sarah Pinder[1,2], Gary Cook[1,2], Ashutosh Kothari[1,2], Arnie Purushotham[1,2]
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Background: In all, 70% of women with breast cancer who require surgical intervention undergo breast-conserving surgery (BCS). Of these 20-25% of patients will require a further surgical procedure due to close or involved margins on histopathology. This increases the risk of physical and psychological morbidity. Therefore, there is a clinical need for novel imaging techniques to assess resection margins intraoperatively.

The aim of this interventional study was to apply two novel imaging techniques, Cerenkov Luminescence Imaging (CLI) directly detecting light emitted by a radiotracer and Flexible AutoRadiography (FAR) by applying a thin, flexible scintillating film to detect emitted activity indirectly to assess excision margins intra-operatively in women undergoing BCS.

Method: A single-arm interventional study was designed to evaluate the diagnostic accuracy of these dual-modality imaging techniques in conjunction with 18-Fluorodeoxyglucose (18F-FDG) to assess tumour margins in women undergoing BCS. Axillary lymph node surgery (sentinel lymph node biopsy or axillary lymph node clearance) was performed as standard of care. CLI-FAR imaging was performed using the LightPath system, an in vitro diagnostic device designed to locate and identify positron-emitting radionuclides within surgically excised specimens.

The study included patients with invasive breast cancer who were 18 years old, had not received any previous surgery or radiotherapy to the ipsilateral breast, were not pregnant or lactating and with no known hypersensitivity to 18F-FDG. Patients were injected with 250MBq +/- 10MBq of 18F-FDG 90-180 minutes before surgery and imaging of the specimen intraoperatively. The surgically excised tumour was initially imaged using an x-ray machine, and margins of suspicion were then imaged using CLI-FAR. Any suspicious margin underwent an immediate re-excision in the form of cavity shavings. The CLI-FAR margin and re-excision data were compared with final histopathology. A margin of 1mm of healthy tissue for invasive cancer and associated DCIS were defined as a clear margin. The histopathologists were blinded to the results of CLI-FAR.

Results: In all, 52 specimens were imaged in 50 patients with a total of 100 margins reviewed using CLI-FAR.

True Positive	10
False Positive	1
True Negative	86
False Negative	3
Total number of margins assessed	100

These results showed a margin specificity of 98.9% and sensitivity of 76.9%. The positive predictive value was 90.9% and negative predictive value 96.6%. In all, 10 margins in 8 patients were identified as positive on CLI-FAR imaging, which was acted upon intraoperatively. In these patients, all initial margins were also positive on histopathology, but cavity shavings were benign on 7 and therefore these patients avoided a second operation.

Conclusion: CLI-FAR imaging presents a promising, technique for intraoperative assessment of tumour margins in BCS. Future work will examine this novel imaging approach in women undergoing breast-conserving surgery for pure ductal carcinoma in situ.

Targeting ECM remodelling as a therapeutic strategy in Invasive Lobular Carcinoma
Theme: Treatment/Novel agents

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Background: Invasive lobular carcinoma (ILC) is a subtype of breast cancer defined by its unique histological presentation, often exhibiting a 'single file' growth pattern with cells distributed linearly in the stroma. Previous work has identified that ILC cells overexpress collagens and elastin as well as LOXL1, a collagen cross-linking enzyme belonging to the lysyl oxidase (LOX) family that can promote invasion and metastasis through remodelling of the extracellular matrix (ECM). The clinical stage pan-LOX inhibitor PXS-5505 has demonstrated anti-tumour potential through the disruption of the collagen matrix in models of pancreatic and myeloid cancer and exhibits an excellent safety profile. Given that ILCs are enriched for an ECM-remodelling signature, we propose that inhibition of LOX/L be investigated as a therapeutic strategy in the treatment of ILC.

Methods: By utilising the mouse intraductal model (MIND) to xenograft ER+ ILC lines into the milk ducts of mice, we can faithfully recapitulate ILC disease progression including ECM remodelling. We used 3 intraductal xenograft models of ILC (2 ER+ and 1 triple negative) to examine their response to oral dosing of PXS-5505, and in the ER+ models in combination with ovariectomy (OVX) to model aromatase inhibition (AI). Response was measured by bioluminescent monitoring of tumour growth and metastatic burden, and histological evaluation of proliferation and collagen organisation.

Results: Treatment with PXS-5505 alone significantly decreased primary tumour radiance compared to vehicle in the SUM44 model (p=0.0013), and had near-significant effects in the MM134 (p=0.1729) and IPH-926 (p=0.0809) models. The combination of PXS-5505 with hormone deprivation significantly reduced tumour radiance compared to vehicle (p=0.0322) and OVX alone (p=0.0451) in the ER+ MM134 model, and compared to vehicle only in the ER+ SUM44 model (p=0.013). In the metastatic ER- IPH-926 model PXS-5505 significantly reduced metastatic

dissemination to the lungs compared to vehicle as measured by ex vivo radiance (p=0.013). Tumour progression is associated with an increase in collagen fibril alignment and density. We observed significant decreases in collagen density in the primary tumours when treated with PXS-5505 alone (IPH-926) and in combination (MM134 and SUM44). This was accompanied by significant reductions in proliferation as measured by % Ki67 positivity.

Conclusion: These data indicate that modulation of ECM remodelling may prove effective in the treatment of ILC. The additional benefit of PXS-5505 to standard of care therapy in the treatment of ILC may occur as a result of the prevention of tumour cell-derived collagen remodelling, a process upon which ILC cells rely.

Age-associated microenvironmental changes highlight the role of PDGF-C in ER+ breast cancer metastatic relapse
Theme: Metastatic breast cancer

Frances Turrell[1], Rebecca Orha[1], Naomi Guppy[1], Andrea Gillespie[1], Matthew Guelbert[1], Chris Starling[1], Syed Haider[1], Clare Isacke[1]
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Patients with oestrogen receptor (ER)-positive breast cancer are at risk of metastatic relapse for many years or even decades after primary tumour resection and treatment, a consequence of dormant disseminated tumour cells (DTCs) reawakening at secondary sites. Further understanding of how the microenvironment at these sites regulates tumour cell survival and subsequent exit from dormancy is required to address the challenge of metastatic relapse in ER+ breast cancer patients. Moreover, given patient demographics, it is crucial we determine the impact of an ageing microenvironment on these processes.

We characterised syngeneic ER+ mouse mammary tumour models and assessed their metastatic ability, following orthotopic or intravenous tumour cell inoculation, in young (3-month-old) or aged (>12-month-old) mice. Parallel experiments were conducted in mice treated intranasally with bleomycin to assess how a fibrotic lung microenvironment affects the outgrowth of DTCs. RNA-seq analysis on aged and young mouse lungs from naïve mice or mice bearing ER+ mammary tumours was performed to identify age- and metastasis-associated changes. To interrogate the role of the age-associated factors in metastatic relapse and the mechanisms of tumour cell-stroma crosstalk, we employed genetic knockdown or pharmacological inhibition in dormancy assays and co-cultures, and spontaneous and experimental metastasis experiments.

Our work demonstrates that ER+ mouse mammary tumours are inefficient at spontaneous metastasis in young mice, with DTCs displaying a dormant phenotype. In contrast, an aged or fibrotic lung microenvironment supports the outgrowth of the DTCs. Many genes involved in fibroblast activation and fibrosis are differentially expressed in the aged mouse lungs and further altered in the metastatic lung, including Pdgfc which encodes the pro-fibrotic factor platelet-derived growth factor (PDGF)-C. In young mice, low-level Pdgfc expression by DTCs has a role in their maintenance at secondary sites but is insufficient to support the development of macrometastases. Raising DTC numbers using experimental metastasis models partly overcomes this deficiency, with macrometastatic outgrowth reversed by tumour cell Pdgfc knock-down. By contrast, the PDGF-C-high microenvironment of ageing or fibrotic lungs promotes DTC proliferation and upregulates tumour cell Pdgfc expression stimulating further stromal activation, events that can be blocked by pharmacological inhibition of PDGFRα or with a PDGF-C-blocking antibody.

In summary, these data demonstrate that an aged lung microenvironment supports the metastatic outgrowth of ER+ DTCs, highlighting the opportunity to target PDGF-C signalling to limit metastatic relapse in ER+ breast cancer as well as the importance of using age-appropriate models in pre-clinical studies.

Session 6.1 - Young women with breast cancer

Preservation of fertility in young women after breast cancer treatment
Julia Kopeika, Guy's & St Thomas NHS Foundation Trust, London, UK

Fertility preservation (FP) has been increasingly recognised as an integrative part of cancer care in patients of reproductive age. In many parts of the UK, FP provision remains patchy.

This talk aims to cover the current data on long term fertility outcome for women who undergone gonadotoxic treatment for breast cancer. Factors that need to be taken in consideration when pre-chemotherapy counselling/assessment is performed are discussed. Management of patients with hormone sensitive cancers is also outlined. All modern methods of fertility preservation are described with details of the timeline, risks and benefits. Long term outcome of natural and assisted conception is presented in young patients going through breast cancer treatment during reproductive age.

Endocrine therapy for pre-menopausal women
Judy King, Royal Free Hospital, London, UK

Presentation details to follow…

Managing side-effects of young women with early breast cancer
Anne Armstrong, The Christie NHS Foundation Trust, Manchester, UK

Presentation details to follow…

Session 6.2 - What have we learnt from prospective longitudinal epidemiological studies?

Generations Study
Montserrat Garcia-Closas, Institute of Cancer Research, London, UK

Presentation details to follow…

Million Woman Study
Gillian Reeves, Oxford University, Oxford, UK

Presentation details to follow…

Prospective studies of benign breast disease
Mustapha Abubakar, National Cancer Institute, Rockville, USA

In the United States alone, about 1.6 million women undergo breast biopsies annually, a figure that is expected to continue to rise with the increasing promulgation of mammographic breast density notification laws. Although the majority (>70%) of screening-indicated breast biopsies are non-malignant (i.e., normal or benign), the absence of malignancy on biopsies does not translate to the absence of risk for future invasive breast cancer development. Indeed, ~30% of all invasive breast cancers tend to occur among women with a previous diagnosis of benign breast disease (BBD). BBD is an agglomeration of histological entities, and BBD-related breast cancer risk varies according to lesion type, i.e., non-proliferative disease (NPD), proliferative disease without atypia (PDWA), or atypical (ductal or lobular) hyperplasia (AH). Proliferative diseases comprise ~30% of all BBD biopsies and patients have an almost 1.5-fold increased risk of breast cancer, which can be up to 4-fold increased risk in the presence of AH or multiple foci of atypia. However, women with AH comprise only ~4% of all BBD patients and in absolute terms fewer breast cancers will occur in these women than in those with NPD (~70% of all BBDs). Thus, there is the need to uncover additional tissue biomarkers that can aid to further stratify women with BBD into different breast cancer risk categories. In his presentation, Dr. Abubakar will discuss his ongoing work within BBD cohorts that are focused on leveraging state-of-the-art computational pathology algorithms to analyze epidemiologically annotated histological images to uncover novel features that can help inform breast cancer risk prediction and treatment decision-making following BBD.

Session 6.3 - New developments in breast cancer diagnosis and treatment

Circulating tumour DNA dynamics for early assessment of recurrence risk
Nicholas Turner, Institute of Cancer Research, London, UK

Presentation details to follow…

Extending the promise of digital pathology
Sarah Pinder, Kings College London, London, UK

Presentation details to follow…

What would GRAIL mean for breast cancer detection and management
Mark Middleton, University of Oxford, Oxford, UK

Presentation details to follow…

Dynamic Biobanking for Advancing Breast Cancer Research
Theme: Other

Maryam Abdollahyan[1], Emanuela Gadaleta[1], The Breast Cancer Now Tissue Bank[1,2,3], Penelope Ottewell[2], Angela Cox[2], Valerie Speirs[3], Louise Jones[1], Claude Chelala[1]
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Longitudinal biospecimens and data advance breast cancer research through enabling precision medicine approaches for identifying risk, early diagnosis, improved disease management and targeted therapy. Cancer biobanks must evolve to provide not only access to high-quality annotated biospecimens and rich associated data, but also the tools required to harness these data. We present the Breast Cancer Now Tissue Bank (BCNTB) as an exemplar of a dynamic biobanking ecosystem that hosts and links longitudinal biospecimens and multimodal data including electronic health records, genomic and imaging data, with integrated data sharing and analytics tools. We demonstrate how such an ecosystem facilitates access to breast cancer biospecimens and data to support researchers and maximise research outputs for patient benefit.

Association between built environment factors and post-menopausal breast cancer risk: Alberta's Tomorrow Project
Theme: Other

Mohadeseh Ahmadi[1], Trevor Dummer[2]
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Background: Breast cancer is the most common cancer in women. In 2020 approximately 2.3 million cases of breast cancer were diagnosed worldwide, of which 685,000 resulted in death. Genetic factors and inherited mutations make up only a modest proportion of cases, while modifiable environmental and lifestyle factors play a significant role, with nearly 40% of breast cancer cases attributable to these factors. With increasing urbanization over the past few decades, characteristics in the built environment may contain important modifiable breast cancer risk factors.

Objective: The overarching aim of this study is to assess the impact of traffic-related air pollution (TRAP), residential greenness, and walkability on the risk of breast cancer in postmenopausal women, utilizing incident cancer data from Albert's Tomorrow Project (ATP) cohort linked to geographic datasets from the Canadian Urban Environmental Health Research (CANUE). The project will 1. Evaluate the risk of breast cancer in relation to TRAP – NO2, SO2, PM2.5, and O3 in a cohort of Albertans; 2. Evaluate the risk of breast cancer in relation to walkability and greenness in a cohort of Albertans.

Method: Cox-proportional hazards regression is being used to model time-to-event breast cancer diagnosis in relation to TRAP, greenness, and walkability. A change-in-effect model building strategy was used to assess for confounders. The likelihood ratio test (LRT) will be routinely performed to examine the significance of effect modifiers and independent predictors of the model.

Results: The study encompassed 14,669 participants, consisting of 544 post-menopausal breast cancer cases and 14,125 post-menopausal non-breast cancer individuals. We developed a total of five models: two for NO2 (measured at baseline and file year), two for greenness (measured at baseline and within 1000 meters of residence), and one for walkability. The adjusted HR for baseline greenness was 1.03 (95% CI = 0.93, 1.15) for each one IQR increase in NDVI (normalized difference vegetation index). For average greenness measured within 1000 meters, the adjusted HR was 0.96 (95% CI = 0.87, 1.06) for each one IQR increase in NDVI. Similarly, the adjusted HR for baseline NO2 was 1.04 (95% CI = 0.88, 1.21) for every 10 ppb (parts per billion) increase in NO2. The HR for NO2 concentration at file year was 1.02 (95% CI = 0.84, 1.24) for every 10 ppb increase in NO2. Finally, the walkability model had HRs of 0.9952, 1.1244, 1.3095, and 1.1376, for quintiles 2 through 5 relative to quintile 1 (least walkable), respectively.

Implications: The findings of this longitudinal prospective study, using nationally available exposure datasets, will support policy makers and public health planners to understand the impact of built environment modifiable cancer risks.

Correlation Between Radiological Findings and Histopathological Diagnosis of Breast Diseases: Retrospective Review Over Sixth Years in King Fahad University Hospital in Eastern Province, Saudi Arabia
Theme: Pathology

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A critical aspect in the determination of treatment plans for breast cancer patients is the preoperative radiological and histopathological assessment of the mass. Thus, This study aims to establish a correlation between radiological findings and histopathological results in regard to the breast imaging-reporting and data system scores, size of breast masses, molecular subtypes and suspicious radiological features, as well as to assess the concordance rate in histological grade between core biopsy and surgical excision among breast cancer patients, followed by analyzing the change of concordance rate in relation to neoadjuvant chemotherapy in a Saudi population. A retrospective review was conducted over 6-year period (2017-2022) on all breast core biopsies of women preceded by radiological investigation. Chi-squared test ($\chi 2$) was performed on qualitative data, the Mann-Whitney test for quantitative non-parametric variables, and the Kappa test for grade agreement. A total of 641 cases were included. Ultrasound, mammography, and magnetic resonance imaging demonstrated diagnostic accuracies of 85%, 77.9% and 86.9%; respectively. magnetic resonance imaging manifested the highest sensitivity (72.2%), and the lowest was for ultrasound (61%). Concordance in tumor size with final excisions was best in magnetic resonance imaging, while mammography demonstrated a higher tendency of overestimation (41.9%) and ultrasound showed the highest underestimation (67.7%). The association between basal-like molecular subtypes and the breast imaging-reporting and data system score 5 classifications was statistically significant only for magnetic resonance imaging ($p=0.04$). Luminal subtypes demonstrated a significantly higher percentage of speculation in mammography. Breast imaging-reporting and data system score 4 manifested a substantial number of benign pathologies in all the 3 modalities. A fair concordance rate ($k= 0.212$ & 0.379) was demonstrated between excision and the preceding core biopsy grading with and without neoadjuvant therapy, respectively. The results demonstrated a down-grading in cases post-neoadjuvant therapy. In cases who did not receive neoadjuvant therapy, underestimation of tumor grade in biopsy was evident. In summary, magnetic resonance imaging had the highest sensitivity, specificity, positive predictive value and accuracy of both diagnosis and estimation of tumor size. Mammography demonstrated better sensitivity than ultrasound and had the highest negative predictive value, but ultrasound had better specificity, positive predictive value and accuracy. Therefore, the combination of different modalities is advantageous. The concordance rate of core biopsy grading with excision was not impacted by neoadjuvant therapy.

Stress Hormone Modulation of Migration and Invasion in Breast Cancer Cell Lines: A Comparative Analysis
Theme: Metastatic breast cancer

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Breast cancer metastasis presents a significant clinical challenge with critical implications for patient outcomes. Understanding the impact of stress hormones and hormone receptors on cancer cell migration and invasion is crucial for targeted therapy development. This study examined the migratory and invasive behaviours of two breast cancer cell lines—MDA-MB-231 and its brain-metastatic variant, MDA-MB-231-Br-alongside the murine triple-negative breast cancer cell line 4T1, in response to stress hormone treatments.

Migratory and invasive potential were assessed using 8µm-pore cell-chemotaxis/collagen-invasion assay kits. Serum-starved cells (1x10^5 cells/well) underwent 24-hour treatments with stress hormones -Corticosterone (500nM) and Norepinephrine (1uM) -as well as their respective inhibitors -Relacorilant(500nM) and Propanolol (1uM). Migration and invasion percentages were quantified via fluorescence measurements and statistically analyzed using One-Way ANOVA.

MDA-MB-231-Br cells exhibited higher migration rates than their MDA-MB-231 counterparts. Corticosterone and norepinephrine led to notable increases in MDA-MB-231-Br cell migration. Norepinephrine induced a significant migration surge compared to control ($p<0.01$). While propranolol, a beta-adrenergic receptor antagonist, reduced migration, this reduction was not significant. Conversely, MDA-MB-231 cell migration remained stable across treatment groups, displaying a trend towards increased migration with hormonal stimuli and decreased migration with hormone inhibitors. However, these changes did not reach statistical significance, except in the

hydrocortisone + norepinephrine group, where the glucocorticoid receptor antagonist significantly reduced migration.

Murine 4T1 cells showed distinct responses to hormonal treatments compared to their human counterparts. Corticosterone treatment resulted in a non-significant migration decrease, but the concurrent administration of hormones and inhibitors significantly reduced migration ($p<0.03$).

Both human and murine cells were exposed to varying dexamethasone (Dex) concentrations, a synthetic glucocorticoid used in chemotherapy management. In 4T1 cells, migration decreased with dexamethasone addition, remaining constant at lower concentrations and significantly decreasing at the highest Dex concentration ($p<0.03$). Conversely, MDA-MB-231 cells exhibited significant migration increases at the lowest Dex concentration (10nM) ($p<0.01$), followed by a gradual decrease inversely proportional to Dex concentration.

Invasion significantly increased in samples treated with Norepinephrine ($p<0.004$ for MDA-MB-231-Br and $p<0.0003$ for MDA-MB-231). Although invasion also rose in samples treated with Corticosterone alone or Corticosterone and Norepinephrine, these changes were not statistically significant. A significant invasion decrease was observed in samples treated with Norepinephrine compared to those treated with Norepinephrine and Propranolol ($p<0.0007$). The increase in invasion for both cell lines was mitigated by the addition of the two receptor antagonists, highlighting their therapeutic potential.

In conclusion, this study reveals distinct migratory responses to hormonal modulation in human and murine breast cancer cell lines. It underscores the influence of the tumour microenvironment on cell behaviour, emphasizing the need for relevant models in cancer metastasis research. These findings highlight the complexity of stress-driven migration and invasion in breast cancer and advocate tailored therapeutic strategies, showcasing the therapeutic potential of glucocorticoid and beta-2 adrenergic receptor antagonists.

Streamlining the multidisciplinary meeting to prioritise discussion of patients with breast cancer
Theme: Other

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Introduction: Multi-disciplinary meetings (MDM) are part of the gold standard of care for patients with cancer. The increasing incidence of cancer and the number of cases scheduled for discussion at MDM requires streamlining to manage the workload, improve efficiency and ensure high-quality patient care.

This study aims to assess the feasibility of implementing a protocol to remove patients with benign diseases from discussion at the MDM without compromising patient safety.

Methods: A prospective review of benign patients of 218 MDMs at Guy's Hospital was undertaken from the period of 4th January 2021 to 13th March 2023. A detailed protocol was designed and implemented, resulting in patients with benign disease which met specific criteria being removed from the MDM, and a clear management/outcome plan as per the protocol was applied and recorded. A surgical fellow was given this responsibility following a pre-MDM discussion with a Surgical Consultant.

Results: On average, 37 patients were discussed at an MDM and of these 34.2% of cases were benign. Implementation of the protocol resulted in 82% of benign cases being removed from MDM discussion. Where there was any area of dubiety or the case was deemed complex, these benign cases were retained for discussion by the MDT.

Conclusion: Implementation of the benign breast disease protocol can safely remove patients with benign disease from discussion at the breast MDM with a view to decreasing the caseload thereby allowing the discussion to focus on patients with a diagnosis of cancer.

CDK4/6 inhibitors compared to weekly paclitaxel for treatment of ER+/HER2- advanced breast cancer with impending or established visceral crisis: a retrospective study
Theme: Metastatic breast cancer

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Background: Oestrogen receptor-positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer (ABC) with visceral crisis (VC) or impending VC (IVC) is associated with a poor prognosis, and rapidly effective treatment is required to reverse organ dysfunction. Chemotherapy is commonly given instead of CDK4/6 inhibitors (CDK4/6i) based on the theory it may be more rapidly efficacious and have better survival outcomes. However, there is little published evidence to confirm which treatment is superior in IVC/VC. This study compared the outcomes of patients with ER+/HER2- ABC and IVC/VC treated first line with a CDK4/6i or weekly paclitaxel.

Methods: Patients with ER+/HER2- ABC who received treatment with a CDK4/6i or weekly paclitaxel at a large UK tertiary cancer centre from 1-Mar-2017 to 30-Jun-2021 were retrospectively identified. Patients were excluded if they had received previous CDK4/6i or any other systemic therapy for ABC, but previous single-agent endocrine therapy (ET) for ABC was allowed in the paclitaxel cohort. Hospital electronic records were screened for evidence of IVC/VC affecting the liver, lungs/mediastinum, gastrointestinal tract and/or bone marrow. Criteria for identifying IVC/VC were based on the international ESO-ESMO ABC guidelines. Baseline demographics, clinical data and survival outcomes were recorded up to 30-Jul-2022.

Results: 27/396 (6.8%) patients with ABC who received CDK4/6i and 32/86 (37.2%) who received paclitaxel had IVC/VC. Table 1 shows the baseline characteristics of patients with IVC/VC. 92.6% of patients in the CDK4/6i cohort received palbociclib. Median time to treatment failure (TTF), progression-free survival (PFS) and overall survival (OS) were all significantly longer in patients treated with CDK4/6i compared to paclitaxel: TTF 17.3 vs. 3.5 months (HR 0.33, 95%CI 0.17-0.61, p=0.0002), PFS 17.8 vs. 4.5 months (HR 0.38, 95%CI 0.21-0.67, p=0.002), OS 24.6 vs. 6.7 months (HR 0.37, 95%CI 0.20-0.68, p=0.002). The median time to first improvement in IVC/VC was similar in the CDK4/6i and paclitaxel cohorts (3.9 vs. 3.6 weeks, p=0.773). Disease control at 4 months was not significantly different in patients who received CDK4/6i compared to paclitaxel (77.8% vs. 59.4%, p = 0.168). In multivariate analysis, when considering organ in IVC/VC (liver-only vs. lung-only vs. other), ET-resistance vs. ET-sensitivity, presence of IVC vs. VC, de novo vs. recurrent disease and performance status (0-1 vs. ≥2) as covariables, treatment with CDK4/6i was independently predictive of a longer PFS (HR 0.31, 95%CI 0.12-0.78, p=0.015).

Table 1: Baseline characteristics of patients with IVC/VC receiving CDK4/6i or weekly paclitaxel

	CDK4/6i n=27 (%)	Paclitaxel n=32 (%)	p value
Age (years)			
Median	59	57	0.589
Range	27-86	39-85	
Menopausal status			
Pre-menopause	6 (22.2)	6 (18.8)	0.485
Peri-menopause/unknown	4 (14.8)	2 (6.3)	
Post-menopause	17 (63.0)	24 (75.0)	
Performance status			
0	6 (22.2)	7 (21.9)	0.037
1	18 (66.7)	10 (31.3)	
2	2 (7.4)	11 (34.4)	
3	1 (3.7)	3 (9.4)	
4	0 (0)	1 (3.1)	
De novo/recurrence			
De novo	11 (40.7)	2 (6.3)	0.003
Recurrence	16 (59.3)	30 (93.8)	
Metastatic sites			
Lung/pleura	19 (70.4)	17 (53.1)	0.523
Liver	17 (63.0)	27 (84.4)	
Bone	19 (70.4)	25 (78.1)	
Abdominal/peritoneal	6 (22.2)	6 (18.8)	
Adrenal	0 (0)	2 (6.3)	
Brain	0 (0)	1 (3.1)	
Number of metastatic sites			
1	1 (3.7)	2 (6.3)	0.696
2	7 (25.9)	12 (37.5)	
3	12 (44.4)	11 (34.4)	
4	6 (22.2)	4 (12.5)	
5	1 (3.7)	2 (6.3)	
6	0 (0)	1 (3.1)	
ET sensitivity/resistance			
Sensitive or naive	13 (48.1)	6 (18.8)	0.035
Primary resistance	4 (14.8)	4 (12.5)	
Secondary resistance	10 (37.0)	22 (68.8)	
Previous single-agent ET for ABC			
Yes	0 (0)	9 (28.1)	0.003
No	27 (100)	23 (71.9)	
IVC or VC			
IVC	16 (59.3)	8 (25.0)	0.009
VC	11 (40.7)	24 (75.0)	
Organ in IVC/VC			
Liver	16 (59.3)	20 (62.5)	0.284
Lung/mediastinum	7 (25.9)	4 (12.5)	
Gastrointestinal	2 (7.4)	2 (6.3)	
Bone	1 (3.7)	2 (6.3)	
Multiple	1 (3.7)	4 (12.5)	

Conclusion: Patients with ER+/HER2- ABC and IVC/VC treated with a CDK4/6i had better outcomes and a similar time to improvement in IVC/VC compared to patients treated with weekly paclitaxel. CDK4/6i should be considered as the preferred first line treatment option for patients with IVC/VC, which is in agreement with results from the recently presented RIGHT Choice randomised clinical trial.

How comfortable are you in consulting pregnant and lactating women for breast imaging?
Theme: Genetics/Screening/Early detection

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Introduction: Pregnancy associated breast cancer accounts for 3% of breast cancer diagnoses. Many women are BRCA carrier or with significant family history of breast cancer. However, due to the concern of radiation and contrast exposure to the mother and fetus, many practitioners have advised delayed imaging or breastfeeding cessation, which may delay cancer detection and cause pain and emotional distress to the patient. This is particularly stressful for high risk women who have to continue breastfeeding between pregnancies over years and not able to have surveillance imaging for prolonged period. For example, a BRCA carrier mother of two who was pregnancy twice over four years and breastfeeding for each pregnancy. This may result in up to 6 years delay in breast imaging.

Methods: We conducted an online questionnaire to assess current understanding and practice in imaging pregnant and lactation in the local trust.

Results: Twenty-four responses received from breast surgeons, speciality breast doctors, radiologists, mammographers and clinical geneticists.

54% aware of the negligible radiation risk of mammography examination. 25% would perform diagnostic mammograms, while 75% would postpone surveillance mammograms during pregnancy and lactation.

46% understood the moderate radiation risk from CT but safe to perform CT in pregnancy if required. 60% had concern or uncertainty about the safety of administering iodinated contrast for CT in pregnant women.

25% participants would not perform diagnostic MRI breasts with contrast in pregnant women while another 25% responders would consider them on a case-by-case basis. 50% were unsure.

75% agreed it is safe to administer local anaesthesia in both pregnant and lactating women.

Only 2 participants aware of NHS recommended durations of breastfeeding. There was variable and incomplete knowledge on the impact of their advice to interrupt breastfeeding.

Discussion: Results reflected inconsistent understanding among practitioners potentially leading to variable imaging practices which lead to compromised patient care and patients' anxiety. Practitioners should be reassured that most imaging could be safely performed during pregnancy and lactation, except MR breasts in pregnancy, according to RCR guidelines.The diagnostic value of mammogram may be compromised by the dense lactational breast tissue, but the imaging quality can be optimised by breastfeeding or milk expression immediately prior to imaging. We hope improved knowledge will support both practitioners in the informed decision making process when counselling pregnant and breastfeeding women for appropriate breast imaging.

Contrast-Enhanced Mammography (CEM) versus Dynamic Contrast-Enhanced MR Breast (DCE-MR Breast) in local staging of breast cancer: A comparison of the sensitivity and background parenchymal enhancement
Theme: Other

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Background / Objective: To allow the safe practice of breast-conserving surgery, accurate preoperative estimation of disease extent is extremely crucial. Dynamic contrast enhanced MR breast (DCE-MR breast) has been the gold standard imaging for pre-operative assessment for its high sensitivity in detecting additional lesions and more accurately sizing the lesions in comparison with conventional imaging. In the last decade, contrast enhanced mammography (CEM), a mammography technique that involves contrast injection has gained increasing popularity as a potential alternate technique to MR breast. We aim to evaluate the performance of contrast enhanced mammography (CEM) by comparing its sensitivity and background parenchymal enhancement with DCE-MRI breast.

Methods: This is a single centre, retrospective study on newly diagnosed breast cancer patients who had CEM and DCE-MR breast for local staging at our institute from 1st Jan 2019– 31st Jan 2023. Patients who were receiving treatment prior to imaging and external referrals were excluded.

The background parenchymal enhancement (BPE) of both examination were graded minimal-mild and moderate-severe.

In this study, the sensitivity of examinations was defined by the number of lesions detected including benign and malignant pathology.

Results or Findings: A total of 62 CEMs performed during the study period. Nineteen patients had DCE-MRI within 2 weeks following CEM (age range 30-71).

Minimal-mild BPE on 15 CEM versus 14 DCE-MRI. Moderate-severe BPE on 4 CEM versus 5 DCE-MRI. A total of 16 CEM and DCE-MR demonstrated similar degree of BPE (74%), thirteen cases of which had minimal-mild BPE and three cases moderate-severe BPE. In 5 DCE-MRI with moderate-severe BPE, three had similar BPE on CEM while two had less significant minimal-mild BPE.

Nine patients had unilateral unifocal lesions. Another nine patients had unilateral multifocal lesions. The sensitivity of both CEM and DCE-MRI were consistent in 15 cases (79%). Four with discordant sensitivity (21%) demonstrated moderate-severe BPE on both examinations. Of note, there were 3 cases with deep lying lesions which were detected on both CEM and DCE-MRI but DCE-MRI is more superior in delineating the posterior extent of disease.

Fifteen patients were premenopausal and four were postmenopausal. Similar BPE and sensitivity on both CEM and DCE-MRI observed in 74% premenopausal (11/15 cases) and 75% postmenopausal women (3/4 cases).

Conclusions: There is no significant difference of BPE between CEM and DCE-MRI breast. The sensitivity of CEM with minimal-mild BPE is comparable with DCE-MR breast. Moderate BPE remains a limiting factor for both CEM and DCE-MRI. Switching from DCE-MRI to CEM to decrease BPE as a limiting factor may not be beneficial.

Limitations: Small sample size. Some imaging was acquired at different phases of menstrual cycle in premenopausal women.

Sleep disturbance amongst the breast cancer population - a single-centre prospective experience
Theme: Living with BC/QoL/Patient perspective/Supportive care

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Background: Sleep disturbance is one of the commonest symptoms experienced by cancer patients across all stages of the disease and during all phases of treatment. Research has shown that as many as 61% of patients experience difficulties with sleep, which in turn negatively impacts on health-related quality of life factors including

fatigue, mood, pain sensitivity, cognitive functioning and physical activity. In 2019 a systematic review concluded that improving sleep disturbance in breast cancer patients can reduce depressive symptoms and anxiety, thereby leading to better adherence to cancer therapies and improvements in both understanding of treatment and physical symptoms.

This research aimed to investigate the prevalence of sleep disturbance amongst the breast cancer population within our cancer centre and evaluate its impact on patients' quality of life.

Methods: Between 1st June to 31st August 2023, breast cancer patients cared for at Mount Vernon Cancer Centre were invited to complete a sleep questionnaire developed from validated surveys. Data was collected prospectively and a total of 52 responses were recorded.

Results: The study cohort comprised 18 patients with early breast cancer and 33 with metastatic disease; one participant did not disclose their disease status. 100% of respondents were female and the median age of participants was 58 years (range 37-79).

52% of patients (27/52) reported trouble sleeping and the majority (22/27) experienced symptoms for more than 3 months.

Of the participants who reported sleep disturbance only 30% (8/27) expressed a wish to discuss treatment options to improve sleeping patterns, whilst a larger proportion, 68% (17/27), were 'not sure' or preferred not to discuss potential treatment with their oncology team.

Amongst patients without sleeping difficulties 48% (12/25) reported symptoms of fatigue, 20% (5/25) experienced poor concentration and 12% (3/25) described mood disturbances. In contrast, of the respondents who did experience sleep disturbance a greater proportion reported symptoms of fatigue [81% (22/27)], poor concentration [52% (14/27)], and mood disturbance [(37% (10/27)].

Where difficulty sleeping was encountered, 86% (23/27) of patients had not been offered treatment by a healthcare professional. The remaining 14% (4/27) were offered treatment in the community by their General Practitioner.

Conclusions: The dataset collected confirms the high prevalence of sleep disturbance amongst our breast cancer population, in keeping with the current literature. In our cohort, patients with poor sleep had higher rates of fatigue, poor concentration and mood disturbance. Interestingly, despite a high proportion of patients reporting sleep difficulties, the majority were unsure or did not wish to discuss methods to improve their symptoms. Finally, discussions with patients regarding their sleeping patterns were not fully explored by our oncology teams, potentially leading to missed opportunities to improve patients' overall quality of life.

SENTINUS: Technical feasibility and diagnostic accuracy of contrast enhanced ultrasound to identify sentinel lymph node metastases in breast cancer patients following training of imaging specialists
Theme: Trials in progress

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Background: Sentinel lymph nodes (SLN) can be identified and biopsied in the breast clinic using intradermally injected microbubbles and contrast enhanced ultrasound (CEUS). Standard B-mode axillary ultrasound has limited accuracy for axillary staging but published evidence indicates that the addition of CEUS offers better test performance. In a large prospective dataset, less than 2% of patients with a normal B-mode axillary ultrasound and a benign CEUS SLN core biopsy had 2 or more axillary lymph nodes (LN) macrometastases found at the end of surgical treatment. These results were not just confined to patients with favourable tumour characteristics and also included those with large (>50mm) and multifocal cancers. The SENTINUS study was therefore designed as a prospective multicentre pilot study to: 1) Determine whether experienced imaging specialists in up to 5 UK Breast Centres can be trained to consistently identify, core biopsy and clip mark axillary SLN in patients with breast cancer

and 2) determine the overall diagnostic accuracy of a CEUS SLN core biopsy as a test to identify SLN metastases as compared to the reference standard of axillary surgery.

Methods: 10 Imaging specialists from up to 5 UK breast units will be trained to perform the CEUS SLN core biopsy procedure.
250 patients newly diagnosed with invasive breast cancer with planned primary surgery will then be recruited from the Breast Centres to undergo the CEUS SLN core biopsy procedure. Technical feasibility will be assessed by 75% of imaging specialists achieving; >85% visualization of tumour draining axillary SLN, >80% successful core biopsy (LN tissue retrieved) rate and >80% concordance with SLN identified surgically with SLN excision.Diagnostic performance will be assessed by calculating the overall pooled sensitivity, specificity, positive predictive value, negative predictive value of CEUS SLN core biopsy as a test to identify SLN metastases as compared to axillary surgery and the prevalence of LN metastases. An overall sensitivity >50% will be considered acceptable.

Results: All imaging specialists have been trained and teaching materials (including videos and a website) have been produced. The study is now recruiting with 41 patients recruited to date.

Conclusion(s): Despite a slow set up, mainly because of the COVID19 pandemic and then MHRA delays with substantial amendments, the study is now recruiting. If successful, this research will lead to a larger study to investigate whether a CEUS SLN core biopsy can safely replace axillary surgery for the majority of patients diagnosed with early breast cancer. In addition, the CEUS SLN biopsy procedure could give patients and their clinical teams information about LN metastases much earlier in the diagnostic pathway, thus helping with treatment planning decisions.

Accuracy of MRI in Breast Cancer Imaging- A Study into Radiological and Pathological Concordance
Theme: Other

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[1]Nimdta

Introduction: Breast Magnetic Resonance (MRI) Imaging is the gold standard in assessment of tumour size, disease extent and in monitoring response to chemotherapy in breast cancer patients. In patients undergoing neoadjuvant chemotherapy (NACT), pre-treatment MRI is used for accurate loco-regional staging and to assess for contralateral disease. Post-treatment MRI is used to assess extent of residual disease and to guide surgical planning. The aim of this audit was to investigate radiological and pathological concordance in patients with breast cancer who had MRI and in some cases second look ultrasound imaging.

Method: A retrospective audit was performed on all patients, both male and female who had breast MRI imaging between 1st January and 31st December 2021.
Pre- and post-treatment MRI studies of patients having neoadjuvant chemotherapy were included.
Histopathological results of all patients who underwent surgery were collected from the electronic care record. Pathological response was compared with Radiological response.
In addition, histopathological results were analysed for those patients who had undergone second look ultrasound after initial breast MRI.

Results:
104 breast MRI studies were performed on 95 patients between 1st January -31st December 2021.
16 patients who had no subsequent surgery were excluded.
32/79 patients were undergoing neoadjuvant chemotherapy.
46/79 patients had newly diagnosed invasive lobular cancer.
1/79 patient had indeterminate/high grade DCIS
Of those patients undergoing NACT, 25/32 (78%) had 2 MRI studies, one prior to NACT and one on completion NACT/prior to surgery.
8/32 (25%) patients undergoing NACT had second look imaging following pre-treatment MRI. Second look imaging found further malignancy not picked up on initial ultrasound/mammogram in 6/8 (75%) patients undergoing NACT.
Radiological (MRI) and pathological concordance was found in 80% (20/25) of NACT patients.
Complete radiological/pathological concordance was found in 9/12 (75%) of cases and partial radiological/pathological concordance was found in 11/13 (85%)
12/46 (26%) of patients who had MRI for invasive lobular cancer had 2nd look imaging after MRI. 2nd look imaging demonstrated further malignancy in 7/12 (58%)

Conclusion: MRI imaging is accurate in initial staging, identification of multifocal disease and in prediction of treatment response to NACT. MRI is also accurate in detection of invasive lobular carcinoma.

Single centre experience of the adoption of self-administered HER2-directed therapy in patients with breast cancer
Theme: Treatment/Novel agents

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Self-administration (SA) of systemic anti-cancer therapy (SACT) offers greater convenience and shared decision making for patients whilst alleviating pressure on services.
The aims of this study were to quantify the uptake/acceptability of SA of subcutaneous trastuzumab (scT), to evaluate safety, patient perception and the chair capacity released.

Methods: scT patients were offered SA training. The competency-based training, under the supervision of a chemotherapy-trained nurse, consisted of a minimum of 3 sessions. Patients were provided with printed and electronic material (via an App) on how to self-administer. Once deemed competent, pre-filled scT was shipped to the patients' home in a temperature-controlled environment. All patients were assessed by telephone one day before and after SA using the Common Terminology Criteria for Adverse Events. The number of administrations between Feb-22 and June-23 was analysed. A telephone survey using a validated questionnaire Self-Management Assessment scale (SMASc) was also undertaken.

Results: Of 46 breast cancer patients receiving single agent scT, 32 agreed to be trained. 2 patients were undergoing training, 6 patients declined and 6 were ineligible based on inclusion criteria.
The median age of 32 patients that participated was 62, (range 27-77). The average distance from home address to the centre was 11.7 miles (range 3.5-27.9). 25 (78%) patients were Caucasian, 4 (13%) Asian and 3 (9%) African/Caribbean. Patients had received an average of 10 scT in hospital (median 5, range 1-103) before starting the training. They required an average of 3 training sessions (median 3, range 1-4). In the 32 patients studied, a total of 302 SA injections (302hrs saved) were delivered. No Grade 3/4 toxicities or infusion-related reactions were reported.

25 of the 32 patients responded to SMASc questionnaires utilising the six-point Likert scale. Patients reported average scores of 5.32(median 6) and 5.56 (median 6) respectively, for questions relating to information about their condition and sufficient training to self-administer. They felt that they had sufficient support to participate in the programme (average 5.56 median 6).

80% would recommend this programme and 88% felt they had benefited. Comments from patients themed around the value of support provided, ease of administration and time saved.

Discussion: Programs such as these empower patients and carers to take a more active role in managing their condition with consequent reduced hospital attendance. Safety and acceptability for those patients who agreed to the program has been confirmed. Success of this program with sc T has enabled expansion to incorporate self-administration of Phesgo (sc trastuzumab and pertuzumab) with 31% (14/45) of the current Phesgo patient cohort enrolled onto the programme within 2 weeks of roll out and the first patients self-administering their treatment from August 2023. With the continued expansion of treatments, we encourage stakeholders to consider SA of SACT as an option. Formulation of treatments conducive to patient SA is a key component to this.

Digital image analysis and a novel set of cell line samples as aids in the development of a quantitative external quality assessment programme for Ki-67
Theme: Other

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Background: Ki-67 is a biomarker of proliferation, however, its value is hampered by lack of analytical reproducibility.
We report here on the results of work using cell line controls analysed by digital image analysis (DIA) as a first step towards providing an EQA.

Methods: A FFPE cell line microarray (CLMA) was produced. It was comprised of cores taken from a pure population of Sf9 caterpillar cells, together with cores of Sf9 cells mixed with four different human BC cell lines: BT-20 (85% BC cells), ZR-75-1 (75%), BT-474 (65%) and BT-483 (55%). Sections from the CLMA were mounted onto glass microscope slides together with sections from a FFPE tonsil sample and two BC samples. Unstained sections were distributed to laboratories; after routine IHC-staining for Ki-67 they were returned and centrally visually assessed for quality and subjected to DIA.

Results: Slides were returned by 37 laboratories.

Two distinct groups were identified. The first (n=27) were negative or showed low Ki-67 scores (mean=1.1%, 95% CIs: 0.2-1.9%), the second (n=10) displayed a step-change in scores (mean=49.9%, 95% CIs: 33.2-66.7%); the means of the two groups were significantly different ($P<0.0001$). When Ki-67 scores for each of the tissue samples were dichotomized the means of those groups differed significantly for the two BC samples ($P<0.001$), but not for tonsil.

Quality scores did not differ significantly between the two groups. However, when slides bearing Sf9 cores demonstrating aberrant Ki-67 scores were visually examined nuclear staining was clearly visible, and non-specific nuclear staining could also be identified in the matched BC tissue samples, but not in the tonsil sections.

Correlation of Ki-67 scores between the four BC cell line cores and each of the BC tissue samples was examined using Pearson's correlation statistics. The r statistic range was 0.57-0.71 in comparisons between BC cell line cores and the BC-high sample, and 0.53-0.70 for those with BC-low; in each case BT-483 showed the highest correlation score and BT-20 the lowest. A similar analysis was undertaken between the tonsil and the two BC tissues. The r statistic for correlation between tonsil and BC-high scores was 0.72; it was 0.64 for those between tonsil and BC-low.

Conclusions: By using a pure population of Sf9 cells we have developed a sensitive indicator of non-specific nuclear staining in Ki-67 stained slides which identifies the presence of the artefact.

Cores made from Sf9/BC cell line mixtures (especially BT-483) produce Ki-67 scores which correlate with those obtained in breast cancer samples at a similar level to those achieved between tonsil and BC samples; cell line mixtures can be adjusted to show Ki-67 scores clinically relevant ranges, and they do not show the biological variations seen in tissue controls.

Patient and Public Involvement (PPI) – It's role in keeping the ATNEC trial open to recruitment.
Theme: Living with BC/QoL/Patient perspective/Supportive care

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Background: The ATNEC study is a phase III, randomised, multi-centre trial investigating whether axillary treatment can be avoided in cT1-3N1M0 breast cancer patients with no residual axillary nodal disease post-neoadjuvant chemotherapy (NACT).

Patients with no residual disease on sentinel node biopsy, post-NACT, are randomised (1:1) to axillary treatment (nodal radiotherapy or axillary nodal clearance) vs. no further axillary treatment.

The ATNEC study opened at the height of the COVID-19 pandemic (December 2020), which impeded initial recruitment. After completing the 18-month pilot phase of the study in Summer 2022, ATNEC underwent a review by its funder, the NIHR HTA, to assess the feasibility of continuing the trial, given that recruitment had fallen behind target.

In preparation for this review meeting, the PPI team decided to find out whether patients and the public thought it would be acceptable to discontinue the trial or whether it should stay open. For this purpose, the PPI team developed the following question:
'Is the ATNEC research question one which needs answering or should eligible patients simply be treated according to their oncology centre's current standard of care?'

Method: As valued members of the Trial Management Group (TMG), the PPI team were aware of current recruitment figures and targets. They decided to run a patient focus group to try to find out what patients thought. It was possible that patients might think that the funder's money could be better spent on other research and, as TMG members, it was possible that the PPI team were biased in favour of keeping the trial open.
They invited members of Independent Cancer Patients' Voice (ICPV) to take part in a focus group using the Teams virtual platform. ICPV have experienced members who are knowledgeable about clinical trials and who have a lived experience.

Results: ICPV members met for one hour, facilitated by two members of the PPI team, and discussed the question in detail. Their conclusion was: 'The research question is unanswered and important and so the trial should continue'.

The PPI team included this conclusion in a report from the patients' perspective which was then incorporated into the monitoring report to the funders.

At the ATNEC Trial's funding review meeting, the PPI section of the report was discussed and was deemed to carry weight. The funders agreed that the trial should remain open to recruitment.

Conclusion: The PPI team continue to be an essential part of the ATNEC research team. Their opinions are constantly sought, listened to, and valued. Most importantly, the PPI team set out to obtain an unbiased, wider patient opinion on the future of the study and presented this to the funders, rather than simply presenting their own agenda.

Trial Registration: ISRCTN 36585784 ClinicalTrials.gov: NCT04109079

A pilot study of the impact of a personalised online yoga and wellness programme on quality of life in women treated for breast cancer
Theme: Prevention/Lifestyle

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Background: Yoga and physical activities such as strength training are known to be beneficial in symptom management and improving quality of life amongst breast cancer patients and women who have been treated for the disease.

A systematic review in 2022 concluded that there were significant benefits of yoga intervention in various aspects of quality of life, fatigue, nausea/vomiting, sleep quality, anxiety, depression, and distress. [1]

Methods: 10 patients were enrolled onto the pilot programme at no cost to the patient. They agreed to fill in questionnaires (adapted from EORTC QLQ-C30 quality of life questionnaire with permissions) pre programme and post programme for quantitative as well as qualitative evaluation.

The Gentle Recovery programme (gentlerecovery.co.uk) consists of 12 modules of low impact but effective yoga and oncology exercise sessions. These whole-body conditioning sessions begin with regaining a healthy posture and core strengthening. Progressing steadily to regain joint mobility, all-body strengthening, shaping and toning. 12 relaxation audio sessions and access to the community tree, online journal and tutorials, full of helpful tips on topics such as; nutrition, sleep, stress management, emotional wellbeing and intimacy, fatigue management and lymphoedema were also included. [2]

Results: Patients felt better during and after the programme.
Average scores in many of the EORTC questions improved with progression through the modules, particularly the questions regarding dissatisfaction with body, attractiveness, pain in shoulder/arm and arm movements, however patients remained anxious about their health.

Question of shortened EORTC QLQ-C30	Average score before	Average score after	% change
Have you worried about your health in the future?	3	3.4	+11.8
Have you felt less physically attractive?	2.64	2.6	-1.5
Have you been dissatisfied with your body?	2.73	2.4	-13.8
Have you had pain in your arm or shoulder?	1.91	1.8	-6.1
Have you had problems raising your arm or moving it sideways?	1.8	1.4	-28.6
Have you had pain in the area of your affected breast?	2.27	2.0	-13.5
Has your breast been swollen?	2.09	1.8	-16.1
Have you had problems with joint stiffness?	2.78	2.6	-6.9
Have you had problems with painful joints?	2.18	1.6	-36.3
Have you had problems with painful muscles?	2.2	1.4	-57.1

Direct quotes included: "This is the first time I have stopped and really considered what my body and mind have been through. It has been a bit of an awakening moment."
"I definitely feel that my whole body is getting a workout. The relaxation is intense in a good way because it's amazing how, if you allow yourself, you can be absorbed into the space."
"This course is changing the way I am looking at exercise.
Thank you so much for accepting me onto this programme – it is honestly making me so much more aware of my body and the impact breast cancer has had. There are the obvious scars but, looking at the wider impact is going to make such a difference."
"This programme helped me physically but also emotionally. I thought I was doing ok, because I was getting out and about but, doing the programme slowed me down to really focus on how my body and mind were feeling."

Conclusion: Regular guided exercise sessions, reflection and peer support have a positive impact on emotional and physical recovery from breast cancer treatment. The programme will be offered to patients with financial support from charity funds. We will continue to monitor EORTC scores and feedback on the programme.

A Novel Way to Increase Recruitment to a National Multicentre Study. The ChamPionSE Scheme for the ABS ASPIRE Breast Pain Pathway Rapid Evaluation Project
Theme: Other

Kathryn Ellis[1], Jo Fields[2], Suzanne Halliday[3], Rajiv Dave[1], Thomas Hubbard[4], Jennifer Hu[5], Anna Isaac[6], Alice Cui[7], Ramsay Cutress[8], Shelley Potter, Karina Cox[9], Leena Chagla[10], Chris Holcombe[11]
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Background: There is increasing evidence that the symptom of breast pain is unrelated to breast cancer. Consequently, new approaches to manage breast pain are needed, that avoid resource intensive diagnostic clinics, yet provide patients with the specialist support required. The ABS ASPIRE project has been developed to evaluate, rapidly and efficiently, new pathways for the management of breast pain. The ASPIRE steering group has developed a novel way to encourage participation in the project by developing the 'ChamPionSE' scheme (Champions for Pathway Service Evaluation) which provides a structure for the development of a quality improvement initiative for supporting recruitment. Often, the 'champion' will be trainee clinicians such as surgical registrars and trainee advanced clinical practitioners (ACPs), implementing the ASPIRE project in their local unit. Those participating in the ChamPionSE scheme, receive formal recognition of engagement in a quality improvement project from the Association of Breast Surgery.

Method: Essential project activities are assigned to the 'ChamPionSE', including data collection, reporting study progress, and promoting the study locally. Incentives include opportunities for research activity, management and quality improvement exposure, a certificate of completion from the ABS, allocated CPD points, and acknowledgement in research publication. In addition, 'champions' who also recruit into the project have the opportunity to gain a bursary for attendance at the ABS conference, in the highest recruiting sites.

Results To end of August 2023: 22 units have signed up to the evaluation. Of these 22, 13 units have started data collection. Five people have signed up to the ChamPionSE scheme, including three surgical registrars, 1

international oncoplastic fellow, and a trainee ACP. At the time of writing, 485 patients have been entered into the evaluation, 78 of these have been recruited by ChamPionSE. However, the top two recruiting sites do not have a ChamPionSE.

Conclusion: The ChamPionSE scheme was initiated to maximise, formalise, and evidence the learning opportunities available to trainees in participation. Recent collaborative studies have noted a lack in engagement from this group, and in this current study 41% of registered units have yet to commence data collection. Furthermore, the largest volume recruiting sites do not correlate with those signed up to the ChamPionSE scheme. Despite the enhanced incentives compared to previous collaborative projects, there remains inadequate engagement with the ChamPionSE scheme. This will be evaluated further, to understand the barriers to engagement with the scheme amongst trainee surgeons and ACPs, particularly in the current health climate where service pressures impact professional development.

Can patients with breast pain successfully exclude any other breast symptoms without the need for clinical examination in primary care?
Theme: Other

Katy S Ellis[1]
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Background: With referrals exceeding the available clinical capacity, breast units nationally are overwhelmed. Many patients are now waiting longer than necessary for an appointment.

Breast units are adapting and creating new pathways for specific condition such as breast pain, as there is increasing evidence suggesting breast pain is not a symptom that is related to breast cancer. Breast pain, however, is a common condition and is responsible for up to 20% of referrals into a breast unit. This is despite national guidance stating that in most cases it is best managed in primary care.

It is common for patients to attend their primary care facility with a solitary symptom of breast pain but then found on examination by their primary care clinician to have a palpable finding on examination. In most cases this palpable finding would exclude them from a breast pain pathway and would prompt assessment in a one stop clinic. This finding along with the referral into secondary care, increases anxiety along with the patient having to wait for an extended period to be reassured in a one stop clinic.

An assessment tool which requires further validation has been created. This could be used to assist primary care clinicians in assessing these patients over the phone, but first it is crucial that we establish the patients' ability to assess themselves.

Method: A retrospective internal audit will assess patients who have been referred into secondary care with a solitary symptom of breast pain with or without a finding on clinical examination in primary care. Recorded will be the patient findings prior to seeing the primary care clinician, the findings of the primary care clinician, the findings of the secondary care clinician and the ultimate outcome.

Results: Results will show any discrepancies between patient findings, primary care and secondary clinicians and the ultimate outcome. This will hopefully support the idea that patients are well equipped to rule out any palpable findings alongside those of breast pain, and may support the idea that patients can be assessed without the need for clinical examination.

Conclusion: Telephone consultations in primary care are proven to be cost effective when deemed clinically appropriate. If patients are proven to accurately assess themselves for further symptoms, a validated assessment tool for breast pain could be implemented for use in non-face to face consultations. A telephone assessment of breast pain patients in primary care may reduce the demand on primary care clinicians, diagnose and treat patients earlier relieving anxiety, and in addition reduce the need for referral into secondary care. This would ultimately create capacity in one stop clinics for those who really need it.

Risk of incomplete ovarian function suppression (OFS) using gonadotropin-releasing hormone (GnRH) agonists and antagonists in premenopausal women with estrogen receptor (ER)-positive breast cancer
Theme: Treatment/Novel agents

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Background: Ovarian function suppression (OFS) is used as part of treatment for high-risk early or advanced estrogen-receptor positive (ER+) breast cancer in premenopausal women. Gonadotropin-releasing hormone (GnRH) agonists and antagonists can be used for OFS which may be incomplete but the extent to which this occurs is not well established. The implications of such incomplete suppression are not known, but based on the mechanism of action of aromatase inhibitors (AI) it is likely that in particular when OFS is used in combination with an AI, treatment would be ineffective if there exists residual ovarian function. Current guidelines do not suggest assessing for OFS, in part due to the lack of an agreed definition for OFS. No systematic review has been carried out to assess the success of OFS to the best of our knowledge. We therefore conducted a systematic review to assess how frequently OFS is incomplete in different settings.

Methods: We searched MEDLINE and EMBASE for studies which include information on the risk of OFS using GnRH agonists and antagonists in premenopausal women with ER+ breast cancer. The protocol was registered on PROSPERO (CRD42023395920) and is available at www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023395920.

Briefly, we included studies which included premenopausal women with ER+ breast cancer who are treated with a GnRH agonist or a GnRH antagonist for OFS (alone or in combination with other treatments). Only English language articles were included. There were no restrictions on the types of study. Case reports were included for qualitative synthesis. Studies including women treated with ovarian ablation using oophorectomy or radiotherapy were excluded. The main outcome of interest was incomplete OFS, based on any definition. Additional outcomes of interest were serum estradiol (E2), estrone (E1), estrone sulfate (E1S), luteneising hormone (LH), follicle-stimulating hormone (FSH), other hormones, and amenorrhoea.

Results: We have completed full-text screening and have provisionally included up to 130 papers. Included papers presented data from trials, such as the SOFT-EST sub-study and TREND trial, as well as observational studies including case reports and case series. Several studies have shown that in a subset of patients there may be incomplete OFS at least at some point during treatment. We will present results based on analysis of included studies, discussing incomplete OFS, and measurements of relevant hormonal levels.

Conclusions: Some patients with ER+ breast cancer receiving GnRH agonists have incomplete OFS either at isolated time points or persistently throughout treatment. Future research is needed into the implications of incomplete OFS, the development of clearly defined criteria for its definition, its causes, and the evaluation of potential changes to treatment strategies in the context of incomplete OFS.

Mini Review: Breast Cancer Care in Individuals with Differences of Sexual Development
Theme: Genetics/Screening/Early detection

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Disorders or differences of sexual development encompasses an important group of conditions that affects up to 1 in 5,000 live births. Many individuals living in the female gender includes Turner syndrome, congenital adrenal hyperplasia and conditions with 46XY karyotype such as gonadal dysgenesis (Swyer syndrome). Individuals are commenced on high dose oestrogen to initiate and maintain development of secondary sexual characteristics such as breasts which is paramount in them identifying in the female gender.

We highlight the first case of a patient with Swyer syndrome who was treated with long term oestrogen therapy and later developed breast cancer. In individuals with gonadal dysgenesis, testicular malignancy is a recognised risk and is screened for. Prolonged exposure to exogenous and endogenous hormones can increase the risk of breast cancer however how much this risk increases in those taking high dose hormones is not documented in the literature. We aim to highlight the importance of breast cancer treatment and surgical reconstruction in this group and whether they should be considered for early breast cancer screening.

Conclusion
It is imperative that triple assessment is undertaken in every patient with a breast lump, regardless of gender identification. Clinicians must not delay investigations in this patient group due to a misunderstanding of their condition. Those on long term hormone supplementation should be entered into the breast screening program at an earlier age with Magnetic Resonance Imaging surveillance. Careful consideration of post treatment endocrine therapy is required and under the care of the multi-disciplinary team.

Exploring outcomes and experiences of women denied immediate breast REconstruction after maSTectOmy for bREast cancer during the COVID-19 pandemic - The RESTORE C19 Study
Theme: Surgery

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Introduction: 40% of the 55,000 women diagnosed with breast cancer each year in the UK undergo mastectomy and NICE recommend that immediate breast reconstruction (IBR) should be offered to improve quality of life. During the COVID-19 pandemic, however, this offer was withdrawn to prioritise frontline care. The RESTORE C19 study aimed to use mixed methods to explore outcomes, lived experiences and views of women not offered IBR during the pandemic.

Methods: Women not offered IBR between March and October 2020, were identified via B-MaP-C, a prospective multicentre cohort study that documented changes in breast cancer treatment decisions during the pandemic. All patients were followed up between December 2021 and July 2022 to explore their ongoing management including whether they had undergone, were awaiting, or had decided against delayed breast reconstruction (DBR). Descriptive statistics were used to summarise results.

Semi-structured qualitative interviews were undertaken with a purposive sample of women to explore their experiences in more depth. All interviews were transcribed verbatim and analysed thematically, with data collection continuing until saturation was achieved.

Results: Of the 366 women identified as being denied IBR, complete follow-up was available for 311 (85%). Women had a median age of 50 (range 27-83). Most (77%) presented with symptomatic breast cancer and had no significant comorbidities.

At between 21-28 months follow-up, almost a fifth (n=58, 19%) had decided against DBR. Of the remainder, approximately 60% (n=149) had had a surgical consultation to discuss DBR and around a third (n=91) had been referred to plastic surgeons to discuss autologous options. However, only 21 (8%) women had actually received a DBR procedure.

Eighteen women with a median age of 48.5 (range 34-67 years) who had undergone mastectomy 2.5-3 years previously were interviewed. This included nine women who had decided against or were unsure about DBR; five who had either received or awaited DIEP reconstruction and four who had either received or awaited symmetrising mastectomy. Whilst all women reported feeling "grateful" for the treatment they received, some reported feeling "abandoned" by healthcare professionals, and others the need to chase breast surgical teams for care, advice and support. Many women described how their desire for symmetry, either with breast reconstruction or symmetrising mastectomy had “paled into insignificance” in the months and years following their treatment.

Conclusions: The impact of COVID19 continues to be felt by women treated for breast cancer during the pandemic with the majority of those denied IBR either still awaiting delayed procedures almost three years after their initial mastectomy or deciding against further surgery.

There is a need for individualised support to provide these women with equitable and timely access to DBR and/or symmetrising mastectomy depending on patient preference to help them move on with their lives.

Inhibition of zinc transporters significantly reduces breast cancer cell motility, in vitro
Theme: Metastatic breast cancer

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Background: As a primary cause of breast cancer-related mortality, prevention of cancer metastasis remains a significant area of unmet clinical need. Therefore, identification of druggable molecules, mediating the acquisition of highly motile/invasive phenotypes, is a priority for the prevention of breast cancer spread. ZIP6 and ZIP10, homologous members of the SLC39A zinc importers, are crucial drivers of mitosis and epithelial-to-mesenchymal transition. Previous data suggests that ZIP6 and ZIP10 may also be functionally important mediators of cell migration. This study aimed to validate this in two clinically relevant breast cancer models, using newly-developed ZIP6/ZIP10 inhibitors. Further, this study is the first to use immunofluorescence to examine ZIP6/ZIP10 localisation and interaction during migration, to begin to unravel the mechanism underlying this process. With the well-documented clinical associations between ZIP6/ZIP10 expression, regional lymph node invasion and breast cancer metastasis, it is hoped that these data can expand the clinical relevance of emerging anti-ZIP6/ZIP10 agents to not only restrict breast tumour outgrowth, but also metastatic dissemination of these tumours.

Methods: 18-hour wound healing and transwell migration assays were performed +/- a ZIP6/ZIP10 inhibitor, using serum as a migratory stimulant and fibronectin as a substrate. For immunofluorescent interrogation and proximity ligation assays (PLA), cells were seeded onto fibronectin-coated coverslips and stimulated with serum for 1 hour prior to fixation, +/- ZIP6/ZIP10 inhibitor. An 18-hour nocodazole treatment arm was also included in PLA to enrich loosely-adhered cellular fractions. ZIP inhibitors used in this study took the form of monoclonal antibodies raised against the N-terminal regions of ZIP6 and ZIP10, known to restrict zinc influx through these transporters.

Results: Functionally, both ZIP6 and ZIP10 inhibition resulted in significantly reduced wound healing capacity and transwell migration of MCF-7 cells, whereas ZIP10 inhibition alone was associated with a significant reduction in migratory capacity of MDA-MB-231 cells across both assays. When examined by immunofluorescence, localisation of both ZIP6 and ZIP10 was observed in membrane structures associated with establishment of cell polarisation and adhesions, namely early protrusions, lamellipodia and membrane “blebs” enriched in low-adhesion contexts. Inhibition of ZIP6 or ZIP10 in MDA-MB-231 cells visibly confused cell polarisation, with ZIP10 inhibition associated with the greatest disruption. Proximity ligation assay confirmed the co-localisation of several proteins predicted to be within ZIP6/ZIP10 interactome to early migratory structures, suggesting ZIP6/ZIP10 function as part of a multi-protein complex.

Conclusions: Together, these results suggest that ZIP6 and ZIP10 are functionally relevant mediators of cancer cell migration, with potential roles in nascent adhesion dynamics and cell polarisation. This work indicates that ZIP6/ZIP10 inhibitors may represent novel anti-migratory agents that may have the potential to reduce metastatic potential of breast cancer.

Single cell analysis of paired lymph nodes and primary tumors in breast cancer patients
Theme: Metastatic breast cancer

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A sentinel lymph node (SN) is the primary node draining the tumor and is assumed to be affected early in the metastatic process. The sentinel node holds a key position in the immune response against tumor in breast, and represents a unique connection between the tumor and the host immune response. We hypothesize that the immune profile in the primary tumor and the paired lymph node (LN) is different during tumor progression.

3.6 million single cells from paired primary tumor and lymph nodes from 28 breast cancer patients (Oslo2 cohort) was analyzed by single cell mass cytometry (CyTOF) with a 47 antibody immune panel and characterized by a semi-automatic gating approach (FlowSOM).

Tumor cells were found in 11 LN. When analyzing the leucocytes from LN we identified a significant difference in immune cell type skewing towards higher abundance of memory CD4 and CD8 T cells expressing an exhausted phenotype in LN with metastasis. In addition, a higher abundance of activated Tregs and significantly lower abundance of resting Tregs was found in the metastatic LNs compared to the sentinel lymph nodes. The change in immune composition and exhaustion was correlated to the metastatic tumor burden. The skewing towards an exhausted immune profile was also found in larger primary tumors compared to smaller primary tumors.

We further analyzed tumor cells from 8 patients with paired primary tumor and LN. No differences were identified in the primary tumor when stratified by LN status, but LNs with smaller metastasis expressed lower levels of epithelial markers essential in the Epithelial-to-Mesenchymal Transition such as E-cadherin, Pan Cytokeratin and EpCAM – this in contrast to the LN with manifested metastasis in the axilla which expressed higher levels of epithelial markers and lower levels of mesenchymal markers such as Vimentin and CD44.

We identified a skewing in the immune profile from a naive phenotype towards a memory and exhausted phenotype in CD8 and CD4 T cell population in LN with manifested metastasis. We also identified that tumor cells in smaller metastatic tumors resembled a “mesenchymal like” phenotype compared to in the larger manifested tumors. These results suggest that the immune suppression is correlated with the tumor burden.

Implementation of Breast Cancer Choices: how a web-based patient decision aid for decisions about BRCA testing is implemented in real-world, mainstream cancer care settings
Theme: Genetics/Screening/Early detection

Rebecca Foster[1], Gillian Crawford[2], Lesley Turner[3], Kelly Kohut[1,4], Kate Morton[1], Lucy Side[2], Jackie Chandler[5], Kate Lippiett[1,6], Diana Eccles[7], Claire Foster[1]
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Background: Decisions about germline genetic testing can be complex and personal with implications for patients and families. Many breast cancer patients can choose testing at the time of diagnosis. Genetic testing is increasingly being offered at point of care in oncology and breast clinics, however, mainstream cancer care clinicians may lack the necessary skills and time to inform and support patients.

Web-based patient decision aids (PtDA) could offer an effective solution, providing a patient-facing resource with information and decision support about genetic testing. Breast Cancer Choices (BCC) is one such PtDA, co-developed through an evidence based, patient focussed process.

We aimed to evaluate the impact of BCC on genetic testing decision making and clinician experiences in mainstream care. We analysed changes in Decisional Conflict (uncertainty about a course of action), acceptability to users, and barriers to and facilitators of implementation of the PtDA in real-world settings.

Methods: Health professionals at six hospitals in Wessex and the Channel Islands were introduced to the study by a Consultant Genetic Counsellor during training and set-up activities, before starting mainstream breast cancer genetic testing. At each participating hospital, women were signposted to BCC by their health professional who gave them a flyer with a weblink and QR code.

Website users were asked to complete a Decisional Conflict questionnaire at the start and end of their PtDA session, and an acceptability questionnaire.

Usage was monitored through Google Analytics. PtDA implementation is documented throughout the study, tracking adaptations to implementation. Interviews with users and health professionals are planned.

Results: Between May 2022 and September 2023, 117 mainstream cancer genetics tests were ordered by breast teams in the study area. BCC flyers were given out when possible and 35 women used BCC.

On average, users spent 21.7 minutes on BCC and logged in 1.32 times. Mean Total Decisional Conflict fell from 42.2 to 8.3 for 11 users who completed the measure before and after using BCC (0-100 scale). Acceptability of the PtDA was high; 10/12 users gave positive responses to all acceptability questions.

Health professionals identified time pressures, low staff numbers and uncertainty about when best to talk about genetic testing as barriers to implementation of the PtDA. These were closely linked to concerns about the introduction of new work practices related to mainstream cancer genetic testing.

Conclusion: Not all eligible patients were offered BCC during the study period. However, when used, BCC was associated with a reduction in Decisional Conflict and high acceptability ratings. Barriers to implementation were identified, centred on integrating BCC signposting into new mainstream genetic testing processes. This is an on-going study and further work is required to identify facilitators to effective signposting of BCC to patients making decisions about genetic testing.

ATNEC – Patient Experience Sub-Study (IRSCTN: 36585784): What Patients Think About Taking Part in Breast Cancer Treatment De-Escalation Trials
Theme: Living with BC/QoL/Patient perspective/Supportive care

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Background: Recruitment to de-escalation trials is challenging because of strong patient and clinician preferences and worry around 'under-treatment'. ATNEC is a phase III, randomised (1:1), multi-centre trial to assesses whether axillary treatment can be de-escalated, post-surgery, in T1-3N1M0 breast cancer patients who have no residual nodal disease post-neoadjuvant chemotherapy. Understanding why patients do/do not wish to participate is important as it can influence recruitment strategies.

Methods: ATNEC has registered 518 patients of which 243 have been randomised against the 1900 target. The patient experience sub-study uses semi-structured interviews to explore how patients process information about the trial and their decision to take part.

Results: Nineteen trial participants have been interviewed and talked openly about their personal cancer pathway and their decision-making process regarding the trial.
Initial analysis suggests that participation is often altruistic:
'…there wasn't really much of a decision to make….. I just thought to myself, well, anything that I can do to try and help people in the future then….why wouldn't I do that? [TNO 0001]
Understanding of lymph nodes and axillary treatment ranges from a little:
Interviewer: 'And before that did you have any understanding of why……they might want to take out lymph nodes from under your arm?' Participant: 'Uh, I think I'm gonna say no to that.' [TNO 0011]
to a lot:
'…what I understood from that was the lymph nodes are really, really good at holding on to the cancer for like a really long time.' [TNO 0001]
All participants interviewed who have been randomised to no further axillary treatment have said they are happy with this allocation. One participant randomised to receive axillary radiotherapy is concerned about potential side-effects: 'I'm having great reservations about going ahead and having radiotherapy.' [TNO 0035]

Conclusion: Patients taking part in the ATNEC trial do not appear to be worried about de-escalation of treatment. Apart from altruism, a reduction of potential treatment side-effects is a key motivating factor for participation. Patients who decline randomisation tend to have a preconceived treatment preference possibly guided by initial contact with the clinical team. Exploring information exchange is a key to successful recruitment.

FAST MRI - Diagnostic Yield study for Average MammOgraphic screeNing Density (DYAMOND): Protocol of a trial in progress
Theme: Trials in progress

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Design: FAST MRI: DYAMOND is a 42-month, prospective multicentre diagnostic yield, single arm study funded jointly by the Medical Research Council and National Institute of Health and Care Research through the NIHR's Efficacy and Mechanism Evaluation (EME) scheme (NIHR150502). It is sponsored by North Bristol NHS Trust.

Participants: Women aged 50-52 years, invited for their first (prevalent) mammogram within the population-risk NHS Breast Screening Programme, who have BI-RADS "B" mammographic density and have not been recalled for further investigations from their screening mammogram.

Intervention: All study participants will have a FAST MRI (First post-contrAst SubtracTed) of the breast.

Research Outcomes: Primary outcome: the number of cancers missed by mammography but detected by FAST MRI.

Secondary outcomes: grades, sizes and stages of cancers detected, recruitment rates, recall rates, biopsy rates, any adverse reactions to FAST MRI and intervention acceptability to participants (including embedded qualitative sub-study).

Public and Patient Involvement and Engagement (PPIE)
PPIE has been integral in the planning of the research question and study design:

- The FAST MRI programme's core aim is to reduce the number of breast cancers diagnosed at a late stage through being undetected on a mammogram. Input from women living with metastatic lobular cancer (diagnosed late due to masking on mammogram) emphasised the human cost of late diagnosis.
- Breast Density Matters UK, campaigns for supplemental screening for women with high mammographic density. They understand that there is a knowledge gap about whether FAST MRI could find cancers missed by mammography for women with average density. They acknowledge that the exclusion of women with high mammographic density from this particular study is a necessary step in the optimisation of breast screening for all.
- Our PPIE contributors highlighted the importance of keeping MRI scan times short and that the absence of ionising radiation is an important advantage of FAST MRI over mammography. They expressed their appreciation of the fine balance of risk vs. benefit in breast cancer screening. The clinicians and PPIE members discussed the literature and estimates of false positive biopsies from FAST MRI and collaboratively developed the proposal's strategy for dealing with MRI 3 (uncertain) results.

One of our Lay Co-Applicants is a member of the Trial Management Group and the other is a member of the Trial Steering Committee, ensuring public and patient views are represented in all aspects of study delivery and operational oversight.

Statistical design: Planned sample size = 1000. A Fleming's two-stage design will be used to assess the number of additional cancers detected by FAST MRI. This design allows for early stopping after stage one, which would save patients, funding costs and time continuing to the end of the study if the question could be answered earlier.

Can preoperative upfront magnetic (Magseed®) localisation of impalpable screen detected breast lesions improve workflow and simplify patient pathways?
Theme: Surgery

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Magseed localization of impalpable breast lesions has been shown to be an effective non-inferior alternative to wire guided localization. We speculated that in a pre-defined cohort of patients, insertion of a Magseed at the time of initial biopsy would improve workflow by decreasing radiology clinician appointments in addition to improving the patient pathway by reducing interventional procedures with associated anxiety and discomfort.

Patients were identified prospectively in screening assessment clinics against a set of selection criteria including lesion feature, lesion size, breast background density, nodal status and previous history. It was the audit design intention to have a second opinion on features and suitability prior to intervention.

Twenty patients were initially audited. All cases were confirmed as invasive carcinoma, concordant with malignant radiological features. All patients proceeded to breast conserving surgery, 19/20 having clear margins at initial excision surgery. Pathological subset was 16/20 invasive ductal carcinoma, 4/20 lobular carcinoma. Pre-operative MRI was not performed in the lobular cohort due to artefact from the Magseed, which may have been considered had this intervention not taken place.

Breast density was largely fatty, with 17/20 being BIRADS A or B. Three cases were retrospectively classified as BIRADS C, within this category lobular carcinomas predominated.

Conclusions; Within a predefined patient cohort, of small, mass like screen detected lesions, upfront Magseed placement at the time of biopsy reduces radiological intervention, beneficial for patients and workflow of clinical teams without adversely altering final outcome. Double reporting of the case features against the selection criteria is superior to single clinician selection.

Practice patterns in ongoing neoadjuvant ATNEC trial for patients with cT1-3N1M0 breast cancer: node marking, response to neoadjuvant chemotherapy (NACT) and breast conservation rates
Theme: Early breast cancer

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Background: In the ATNEC trial (ISRCTN 36585784), cT1-3N1M0 patients receive NACT followed by sentinel node biopsy (SNB). If the sentinel nodes (SNs) have converted to benign (ypN0), patients are randomly assigned to Axillary Treatment vs no Axillary Treatment.

Node marking is recommended in the study and sites are offered training to enable them to adopt node marking in a standardised way. Additionally, the study has in-built radiotherapy quality assurance program.
Objectives: To prospectively evaluate the practice patterns and response to NACT, uptake of node marking by centres, marked node identification rates, and breast conservation rates in the ongoing UK ATNEC trial. The trial aims to recruit 1900 patients.

Methods: Data for all patients who were randomised (December 2021 - April 2023) across 70 UK centres were included in these analyses. Patients were cT1-3N1M0 at presentation, received NACT and were found to have no residual nodal disease (ypN0) on SNB.

Results: Among the 146 randomised patients (median age 54 [range, 28-77] years) (median BMI 26.5 [range, 17.6-51.1]), 54% (79) were post-menopausal, 74% (108) underwent breast conserving surgery (BCS) and 26% (38) mastectomy.

At presentation, 12% (17) were T3, 66% (97) T2 and 21% (31) T1. 73% (107) had grade 3 tumours. 60% (88) were HER2 positive, 31% (45) triple negative and 9% (13) HER2 negative (ER or PgR positive). 56% (77) had an anthracycline and taxane based NACT and 40% (54) had a platinum containing regimen.

Median of 4 nodes [interquartile range, 3-5] were removed during SNB. Among the 138 patients with node marking data, the involved node was marked for 102 (74%) randomised participants. The marked node was removed in 98 (96%) of the 102 patients that had nodes marked. Of those 98 that had the marked node removed, the marked node was identified as the sentinel node in 88 (90%) of these cases.

Of the 139 randomised patients with data for breast tumour post-NACT, 69% (96) had complete pathological response, 9% (13) DCIS only, 22% (30) invasive cancer. Among the 77 patients with complete breast tumour response on imaging, 17% (13) had residual DCIS/invasive cancer. 52% (29/56) of patients with partial response or stable breast tumour on imaging had no residual tumour on histology (ypT0).

Of the 138 patients with data on post-NACT imaging assessment of the axilla, 14% (19) had partial or stable disease but complete pathological response on histology.

Conclusions: Majority of patients undergoing NACT in the UK have HER2 positive or triple negative breast cancer. Although 69% patients had a complete pCR (ypT0) in the breast, BCS rates remain low. 3 in 4 patients randomised had their node marked, with a 96% intra-operative identification rate; demonstrating that ATNEC has successfully rolled out node marking in the UK.

Prevalence and referral sources of metastatic breast cancer at the Kent Oncology Centre Maidstone & Tunbridge Wells; 2019 - 2023
Theme: Metastatic breast cancer

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Introduction: The National Cancer Intelligence Network recommended, in 2012, that all units should capture data on recurrent and metastatic breast cancer (MBC), following a pilot of 15 breast units in England (NCIN Data Briefing, June 2012).
Despite this, prevalence of MBC in England had not been reported until Palmieri et al reviewed NHS England's Hospital Episode Statistics (HES) 2016-21 database (Palmieri et al JAMA Network Open, 2022;5 (12). The estimates indicated a prevalence of 57, 215 cases, which has risen steadily over the past 5 years.
A Metastatic Breast Cancer service (MBCS), comprising of Nurse Consultant, Clinical Nurse Specialists and Cancer Support Workers, has been developed in our Trust since 2018. We collected local data to explore incidence, prevalence and sources/modes of referral.

Methods: The MBCS prospectively collected details of patients referred from multiple sources, including those referred directly to palliative care. The Kent Oncology Management System and hospital case notes were interrogated. Records were analysed, annually from January 2019 to September 1, 2023, including the two 'Covid years' (2020 and 2021). The following data was collected: MBC prevalence, incidence, deaths, referral source, method of presentation, basic biological characteristics.

Results: MBC patients on active treatment increased by 69% (152 to 257) over the period (Table 1).

Number of active metastatic breast cancer patients				
1 Jan 2019	1 Jan 2020	1 Jan 2021	1 Jan 2022	1 Jan 2023
152	181	199	205	257

Table 1

The number of new patients referred to the MBCS rose steadily over the period from 71 (2019) to 98 (2022) except for 2021 (73), which may reflect the impact of the Covid pandemic.
Deaths remained largely stable over the period 2020-2022.

The proportion of presentations with 'De novo' MBC (first presentation of breast cancer) reduced from 31% (2019) to 21% (2022), varying over the 'Covid years' (20% (2020) and 30% (2021) respectively).

Presentation through emergency care (EC) increased from 18% (2019) to 29% (2022), with 27% and 28% respectively during the two 'Covid years'.

GP referrals (via 2 week wait or direct to investigation) fell from 43% (2019) to 38% (2022), though an increase was seen during the 'Covid years' (47% and 45% respectively).

Conclusion: We believe this is the first detailed prospectively collected prevalence and incidence data of MBC in the UK. The rising prevalence is consistent with the estimates by Palmieri et al. Most MBC patients are on active treatment, reflecting the increased pressure on breast oncology services.
A worrying steady increase in presentations via EC (29%) was seen, and more than double that reported in the 2012 pilot (13%).
This, and the substantial proportion of de novo presentations, may reflect the impact of COVID-19 on GP access and changes in how and where patients are followed up. These data will inform workforce planning and demonstrate a need for increased patient and GP education regarding symptoms of systemic relapse of breast cancer.

Bespoke muscle resistance exercise (MRE) programme for use in a future clinical trial, following patient engagement program (PEP) in patients with advanced breast cancer (ABC)
Theme: Prevention/Lifestyle

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Background: Muscular resistance exercise has been investigated in early breast cancer but there has been little evaluation in ABC. Cancer guidelines suggest the use of physical activity, including MRE, to improve fatigue (National Comprehensive Cancer Network, 2020; European Society of Medical Oncology 2020) but improvement in other outcomes in ABC are less clear. In clinical trials, adherence to exercise intervention has been a challenge and has hampered investigation of other outcomes. Little data exists evaluating the possible reasons for this poor adherence and compliance. In preparation for an exercise component as part of lifestyle intervention trial in ABC, a PEP was undertaken to evaluate an on-line web-based exercise program. Results would support continued usage of the program or creation of a new program.

Methods: A commercially available program was used containing a library of exercises created for multiple disease types. There was no voice over. Involving an exercise science professional, 2 sets of muscular resistance exercise programmes were created (A &B), selecting exercises for upper and lower limb major muscle groups. Set A and B differed, with A involving younger leaner demonstrators and B older, less lean. Volunteers were asked to view the sets and complete a survey. The results of the survey, involving 21 volunteers of which 43% were over 60 years and presented previously, indicated that the following main modifications were needed to a program: use of demonstrators similar to patient's habitus and use of a voice-over to guide exercises. A short test video was produced incorporating these and other visual changes and viewed by a focus group of four volunteers.

Results: The focus group concluded that the new visual and audio changes would allow them to more easily perform the exercises and increase the likelihood of compliance compared to the on-line program. The group advised involvement of a more diverse demonstrator group and further improvements to the voice-over. A professionally produced video has now been made with all the above changes.

Conclusions: This PEP indicates that is necessary to review exercise programmes with patients and not assume they are all suitable for use in clinical trials. We believe a PEP of this kind with the resultant bespoke video is the first produced involving patients with ABC. This video will now be evaluated in a much larger diverse PPE which will help the development of a national UK clinical trial of exercise in ABC

Elucidating the Functional Mechanisms of a Novel PTEN Long Non-Coding RNA in Breast Cancer
Theme: Preclinical research

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Background: A common alteration in breast cancer is the inactivation of the tumor suppressor gene, PTEN (phosphatase and tensin homolog). PTEN prevents the overstimulation of the AKT pathway, slowing down cell proliferation. Thus, cancer cells utilize different approaches to shut down the expression of PTEN including mutations, promoter methylation, and post-translational modifications. While reduction of PTEN using these mechanisms explains a large number of cancer cases, in some cancer patients, including breast cancer, PTEN reduction cannot be explained by these mechanisms, suggesting an unknown pathway. We thus explored a post-transcriptional mechanism for regulating PTEN expression, specifically the splicing of its first intron, which is a minor intron. We have previously shown that minor introns can act as molecular switches that regulate the expression of the genes that harbor them. We thus hypothesized that the regulation of PTEN pre-mRNA splicing presents a novel mechanism by which breast cancer cells alter PTEN expression.

Methods: We used several breast cancer cell lines to determine PTEN expression and the status of its minor intron splicing. Real time qPCR and western blot were used to confirm splicing alterations and protein changes, respectively. To test if PTEN expression is indeed dependent on splicing, we used antisense oligonucleotides to alter the splicing of PTEN's minor intron. We then used 3'RACE to check if the minor intron contains any premature cleavage and polyadenylation (PCPA) signals. Overexpression of PTEN's novel long noncoding RNA (lncRNA) was done using a plasmid, followed by cell proliferation measurement to determine whether the lncRNA affects breast cancer cell growth and progression.

Results: RNA sequencing data analysis confirmed that PTEN's minor intron is inefficiently spliced in breast cancer cells. Our data also showed that the unspliced minor intron is cleaved and polyadenylated, supporting our hypothesis that in breast cancer cells the low efficiency of PTEN minor intron splicing leads to the production of a previously unidentified PTEN lncRNA. Cell proliferation assays showed that the deregulation of PTEN minor intron splicing leads to an increase in cell proliferation. Interestingly, the change in cell proliferation was decoupled from the decrease in PTEN protein and more consistently correlated with the production of PTEN lncRNA. Remarkably, overexpression of the PTEN lncRNA showed a significant effect on cell proliferation independent of any change in the endogenous PTEN mRNA or protein.

Conclusion: We conclude that breast cancer cells actively accumulate unspliced PTEN which is processed into a lncRNA that seems to alter cell proliferation independently of the PTEN protein. We are currently exploring the underlying mechanism of action of PTEN lncRNA. More specifically sponging of miRNAs and/or RNA binding proteins. Our preliminary data points to a specific miRNA that could be sequestered by PTEN lncRNA to inhibit its function.

Targeting zinc transporters provides a potent treatment for triple negative and tamoxifen-resistant breast cancer preclinical mouse models
Theme: Treatment/Novel agents

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Background: Triple negative breast cancers (TNBCs) present a clinical challenge with regards to treatment, their aggressive nature and higher risk of recurrence and metastasis. Zinc has been implicated in cancer, with breast cancer tissue exhibiting higher levels of zinc compared to normal breast tissue. Furthermore, our group have demonstrated how zinc drives the aggressive growth of tamoxifen-resistant breast cancer. We have discovered how zinc transporters ZIP6 and ZIP10 are essential for mitotic initiation in cells and our own ZIP6 and ZIP10 antibodies have inhibited cell division in multiple breast cancer cell lines. This work has been expanded to demonstrate inhibition of tumour growth in TNBC and tamoxifen-resistant xenograft mouse models.

Methods: 6-week-old female athymic nude (Charles River: 490) and NSG (Charles River: 614) mice were subcutaneously injected bilaterally in their flanks with $5x10^5$ MDA-MB-231 and $1x10^6$ MCF7 tamoxifen-resistant (TAMR) cells respectively (both with 50% Matrigel). Treatment via intraperitoneal injection (IP) of isotype IgG control or zinc transporter antibodies began once tumours reached 4x4-6x6mm. Tumours were calliper measured at 4-day intervals. Treatment intervals and antibody doses were assessed.

10-week-old female BALB/cByJ mice (Charles River: 627) were administered IgG and ZIP6 antibody at 0.1mg/Kg for 4 consecutive doses at 4-day intervals. At endpoint, peripheral blood was analysed by flow cytometry for various immune cell markers.

Results: Initial experiments using the ZIP6 antibody demonstrated an ability to inhibit the growth of TNBC xenograft tumours by 70% compared to the IgG control. Further experiments showed the optimal dose for this ZIP6 antibody was as low as 0.1mg/Kg. Furthermore, dosage intervals were optimised discovering that dosing at 4-day intervals was most effective at reducing tumour growth.

Importantly, ZIP6 antibody treatment can preferentially inhibit the growth of tamoxifen-resistant breast cancer xenografts compared to tamoxifen-sensitive counterparts. Interestingly, during all treatments, mice exhibited no adverse effects which was confirmed by demonstrating no effect on immune cells in immune competent mice. Furthermore, the tamoxifen-resistant xenografts were treated for almost 200 days with no observed adverse effects, suggesting good tolerance.

The TNBC xenograft experiments have now been expanded to compare ZIP10 antibody effects with ZIP6 antibody effects and a combination treatment with both antibodies simultaneously. Excitingly, all treatments successfully inhibit tumour growth but the combination of ZIP6 and ZIP10 antibodies demonstrates further tumour growth inhibition.
Conclusions: We have demonstrated that inhibition of the two zinc transporters essential for mitosis can significantly reduce the growth of triple negative and tamoxifen-resistant breast tumours in animals. The low dose required and lack of adverse side effects should enable these agents to move towards clinical use. It is hoped that these antibodies will provide a new effective treatment for both triple negative and tamoxifen resistant breast cancers which represent a clinical unmet need.

Neoadjuvant radiotherapy prior to mastectomy and breast reconstruction – a systematic review of oncological and aesthetic outcomes
Theme: Surgery

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Background: Neoadjuvant radiotherapy (NART) prior to mastectomy and immediate breast reconstruction for locally advanced breast cancer has the potential to reduce the deleterious impact of radiotherapy on the reconstructed breast and expedite treatment without impact on short-term oncologic control. The PRADA feasibility study has previously demonstrated that microvascular reconstruction is technically feasible and safe in modern breast oncology practice. We present a systematic review examining the oncological and aesthetic outcomes for NART prior to mastectomy and immediate breast reconstruction reported in the published literature.

Methods: A prospectively registered search of Medline (Ovid), EMBASE (Ovid), EMCARE (Ovid) and CINAHL (EBSCO) databases was performed in August 2023 for studies reporting NART prior to mastectomy and breast reconstruction. Oncological and aesthetic outcomes were extracted with risk of bias (ROBINS-I) and methodological quality assessed (STROBE checklist) for each study.

Results: Twenty published articles (19 journal articles and 3 abstracts) were identified reporting the outcomes of 1,258 patients with median follow-up between 19.0-212.4 months. Patients received neoadjuvant chemotherapy in 20 studies. Most studies were of low methodological quality and at serious risk of bias. Rates of pathological complete response (PCR) ranged from 16.6-77.8% (median - 45.0%). Rates of locoregional recurrence and overall survival ranged between 0-21.7% (median - 2.0%) and 82.0-98.3% (median - 8.4%) respectively. Rates of distant metastases ranged from 0-31.9% (median - 7.8%) Overall complication rates ranged from 2.2-66.6%. Rates of flap loss or necrosis ranged from 0-7.6% (median - 0.5%). Rates of revisional procedures ranged between 1.9-35.3%. Patient-reported outcomes were reported in 7 studies and were mostly ‘good’ or ‘excellent’.

Domain	No. of Studies (n=)	Result *Median (Range)*
Oncological Outcomes		
Pathological Complete Response	16	45.0% (16.6-77.8%)
Locoregional Recurrence	13	2.0% (0-21.7%)
Distant Metastases	11	7.8% (0-31.9%)
Survival (Overall / 5-year)	5	88.4% (82.0-98.3%)
Post-operative Complications		
Overall Complications	11	2.2-66.6% (Range only)
Seroma formation	6	10.1% (4.8-63.0%)
Haematoma formation	9	3.6% (0-11.5%)
Wound dehiscence	4	5.0% (2.5-6.4%)
Wound Infection	9	4.8% (0-19.1%)
Mastectomy Skin Flap Necrosis	10	5.3% (1-12.0%)
Scar Revision	4	7.7% (2.6-35.0%)
Reconstructive Outcomes		
Reconstructive Failure	3	5.7% (3.8-6.3%)
Flap Loss	9	0.5% (0-7.6%)
Fat Necrosis	4	2.2 (1.0-18.2%)
Surgical Revision	5	1.9-35.3% (Range only)
Assessments of Cosmetic Outcomes	7	Qualitative Data Only

Summative Table of Systematic Review Findings

Conclusion: The published literature described a heterogeneity of outcomes for patients undergoing PRT prior to mastectomy and breast reconstruction. This reflects a large number of small retrospective single-centre cohort studies of low methodological quality and at risk of bias. There is a clear need for a prospective pragmatic randomised controlled trial appraising the outcomes of PRT in the context of immediate breast reconstruction to accurately determine whether re-sequencing the order of adjuvant therapies leads to clinical benefit.

I'm sure it is good for me but I don't quite understand why – patients' experience of adjuvant bisphosphonates for early breast cancer

Theme: Early breast cancer

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Background: Bisphosphonates (BPs) are used to prevent bone loss in osteoporosis and to treat patients with skeletal metastases. In addition, multiple clinical studies in early breast cancer have demonstrated that BPs can reduce disease recurrence and improve survival, but only in postmenopausal women. In 2018, NICE recommendations resulted in BPs becoming UK standard of care for postmenopausal women with early breast cancer. But what is the experience of patients following this major change in practice? To explore this, we conducted a survey with the following aims:

- To provide real-world data regarding patients' experience with adjuvant BPs
- To explore patients' general understanding of why they receive adjuvant BPs
- To determine any difficulties or side effects of this treatment

Methods: In collaboration with Breast Cancer Voices, a Breast Cancer Now patient group, we developed a 30-question survey that was approved by the University of Sheffield Ethics committee and subsequently distributed through the Breast Cancer Voices monthly newsletter. We used Survey Monkey and the results were analysed by descriptive statistics.

Results: 32 responders agreed to complete the survey of which 25 were eligible and included in the analysis. Of the patients who were offered adjuvant BPs, 90% indicated that they received the full course of therapy, 5% did not complete the full course, and 5% were still receiving adjuvant BPs when they participated in the survey. None of the patients stated that they had refused adjuvant BPs. The most commonly offered adjuvant agent was intravenous Zoledronic Acid (90%), with 10% receiving oral Ibandronic Acid. All participants understood that adjuvant BPs prevent bone metastasis, whereas only half of the responders (55%) indicated that the agents were

offered for prevention of breast cancer recurrence. 41% stated that they received enough information about the use of BPs after their surgery, while 32% replied that they only had some information and 14% had minimal information for the use of these agents. The most common side effects experienced were joint pain and fatigue (both 50%), followed by flu-like symptoms (45%) and muscle pain (35%). However, 30% of the survey participants reported no side effects at all.

Conclusion: The responses suggest that despite some expected side effects, adjuvant BPs are well tolerated, and patients were motivated to complete the course of therapy. However, patients did not have a good understanding of the purpose of the treatment and would welcome better information. Further work at a local and national level is needed to ensure narrowing of patients' knowledge gap relating to the benefits of adjuvant BPs and why they are offered.

Acknowledgments: The survey was conducted in collaboration with Breast Cancer Voices (Breast Cancer Now group). We thank all the participants for their contribution to this study.

Axillary management of a positive sentinel lymph node biopsy in the era of Abemaciclib in early Breast cancer
Theme: Surgery

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Background: Abemociclib is a CD K 4+6 inhibitor licensed for oEstrogen Receptor (ER) +ve Human Epidermal Receptor (HER) 2 -ve early breast cancer to reduce recurrence and improve survival. It is indicated in patients with high risk of recurrence (≥4 positive axillary lymph nodes (ALN) OR 1 – 3 +ve ALN and either grade 3 (G3) disease or tumour size ≥5cm) based on the MonarchE trial. Therefore patients with 1-3 +ve ALN at sentinel lymph node biopsy (SLNB) with no other high risk features may be recommended completion Axillary Node Clearance (ANC) in preference to axillary radiotherapy to potentially obtain ≥4 +ve ALN. Therefore, patients may undergo more morbid axillary surgical treatment with an unquantified (possibly low) chance of qualifying for abemociclib in an era of surgical de-escalation and axillary radiotherapy. This study investigates patients with a +ve SLNB not initially meeting criteria for abemociclib and how many would have been subsequently eligible on achieving ≥4 +ve ALN at completion ANC.

Methods: All patients at a single UK institution diagnosed with ER+ve HER2-ve early breast cancer with a +ve SLNB and subsequent completion ANC between 01/01/2018 – 03/08/2022 were included (local audit 22-5734). Patients were identified by operation codes and clinical notes were reviewed. Statistical analysis performed with chi-squared test and student t-test, statistical significance $P<0.05$.

Results: 67 patients had +ve SLNB with completion ANC; 40 remained after exclusions (Neoadjuvant Chemotherapy (7), ER-ve or HER2+ve (10) and mis-coding (10)). 23/40 were eligible for abemociclib regardless of ANC findings (≥4 +ve SLN at SLNB (8), tumour ≥50mm (9), G3 (7)) leaving n=17 for analysis.

11/17 (65%) had no additional +ve ALN at ANC, 13/17 (76.5%) had a total <4 +ve ALN. Only 4/17 (23.5%) had a total ≥4+ve ALN.

Predictors of total ≥4+ve ALN were investigated; There was no statistical significant difference between <4 vs ≥4+ve ALN for breast operation, tumour type, grade or size, NPI, number of lymph nodes retrieved at SLNB, percentage yield of +ve SLNB (>50%, >75%, 100%) and ALN Ratio ($P>0.05$). The only outcome predictor was having only 1 +ve SLNB; all 8 of these patients had total <4 +ve ALN (vs 0 had ≥4+ve; $P = 0.029$).

Conclusions: This study demonstrates that patients who do not initially qualify for abemociclib after SLNB remain unlikely to after completion ANC, with less than a quarter achieving ≥4+ve ALN. There were no predictors of which patients may have a total ≥4+ve ALN (apart from no patients with 1 +ve ALN at SLNB had a total ≥4+ve ALN). These results suggest that the potential to achieve ≥4+ve ALN to qualify for abemociclib should not be a rationale for recommending completion ANC after a +ve SLNB.

External Breast Forms and the custom fit fallacy; why our innovative custom fit system fails.
Theme: Living with BC/QoL/Patient perspective/Supportive care

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In the field of external breast prosthesis, many teams across the world have been exploring a fully customised breast form. With each approach there are similar pathways; usually using a 3D scan to model the patient's shape needs before the creation of the prosthetic and a fitting process takes place. Although our Boost prosthetics are hugely different to the traditional silicone gel construction, we were recently supported by Innovate UK to explore this pathway through a feasibility study project. Our aim was to create a process to capture data and use this to model a custom Boost, with the projection and footprint of the breast form tailored to the customer's individual size needs. With a partner who had developed a brand-new, as yet unreleased 3D-print resin compatible with the high-quality medical grade silicone that Boost requires, we thought we were on to something. It would be possible, if our R&D programme worked, to produce a fully custom breast form for as little as £400 with a user experience that focussed on non-medical settings. We tested our hypothesis with some success, producing low-cost custom breast forms for a small trial group of women. Data capture, accuracy and the digital technology was a challenge, but the creation of the moulds and the custom breast forms was straightforward. We had proven it was possible. But was it actually needed? Was that what our customers wanted? No, actually it wasn't. What they wanted was a Boost that worked for them, but that did not necessarily mean they really wanted to have a custom one. Customisation was not a desirable option; it was a last resort. Our study shows just why human-centred design, and women-led co-creation is essential when developing products for women after mastectomy. Our project was a technical success, but failed where it mattered the most. Sharing the outcomes, our approach to innovation and the process behind our R&D programme, our presentation will highlight the importance of delivering innovation through a human-centred methodology.

The Impact of Body Mass Index on Pathological Complete Response Following Neoadjuvant Chemotherapy in Operable Breast Cancer
Theme: Prevention/Lifestyle

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Introduction: Breast cancer is a global health concern, impacting women with an incidence rate of 11.7% and a mortality rate of 6.9%. Pathological complete response (PCR) following neoadjuvant chemotherapy (NACT) is associated with improved survival outcomes in Breast cancer patients. Higher proportion of adults (63.5%) in the UK are found to have an elevated body mass index (BMI) which has been increasing over time.

Objective: We aimed to determine the rate of pathological complete response in breast cancer patients receiving neoadjuvant chemotherapy in our trust and compare pathological complete response rates in those with a normal body mass index (18-24.9) and those with an elevated body mass index (≥25).

Material and Methods: The study included females with biopsy-confirmed operable breast carcinoma and underwent surgery after neoadjuvant chemotherapy between January 2018 and December 2022. Patients were categorized into two body mass index (BMI) groups, normal (18-24.9), and elevated (above normal) (≥25). Pathological complete response was defined as ypT0/Tis ypN0, ypT0/Tis, or ypN0. Descriptive analyses were performed. Univariate and multivariate logistic regression was performed using R software.

Results: A total of 230 breast cancer patients were included, 68 (30%) had a body mass index between 18-24.9, 162 (70%) had an elevated BMI (≥25). Normal body mass index patients had the highest pathological complete response (PCR) rate (59%), while those with an elevated body mass index had a lower PCR rate (34%) ($p<0.001$). A normal body mass index (BMI) remained an independent predictor of pathological complete response (PCR) after controlling for age, Her2 status, and presence of stage 2 and stage 3 disease at diagnosis. (OR=1, 0.34; for normal and elevated BMI respectively, p value<0.001) (Table 1).

Variables		Odds ratio (PCR Yes)	CI		P value
			2.50%	97.50%	
Age (years)		0.99	0.96	1.01	0.241
Stage at diagnosis	I	1			
	II	0.78	0.31	1.95	0.60
	III	0.53	0.17	1.58	0.25
BMI	Normal	1			**0.001**
	Above Normal	0.34	0.18	0.66	
Triple negative	No	1			0.67
	Yes	0.83	0.33	2.00	
ER	Negative	1			**<0.001**
	Positive	0.16	0.06	0.37	

Table 1: Multivariate analysis

Conclusion: In our cohort, patients with an elevated body mass index (BMI) had a lower rate of pathological complete response (PCR) after neoadjuvant chemotherapy (NACT) than patients with a normal body mass index (BMI). The reasons remain unclear but may involve impact of insulin resistance on tumour cell pathways. Further studies are required to validate our findings and to establish underlying mechanisms, however, this study highlights obesity as an important public health issue.

Osteopontin (OPN) as a Potential Biomarker for Early Detection of Ductal Carcinoma in Situ (DCIS)
Theme: Pathology

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Background: This paper evaluates the current NHS guidelines for biomarkers used to detect breast cancer and explores the potential use of osteopontin as a DCIS progression biomarker. Additionally, the potential use of osteopontin as a biomarker was assessed in a retrospective cohort of patients with DCIS.

Methods: Literature review
Methodology incorporated evidence from credible journals, from the PubMed and SCOPUS websites, in relation to the properties of osteopontin and its use as a potential breast cancer biomarker, and an investigation into the current guidelines of biomarkers. An exclusion criterion was used to refine results and ensure relevancy and decreased bias by checking affiliations. Altogether, 12 relevant papers were collated.
QuPath pathology analysis
QuPath software was used on DCIS biopsy slides to produce H-values to be analysed and retrieved statistical data for each category as follows: pure DCIS, DCIS recurrence, and DCIS invasion. H-values were retrieved from the analysis to calculate the expression of osteopontin from each data set category.
Statistical analysis
The data sets from each category of DCIS (pure, recurrence, invasion) were averaged and the standard deviation was calculated.
Vijay Sharma calculated the survival curves for each data set.

Results: The key findings demonstrate a pattern between a high expression of osteopontin and the likelihood of progression into invasive breast cancer and recurrence of DCIS. As the severity of the cancer increases, so does the presence of osteopontin.
Additionally, according to the survival curves calculated, a lower expression of OPN indicates a longer survival time and a higher expression of OPN suggests a shortened survival period, which were measured in months.

Conclusions: There is capacity to use osteopontin concurrently with currently used biomarkers and guidelines to help guide clinical decision making in patients with DCIS. There is scope to explore therapies that could be offered from identifying a patient as 'OPN positive'. This would be especially beneficial in patients who may be classed as 'triple-negative' for breast cancer receptors. There is a necessity for further research with a larger sample to extrapolate data and find similar data or the opposing results. More broadly, this research could supplement investigations for other cancers linked to the excessive expressionof osteopontin as a biomarker, which includes colon cancer, ovarian cancer, hepatocellular carcinoma and glioblastomas, amongst others.

Keywords:
- Osteopontin-c (OPN-c), SPP-1 gene, oestrogen (ER) receptor, progesterone (PR) receptor, HER-2 receptor
- DCIS, breast tumour, breast cancer, pre-malignant breast tumour, invasive breast cancer, ductal carcinoma in situ, breast metaplasia,
- Prognostic biomarkers, guidelines, cancer detection

Roll out and influence on practice of the Talking about Risk, Uncertainties of Testing in Genetics (TRUSTING) educational programme
Theme: Genetics/Screening/Early detection

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Background: The significant capacity issues in family history clinics make calls for genetic testing of all breast cancer patients problematic. There is a need for mainstreaming of services by health care professionals (HCPs) who are not always familiar with genetic counselling. Following the successful development and evaluation of the TRUSTING programme for breast cancer HCPs (Fallowfield et al. BJC 2022), we trained facilitators to roll out workshops across the UK and probed its influence on mainstreaming within clinics.

Methods: HCPs (1 surgeon, 3 oncologists, 1 nurse specialist) who had attended original TRUSTING evaluation workshops, were trained to facilitate in pairs the 8-hour programme. SHORE-C organised dates, venues, recruitment of participants, pre workshop assessments, CPD points and prepared the data for workshop presentations. Participants completed 3 assessments pre-workshop: - 1) the Intolerance to Uncertainty Scale, 2) a 10-item questionnaire exploring self-confidence when discussing/explaining/advising patients about different aspects of BRCA testing, results, and treatments, and 3) an 18-item multiple choice knowledge questionnaire about gene testing in breast cancer. Both self-confidence and knowledge were re-tested post workshop together with feedback questions about the facilitator's approach and overall satisfaction with the event. Follow-up questionnaires were sent 3-12mths later examining what impact TRUSTING workshops had on participants' own practices and how mainstreaming was working in their centre.

Results: 120 participants (61 surgeons; 42 nurses; 8 oncologists; 9 other) attended 12 workshops held in Scotland, Southwest & Southeast, Northern England, London, and Wales. There were significant improvements post workshop in knowledge scores (mean change = 6.57; 95% CI 5.97 to 7.16; $p<0.001$), self-confidence (mean change = 2.64; 95% CI 2.33 to 2.95; $p<0.001$) and overall feedback showed uniformly high ratings for the facilitators' approach (mean range 9.65 to 9.90 /10). Most found workshops useful, enjoyable, and informative and 98% would definitively recommend them to colleagues. Follow up data (n=68 to date) revealed that attendance had significantly impacted individuals' own practices with 59% reporting it had improved the way they discussed genetic testing with patients. When asked about mainstreaming more generally, 16% said it had not yet started, 3% thought it was problematic and 81% felt it was either going OK or working very well. Not all participants had roles that allowed them to influence mainstreaming pathways within their hospitals but recognised how much TRUSTING could help. A majority (85%) wanted further workshops about: - other significant genes, risk reducing treatments (78%) and methods of testing (62%).

Conclusions: Discussing the implications that having a pathogenic gene alteration has for patients' treatment and risk-reducing interventions is complex when patients are already coming to terms with a breast cancer diagnosis. The TRUSTING educational programme is an effective means of helping HCPs now involved in the mainstreaming of genetic testing.

Interplay between tumor size and vitamin D receptor (VDR) polymorphisms in breast cancer prognosis: A prospective cohort study
Theme: Genetics/Screening/Early detection

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Background: Vitamin D and its receptor (VDR) have in some studies been shown to counteract tumor progression and enhance different treatments, which merits further investigation. The aim was to investigate the associations between four VDR SNPs (Taq1, Tru91, Bsm1 and Fok1) and breast cancer prognosis in different treatment groups.

Methods: VDR genotyping was performed using Oncoarray on bllod samples from 1017 patients with primary breast cancer who were included in the BCBlood cohort between 2002 and 2012 in Lund, Sweden. Patients were followed for up to 15 years. Clinical data and patient information were collected from medical records and questionnaires. Cox regression was used for survival analyses to analyze associations between VDR genotypes and prognosis.

Results: Genotype frequencies were as follows: Fok1 (AA 15.7%, AG 49.1%, GG 35.1%), Bsm1 (CC 37.2%, CT 46.1%, TT 16.7%), Tru91 (CC 77.8%, CT 20.7%, TT 1.5%), and Taq1 (AA 37.2%, AG 46.2%, GG 16.6%). During follow up there were 195 breast cancer events. The homozygous variants of Taq1 and Bsm1 were associated with 40% reduced risk of breast cancer events, adjusted HR=0.59 (95% CI 0.38–0.92) for Taq1 and adjusted HR=0.61 (95% CI 0.40–0.94) for Bsm1. There was a borderline interaction between tumor size and having at least one variant G-allele in Fok1 (Pinteraction=0.058). In patients with small tumors (pT1) G-allele carriers had a nearly double risk of breast cancer events adjusted HR=1.83, 95% CI 1.04–3.23) but this was not seen in patients with large tumors (pT2/3/4), adjusted HR=0.80, 95% CI 0.41–1.59). No interactions between V genotypes and adjuvant treatments regarding breast cancer prognosis were detected.

Conclusion: V genotypes were significantly associated with breast cancer prognosis and the association might be modified by tumor size. Further research is needed to confirm the findings and elucidate their potential clinical implications.

Zinc transporters: a potent therapeutic target for treatment of triple-negative and tamoxifen-resistant breast cancers
Theme: Treatment/Novel agents

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Background: It has long been established that cellular influx of zinc through specialised membrane transporters is indispensable for initiating normal mitotic signalling cascades that drive cell division. Previously, we identified the coordinated activity of two transporters, ZIP6 and ZIP10, as the primary regulators of this process, with their dysregulation often associated with cancer development. Utilising novel inhibitory ZIP6 and ZIP10 monoclonal antibodies, we explored the therapeutic potential of these agents in breast cancer lines representing major areas of unmet clinical need including triple-negative and anti-hormone resistant breast cancer.

Methods: In vitro response to our anti-ZIP6 antibody was assessed in triple-negative and tamoxifen resistant breast cancer models, as well as a model of oestrogen receptor positive (ER+), anti-hormone sensitive breast cancer. Anti-ZIP10 antibody assessment was restricted to triple-negative and ER+ models only. Mitotic activity in response to antibody treatment was evaluated using immunofluorescence detection of phosphorylated HistoneH3S10, coupled with functional assessment of active proliferation using cell counting assays.

Results: Treatment with our anti-ZIP6 antibody significantly reduced HistoneH3S10 phosphorylation across all models in vitro, though a significantly preferential response was noted in triple-negative and tamoxifen resistant cells when compared to the ER+ model. This particular trend was conserved with functional assessment of proliferation, where anti-ZIP6 antibody did not significantly affect ER+ cell growth but significantly reduced that of triple-negative and tamoxifen resistant models. This result was sustained in later in vivo studies, with a vast decrease in tumour volume of triple-negative and tamoxifen resistant tumour bearing mice versus control cohorts. Treatment with anti-ZIP10 antibody significantly attenuated both HistoneH3S10 phosphorylation and cell proliferation in triple-negative cells, whilst the effect on ER+ models was limited, suggesting a specific preference in triple-negative disease. Though significant variation in HistoneH3S10 phosphorylation was observed in triple-

negative cells, anti-ZIP10 treatment displayed comparative functional efficacy versus proliferation when compared with anti-ZIP6 treatment, eluding to different mechanisms of action of the 2 closely related transporters.

Conclusions: Together, these results highlight the therapeutic potential of novel anti-zinc transporter antibodies, specifically those targeting ZIP6 and ZIP10, as monotherapeutic agents for treatment of clinically relevant breast cancer subtypes. Moreover, the indication that ZIP6 and ZIP10 may have different mechanistic roles in mitosis may elude to wider uses of these agents for therapeutic intervention and, with further work, may enable the implementation of novel treatment strategies.

Models for predicting the risk of breast cancer: a systematic review
Theme: Genetics/Screening/Early detection

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Background: Predicting the risk of breast cancer (BC) can help with early diagnosis, treatment, and prevention strategies. In particular BC risk prediction models may be used to identify individuals at a higher risk of BC who may benefit from earlier or more frequent screening, and in the context of genetic counselling among high-risk individuals with known high-penetrance mutations in cancer predisposition genes or strong family history suggestive of a hereditary component, to inform decisions on surveillance or prevention strategies. Models typically utilize demographic, genetic, or imaging-derived variables. This systematic review summarizes all developed models for BC risk in general and high-risk populations, and their discriminatory ability and calibration.

Methods: MEDLINE and Embase were searched for studies developing and/or validating models estimating risk of developing BC in women and/or men. After removal of duplicates, 9,509 titles and abstracts were screened, yielding 359 full-text reviews. The included studies either (i) developed a new model to predict BC risk in general or high-risk populations, (ii) extended an existing model, or (iii) validated a model in a new population.

Results: A total of 108 studies developing new models for BC risk prediction were included in this review. Sample sizes ranged from 299 to 2,392,998 for cohort studies, and from 133 cases with 113 controls to 95,075 cases with 75,017 controls for case-control studies. 69 studies focused on predicting lifetime BC risk, while other outcomes included: 5-year BC risk (n=19), 10-year BC risk (n=17), short-term risk (n=5), overall risk by a certain age cut-off (n=3), 3-year BC risk (n=1), oestrogen and progesterone receptor (ER and PR) positive BC risk (n=2) and contralateral cancer risk (n=1), with several studies assessing more than one outcome. 91 studies developed models in the general population and 17 in high-risk populations. Areas under the receiver-operating characteristic curves (AUCs) ranged from 0.51 to 0.96. For studies reporting calibration using observed/expected events (O/E) ratio (n=8), the range was 0.84 to 1.10. External validation was reported in the original paper for 18 models. 46 studies extended existing models, some of which included validation, and there were 51 external validation studies of one or more models. Models which were frequently enhanced or validated in new populations included the Gail model, the Tyrer-Cuzick/IBIS model, BOADICEA, the Rosner-Colditz model, and polygenic risk scores.

Conclusions: The predictive ability of BC risk prediction models varied, with models including both demographic and genetic factors or demographic and imaging/biopsy factors tending to perform better than models based on demographic variables alone. Further research into the utility of different models, alongside clearer reporting and validation of models in diverse populations and settings, in prospective studies representative of their target population, is required to ensure clinical relevance.

Breast Cancer MDT Standard of Care Audit St George's Hospital
Theme: Other

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Introduction: The Case for change
As patient numbers and complexity increase, our breast MDT meeting overruns by up to 50%. Our 2021 breast MDT review concluded that though our decisions were good, not all cases were sufficiently well prepared, leadership was not invariably clear and output documentation required improvement. We agreed a lead every week for surgery, oncology, radiology and histopathology and improved concentration on quality input and outcome documents. These changes did not achieve the timeliness required. Patients at the latter end of the list received ever briefer discussions. The quality of outcome was at risk of being dependent on order of placement. Options to improve included more time, fewer patients or smarter preparation.

Methods: The SoC Team core of 5 was preferred, a core of 3 materialised (surgeon, radiologist, medical oncologist). Histopathology reports were taken as read. Breast SoC MDT ran the evening before the morning MDT for 4 weeks [time 2.5-4 hours]. Each patient was discussed in detail - an SoC decision made when all 3 agreed. 18 -26 clinicians attend main MDT. Each case rediscussed in main MDT the following day to assess accuracy and quality of SoC decision.

Results: 157 patients discussed in 4 SoC MDTs. 106/157 a SoC decision was made. 51/157 no SoC decision was possible. 8/106 SoC decisions reversed in main / subsequent MDT. > 92% SoC decisions were upheld by the Whole MDT. Reasons to alter SoC decision included - complex neo-adjuvant /axillary plan, complex benign lesion, patient choice, subtle radiology difference, SOC omission, best interest treatment plan. 20% patients no performance status or staging information.
8% histopathology not ready for SOC MDT but available in main MDT. Main Breast MDT never ran over. 3 of 4 weeks completed main MDT with 30 minutes to spare. Time used for presentations of conference data, a local Audit, PSFU planning, general team building.

SoC MDT team described improved satisfaction but more intense responsibility and fatigue. Whole MDT opinion that quality of Breast MDT clinical decision increased from 4.1/5 to 4.3 /5. Whole MDT opinion that quality of the breast MDT outcome record improved from 3.4/5 to 4.2/5. Some MDT participants disliked SoC process, felt less included and preferred to present their own patients.

Conclusions: Health economics: 2 hour SoC Breast MDT considerably cheaper than 1 additional hour of main MDT. By removing straightforward patient plans, more clinician time freed for complex discussion of difficult cases. Patient experience improved by timely clinic starts. For future SoC MDTs, 5 groups of SoC decisions agreed. SoC MDT only reviews patients considered suitable. Those cases not rediscussed in main MDT. SoC MDT decisions are efficient, accurate and comparable or of improved quality to the main breast MDT.

Acceptability of de-intensified screening for women at low risk of breast cancer: a randomised online experimental study in England
Theme: Genetics/Screening/Early detection

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Background: Risk-stratified approaches to breast screening show promise for increasing benefits and reducing harms. But the successful implementation of such an approach will rely on public acceptability. To date, research suggests that while increased screening for women at high risk will be acceptable, any de-intensification of screening for low-risk groups will be met with less enthusiasm. We report findings from a population-based survey of women in England approaching the age of eligibility for breast screening to compare the acceptability of current age-based screening with two hypothetical risk-adapted approaches for women at low risk of breast cancer.

Methods: We carried out an online survey of 1,579 women aged 40-49 who had no experience of breast cancer or mammography. Participants were recruited via a market research panel, using quotas for education and ethnic group, and were randomised to view information about: 1) standard NHS age-based screening; 2) a later screening start age for low-risk women; or 3) a longer screening interval for low-risk women. Primary outcomes were

cognitive, emotional, and global acceptability, measured using 6, 2 and 1 item, respectively. We used ANOVAs and regression to compare acceptability between groups and explore demographic and psychosocial predictors.

Results: All three screening approaches were judged to be acceptable on the single-item measure of global acceptability (mean score >3 on a 5-point scale). However, scores for all three measures of acceptability were significantly lower for the risk-adapted scenarios than for age-based screening. There were no differences between the two risk-based scenarios. In multivariable analysis, higher knowledge was a significant predictor of cognitive and emotional acceptability.

Conclusion: We found no difference in the acceptability of later start age vs. longer screening intervals for women at low risk of breast cancer in a large sample of women who were screening naïve. Although acceptability of both risk-based scenarios was lower than for standard age-based screening, overall acceptability was reasonable. The positive associations between knowledge and both cognitive and emotional acceptability suggests clear communication about the rationale for de-intensified screening may enhance acceptability.

Pre- and postoperative antioxidant use, aryl hydrocarbon receptor (AhR) activation and clinical outcome in different treatment groups of breast cancer patients
Theme: Prevention/Lifestyle

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Background: Dietary supplements with antioxidant properties are common among cancer patients. Antioxidant supplements might interfere with adjuvant breast cancer treatments but results from earlier studies are inconclusive. It is also possible that metabolic pathways are involved in the interactions between antioxidants and adjuvant treatments, such as the aryl hydrocarbon receptor (AhR) pathway. The purpose of this study was to investigate pre- and postoperative antioxidant use in relation to clinicopathological characteristics and prognosis in different breast cancer treatment groups.

Methods: Pre- and postoperative antioxidant (vitamin A, C, E, carotenoids, or Q10) or multivitamin use was self-reported by patients with primary breast cancer from Lund (n=1855) and Helsingborg (n=478), Sweden. Patients were followed for up to 15 years. Clinical data were obtained from patient charts. Tumor-specific AhR protein levels in the cytoplasm (AhRcyt) and nuclei (AhRnuc) of invasive tumor cells were analyzed with immunohistochemical methods on tissue microarrays. AhR levels were available for 920 patients included in Lund 2002–2012. AhR and its downstream marker CYP1B1 were also analyzed with western blot in MCF-7 and MDA-MB-231 cells.

Results: About 10% of patients used antioxidants. AhRnuc positivity was twice as common in preoperative antioxidant users compared to non-users. In mechanistic studies vitamin C increased AhR levels and its downstream target CYP1B1, indicating AhR activation. There were significant interactions between tumor AhRnuc status and preoperative antioxidant use in relation to clinical outcome. In all patients, antioxidant use (other than multivitamins) at both visits was associated with poorer prognosis, while use only at the follow-up visit was associated with better prognosis, compared with no use at either visit.

Conclusion: The clinical impact of antioxidants depended on antioxidant type, timing of use, and tumor AhR activation. Antioxidants may influence clinical outcome by activation of the master regulator AhR in addition to interference with free radicals. Further studies are needed to identify breast patients that might improve or worsen their prognosis when using antioxidants postoperatively.

Impact of Prosigna test on treatment decision in lymph node negative early breast cancer - a prospective multicenter study (EMIT1)
Theme: Early breast cancer

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Background: EMIT1 is a national, observational single-arm trial designed to assess the value of the Prosigna PAM50/ROR test as a routine diagnostic tool, examining its impact on adjuvant treatment (tx) decisions vs standard histopathology, clinical outcomes, long-term side effects and cost-effectiveness. Here we present the impact of Prosigna on tx decisions.

Material and methods: Patients (pts) with HR+/HER2- pT1-T2 pN0 early breast cancer (EBC) were included. Prosigna test and standard histopathology assessments were performed on all tumors. Clinicians' tx decisions were recorded before and after the Prosigna results were disclosed. Descriptive statistics, Pearsons' r and R2 were executed.

Results: Of 2194 patients included (2019-2022), 2164 tumors had conclusive Prosigna result; 62% were Lum A, 36% Lum B, 1% HER2 enriched and 1% Basal-like. The ROR score was ≤40 in 49% of tumors, 41-60 in 31% and >60 in 20%. Based on national guidelines for risk profile assessment, the pre-Prosigna tx decisions were: no systemic tx (NT) in 27% of pts (low risk), endocrine tx only (ET) in 38% (intermediate risk) and chemotherapy (CT) followed by ET (CT-ET) in 35% (higher risk). Post-Prosigna tx decisions were 25%, 51% and 24%, respectively. Adjuvant tx changed in 29% of pts, including 21% change in CT use. For pts assigned to CT pre-Prosigna, 45% were de-escalated to ET post-Prosigna. For pts allocated to ET, 12% were escalated to CT-ET and 8% de-escalated to NT. For pts allocated to NT, 18% were escalated to ET/CT-ET. For pts with pT1c-2 G2 and intermediate Ki67 (0.5-1.5x hospitals own median Ki67), the pre-Prosigna tx decision varied widely across hospitals (i.e. use of CT <5–51%). Post-Prosigna, the variability in CT use was markedly reduced (8–24%). Overall, the correlation between Ki67 and ROR score was moderate (r=0.66) with large variation between hospitals (r=0.49-0.83/R2=0.24-0.68). The median ROR score increased by increasing grade, but the ROR score-ranges were wide (for G1 0-79, G2 0-90, G3 16-94).

Conclusion: The Prosigna-test result changed adjuvant tx decisions in all EBC clinical risk groups, markedly decreased the CT use for pts with higher clinical risk and reduced treatment decision discrepancies between hospitals.

A review into the role of validated tools, predict and nottingham prognostic index, for guiding decisions on tumour profiling test referrals within our trust
Theme: Early breast cancer

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Background: In 2018, NICE published diagnostic guidance on the use of tumour profiling tests to guide adjuvant treatment decisions in early breast cancer. These provide clinicians with information on the risk of recurrence for their patient's cancer, which helps guide decisions around adjuvant chemotherapy. To identify suitable patients for referral, validated tools such as Predict and Nottingham Prognostic Index (NPI) utilise clinical information to highlight those at an intermediate risk of recurrence, who are eligible for a genomic test. There is variation across the UK, with Trusts either solely using NPI, Predict, or both. We aimed to review our data on patients referred for Prosigna to explore potential variations between the two.

Methods: This retrospective study identified 90 patients referred for Prosigna at our Trust between Dec 7, 2020 to Feb 10, 2023. Eligible patients included those with hormone receptor positive, HER2 negative, and node-negative disease that had completed breast surgery. 4 patients were deemed ineligible for the study due to incomplete information and node-positive disease.

Results: Amongst the 86 eligible patients, 54.6% (47) had an intermediate or high risk of recurrence (RoR) score.

In comparison to Predict, NPI identified 29 further subjects eligible for Prosigna testing. Of these, 15 were deemed to have an intermediate or high RoR score, warranting discussions surrounding adjuvant chemotherapy. 93% (14) had grade 2 disease with tumour size 2-3cm. Ultimately, 5 of the 15 received adjuvant chemotherapy. The remainder declined treatment or chemotherapy was deemed unsuitable.

Conclusions: Utilisation of NPI identified a greater number of patients within our Trust eligible for Prosigna testing compared to Predict. With 5 additional patients receiving adjuvant chemotherapy for high risk disease, this is a positive indicator for its continued use in this setting; particularly for those with 2-3cm, grade 2 disease.

These findings additionally support a review of the clinician's role in undergoing preliminary discussions surrounding adjuvant chemotherapy with our patients before a referral for tumour profiling tests. This would be in an effort to reduce unnecessary Prosigna testing/costs.

The HER2-RADiCAL study (Response ADaptive CAre pLan) – Tailoring treatment for HER2 positive early breast cancer

Theme: Trials in progress

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Background: Pathological complete response (pCR) following neoadjuvant systemic anti-cancer therapy (neoSACT) identifies a population of patients with HER2-positive early breast cancer (HER2+ EBC) at low risk of recurrence, particularly with cancers of lower clinical TNM stage at diagnosis. Here, the balance of toxicity associated with the current treatment pathway may be disproportionate to absolute clinical benefit. HER2-RADiCAL (ISRCTN81408940) seeks to reduce the treatment burden and healthcare costs of treating HER2+ EBC by testing the hypothesis that pCR can be used as a functional response biomarker to select patients who can receive less systemic therapy with minimal/no loss of efficacy.

Methods: HER2-RADiCAL is a response-directed interventional cohort/threshold-crossing study embedded within a real-world data-driven clinical pathway. Patients with ER-positive or negative HER2+ EBC with cT1N1/cT2N0-1 stage at diagnosis are eligible after completion of routine neoSACT and locally determined pCR (ypT0/Tis ypN0). Patients with pathological features consistent with previous malignant involvement in >4 nodes are not eligible. Adjuvant trastuzumab +/- pertuzumab may have continued before study entry provided no more than 9 cycles of trastuzumab have been received. After registration, all participants receive a total of 9 cycles of trastuzumab including those administered before study entry. Participants receive no further pertuzumab and no adjuvant chemotherapy. Adjuvant endocrine therapy, bisphosphonates and radiotherapy are given as per standard care. Central pathology review of pCR status will be conducted in a subset of cases.

The primary endpoint is relapse-free interval. Recruitment of 720 participants over 3.5 years will provide 90% power to exclude an event rate >6.5% at 3 years (expected event rate ≤4%). Secondary endpoints include relapse-free survival, invasive breast cancer-free survival, invasive disease-free survival, distant recurrence-free interval, breast cancer-free interval, overall survival, treatment pathway adherence and cost-effectiveness. An interventional cohort / threshold crossing design was preferred to a randomised non-inferiority trial based on the known event rate in this population which is sufficiently low such that any deviation from this expected event rate would indicate failure of the reduced therapy strategy.

Health economic modelling will compare the protocol-driven study cohort with two comparator pathways: a non-response adapted maximum therapy pathway (standard pathway prior to the study) and a real-world representative pathway derived from pseudonymised data for all patients treated for HER2+ EBC within the UK NHS. A Study Within a Trial (SWAT) will explore identification of factors influencing patient decision-making for participation in studies of response-adapted reduction in treatment.

Result and conclusions: At 5th September 2023, 24 research sites have opened with 44 participants recruited. Responding to continued use of anthracycline-based regimens in UK practice, eligibility criteria have recently been extended to permit entry of patients who have received anthracycline-containing neoSACT. For further information contact her2radical-icrctsu@icr.ac.uk.

The impact of a breast cancer diagnosis on lifestyle behaviours - a mixed methods study
Theme: Prevention/Lifestyle

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Background: To explore the impact of a breast cancer diagnosis on lifestyle changes and explore barriers and facilitators to behaviour change relating to these lifestyle factors.

Methods: Online survey and interviews with women up to 10 years post breast cancer diagnosis. A descriptive analysis of survey data, and thematic analysis of interviews was conducted.

Results: One hundred and forty-one completed the survey and 21 interviews were conducted. Of the survey respondents 71% continued to consume alcohol, only 35% met the UK exercise recommendations of 150 minutes of moderate to vigorous exercise a week, and 66% participants consumed the recommended 5 portions of fruit and veg per day. Lifestyle changes post diagnosis were reported with 46% drinking a lot (26%) or a little less (20%), 51% doing more physical activity, and 61% eating healthier. While around half were motivated to further improve diet and exercise, few were motivated to change alcohol consumption. Barriers to lifestyle changes included time constraints, lack of knowledge and social inclusion. Facilitators for lifestyle changes related to short-term gain (improved mental health, sleeping better, losing weight) and long-term consequences of preventing recurrence and other illnesses.

Conclusions: The period after cancer may be an opportunity to engage in a dialogue about lifestyle behaviour change. Findings highlight the need to respect health related barriers as well as conflicting priorities of cancer survivors. Tailored messaging is needed to provide equal weight to short term benefits of lifestyle change as well as the long-term benefits.

Results of survey on De-intensification of breast or chest wall radiotherapy following pathological complete response to neoadjuvant chemotherapy in the early breast cancer patients
Theme: Radiotherapy

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Background: Over the last decade, with the advancement of systemic treatment and the increasing use of neoadjuvant chemotherapy (NACT), a significant proportion of patients are achieving pathological complete response (pCR) at surgery. Following surgery, patients with T1-3N0 early breast cancer (EBC) who undergo breast-conserving surgery (BCS) and T3N0 patients who have mastectomy are offered post-operative radiotherapy to breast/chest wall (CW) regardless of whether they have had a pCR to NACT. Those patient who were initially N0 but show evidence of fibrosis or 'response' in the nodes are also offered breast/CW and nodal radiotherapy. This current standard of care stems from the landmark EBCTCG large meta-analyses proving adjuvant radiotherapy roughly halves the rate of loco-regional recurrence and reduces breast cancer related deaths when compared to observation alone. However, the landscape of breast treatments has rapidly evolved since these trials with improvement in systemic treatment options, surgical techniques and imaging. Considering the higher rates of pCR, the role for adjuvant breast/CW radiotherapy is questionable in early breast cancer patients (i.e. T1-3N0). To our knowledge, there is no ongoing or planned trial in UK to answer this important question. Hence, we did this survey to gather the opinion of UK breast cancer community to see if there is a willingness for such a clinical trial.

Method: Online questionnaires were created on survey monkey and circulated in April 2023 among the UK breast cancer community (surgeon, oncologists, nurses and patients) via UKBCG, UKBI and ABS platforms. We collected opinions until early June 2023. Separate questionnaires were created to gather the opinion of doctors and patients.

Results: Survey was well received. 76 doctors and 28 patients responded to the survey. Out of 76 responders, 57 were oncology colleagues and 19 were surgeons. Colleagues participated from all over the UK with highest responders from North West followed by London (12/76), Midlands (10/76) and the Southwest (10/76). Over 90% of colleagues supported the need for a prospective randomised trial to answer this question and would be willing to enter patients in such a trial. There was higher variation noted among patients but more patients were willing to omit radiotherapy than omitting surgery.

Conclusion: These results highlight that the UK community supports the idea of a prospective clinical trial to answer the important question of De-intensification of breast or chest wall radiotherapy following pathological complete response to neoadjuvant chemotherapy (NACT) in early breast cancer (EBC) patients.

Assessment of response to neoadjuvant chemotherapy in patients with T1-T3 node negative breast cancer- single centre experience
Theme: Early breast cancer

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Background: In recent years, with the increasing use of neoadjuvant chemotherapy (NACT), 10-75% of breast cancer patients are achieving pathological complete response (pCR) following surgical resection. The higher rates of pCR are seen in the higher risk HER2+ and triple negative molecular subtypes. In Tryphaena and Neosphere trials pCR was achieved in ~60% of HER2+ patients whilst in the recent Keynote-522 trial of neoadjuvant pembrolizumb in triple negative (ER-PR-HER2-) disease ~65% of patients achieved pCR. Pathological complete response to NACT has been considered as a useful surrogate marker for improved survival. Rate of pCR is not well studied in T1-T3 node negative patients at presentation, this might be helpful to estimate the patient population for future de-escalation studies. With this aim in mind, we did a retrospective analysis of assessment of response to NACT in T1-T3N0M0 breast cancer patients at our tertiary cancer centre.

Methods: In this study, we did the retrospective analysis of patients who presented with T1-T3N0M0 breast cancer and were treated between 1st Jan 2022 to 31st Dec 2022 at Clatterbridge cancer centre, UK. Data was collected using electronic notes and analysed using SPSS version 29.

Results: Total of 103 patients were identified meeting the criteria. All were females, median age was 55 years (range: 31-82 years), 53 (51.5%) patients were ER-ve and 50 (48.5%) were ER+ve, 56 (54.4%) were Her2-ve and 47 (45.6%) were Her2+ve, 37 (35.9%) were triple negative (TN). Among the whole population studied, the pCR seen in 65 (63.1%) patients. On subgroup analysis, 48% of ER+ patients, 53.2% in HER2+ve patients and 81.1% of TN patients showed pCR at the time of surgery post NACT. 14 (13.6%) patients who were cN0 at presentation, did show at least a single node fibrosis on sentinel node biopsy at the time of surgery.

Conclusions: As expected we observed higher rate of pCR in TN and Her2+ patients than in other subgroups. Although only node negative patients included, our results are in line with the landmark trials published. These results will be helpful in estimating the patient population who may be eligible for de-escalation studies in future.

Axillary Lymph node Micro-metastasis and Oncotype DX Recurrence Score: Impact on adjuvant treatment in early breast cancer
Theme: Early breast cancer

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Background: Early Breast cancer (pT1-2) patients diagnosed with lymph-node micro-metastasis (Nmic) in sentinel node biopsy (SNB) are not considered for further axillary treatment in non-neoadjuvant setting as evidence support no impact of Nmic on overall and recurrence free survival. Concurrently, the Oncotype DX Recurrence Score (RS) has proven invaluable in guiding chemotherapy recommendations within the NHS healthcare system. In this study, we endeavour to investigate the potential correlation between micro-metastasis and the need for adjuvant chemotherapy as determined by RS.

Methods: We conducted a retrospective analysis of breast cancer patients with micro-metastasis who underwent RS assessment between 2015 and 2023. Data were sourced from the Oncotype portal, histopathology reports, and multidisciplinary notes within the Nottingham Breast Institute's online hospital system.

Results: A total of 750 patients were recommended for Oncotype Dx by the MDT during the studied period. Among these, 79 patients exhibited micro-metastasis in SNB. Based on their Nottingham Prognostic Index (NPI) scores falling within the range of 3.4-5.4, they were classified as intermediate risk.

Of these intermediate-risk group patients on the basis of NPI, 20 patients (25.3%) received chemotherapy as adjuvant therapy. 10 patients of these chemotherapy recipients had a high RS score (>25), and the remaining 10 patients received chemotherapy due to high risk factors for recurrence such as young age, the presence of lympho-vascular invasion (LVI), high tumour grade, or high NPI scores, despite having RS scores of 7-25 (low-to-intermediate risk) after discussion in MDT. Importantly, 59 patients (74.6%) with micro-metastasis and an Oncotype score <25 were not recommended for chemotherapy. With an average follow-up duration of 42.6 months, all patients in the non-chemotherapy group remained disease-free. Conversely, two out of the ten patients who received chemotherapy due to a high RS score developed metastatic disease, with a mean survival time of 40.5 months and an average disease-free interval of 12 months.

Description	Total	T1-2 Nmic	Nmic with RS <25	Nmic with RS >25	Chemotherapy offered to
Number of patients	750	79	69	10	20
Percentage	-	10.5%	97.3%	12.6%	25.3%

Conclusions: The introduction of Oncotype RS assessment has led to a decreased requirement for chemotherapy in patients with early breast cancer (pT1-2, Nmic) displaying micro-metastasis in sentinel nodes. Micro-metastasis, while contributing to elevated NPI scores, does not inherently mandate the administration of chemotherapy. This study underscores the significance of individualized treatment decision-making in breast cancer patients, offering a tailored approach based on precise RS data. It may also be an indication to modify the current NPI scoring system.

Interval Breast Cancer in a One-stop symptomatic Breast Unit
Theme: Other

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Introduction: Over half of all breast cancer diagnoses arise from symptomatic one stop breast clinics. Whereas the National Breast cancer screening service has strict sensitivity guidelines, such rigorous quality control does not exist in the same way in the symptomatic one-stop breast clinic setting. As a surgeon led clinic, we audited the sensitivity of one-stop clinic for cancer detection and interval cancer rates, comparing it with standards defined in the National screening service as well as other documented one stop clinic missed cancer rate studies.

Methods: All the new patients attending symptomatic one stop clinic across a two-year period between Jan 2019-Dec 2020 were identified. Retrospective data was collected on patients with new cancer diagnosis. Of the patients who had new cancer detected, any previous visits to the department in the last three years were identified. Data on triple assessment on previous visit was collected. Sensitivity of one stop clinic and interval cancer rate was calculated. Patients with past history of breast cancer, under surveillance were excluded.

Results: 6136 patients were seen in symptomatic clinics over the two-year period between Jan 2019 and Dec 2020. Of those, 217 patients were identified to have a new cancer diagnosis from clinical examination, imaging and core biopsy. 204 patients had been diagnosed on their initial attendance at the clinic. Thirteen of those patients were diagnosed with a new cancer having been seen within the three years prior to their diagnosis in the breast unit. After thorough review of clinic letters, examination findings and imaging, we found 2 patients where mammographic imaging in retrospect showed a missed / interval cancer.

The interval cancer rate therefore is 0.06 % while the sensitivity of the one-stop symptomatic clinic is 93.98%.

	Age Groups						
Cohort	<40	40-49	50-59	60-69	70-79	>>80	Total
Total Patients Seen	1240	1309	1171	1103	757	556	6136
Discharged	1234	1289	1140	1070	696	504	5933
Cancer diagnosis at initial referral	6	20	31	33	61	52	203
Cancer diagnosis at subsequent referral	0	2	4	3	2	2	13
Sensitivity %	100%	98.1%	88.57%	91.67%	96.8%	96.3%	93.98%

Conclusion: The missed cancer rate and sensitivity of the one-stop symptomatic clinic is comparable to that found by the Bristol Breast Care Centre (2020) and the outcomes reported by the National Health Service Breast Screening Programme. The performance of the unit in question is exceptional against current standards.

Mode of Recurrence/ Metastasis Detection in Breast cancer survivors
Theme: Living with BC/QoL/Patient perspective/Supportive care

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Follow-up of patients after primary treatment of breast cancer is aimed to detect recurrences at an early/ asymptomatic stage. Cochrane review of the randomized control trials suggests that follow-up programs based on regular physical examination and yearly mammogram alone are as effective as more intense approaches based on regular performance of laboratory tests and imaging in detecting recurrence, overall survival, and quality of life. This study's objective was to assess the pattern of detection of Metastasis/local/regional recurrence in Breast cancer survivors treated in a single center in Southwest Wales.

Material and methods: This was a retrospective review of patients diagnosed between 2016 and 2017. Their initial presentation clinical parameters and stage of diagnosis, and the treatment received was documented. The patients were followed up for 5 years and any event (defined as local recurrence, regional recurrence, metastasis, or death) was recorded. Patient's records were also reviewed to identify the cause of death. At the time of the event, the mode of presentation/detection was also recorded.

Results: A total of 494 patients were diagnosed with breast cancer who had therapeutic surgery (breast conserving surgery or mastectomy) between 2016 and 2017. Patients were routinely followed up, annually, in the clinic from 2017 to 2023. Of the 494 patients, 33 patients (6%) were diagnosed with a recurrent/ metastatic event. Breast cancer local recurrence rate was 1.4% (6 patients).

Regional axillary recurrence rate was 1% (4 patients) and distant metastasis rate was 4.4% (20 patients). 79.5% (26/34) of the patients were symptomatic at the time of diagnosis of recurrence/ metastasis. 20.5% (7/34) of the patients were asymptomatic. GP referral was the main route of recurrence/metastasis detection at 50%, followed by on-demand follow-up examination (breast team) at 26.9%. Among other routes, 18.2% cases were investigated by other specialties.

Routine annual follow-ups in breast clinic only identified 6 patients (all with loco-regional recurrent disease, with one patient also having synchronous distant metastasis. The three cases of local recurrence would have been detected on surveillance mammograms – clinical exam did not add to the early detection. Three cases of regional recurrence were detected on clinical/ US exam and would have been missed on surveillance mammograms – All three cases had high risk biology and did not receive chemotherapy.

Conclusions: High self-referral rate shows that the open access clinic has enabled the patients to seek medical attention immediately when a concern arise. Routine follow-up performed well in detecting local and regional recurrence, but detection of distant metastasis remains a challenge. Metastasis detection heavily relies on referral from GP, other specialties and self-referral.

ATNEC: A multicentre, randomised trial investigating whether axillary treatment can be avoided in cT1-3N1M0 breast cancer patients with no residual axillary nodal disease post-neoadjuvant chemotherapy
Theme: Trials in progress

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Background: Neoadjuvant chemotherapy (NACT) results in eradication of cancer in the axillary nodes in 40-70% of patients. This raises questions about the benefit of further axillary treatment in patients with no evidence of residual nodal disease (ypN0) post-NACT.

Design: ATNEC is a phase III, randomised (1:1), multi-centre trial, with embedded economic evaluation. Patients with proven axillary node metastases on needle biopsy receive NACT followed by sentinel node biopsy (SNB). If the sentinel nodes have converted to ypN0, ATNEC randomises patients to axillary treatment (nodal radiotherapy [ART] or axillary nodal clearance [ANC]) vs. no further axillary treatment.

Stratification:
Institution, type of surgery (breast conserving surgery vs mastectomy), receptor status (triple negative vs HER2 positive vs ER positive and/or PR positive and HER2 negative).

Inclusion criteria:
- Age ≥ 18
- cT1-3N1M0 breast cancer at diagnosis (pre-NACT)
- FNA or core biopsy confirmed axillary nodal metastases at presentation
- ER and HER2 status evaluated on primary tumour
- Received standard NACT as per local guidelines
- Imaging of axilla to assess response to NACT as per local guidelines
- Dual tracer SNB post-NACT and at least 3 nodes removed (sentinel nodes and marked node)
- No evidence of nodal metastases post-NACT (ypN0)

Exclusion criteria:
- Bilateral synchronous invasive breast cancer
- SNB prior to NACT
- Previous ipsilateral axillary nodal surgery
- Previous cancer within last 5 years or concomitant malignancy (exceptions listed in protocol)

Aims: To assess whether omitting further axillary treatment (ART or ANC) for patients with early-stage breast cancer and axillary nodal metastases on needle biopsy - who post-NACT have no residual nodal disease on SNB - is non-inferior to axillary treatment in terms of disease-free survival, and lymphoedema at 5 years.

Statistical methods: All analyses will be carried out on an intention-to-treat basis to preserve randomisation, avoid bias from exclusions and preserve statistical power.

Radiotherapy Quality Assurance (RTQA):
ATNEC has in-built RTQA coordinated by the RTTQA group. The RTQA monitors protocol compliance ensuring clinical outcomes reflect differences in randomisation schedules rather than departures from the protocol. ATNEC is the only UK trial that offers QA for IMC radiotherapy.

Screening Data:
ATNEC collects screening data to monitor acceptance rates and reasons why patients decline the trial to identify ways to improve recruitment. Data until 31-Aug-23 shows 77% of eligible patients were approached (733/955) and, of those approached, 45% were consented (329/733). Most common reasons for not consenting (33%; 241/733) were preference for axillary treatment (34%), no reason documented (28%), patient unsure/anxious (8%) and preference for no axillary treatment (7%).

Target accrual: 1900

Status: Recruiting. As of 15-Sep-23: 72 sites, 495 patients enrolled, 229 randomised. ATNEC is open to new sites (UK & International)

Trial Registration:
ISRCTN: 36585784
ClinicalTrials.gov: NCT04109079

Evidence of significant differences in the quality of PD-L1 immunohistochemical testing in triple negative breast cancer: results from external quality assessment
Theme: Other

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Background & objectives: PD-L1 inhibitors are used as first line treatment options in TNBC. A number of companion immunohistochemistry (IHC) assays are available to aid in selecting patients who may benefit from treatment. Laboratories can also develop and validate their own laboratory developed tests, LDTs.
UK NEQAS ICC & ISH conducts EQA of laboratories testing for PD-L1.
We examined the data that we have collected from all the assessment runs conducted to date, looking for trends over time and associations between assessment score achieved and methodological parameters.

Methods: UK NEQAS prepares and distributes unstained composite slides of FFPE sections of tonsil, TNBC tissues and FFPE cell lines with known PD-L1 expression levels.
Participants stain the slides using their routine method. Returned slides are centrally assessment by an expert panel for technical quality, and semi-quantitatively in comparison to the staining achieved in reference slides.
Data is collected on antibodies and other methodological parameters.
Data from each of the PD-L1 TNBC surveys were collated and analysed looking for significant associations between methodological parameters and test accuracy.

Results: Between 2020-23, 11 assessments were conducted (comprising a total of 352 submissions). The mean number of laboratories subscribed at each run was 32 (range: 16 - 40). These comprised laboratories located in 24 different countries; UK-based laboratories contributed 41% of submissions.

The overall mean quality score for submissions was 12.8 (assessments are scored in the range 4 to 20, with four being unacceptable and 20 excellent), a score 12.8 is in the middle-range (acceptable).

A companion diagnostic assay based on the rabbit monoclonal SP142 antibody (Roche Diagnostic, Indianapolis, USA) was the test employed by most laboratories, N = 292 (83.0%). This test showed a mean quality score of 13.1 (range 10.9 – 15.4). Performance of this assay method showed variations over EQA surveys.

The next most prevalent test used the 22C3 antibody (Agilent Dako), again produced as a companion diagnostic by the company. This was used by 16 of laboratories (4.6%). The mean quality score was 12.3 (range = 8.0 – 16.0).

Detailed examination of the methodologies employed indicated a substantial number of laboratories are not using the assays according manufacturer's recommendations particularly in regard to antigen retrieval and detection methodologies. Comparisons showed a significant association of those laboratories using the assay as indicated with higher quality scores.

Conclusions: This is the results presented here are on the largest series of EQA samples to be reported to date, both in terms of data sets and time period. Analysis of the data has shown significant reproducible performance differences between the different primary antibodies used including those available as in-vitro diagnostics (IVDs). We highlight evidence showing the importance of methodological details in the quality of staining produced.

Ensuring inclusivity of patient participation in clinical trials
Theme: Other

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Background: Several studies have shown that certain groups of patients are underrepresented in clinical trials including non-Caucasian ethnicity, neurodivergence, advanced age, non-English speaking, large Body Mass Index (BMI) and low socioeconomic status. There is a need to ensure adequate representation of these groups to ensure the results of any clinical trial accurately reflect the underlying population base.

Our breast surgery clinical trials unit based at Guy's Hospital in London which has a diverse multi-ethnic population, aims to be wholly inclusive in clinical trial recruitment.

The aim of this study was to review the pathway to recruitment and patients recruited into two clinical trials including the aforementioned sub-groups.

Methods: The Breast Cancer Research Database at Guy's hospital was reviewed, and the English Indices of Deprivation was used to populate the Index of Multiple Deprivation (IMD) for each patient using their postcode. A bespoke questionnaire was undertaken in interview form to assess patients' satisfaction with the pathway for recruitment.

Results: In total, 648 patients were eligible to participate, between September 2020 to May 2023. Of these, 131 (20.2%) were recruited to these two trials. In all, 100% of patients eligible for these trials were approached and screened for participation. Eligible patients had a mean age of 55.1 years. Recruited patients were younger on average than those not recruited (49.1 years vs 56.6 years, $p<0.0001$). Many older patients although initially classified as eligible, had changes in their management plan due to their WHO performance status and other co-morbidities, and were generally more reluctant to participate for various reasons. No patients requiring interpreters participated in the clinical trials.

There was no difference in the deprivation index ($p=0.69$), BMI ($p=0.75$) and neurodiversity ($p=0.22$) between patients recruited into clinical trials and those who were not. Patient feedback showed 95.5% overall satisfaction with the pathway of recruitment.

Conclusion: Using a pathway such as the one used by the Breast Research team at Guy's allows inclusivity of all minority groups in recruitment. The recruitment process was well received by patients, although extra steps may also be taken to reduce language barriers, such as information sheets and videos in the patient's native language where possible.

Talniflumate as a potential supplement in breast cancer treatment?
Theme: Preclinical research

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Background: Although survival of breast cancer is improving across most breast cancer types, triple negative breast cancer survival remains poor due to chemoresistance. Lower expression of Mucin 17 (MUC17, an O-glycosylated glycoprotein) has been shown to correlate with improved patient survival in triple negative breast cancer patients, and in vitro reduction of MUC17 expression can sensitise breast cancer cells to chemotherapy. Inhibition of MUC17 function may improve responses to chemotherapy in patients; however, there are currently no selective MUC17 inhibitors. Talniflumate is an approved anti-inflammatory drug, which is also a mucin regulator. We have assessed whether talniflumate can chemosentisise breast cancer cells in vitro.

Materials and Methods: We used 2 cell lines representing different breast cancer subtypes: triple negative, MDA-MB-468 cells, and ER+ HER2-, MCF7 cells. MTT cell survival assays were used to assess the influence of the chemotherapy agent epirubicin, or talniflumate either alone or in combination. Immunofluorescence imaging was used to assess whether talniflumate decreased expression of MUC17 in vitro.

Results: As expected, epirubicin caused dose- and time-dependent inhibition of proliferation/survival in both breast cancer cell lines. Talniflumate alone also caused inhibition of proliferation/survival causing approximately 30% less cell survival in MCF7 cells at 50µM and 70µM doses. Furthermore, in MDA-MB-468 (TNBC) cell line, there was approximately 20% less cell survival at 20µM and 25µM doses of talniflumate alone. No significant chemosensitisation to epirubicin was seen with talniflumate, however talniflumate's cytotoxic effect was additive with epirubicin. Immunofluorescence demonstrated that MUC17 levels were lower after treatment with talniflumate, suggesting that talniflumate must reduce MUC17 function and that chemosensitisation may well be evident in longer term assays or with staggered dosing.

Conclusions: Talniflumate caused cytotoxicity in breast cancer cell lines, representing triple negative and ER+ HER2- breast cancers. Talniflumate also successfully reduced expression of MUC17, indicating it has potential as a chemosensitizer in longer term assays. We conclude that talniflumate merits more detailed examination as a potential breast cancer therapeutic.

Inhibiting PTP1B in tumour conditioned macrophages promotes breast cancer growth by modulating tumour-promoting genes
Theme: Preclinical research

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Background: Tumour associated macrophages (TAMs) account for 50% of the breast tumour mass. TAMs are programmed to be highly immunosuppressive, promoting tumour development and a high infiltration of TAMs is associated with resistance to immune checkpoint inhibitors and chemotherapy. Our aim is to investigate whether we can rewire TAMs towards an anti-tumour phenotype by using PTP1B inhibitor which has already been shown to slow breast cancer progression through its effects on cancer cells.

Methods: Human monocyte-derived macrophages (hMDM) were conditioned to TAMs by co-culture with T47D (ER+, PR+) and triple negative breast (TNBC) cancer cell line MDA-MB-231. Effects of PTP1B inhibition of TAMs on mammosphere growth were examined by area and viability measurements. Mechanisms by which breast cancer conditioning and PTP1B inhibitor treatment affect mammosphere growth were assessed by gene expression arrays.

Results: Tumour cell conditioned hMDM significantly decreased T47D and MDA-MB-231 mammosphere growth areas by 15±3% and 9±1%, respectively. Following co-culture, PTP1B inhibitor-treated hMDM significantly increased T47D and MDA-MB-231 mammosphere area by 60±10% and 10±8% over non-treated hMDMs. Gene expression arrays revealed T47D mammospheres, generated following co-culture with PTP1B inhibitor TAMs, upregulated the expression of cancer promoting genes such as EMT transcription factors Notch1 and JAG1, supporting the increase in T47D mammosphere area. Oestrogen receptor (ESR1) was also upregulated in T47D mammospheres following co-culture with PTP1B inhibitor treated TAMs. Conversely, MDA-MB-231 mammospheres, generated following co-culture with PTP1B inhibitor TAMs upregulated expression specific tumour promoting genes including Snail1, Notch1 and Oct-4 but downregulated other tumour suppressing genes including VEGFA and SOX-2. However, gene expression changes in MDA-MB-231 tumour conditioned macrophages treated with PTP1B inhibitor support the increase in MDA-MB-231 mammosphere area.

Conclusions PTP1B inhibition of tumour conditioned macrophages affect mammosphere growth, viability and gene expression although this is strongly dependent on the different classes of breast cancer. T47D mammospheres following co-culture with PTP1B inhibitor treated TAMs have an aggressive phenotype and express higher levels of ESR1 which can be targeted with existing therapies such as Tamoxifen.

Going beyond: enabling transcriptomics-based precision breast oncology
Theme: Early breast cancer

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Transcriptomics have revolutionized biomedical research and refined breast cancer subtyping and diagnostics. However, wider use in clinical practice is hampered by the necessity of analyzing large sample sets in batches and the difficulty in comparing transcriptomic data from different sources. Here, we present EMBER, an embedding approach that creates a unified neighborhood of 11000 breast cancer transcriptomes, which can be used to predict phenotypic implications of new transcriptomic profiles on a single sample basis. EMBER accurately captures the five molecular subtypes. Key biological pathways, such as estrogen receptor signaling, cell proliferation, DNA repair and epithelial-mesenchymal transition determine sample position in the neighborhood. EMBER was successfully validated in four independent patient cohorts. Further validation using the pre- and post-treatment samples from the window trial, POETIC, captured clinical responses and identified increased androgen receptor signaling and decreased TGFβ signaling as potential mechanisms underlying primary resistance to endocrine therapy. Of direct clinical importance, we show that the EMBER-based estrogen receptor (ER) signaling score is superior to the immunohistochemical ER index used in current clinical practice to stratify patients for endocrine therapy. As such EMBER provides a calibration and reference tool that paves the way for using RNA-seq as a standard diagnostic and predictive tool for ER+ breast cancer.

"Working together for the better": Patient and Public Involvement (PPI) in the ATNEC Trial – What is our role?
Theme: Living with BC/QoL/Patient perspective/Supportive care

Janice Rose[1], Helen-Teresa Edwards[1], Sophie Gasson[2], Sophie Nicholls[2], Natalie Hammonds[2], Janet Dunn[2], Amit Goyal[3]
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Background: For a long time, patient and public involvement (PPI) in research was considered a 'tick box exercise'. Funders would review grant applications and reject them if there was no mention of PPI. Later, funders became wiser and began to ask, 'What is your budget for PPI activity?' Researchers would scratch their heads and think 'What is there to pay for?'

Not all trials put the same emphasis on PPI, but we are proud of ourselves as the ATNEC PPI team and want to showcase our contributions to the trial so far and outline 'our role'.

Method: To showcase our PPI expertise, we have broken the question 'What is our role?' into four parts, below.

Results: Why are we part of this research team?

We know that funding for research is in demand. As patients, we want to make sure all funding is used wisely and for the benefit of patients.

ATNEC is a treatment de-escalation trial which is assessing the role of axillary treatment in cT1-3N1M0 breast cancer patients. We have been part of the ATNEC TMG from the trial's inception, representing the patient voice and guiding the team to ensure that the trial is accessible to all.

What is our value?

The TMG respect and value our contribution as they recognise that they can only imagine what it would be like to be a patient. We have been there and can speak on behalf of patients who might be invited to take part.

What specifically do we do and how do we do it?

The ATNEC PPI team has been involved at every stage of the trial's development. Our involvement includes:

- Input into all patient-facing trial documents
- Production of a patient information video – Patient/Research Nurse consultation https://youtu.be/s5vqST08HYE (~1000 views)

- Attendance at all TMGs – with a standard PPI agenda item
- Contribution to ATNEC reports, including reports to the funder
- Evaluation of the Patient Experience Sub-study results

Do we do it well?

This is difficult to quantify but the PPI contribution to the latest funder progress report was instrumental in ensuring that the trial remained open to recruitment. Since then, recruitment has increased at a steady rate. Importantly, the PPI team has an excellent rapport with the rest of the TMG and are respected and valued for what they bring to the trial.

Conclusion: The ATNEC PPI team is active and confident and has a strong and respectful working relationship with ATNEC TMG. Our input is valued and is proving to be crucial to continued recruitment to the study. We hope our work will go some way to ensuring that this important research question gets answered.

Trial Registration:
ISRCTN 36585784
ClinicalTrials.gov: NCT04109079

Gut microbiota predict efficacy of neoadjuvant systemic therapy in patients with early breast cancer
Theme: Early breast cancer

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Background: The gut microbiome has been shown to influence the efficacy of some systemic anti-cancer therapies, most notably immune checkpoint inhibition. This prospective study explored the ability of the pre-treatment gut microbiome to predict pathological complete response (pCR) in patients receiving neoadjuvant chemotherapy (NACT) for early breast cancer.

Methods: Faecal samples were collected before first cycle NACT (T1), during (T2), and on completion of NACT (T3) as well as from gender, age and BMI matched healthy control participants (HCs). Microbiome composition was determined by 16S rRNA amplicon sequencing. Faecal short chain fatty acids (SCFA) were quantified with gas chromatography. Enumeration of stromal tumour infiltrating lymphocytes (TILs) and regulatory T cells (Tregs) was performed on pre-treatment diagnostic core biopsies. Random forest (RF) classification was applied to predict pCR based upon clinico-pathological parameters, faecal SCFA measurements and relative abundance of gut microbiota inferred from 16S rRNA sequencing.

Results: Twenty-one patients and twenty-one HCs provided samples. Most patients (19, 90%) received sequential anthracycline-taxane based NACT and all HER2-positive patients also received neoadjuvant HER2-directed therapy. No patients received an immune checkpoint inhibitor. pCR was observed in 6 of 21 patients (29%). Richness of the pre-treatment (T1) gut microbiome was significantly lower in patients without subsequent pCR compared to those patients with pCR or HCs. At T1, mean concentrations (μmol/g) of propionate and butyrate were higher in patients without subsequent pCR vs. patients with pCR: propionate 24.96 vs. 14.6 (p=0.025) and butyrate 27.7 vs. 13.2 (p=0.034). No significant difference in stromal TILs or Tregs was observed between patients with pCR vs. non-pCR. When RF classification was applied to baseline clinico-pathological parameters and readily measurable T1 SCFA data, faecal propionate was the variable most predictive of pCR (model out-of-bag (OOB) error rate = 15.8%, p = 0.010). The addition of 16S rRNA data produced a more accurate model (OOB error = 10.5%, p <0.001) that was entirely dominated by the relative abundance of specific bacterial genera.

Conclusion: Compositional and functional differences were observed in the pre-treatment gut microbiome of patients with subsequent pCR compared to those without pCR. A less diverse microbiome, associated with higher propionate and butyrate production and increased abundance of Lachnoclostridium may abrogate chemotherapy response. In this relatively small cohort, gut microbiota appeared to predict pCR more accurately than clinico-pathological characteristics. Prospective validation of these findings is underway within the NEO-MICROBE BREAST study (ISRCTN13877559).

Rapid Access Breast Oncology Clinic in University Hospital Southampton NHS Foundation Trust: A quality improvement project
Theme: Other

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Background: Recent advances in targeted therapies have improved clinical outcomes but also have increased the number of patients with breast cancer (BC) who require regular outpatient reviews. This may have an indirect effect on clinic access for patients with newly diagnosed BC, progressive disease, or treatment toxicities, causing delays in the patient pathway. We have trialled a new rapid access breast oncology clinic (RABOC) to provide an alternative pathway for patients requiring urgent oncological input.

Methods: Referral criteria for RABOC were a) patients with known BC who require additional monitoring due to systematic anticancer therapy (SACT) toxicity, b) newly diagnosed metastatic BC patients who require urgent commencement of SACT and c) newly diagnosed early BC patients who require urgent (neo)adjuvant SACT. Patients reporting acute toxicities were directed to Acute Oncology Service (AOS). Patients were booked in clinic ≤1 week in advance. RABOC was led by a senior registrar with consultant and CNS support. Fully anonymised data were collected from 05/05/2023 to 08/09/2023. Descriptive statistical techniques were used.

Results: 55 patients were reviewed in this 15-week period. 43 and 12 patients received a face-to-face or telephone consultation, respectively. On average, 4 patients were reviewed per clinic [mean 4, IQR (2-5)]. 35% (n=19) patients were referred by oncology registrars, 22% (n=12) by the Breast CNS team, 15% (n=8) by oncology consultants, 20% (n=11) by Breast surgeons and the remainder by AMU, AOS, and other teams. 35% (n=19) of the patients had newly diagnosed BC requiring urgent chemotherapy. 42% of patients were referred for urgent chemotherapy or change of SACT: 16% (n=9) for (neo)adjuvant, 13% (n=7) for palliative and 13% (n=7) for SACT switch due to rapidly progressive disease. 36% (n=20) and 13% (n=7) were seen for SACT toxicities or cancer-related complications, respectively. 31% (n=17) of patients were receiving chemotherapy, of whom 9% (n=5) were receiving chemoimmunotherapy. 29% (n=16) were on endocrine treatment of whom 11% (n=6) were treated in combination with a CDK5/6 inhibitor.

Fifty percent of patients were seen within 3 days [median 3, IQR (1-7)]. Fifty percent of patients (6 out of 11) referred for first-line chemotherapy received their first cycle within 13 days, IQR (7-14).

23 patients would have been seen in AOS if RABOC appointments have not been available: only 2 of these were referred from RABOC to AOS for the purpose of admission. Over 15 weeks, 15 routine chemotherapy and 16 routine New Patient clinic appointments were released by the RABOC clinic. Feedback from patients and the breast MDT has been very positive.

Conclusion: The RABOC has had a positive impact on patient pathway and oncology service as patients have access to a clinic where they are reviewed rapidly, and delays are minimised in their treatment pathway.

Identifying genetic alterations that sensitise breast cancer cell lines to mTOR inhibitor and ATR inhibitor
Theme: Treatment/Novel agents

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In breast cancer, changes in mTOR signalling are associated with hormone therapy resistance and currently, the mTORC1 inhibitor, Everolimus, is used to treat advanced breast cancer in combination with aromatase inhibitors. The DNA damage response (DDR) pathway is significantly altered in advanced or metastatic cancer and associated with resistance to radiotherapy and chemotherapy. mTOR signalling is activated by growth factors to increase cell growth, proliferation and it also promotes cell survival during stress. The DDR is a signalling cascade that is activated by DNA damage to enhance DNA repair, arrest cell cycle to allow time for DNA repair or initiate apoptosis when the damage is too severe. There are ‘cross talks’ between the DDR signalling and the mTOR signalling pathway that we hypothesise become prominent and important in advanced breast.

From my previous work, we identified that mTOR is required for DNA damage-induced cell cycle arrest by regulating the activity of the DDR protein Chk1. As ATR is directly upstream of Chk1 that phosphorylates to activate Chk1, we are interested in finding out if the combination of mTOR kinase inhibitor (Onatasertib, CC223) with ATR inhibitor (Ceralasertib, AZD6738) could be an effective advanced breast cancer therapy. In addition, identifying genetic alterations that promote sensitivity to the mTOR inhibitor or ATR inhibitor alone or in combination would identify synthetic lethality markers that would allow for personalised treatment.

Using 2D and 3D spheroids cell culture, 12 breast/prostate cancer cell lines were screened to identify cell line that is most sensitive to mTORi and ATRi in combination or alone. There was no significant combination effect observed, but the breast cancer cell lines MDA-MB-453 and T47D showed significant sensitivity to ATRi and mTOR inhibitor alone, respectively. In order to identify genetic alterations in the cell line that allow sensitivity to the drug, we have compiled a list of genes in the PI3K-AKT-mTOR and DDR pathway that are genetically altered in each cell line, and knocking down these genes using siRNA and measuring cell viability.

mTOR signalling is mainly in the cytoplasm and ATR signalling is in the nucleus, however, there are indications that in cancer this is altered, therefore, we are investigating these signalling through cell fractionation/western blotting. Interestingly, we found abundant ATR in the cytoplasm of MDA-MB-453 cells. In addition, we are characterising the two drugs to see how mTORi affect ATR signalling and conversely how ATRi affect mTOR signalling in breast cancer, particularly in the nucleus.

Incidental lobular neoplasia on core biopsy performed for microcalcification and the recommended mammographic surveillance – a small study
Theme: Genetics/Screening/Early detection

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Background: Lobular neoplasia (LN), incorporating the terms lobular neoplasia in situ, classical lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH), is a low grade lobular proliferation of discohesive cells. When this is diagnosed on a breast core biopsy it is given a B3 (with atypia) classification as it is a lesion of uncertain malignant potential and confers an increased risk of malignancy in both breasts as well as an increased upgrade rate in the area of the biopsy. But just how significant is a finding of incidental lobular neoplasia in a core biopsy performed for microcalcification?

Method: All patients who had a core biopsy performed for microcalcification that was reported as B3 (with atypia) for lobular neoplasia (including the terms LN, ALH and classical LCIS) from 2015 to 2021 were identified.

Results: This yielded 106 patients and a total of 110 core biopsies. 94 of these patients (and 95 of the core biopsies) went on to have a vacuum assisted biopsy (VAB). The findings on VAB were lobular neoplasia in 53% (50/95). There was an upgrade to either a lesion highly suspicious for malignancy (B4), DCIS or PLCIS (B5a) or an invasive carcinoma (B5b) in 9 cases giving a VAB upgrade rate of 9.5% (9/95). Of the 95 VABs performed 78 needed management for the finding of lobular neoplasia and the current recommendation is annual mammograms for 5 years. 10 patients did not attend at all for follow up and therefore we had results available for 68 patients. The results showed that many patients did not have their quota of mammograms for a multitude of reasons. Only 22% (15/68) had the annual mammograms for 5 years and these all showed stable appearances with no further abnormality detected. Out of the 68 there were only 3 cases were the mammograms picked up an abnormality which ultimately were 1 case of DCIS and 2 further cases of LN.

Conclusion: The recommendation of annual mammograms for 5 years was followed in less than a quarter of patients however of those that did have the full follow up there were no new abnormalities detected. In the 3 patients who had an abnormality picked up only one was upgraded to DCIS and this was picked up at the first annual mammogram and the other 2 were further LN. Is this pick up rate higher than what would be expected in the population? Is there a true benefit in the recommendation of annual mammograms for 5 years – our very limited data would suggest not.

The Patient Roles and Responsibilities Scale (PRRS): a psychometrically robust and useful tool to measure what matters most to patients
Theme: Living with BC/QoL/Patient perspective/Supportive care

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Background: The importance of measuring the impact of diagnosis and treatment on health-related quality of life (HR-QoL) is long recognised. HR-QoL endpoints are recommended by the Food and Drug Administration and European Medicines Agency and are integral to the ESMO-Magnitude of Clinical Benefit Scale. Each year advances in treatments mean that more patients are living longer with cancer, so it is important to consider if, in these HR-QoL endpoints, we are asking about the things that matter most to them. Development of the PRRS began with asking patients just that question. The 16 core item PRRS was first validated in 135 patients with stage III/IV breast lung or gynaecological cancer or melanoma. Here we present further validation data from breast cancer patients.

Methods: Principal component analysis of the 16 core items identified three subscales: responsibilities and social life, family well-being, and financial well-being, which accounted for 61.5% of total variance. In the initial validation study, Cronbach's alpha was 0.9 for the PRRS-16; 0.79–0.87 for the subscales. PRRS showed good test–retest reliability (ICC-0.86), sensitivity to change and the predicted pattern of correlation with validation measures r = |0.65–0.77|.

Here, the PRRS was administered at baseline to breast cancer patients participating in one of five studies. Acceptability and precision were assessed by missing data rates (threshold set at >15%) and floor/ceiling effects (threshold set as exceeding 70% minimum or maximum score, per item). Internal consistency was assessed using Cronbach's alpha for total score and individual subscales.

Results: The PRRS was completed by 352 breast cancer patients: 92 (26%) were <50yrs old, 132 (38%) 50-60yrs, 92 (26%) 61-70yrs and 36 (10%)>70yrs. One hundred and twenty-two (35%) had early stage cancer while 230 (65%) had locally advanced or metastatic cancer. Missing data rate was extremely low (0.4% overall, maximum 0.6% for any individual item). No items demonstrated floor effects. One item showed above threshold ceiling effects at 70.3% (My family gives up things because of the financial impact of my illness – reverse scored). Cronbach's alpha was 0.93 for the PRRS-16 total score, 0.88 for responsibilities and social life subscale (five items), 0.91 for the family well-being subscale (five items) and 0.84 for financial wellbeing (6 items).

Conclusion: The PRRS is a psychometrically robust measure of the wider HR-QoL impacts of cancer and treatment. This additional validation demonstrates its validity specifically in breast cancer. The scale is acceptable to patients and has good face validity, covering broader aspects of well-being such as caregiving, family life and finances which are highly valued by patients. The PRRS is suitable for use with breast cancer patients in clinical trials, real-world studies and as an aid to clinical conversations around treatment and intervention.

Glucocorticoids and Tissue Transglutaminase 2: implications in Triple Negative Breast Cancer
Theme: Preclinical research

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Background: Tissue Transglutaminase 2 (TG2, Tgm2) is a multifunctional enzyme, which has significant roles in promoting cancer progression such as tumour cell survival, invasion and metastasis. In the context of breast cancer, a pro-metastatic role has been reported, moreover TG2 expression is able to induce the epithelial-to-mesenchymal transition. Glucocorticoid (GC) signalling, mediated through the glucocorticoid receptor (GR), can contribute to tumourigenesis in triple-negative breast cancer (TNBC). The GC cortisol can induce TG2 in TNBC. The exact mechanisms through which stress hormones alter tumour dynamics to invade the complex brain or bone environments is not yet fully understood.

Methods: The role of TG2 on distant metastasis free survival (DMFS) was examined using KMPlotter. A quantitative Proteomics analysis employing TMT-sixplex was carried out using TNBC MDA-MB-231 cells (known to express high levels of TG2) following treatments with 0.5 μM of cortisol with and without 0.5 μM of the GR inhibitor, relacorilant for 24 h. Data analysis, filtering and visualisation was carried out using MaxQuant, Perseus and R.

Results: The KMPlotter analysis revealed a statistically significant reduction in distant metastasis – free survival (DMFS) is observed in patients with higher-than-average Tgm2 expression in ER- breast cancers (p = 0.022). Proteomics analysis identified 44 differentially expressed proteins in response to cortisol treatment alone and in combination with relacorilant. KEGG analysis found significant enrichment in pathways involved in cancer progression which are regulated by TG2, including the Matrix metalloproteinases (MMP) signalling pathway, which have reported a pro-metastatic role in breast cancer. Treatment with relacorilant also led to significant downregulation of NF-kappa-B essential modulator (IKBKG), which is a key regulator of the pro-metastatic NF-κB pathway activated by TG2.

Conclusions: Here we identified key pro-metastatic pathways regulated by TG2, such as MMP and the NF-κB pathway, that potentially underpin the pro-metastatic role of stress hormones in TNBC.

Fibroblast growth factor receptor 1 (FGFR1) and its role in luminal breast cancer
Theme: Other

Therese Sørlie[1,2], MSc Torbjørn Lien[1], Sushil Dhakal[1], Helga Bergholtz[1], Jens Henrik Norum[1]
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Fibroblast Growth Factor Receptor 1 (FGFR1) has emerged as a potential driver of endocrine resistance in a subset of luminal breast cancers, but targeting FGFR1 activity has been largely unsuccessful. Understanding the mechanisms of resistance in the context of FGFR1-dependency is vital for improved treatment stratification of FGFR1-positive breast cancers. Our current research endeavors are directed towards unraveling the intricate mechanistic underpinnings of FGFR1's impact on breast tumor progression, specifically its contribution to endocrine resistance as well as its regulatory role in innate immune sensing and subsequent induction of Type 1 interferons (IFNs). Our investigative efforts have established a direct association between FGFR1 and endocrine resistance in hormone receptor positive T47D breast cancer cells. Moreover, a remarkable and distinct inverse correlation linking FGFR1 expression to the Type 1 IFN response was observed. We found that proliferation of FGFR1-overexpressing tamoxifen-resistant T47D cells is dependent on FGFR1 activity and that these cells were re-sensitized to tamoxifen upon treatment with erdafitinib, a small molecule FGFR1 inhibitor. Moreover, we found that upregulation of genes related to epithelial-mesenchymal-transition correlated with FGFR1 overexpression and was reduced upon FGFR inhibition Furthermore, such inhibition enhanced the expression of IFN-alpha, IFN-beta, TLR7, and TLR9 in T47D cells when stimulated with the TLR7 agonist loxoribine. Our results suggest that targeting FGFR1 in luminal breast cancer cells with aberrant FGFR1 activity has the potential to inhibit tumor growth and re-sensitize resistant tumors to tamoxifen. In addition, that FGFR1 may function as an innate checkpoint and may be exploited by tumor cells to dampen Type 1 interferon responses, thereby inhibiting antitumor immunity in hormone receptor-positive breast cancer.

The Obesity Paradox Associated with Breast Cancer Risk Pre- and Post-menopausal Women
Theme: Preclinical research

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Background: Obesity is a growing health crisis; over 60% of UK adults are classed as overweight or obese. Obese post-menopausal women have a higher risk of developing breast cancer compared to obese pre-menopausal women. Emerging evidence suggests adipocytes play an important role within the tumour microenvironment by adopting a tumour-promoting phenotype. Our study aimed to identify morphological changes occurring in adipocytes in proximity to breast tumour epithelium in pre- and post-menopausal breast tissues.

Methods: Digital whole slide images of H&E-stained samples of tumour and normal contralateral breast tissue were obtained from 4 different biorepositories. Samples were split into 4 groups: 20 unselected, 30 pre-menopausal, 94-postmenopausal, and 33 with known BMI and mammographic density (MD). Adipocytes <1mm from the tumour or corresponding region in the normal contralateral breast were classified as close, and those >2mm as distant. Various size (e.g. perimeter and area) and shape (e.g. aspect ratio and concavity) parameters were extracted from each adipocyte using Particles8 in ImageJ.

Results: As proof of concept, images from the 20 unselected patients were analysed. Random forest analysis revealed that perimeter, area, aspect ratio, and concavity were the most important parameters for further morphology-based classification. Close adipocytes were smaller in size and more elongated (larger aspect ratio) than distant adipocytes ($p<0.0001$). In terms of menopausal status, close adipocytes from pre-menopausal subjects were smaller and more elongated compared to those from post-menopausal subjects ($p<0.001$). Since adipose tissue has an inverse relationship with MD, we investigated whether this, and BMI, influenced adipocyte morphology. Samples were stratified according to the BIRAD system; group 1 being mostly adipose to group 4 with the least. Group 1 adipocytes were the largest and most elongated ($p<0.001$). Patients were further split into lean/healthy (<25.0kg/m2) and overweight/obese (≥25.0kg/m2). The area of close adipocytes increased from lean/healthy to obese individuals. Additionally, in lean/healthy individuals, close adipocyte area decreased with increasing MD. Contrastingly, in overweight/obese individuals, close adipocytes area and MD positively correlated. Immunohistochemical analysis of PLIN1, a protein involved in lipid metabolism, was expressed strongly in adipocytes from these samples, irrespective of BMI/MD.

Conclusions: Morphological changes in close adipocytes may reflect the complex crosstalk occurring between adipocytes and tumour cells. Adipocyte size reduction could be linked to lipid depletion to fuel tumour growth and their altered shape could indicate the adoption of a fibroblast-like phenotype to enhance tumour proliferation and invasion. Future steps will study biomarkers related to adipocyte function and structure to understand the functional changes behind the obesity paradox in pre- and post-menopausal breast cancer.

OPTIMA, a randomised trial to validate the clinical utility and cost-effectiveness of gene expression test-directed chemotherapy decisions in high risk early breast cancer.
Theme: Trials in progress

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Background: Multi-parameter tumour gene expression assays (MPAs) are used to estimate individual patient risk and guide chemotherapy use in hormone-sensitive, HER2-negative early breast cancer. The TAILORx trial supports MPA use for postmenopausal node-negative patients. Evidence for the predictive ability of MPAs, their use in postmenopausal node-positive breast cancer and for premenopausal patients is not robust. OPTIMA (Optimal Personalised Treatment of early breast cancer using Multi-parameter Analysis, ISRCTN42400492) is a prospective international randomised controlled trial designed to validate MPAs as predictors of chemotherapy sensitivity in a largely node-positive breast cancer population.

Methods: OPTIMA is a partially blinded study which recruits women and men age 40 or older with ER-positive, HER2-negative invasive breast cancer and up to 9 involved axillary lymph nodes. Randomisation is to standard management (chemotherapy and endocrine therapy) or to MPA-directed treatment using the Prosigna (PAM50) test. Those with a Prosigna tumour Score >60 receive standard management whilst those with a low score (≤60) tumour are treated with endocrine therapy alone. Endocrine therapy for pre-menopausal women includes ovarian suppression for all participants unless they experience a chemotherapy-induced menopause. Adjuvant abemaciclib is permitted. The trial will be analysed for (1) non-inferiority of recurrence and (2) cost-effectiveness. The key secondary outcome is non-inferiority of recurrence for patients with low Prosigna Score tumours. The efficacy analyses will be performed Per Protocol using Invasive Breast Cancer Free Survival (IBCFS) as the primary outcome measure to limit the risk of a false non-inferiority conclusion. Recruitment of 4500 patients will permit demonstration of up to 3% non-inferiority of test-directed treatment with at least 83% power. HRQoL and economics data collected by the trial will provide a contemporary both personal and societal perspective on treatment costs. An integrated qualitative recruitment study addresses challenges to consent and recruitment, building on experience from the feasibility study which found that a multidisciplinary approach is important for recruitment success. OPTIMA is strongly supported by Independent Cancer Patients' Voice which has helped design all patient documents and which is represented on the TMG.

Results: The OPTIMA main trial opened in January 2017 and will continue to recruit until the end of 2024. Overall recruitment as of 1 Oct 2023 was 3535 (3192 from UK, 343 from Norway). Patient/tumour characteristics are summarised in the table and are well balanced between trial arms. The time between consent and notification of treatment allocation is 14 days or less for 75% of participants. The Prosigna test failure rate is <1%.

Conclusion: OPTIMA will provide robust unbiased evidence on test-directed chemotherapy safety for both postmenopausal and premenopausal women with 1-3 involved nodes, as well as for patients with 4-9 involved nodes and for patients treated with abemaciclib.

Distribution of patient and tumour characteristics

Characteristic		%
Median age in years (range)	56 (40-83)	
Menopause status	Pre	36
	Post	63
	Male	1
Tumour size	<30mm	55
	≥30mm	45
Node status	pN0	3
	pN1mi(sn)	4
	pN1(sn)	28
	pN1	47
	pN2	18
Histologic grade	1	5
	2	63
	3	32

A UK study exploring the attitudes and experiences of patients living with metastatic breast cancer with regard to clinical research: A patient advocate-academic collaborative study
Theme: Living with BC/QoL/Patient perspective/Supportive care

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Background: Clinical trials are key to improving outcomes in metastatic breast cancer (MBC). However, participation is low. Little data exists regarding the attitudes and experiences of patients in relation to clinical research. This study co-developed by a patient living with MBC and researchers aims to explore the experiences and issues related to accessing and participating in clinical research.

Material and Methods: A mixed methods study consisting of an online survey and qualitative interviews. Participants responded to an online questionnaire which contained closed and open questions, this was live between 17th May 2021 and 30th November 2021. Qualitative interviews from a sample of patients who gave their consent were carried out between 15th August 2021 and 22nd November 2021. Descriptive statistical analysis of the quantitative results from the closed questions and thematic analysis of the qualitative data generated by the open-ended questions and interviews were utilised.

Results: 768 eligible responses were received (765 female, 2 male, 1 unknown gender). The greatest proportion of responders were aged 51-60 years (37%), 92% were white (n=708) and 45% employed (n=345). 31% (n=235) were diagnosed with MBC within the last year with 14% (n=107) >5 years ago. 86% (n=660) knew what a clinical trial was. With 23% (n=173) reported an oncologist raising trial participation while 32% (n=243) of patients raising participation with their oncologist. Accessing new treatments (96%, n=737) and playing a more active role in own health (81%, n=619) would encourage trial participation while being unsure of potential benefits (43%, n=333) was the commonest reason for possible non-participation. Preferred sources of information on trials were a consultant (80%, n=612), nurse (61%, n=467) or trial database (29%, n=220). 36% (n=276) were willing to travel for a study increasing to 56% (n=430) if travel costs were covered, and 43% (n=306) would travel worldwide for a study. Of the 14% (107 of 768) who had taken part in clinical trials; 72% (n=77) found it a positive experience. 21 participants were interviewed for the qualitative sub study, with three complementary themes emerging from these namely (1) information about clinical trials/research, (2) barriers to participation and (3) research priorities.

Conclusion: This large UK study provides insights into the experiences and attitudes of patients with MBC in relation to clinical research. It demonstrates that patients are keen to be involved in research but face barriers to inclusions. Key messages include the need to develop patient facing trial databases, importance of clinical staff in the provision of study information and a willingness to travel for a trial but the need for financial support. Addressing the issues identified are key to ensuring MBC patients not only have opportunities to participate in clinical research but also the ability to take up these opportunities.

Deregulation of Minor Introns Splicing in Breast Cancer Cells
Theme: Preclinical research

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Background: Intron splicing is needed for proper gene expression in eukaryotes. This study focuses on a distinct class of noncanonical introns, known as minor introns (mi-INTs) that rely on U6atac snRNP, a vital yet highly unstable component of the minor spliceosome. mi-INTs have been shown to act as molecular switches that dictate the level of expression of the genes that harbor them. Despite their rarity, mi-INTs display a high level of conservation across species and are enriched in genes related to DNA transcription, replication, repair, RNA processing, and translation, suggesting crucial roles in cellular processes that can be deregulated in diseases like cancer. Here, we explored the role of minor intron splicing and its regulation of various breast cancer phenotypes. We hypothesized that the deregulated splicing of mi-INTs contributes to the aggressiveness and therapeutic resistance often associated with breast cancer.

Methods: In a functional knockdown approach, we used antisense oligonucleotides to inactivate the U6atac in MCF-7 and MDA-MB-231 breast cancer cells. We performed qPCR to measure the relative gene expression of spliced and unspliced genes and conducted cell viability assays. Statistical methods were used to classify mi-INTs and identify novel therapeutic targets.

Results: Complete inactivation of U6atac caused rapid and high cell toxicity. It also unraveled distinct splicing trends in 23 genes. While some genes exhibited the anticipated response to minor intron splicing inhibition, a subset of genes showed a unique response. They showed the expected drastic reduction of spliced transcripts, leading to a direct effect on the encoded proteins, however, this was not accompanied with the expected accumulation of unspliced transcripts, suggesting an active mechanism to eliminate these toxic byproducts in breast cancer cells.

On the other hand, mild (~10%) inactivation of U6atac resulted in a surprising decrease in cell viability, comparable to the impact of complete inhibition of minor intron splicing. This suggested a small set of highly sensitive genes that are affected at low doses of U6atac inhibition. These genes seem to be essential for breast cancer cell viability but not normal cells that have low proliferation index. These findings highlight the potential for therapeutic interventions based on low dosage of minor intron splicing inhibition.

Conclusion: These findings not only challenge the conventional understanding of splicing efficiency but also provide crucial insights for future investigations targeting specific genes in a dose-dependent manner. The results underscore the intricate regulatory network of minor intron splicing and its potential impact on breast cancer phenotypes. Furthermore, the identification of novel targetable genes in breast cancer opens new avenues for selectively targeting breast cancer cells, emphasizing the significance of minor intron splicing in the complexity of breast cancer and its potential as a therapeutic target.

"There's always hope": improving access to clinical trials for people living with secondary breast cancer
Theme: Metastatic breast cancer

Sarah Thomas[1]
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Clinical trials can improve outcomes for people living with secondary breast cancer, yet evidence shows that there are barriers to participation and despite innovations in clinical research, little progress has been made to improve the diversity of trial participants over the past two decades.

In 2021, the charity Make 2nds Count, funded a national research study exploring the clinical trials experiences of patients living with secondary breast cancer. The results revealed enormous information barriers surrounding clinical trials and persistent myths that patients are treated as 'guinea pigs' and clinical trials are only for those who have 'run out of options'. This is deeply concerning as secondary breast cancer cannot be cured, and for many, clinical trials offer further treatment options and hope.

Armed with this data, the charity pioneered an innovative informational and support service, working together with the patient community and healthcare professionals, known as the Patient Trials Advocate (PTA) service. This free service aims to equip patients with knowledge about clinical trials, overcome common misconceptions and ensure that patients feel empowered to have clinical trials conversations. It offers patients time with a clinical trials nurse, no matter where they live, where they can discuss their treatment and receive a personalised trials search report based on their eligibility.

Our poster will explore how this unique service was developed and evidence the incredible work of our PTA team in removing barriers to access clinical trials, improving the doctor-patient relationship, promoting the wellbeing of our patient community and giving much needed hope to those facing life-limiting illness.

Delegates will also have the opportunity to hear from our patient community: as part of our poster, there will be a digital display sharing the voices and perspectives of the individuals living with secondary breast cancer who have accessed the service. Their valuable experiences demonstrate not only the informational impact of our work, but also just how important it is to be listened to.

Proliferative, immune and molecular characteristics of oestrogen-receptor positive, human epidermal growth factor receptor negative early breast cancer in patients aged 70 years and older.
Theme: Early breast cancer

Jasmin V. Waterhouse[1,2], Elena López-Knowles[2,3], Anastasia Alataki[2,3], Lila Zabaglo[4], Marta Lubowiecki[2,3], Margaret Hills[3], Kathryn Dunne[2,3], Nicolò M.L. Battisti[1], Matilde Coriano[1], Anh T. L. Dinh[1], Kally Sidhu[4], Ruth Sardinha[3], Alistair Ring[1,2,6], Maggie C. U. Cheang[5,6], Eugene Schuster[2,6]
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Background: The number of older patients with oestrogen-receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) early breast cancer (BC) has increased significantly over the last few decades. Treatment outcomes in this patient group are inferior to those observed in younger patients, with significant variation in treatment. Following loco-regional treatment, adjuvant endocrine therapy (ET) is routinely offered, and adjuvant chemotherapy to those higher risk patients deemed fit enough. Despite this, observed relapse rates can be high, and alternative or complimentary approaches are needed. Relatively little is known about the biological characteristics of this patient cohort which may inform potential therapeutic choices. The BOLD-70 study (NCT05734950) aims to investigate tumour microenvironment, molecular, and genomic features in a population of older patients with early BC.

Methods: The study uses surgical specimens from older (>70 years) postmenopausal women with ER+/HER2- early (stage I-III) BC who were treated with curative primary surgery and adjuvant ET between January 2014 and December 2017. All samples underwent gene expression profiling using BC360TM (NanoString) covering 48 biological signatures (including the validated PAM50 signature, tumour inflammation signature, risk of recurrence, programmed-death ligand 1/2, Rb1 expression) and intrinsic subtypes. The distribution of the proliferation marker

Ki67 and tumour-infiltrating lymphocytes (TILS) were also assessed. Follow-up data was collected up until 5 years post-surgery.

Results: In total 73 patients with a mean age of 78 years (age range: 71-96) were eligible. Fifty-eight (79.4%) were European Cooperative Oncology Group (ECOG) Performance Status (PS) 0-1. Most patients had invasive ductal BC (74.0%, n= 54), a negative lymph node status (56.2%, n=41), and 16 (21.9%) had grade 3 tumours. Forty-three (58.1%) stained highly (≥10%) for Ki67 (mean Ki67 percentage 17.2% (range 0.3-52.6)). Most patients (67.6%, n=48) had no, or minimal immune cells with a mean TILS percentage of 10.3% (range 2.9-43). The most prevalent intrinsic subtype in this dataset was Luminal A (61.6%, n=45), followed by Luminal B (37.0%, n=27), and Her2-enriched (E) (1.4%, n=1). At 5 years post-surgery, 1 patient (1.4%) had experienced a local, and 2 (2.7%) patients a distant recurrence. Using multiple corrections spearman's correlation, preliminary data showed significant correlation of TILS with immunosuppressive signatures, and Ki67 with signatures involved in proliferation. A complete dataset (~100 patients) with a more detailed analysis is anticipated in time of UKIBCS 2024. This will also include an analysis of known mechanisms of cyclin-dependent kinase (CDK) 4/6 inhibitor resistance to estimate response to CDK 4/6 inhibitor treatment in this patient cohort.

Conclusions: Preliminary analysis showed overall favourable prognostic characteristics of older women with ER+/HER2- BC. However, a proportion were at higher risk of recurrence and could be eligible for additional treatment with CDK 4/6 inhibitors. We anticipate comparing final results with a younger cohort.

The challenges of recruiting women with low risk ductal carcinoma in situ to a randomised controlled trial: the LORIS study experience
Theme: Trials in progress

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Background: The LOwRISk DCIS (LORIS) study, trial registration ISRCTN: 27544579, compares conventional surgical treatment with active monitoring in women with ductal carcinoma in situ (DCIS). Recruitment to trials with a surveillance arm is known to be challenging. The research question for this report was: can best practice strategies targeted at patients and recruiting staff, ensure recruitment targets are met and if not, why not?

Methods: Women aged ≥ 46 years with a histologically confirmed diagnosis of non-high grade DCIS were eligible for 1:1 randomisation to either surgery or active monitoring. Trial information was provided via written material and a film, the content of which were informed by public and patient focus groups. Prior to randomisation, all eligible women were invited to complete the Clinical Trials Questionnaire (CTQ), a validated measure examining reasons for or against participation in clinical trials, and to take part in an interview about their decision-making and views on the trial information. Women agreeing to randomisation completed validated questionnaires assessing health status, physical and mental health, and anxiety levels. Initially, four communication workshops were held for recruiting staff. A year into the trial, surveys and semi-structured interviews with recruiting staff explored recruitment challenges. Based on these, some sites were offered refresher site initiation training and communication workshops.

Results: Eighty percent (181/227) of eligible women agreed to be randomised. The CTQ showed altruism and the belief that the trial offered the best treatment were the most frequently selected important reasons for accepting randomisation, whilst worries about randomisation and the influences of others were most frequently selected as important reasons for declining. One hundred women were interviewed, mainly those who accepted randomisation (89, 89%). Most found the study information provided clear and useful. Based on the validated questionnaires, as a group, participants were in good health but >40% had high anxiety levels at baseline. Although communication workshops for site staff (n=37) improved knowledge and confidence, fewer than half said they themselves would join LORIS if eligible or encourage family members and friends to do so. The most common recruitment barriers staff identified were low numbers of eligible patients and patient preference.

Conclusion: There was a lower number of eligible patients than anticipated but recruitment to LORIS was also challenging despite the use of best practice strategies aimed at both patients and recruiting site staff. The influence of salient opinions of others was an important reason for declining trial entry. All staff communicating with potential patients need to be in equipoise and fully support the study to enhance recruitment in similar future trials.

Attitudes to lifestyle interventions in early breast cancer patients: A survey of UK healthcare professionals
Theme: Living with BC/QoL/Patient perspective/Supportive care

Abigail Whittaker[1], Catherine Harper-Wynne[2], Caroline Wilson[3], Constantinos Savva[1], Rebecca Beeken[4], Bernard Corfe[5], Omolade Femi-Ajao[6], Kajal Gokal[7], Michelle Harvie[8], Lucy McGeagh[8], Rachel Rolph[9], John Saxton[10], Caroline Tweedie[11], Guillermo Villacampa[12], **Ellen Copson**[1]
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Background: Up to 23% of UK breast cancer (BC) cases are attributable to modifiable risk factors, primarily obesity, alcohol and reduced physical activity. Obesity at diagnosis is associated with increased treatment-related complications and poorer long-term outcomes. Studies have reported beneficial effects of physical exercise on BC treatment toxicities. Long-term impact of weight loss post diagnosis on BC recurrence remains under investigation but beneficial effects on common co-morbidities including cardiovascular disease are well established. The NICE guidelines for early BC advise that a healthy lifestyle is associated with a lower risk of recurrence and recommend patients should maintain a healthy weight, limit alcohol intake, and engage in regular physical activity. However, there is no formal pathway for providing lifestyle interventions for UK early BC patients post diagnosis. The NCRI Breast Group Lifestyle Working Group (NCRI BCLWG) performed a survey to assess current knowledge basis of UK breast multi-disciplinary team (MDT) members and investigate how they currently incorporate lifestyle advice into their clinical practice, or barriers that prevent this.

Method: A survey of 18 questions was designed by a subgroup of the NCRI BCLWG using Microsoft Forms. It was piloted by 5 health care professionals meeting the eligibility criteria to assess clarity and ease of completion. Amendments were made based on their feedback. Members of UK breast cancer MDTs were invited to participate via an email including a digital link to the survey sent to membership lists of the UK Breast Cancer Group (UKBCG), Association of Breast Surgeons (ABS), UK Oncology Nursing Society (UKONS) and the British Oncology Pharmacy Association (BOPA). Participants were given 4 weeks to complete the survey, with an email reminder sent out at 3 weeks. Participants provided informed consent for publication of anonymous data. Data from survey responses were extracted directly into Microsoft Excel and analysed using simple descriptive statistics.

Results: The survey has been completed by 78 participants: 11 breast surgeons, 49 oncologists, 9 nurses, 3 pharmacists, 6 other. Ninety-nine percent (n=77) agreed that lifestyle advice was important and 95% (n=74) assessed lifestyle factors during clinic interactions.

The main barrier identified to effective delivery was lack of time, with lack of training and detailed recommendations also highlighted. Despite this, 97% (n=76) of respondents stated that time allowing, brief advice was provided. Access to facilities was variable but 96% (n=75) would refer to lifestyle services if available. Further research was strongly supported and a need for further observational and interventional studies to inform optimal clinical care was identified.

Conclusion: Almost all health care professionals surveyed recognised that lifestyle advice is an important aspect of BC care, but time is a significant barrier to delivery. Further research is required to support delivery of lifestyle recommendations in the clinical setting.

Feasibility and efficacy of a randomised pilot study of the North of England Women's Diet and ActivitY - After early Breast Cancer intervention
Theme: Prevention/Lifestyle

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Background: Two thirds of women are overweight at diagnosis of early-stage breast cancer. Observational studies show a link between excess body weight and breast cancer mortality. This randomised pilot study assessed both feasibility and efficacy of a lifestyle intervention [1] in the UK.

Method: This two-arm, parallel group, randomised controlled pilot study recruited; oestrogen receptor positive (ER+ve) HER2 negative stage I-III breast cancer patients, body mass index greater than or equal to 25, within 3 years of completing primary treatment (excluding endocrine therapy). Participants were assigned (2:1) to the lifestyle intervention [1] or usual care. Feasibility outcomes; recruitment rate, data quality, intervention acceptability and adherence. Descriptive efficacy outcomes at 6 months; weight loss, anthropometric measures, dietary change, physical activity and patient-reported outcomes. The study was sponsored by Northumbria University and was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Approval was granted by the North East NHS Research Ethics Committee (19-NE-0358), ISRCTN registration number 15088551.

Results: Feasibility outcomes: Between Feb 2021 and 30th April 2021 information packs were sent to 108 patients, with a 40.7% response rate. Twenty-one women consented to the study, 1 withdrew prior to randomisation leaving 13 in intervention and 7 in control. Data were available for 100% participants at baseline and 85% at 6 months. The overall attendance rate for intervention sessions was 79.6%.
Efficacy outcomes: intervention vs control showed the following changes from baseline to 6 months: body weight -3.3kg vs -1.1kg, hip circumference -3.1cm vs +1.1cm, fruit and vegetable consumption +1.1 vs -0.8, weekly snack consumption -6.1 vs+1.3, daily PA +73min/day vs -31.7min/day with numerical improvements in body image, breast symptoms and arm symptoms in intervention.

Conclusion: The intervention is feasible to deliver across multiple NHS sites in the North of England and has the potential to improve weight loss at 6 months.

[1]Saxton, J.M., et al., Co-designed weight management intervention for women recovering from oestrogen-receptor positive breast cancer. BMC Cancer, 2022. 22 (1): p. 1202.

Audit of Incidental Breast Lesions on Non-Dedicated Imaging: A Six-Month Analysis
Theme: Other

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Background: The evaluation of incidental breast lesions detected through non-dedicated imaging modalities is crucial for ensuring efficient patient care. However, the types of breast abnormalities identified on non-dedicated imaging that warrant referral remain understudied. This audit aims to assess which incidental breast lesions should be referred and how to optimise the referral process.

Methods: All patients seen at the breast clinic following a referral for an incidental breast lesion on non-dedicated imaging between January and June 2023 were retrospectively identified, and demographic data were collected. Data from subsequent mammography, ultrasound, biopsy records and any other imaging (including historical data) available were gathered and analysed for the specified timeframe.

Results: A total of 95 patients, with a median age of 62 years, were identified. When applicable, mammography was performed with a M1 or M2 grading in 47% of cases. 64% of US scans were graded U1 or U2. Biopsies were

offered to 36 patients (38%) due to suspicious findings on ultrasound and/or mammography, of which 12 were proven to be malignant. This gave a positive predictive value for malignancy of 13%. In approximately 12% of cases, the imaging triggering the referral was unavailable at the time of consultation. Of the remaining patients, over 20% did not undergo a formal review of that imaging.

Conclusions: The high percentage of benign breast imaging in our audit made us consider whether our current practice to image all patients for whom a non-breast-dedicated imaging test suggested the possibility of a breast lesion is justified. All the imaging that triggered the referral was reviewed by a dedicated breast radiologist with the aim of characterising which lesions should be referred and how our current practice could be improved. The audit highlights the importance of optimising the clinical pathway to ensure timely and accurate management of incidental breast lesions as well as the efficient use of resources.

Incidental Breast Lesions on Non-Breast-Dedicated Imaging: Identifying Highly Suggestive Malignancies – A Pictorial Review
Theme: Other

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Background: Assessing incidental breast lesions detected through non-dedicated imaging methods is essential to optimise patient care. Nevertheless, there is limited research on the types of breast abnormalities identified on non-dedicated breast imaging that should be referred to the breast unit for further evaluation. This audit aims to identify which incidental breast lesions are most suggestive of malignancy and should be referred to the breast unit based on cases seen between January and June 2023.

Methods: All patients seen at the breast clinic following a referral for an incidental breast lesion on non-dedicated imaging between January and June 2023 were retrospectively identified. Demographic data and information from subsequent investigations were collected and analysed. With the goal of establishing formal referral criteria, a dedicated breast radiologist assessed all the imaging that led to the referral.

Results: Ninety-five patients were referred to our unit for assessment of incidental breast abnormalities detected through non-breast-dedicated imaging. Among them, only 12 patients (12.6%) were diagnosed with breast cancer. The review of cases led us to formulate specific assessment criteria for breast lesions in future referrals, based on distinct features of these lesions on non-dedicated imaging.

Conclusions: Our audit allowed us to identify which types of incidental breast lesions were most suggestive of malignancy. The pictorial review will showcase the characteristics of these lesions, providing guidance for referrals to the breast unit.

The bone anabolic agent losartan reduces progression of lytic lesions in an in vivo model of breast cancer-induced bone disease
Theme: Metastatic breast cancer

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Background: Bone is the preferred site of breast cancer metastasis. A feed-forward vicious cycle is formed when tumour cells promote osteoclast-mediated bone resorption and growth factors released from bone promote tumour cell proliferation, resulting in localised lytic bone lesions leading to bone fragility and pain. Bisphosphonates can slow the growth of bone lesions by preventing osteoclast-mediated bone resorption. However, it is uncertain whether bone anabolic agents can activate osteoblasts to repair bone lesions from solid tumours. Therefore, we investigated the effectiveness of the angiotensin II receptor blocker losartan as a bone anabolic treatment in a murine model of breast cancer-induced bone disease. We investigated whether losartan could limit/repair bone lesions and reduce the detrimental effects to bone integrity and structure.

Methods: 6-week-old female BALB/c nude mice were injected intracardially with 5x105 Luc2+ve MDA-MB-231 breast cancer cells. Once hindlimb tumours were confirmed by bioluminescence imaging and bone lesions detected by in vivo µCT (week0), mice were treated 5 days/week for 3 weeks with 100mg/kg losartan (n=11) or PBS (control, n=9) by oral gavage. Tumour growth was monitored by bioluminescence imaging twice weekly, left

proximal tibiae and distal femora were scanned by in vivo µCT once weekly (VivaCT80 µCT scanner). The size and progression of the lytic bone lesions were analysed by ImageJ software, using 3-D images reconstructed by CTVOX software.

Results: Bioluminescence imaging showed that tumour burden in bone increased from week 1 to 3, with no significant difference between losartan and PBS treated mice, demonstrating that losartan did not reduce tumour growth. In vivo µCT demonstrated a tumour-induced reduction in trabecular bone volume (BV/TV), trabecular number, and trabecular pattern factor in the tibia which progressed at a slower rate in losartan treated mice compared to PBS controls (Table1.).

	Percentage bone volume (BV/TV)		
Weeks	Vehicle	Losartan	Significance
1	8.013	7.715	ns, 0.213
2	5.515	6.643	ns, 0.193
3	2.603	5.588	*, 0.025
Weeks	Trabecular number (Tb.N)		
	Vehicle	Losartan	Significance
1	0.91	0.938	ns, 0.56
2	0.669	0.803	*, 0.0441
3	0.381	0.689	*, 0.0151
Weeks	Trabecular pattern factor (Tb.Pf)		
	Vehicle	Losartan	Significance
1	18.405	18.736	ns, 0.650
2	17.51	16.998	ns, 0.653
3	12.988	14.991	*,0.0464

Table 1.

Although losartan did not cause complete repair of the bone lesions, the percentage bone lesion area was significantly lower after 3 weeks of losartan treatment compared to control (3.422% vs 9.896%, p**0.0072).

Conclusion: Our data are the first demonstration that a bone anabolic agent can limit the development of breast cancer-induced bone lesions in vivo.

Breast Cancer Now's Service Pledge: Using the power of the patient voice to improve breast cancer services

Theme: Living with BC/QoL/Patient perspective/Supportive care

Fran Berry[1], **Catherine Wood[1],** Zoe Harris[1]**,** Kim Giffen[1]
[1]Breast Cancer Now

The Service Pledge was developed by Breast Cancer Now in 2003, in response to patients and clinicians highlighting a need for services to be informed by patient experience. 20 years on, it continues to be a sector-leader in using patient feedback to shape services. The Service Pledge aligns with the NHS Long-term Plan, helping services embed a 21st century model of care, where patients get more options, better support, and properly joined-up care. It has also responded to the innovations and challenges from the COVID-19 pandemic, shifting patient and healthcare professional engagement to virtual meetings, ensuring partnership working could continue regardless of social distancing measures.

By working at a Cancer Alliance level and including all experiences of breast cancer, the Service Pledge focusses on reducing variation whether that is geographically, across different breast cancer diagnoses, or between different demographics. Through co-production, peer learning and sharing best practice, the Service Pledge encourages a culture of continual improvement in breast care teams and hospitals across the NHS.

Patient and hospital staff feedback is collected through surveys and focus groups, analysed, and shared with patients and hospital staff in a detailed report. Local patient representatives are recruited to work with Breast Cancer Now staff and volunteer Patient Advocates to help hospitals identify improvements from a patient perspective. Through listening and learning from each other, patients and healthcare professionals work in true partnership.

Each hospital develops action plans to ensure improvements are SMART and sustainable. The Service Pledge encourages a Plan, Do, Study, Act approach to implementing improvements, bringing together patients and healthcare professionals across a Cancer Alliance to learn from each other's successes and provide peer support to address challenges. To close the feedback loop, leaflets and posters are provided for patients, highlighting the changes made in response to patient feedback.

To date, over 140 breast services across the UK have developed a Service Pledge with their patients, delivering over 400 improvements for primary and secondary breast cancer patients in the past five years. Improvements have included:

- Recruiting a dedicated secondary breast cancer nurse
- Staggering patient arrival times for surgery so patients don't have to arrive early in the morning for afternoon surgery
- Reviewing Holistic Needs Assessment processes to ensure patients get the most out of them

The success of this work is due to the level of engagement and involvement from both local patients and staff across the hospitals, including clinical teams, budget holders and administrative support. Many patients report that being involved in the Service Pledge helps them grow in confidence and turn something negative (their diagnosis) into something positive for others, while healthcare professionals report an improved understanding of patients' perspectives.

Measuring plasma, soluble Semaphorin-4D (SEMA4D): a potential non-invasive biomarker predictive of clinical outcomes within breast cancer patients with bone metastasis
Theme: Metastatic breast cancer

Steven Wood[1], Walter Gregory[2], Fatma Gossiel[1], Richard Eastell[1], Mark Dunning[1], Gabriela Berg[3], Janet Brown[1]
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Background / Introduction: Breast cancer metastasis to bone occurs in > 70% of advanced breast cancer patients at which point the disease is considered incurable, increasing patient mortality and reducing patient quality of life. Current treatments for bone metastasis (e.g. bisphosphonates such as zoledronic acid) are not without side effects, including osteonecrosis of the jaw (ONJ), and therefore biomarkers are urgently required to identify those patients at greatest risk of developing cancer spread to bone to enable personalized medicine initiatives. Semaphorin-4D is a coupling factor expressed by bone resident osteoclasts, which acts to suppress osteoblast differentiation. SEMA4D exists in both membrane tethered and soluble forms.

Purpose: In order to investigate the potential role of plasma SEMA4D as a marker of breast cancer spread to bone, we measured the level of this protein within plasma samples from patients within the prospective, randomized, open label, AZURE trial comparing adjuvant therapy to adjuvant therapy + zoledronic acid (3360 patients).

Methods: Soluble SEMA4D was measured by ELISA within plasma samples from patients within the AZURE trial and SEMA4D levels correlated with patient outcomes recorded over a 10-year follow up period.

Results: In total plasma-samples were available from 808 patients within the AZURE trial. The measured level of soluble SEMA4D followed a log normal distribution within this patient population. Initial analysis of the results did not reveal a statistically significant association of SEMA4D levels with metastatic outcomes (to either bone or non-bone sites) within the total patient population.

Upon further analysis, plasma SEMA4D levels were observed to be lower within patients who did not develop ONJ ($p = 0.000056$) within the study population, compared to patients with ONJ

Circulating levels of soluble SEMA4D also correlated with T4 tumor stage within patients receiving chemotherapy alone (but not within patients receiving endocrine therapy or endocrine therapy plus chemotherapy), $p = 0.001$. Finally, analysis of circulating SEMA4D levels within breast cancer tumor subtypes revealed that circulating

SEMA4D levels correlated with the time to development of bone only metastases within ER-negative patients, within the control arm of the AZURE trial (p = 0.001). This effect was not previously observed within the total AZURE patient population, which encompasses a wide range of breast cancer tumor subtypes. .

Conclusion(s): Measuring plasma levels of soluble SEMA4D may serve as a non-invasive biomarker which can predict breast cancer patient outcomes, including the risk of developing ONJ. In addition, circulating SEMA4D levels correlate with breast cancer tumor stage and time to develop bone metastases within the ER negative patient subpopulation from the AZURE trial.