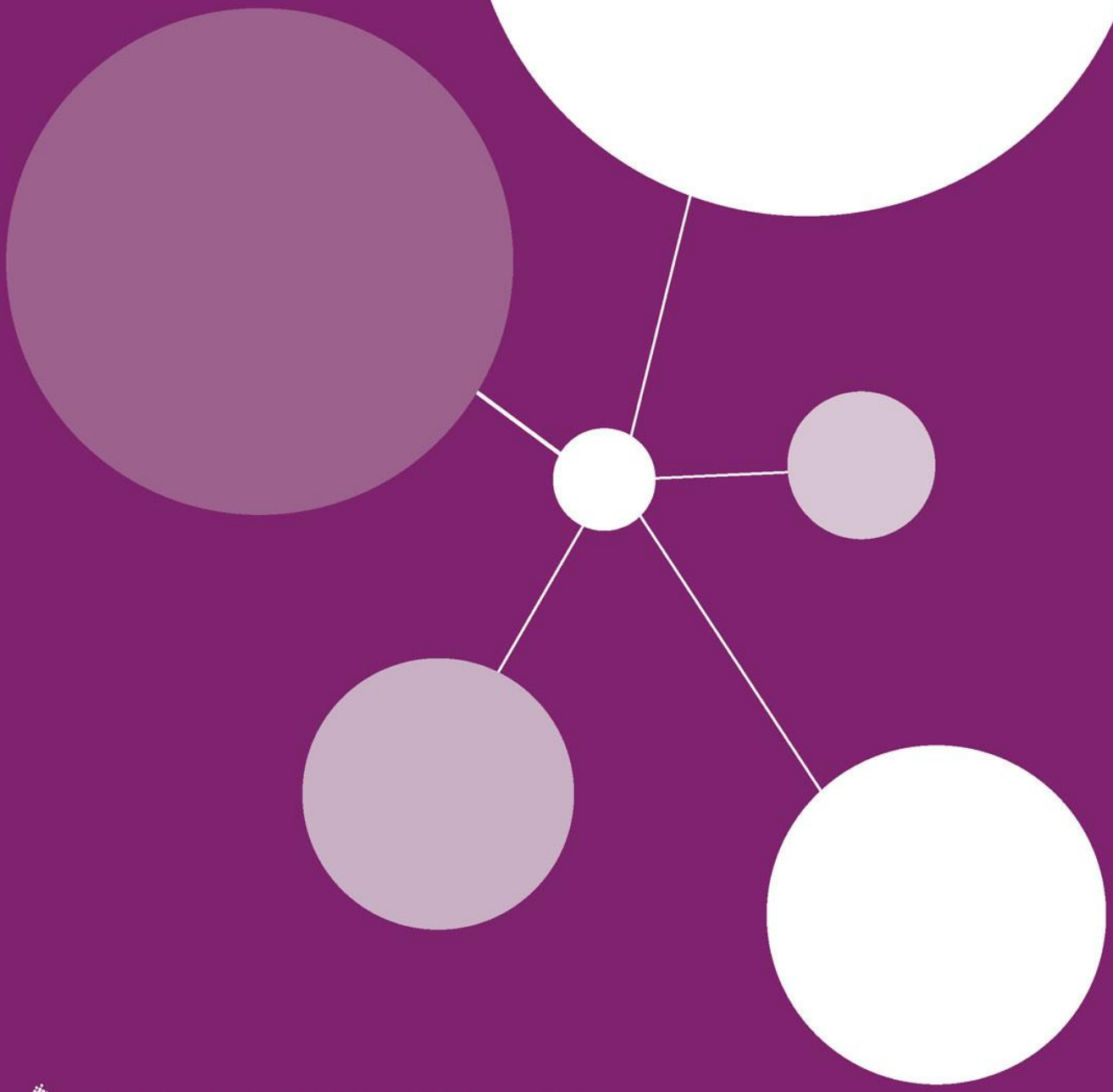
NCRI
National
Cancer
Research
Institute

NCRI Breast Cancer Clinical Studies Group

Annual Report 2017-18



Partners in cancer research

NCRI Breast Cancer CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

Definitive publication of an academic multicentre phase 3 study in advanced breast cancer:

Carboplatin in BRCA1/2-mutated and triple-negative breast cancer BRCAness subgroups: the TNT Trial (Tutt et al Nature Medicine 2018).

The TNT trial is a multicentre UK study of first line chemotherapy in advanced triple negative breast cancer (TNBC). This is one of a small number of contemporary, rare phase III academic studies in advanced breast cancer. It has demonstrated similar response to carboplatin and docetaxel as first line chemotherapy in unselected triple negative disease. In a statistically powered pre-planned subgroup analysis, it has also demonstrated superiority of carboplatin in women with germline BRCA mutations and advanced TNBC. In addition, the study demonstrated in contrast that in BRCAness cases (methylated BRCA-1 BRCA-1 mRNA low and Myriad HRG score high tumours) were not associated with increased response to carboplatin. As significant interaction between basal and non-basal phenotype is driven by high response to docetaxel in the non-basal subgroup.

This is a landmark study in advanced triple negative disease, which demonstrates the ability of UK breast cancer researchers to deliver high quality academic phase III studies with biologically driven hypotheses. The results are practice changing and demonstrate the importance of molecular characterisation in TNBC.

Achievement 2

First results of a large randomised trial

Presentation of POETIC trial results at San Antonio Breast Cancer Symposium December 2017 (Robertson et al SABCS 2017)

The POETIC trial is a large Cancer Research UK (CRUK) funded multicentre UK perioperative study with two coprimary endpoints. The study included 4486 ER positive patients randomised to perioperative aromatase inhibition or no treatment prior to surgery. This study is the only

study to prospectively examine the efficacy of perioperative endocrine therapy, which has for many years been hypothesised to reduce perioperative metastatic seeding.

The study has reported absence of any effect of perioperative therapy on long-term outcome but has provided unequivocal robust data demonstrating the prognostic significance of Ki67 score at baseline and Ki67 score at day 14 of preoperative aromatase inhibition. This outcome is central to the rationale to the POETIC 2 study proposal , which was planned to recruit patients with high Ki67 scores at day 14 to investigate the activity of multiple drugs ability to influence Ki67 and other biomarkers in this group of patients with poor prognosis. While this particular study was not funded but a revised and more ambitious approach incorporating a phase 3 practice changing endpoint is in development based on the concepts arising from POETIC

Achievement 3

Successful funding for an innovative breast cancer de-escalation trial

The SMALL study is a phase 3 non-inferiority design trial to compare standard surgical excision of small grade I screen detected cancers with radiological excision with no surgical intervention. These slow growing cancers with an excellent prognosis may not need the conventional treatment of surgery by wide local excision with pathologically defined clear margins. Advances in techniques for radiologically-guided excision are now widely employed for benign lesion and may be able to replace traditional surgery.

This study illustrates the Breast Cancer CSG strategic aim to trial de-escalation approaches to breast cancer and builds on the previous de-escalation trials shaped by the Breast Cancer CSG such as IMPORT LOW, LORIS, PRIMETIME and Persephone. This study was refined through several rounds of discussion at the UK Breast Intergroup and active involvement of both the Early Disease and Imaging and Translational Subgroups. The funding application was completed with input from a fully multidisciplinary team of surgeons, radiologists, pathologists, clinical and medical oncologists, clinical trial methodologists and patient advocates. The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme has granted provisionally funding for this study, which is a major success and builds on the growing breast cancer de-escalation theme within the portfolio.

2. Structure of the Group

The structure of the Group is largely unchanged. Dr Charlotte Coles has succeeded Professor Judith Bliss as Chair of the Early Disease Subgroup. Professor Iain Lyburn has succeeded Dr Abeer Shaaban as Chair of the Translational & Imaging Subgroup. Dr Anne Armstrong has succeeded Professor Debbie Fenlon as Chair of the Symptom Management Subgroup.

The process for review of proposals for new studies has been standardised with the first place for new ideas to be presented being the UK Breast Intergroup. Immediate feedback is provided via discussion during the meeting and draws on the views of the wider, multidisciplinary UK breast community. This verbal feedback is then summarised into a written format including suggestions for development and a RAG rating is provided to classify the current developmental stage of the proposal. More complex projects or important issues raised are then discussed subsequently at the main CSG.

3. CSG & Subgroup strategies

Main CSG

Improve the outcomes and experience of breast cancer patients and those at risk of developing breast cancer Engagement with patients in all spheres of CSG activity maintains focus on this critical rolling strategic goal.
Increase patient expectation of being involved in a clinical trial This is a continuing focus of the CSG we work with patient groups nationally and locally to promote the value to patients of trial participation. A recurring challenge which is becoming more apparent is the difficulty experienced by individual hospitals is the resource to maintain a wide portfolio which is necessary provide wide access to a suite of clinical trials.
Further the develop the Breast Cancer portfolio The clinical trials portfolio provides a wide range of studies across the entire spectrum of breast cancer from detection treatment of early disease and advanced disease. We have seen the activation of innovative studies such as cTRACk which explores the potential for intervention after completion of standard early disease management where molecular testing indicates impending relapse. Additional novel approaches to understanding the impact of therapy to resistant early disease are now in set up.
Collaborative approach to trial development & participation We are very committed to an inclusive approach to trial development. The breast Intergroup meetings held 4 monthly provide a constructive environment where investigators can share ideas and get immediate feedback from the research community. The CSG provides verbal and written feedback to investigators and encourages groups with similar ideas to pool resource and expertise. The recently funded Small trial provides a clear example of a trial that required extensive collaboration between radiologists, surgeons, clinical oncologists, patient advocates and many more disciplines to develop a successful application.
Improve trials methodology & clinical utility This is a rolling strategic goal the CSG encourages innovative thinking in trail methodology and in trail design. Biomarker driven studies such as ROSCO and the use of $_{CT}$DNA in advanced and early disease studies are examples of trial innovation. Further innovative approaches in surgery are incorporated in current portfolio studies. The importance of patient advocates in all stages of trial development has been established and is now seen as critical to the successful development of trials in answering patient focused questions.

Embed a research culture across the entire patient pathway within all healthcare professionals and in all institutions, provide breast cancer services

The best example for progress in this dimension is the formation this year of the trainee collaborative for oncologists, radiologists and pathologists. This initiative modelled on the surgical research collaboratives will enable trainees to gain experience in conducting collaborative and productive research with published outputs and equip the next generation of consultants to maintain a research based clinical practice.

Optimise trial design to adequately answer specific questions within the confines of the current and future health care environment

The opportunity for studies to be presented and discussed at multiple time points with a wide research base through the existing CSG review structure allows researchers to progressively refine research proposals to take account of practical issues of local delivery and to introduce novel elements at a pace that the NHS can support.

Empower and educate patients and the public to drive research oriented culture within the provision of routine care

Engagement with the media through all outlets available to the CSG is used to drive home the message that progress in breast cancer comes through conduct of research and in particular practice changing clinical trials.

Increase the number of local PIs participating in clinical trials

We have been working with The Association of Breast Surgeons to encourage the integration of research into the working of all breast Units and for the use of MDTs for identification of studies suitable for patients discussed at MDTs. A research session at the 2018 Association of Breast Surgery meeting has been designed to specifically educate and encourage the integration of research into everyday practice in all breast units.

Increase the level of access to and use of tissue from all patients throughout the patient pathway

Access to tissue is a key element of translational research with increasing demand for access to tissues with well annotated clinical outcomes these can be best provided through access to clinical trial sample collections. The establishment of the translational group within the Early Breast Cancer Trial's Collaborative Group (EBCTCG) provides a medium through which groups can collaborate initially by combining translational data from meta-analysis. The expectation now is that better harmonisation of translational methodology across International groups will allow better validation and meta-analysis. New questions requiring the central pooling of samples across multiple trails for analysis are being posed and mechanisms for this type of large scale translational project are being explored. Regulatory issues may slow this process and will need to be carefully negotiated.

Advanced Disease Subgroup (Chair, Professor Carlo Palmieri)

Further develop the Advanced Disease Subgroup portfolio

- Develop Pragmatic Studies
  - Real world data collection
  - No data for efficacy of TDM1 post-progression on Pertz plus Traz
  - N=800 patients treated on Pfizer open access scheme
  - ER+: Sequencing question with introduction of first line CDK4/6
- Systemic Studies that industry will not undertake Sequencing of treatments Toxicity Oligometastatic disease
- Organ specific studies
  - e.g. Liver metastasis (radiofrequency ablation or SIRT)
  - CNS Disease particularly leptomeningeal disease
- Develop platform studies/stratified studies e.g. CNS disease utilising CSF cfDNA

Collaborative approach to trial development & participation

- Engage with other professional groups
  - CT-RAD - RT and systemic therapies Workshop in 2018
  - CM-Path - Standardise SOPs for translational samples
  - Cross-cutting CSG Initiatives - Brain metastasis workshop in 2018
- Engage with pharma
  - Look to develop further 'Alliance type calls'
- Engage with breast cancer clinical community to develop & deliver studies
  - Provide written feedback for trial proposals as a part of UK BI
  - Help less experienced PI develop studies
  - Encourage more colleagues to be PIs
- Ensure successful delivery of current portfolio
  - Provide feedback and advice as needed
- Engage with international groups

Improve trials methodology & clinical utility

- PPI
- Move away from 'paternalistic based' model of recruitment/research
  - Develop patient facing material to aid patients in accessing clinical studies e.g. 'Google' style trial search tool
  - UK Clinical trial gateway-suboptimal
- Help increase patient expectation of being involved in clinical research
- Understanding needs of patients with metastatic cancer in context of studies
  - Factors which may influence trial recruitment
  - Barriers to trial entry
- Understanding questions important to patients
- Integration of PPI in trial development
  - Input at early stage into design
  - Patient facing material
  - Involvement in TMGs
- Trainees/Education
- Support Trainee Research Collaborative
  - Cross speciality: medical oncology, clinical oncology, radiology and pathology
  - Help involve trainees in research & develop future PIs
  - National launch meeting being arranged in 2018
- Ensure trainee involved with a study from its development
  - Input at early stage into design
  - Patient facing material
  - Involvement in TMGs
- Encourage FLIMS proposal and review by group
  - Invite to present at UK BI and to get comments from sub-group
- Invite senior trainees to observe sub-group meetings
- Educate other healthcare professionals regarding benefits of clinical trial

Early Disease Subgroup (Chair, Dr Charlotte Coles)

Further develop the Early Disease Subgroup portfolio

A key achievement has been contribution to development of the SMALL trial proposal: A Phase III, randomised, multi-centre trial addressing overtreatment of small screen-detected breast cancer by comparing standard surgery versus minimally invasive vacuum-assisted excision. This builds on our theme of de-escalation of therapy for lower risk breast cancer patients and has been funded by the HTA programme. The lead applicant is Mr Stuart McIntosh, who is a member of the Early Disease Subgroup and there has also been considerable input from other subgroup members, Dr Coles and Mrs Hilary Stobart (consumer). This trial proposal also had considerable input from the Translational & Imaging Subgroup and is an example of cross-cutting collaborative working between subgroups.

Development of the HER2+ platform trial proposal is ongoing and the subgroup has contacted the National Institute for Health Research (NIHR) regarding a possible funding call for research into effectiveness of HER2 directed therapy. In addition, the group has identified that essential pilot data is required before submitting a proposal which investigates optimal axillary treatment following neo-adjuvant systemic therapy and the lead researcher has taken this forward as a pilot study in key centres.

Adopt a collaborative approach to the development of translational research

Active involvement of the Subgroup has been demonstrated by:

- Written feedback for 9 trial proposals in 2017, via the UK Breast Intergroup meetings (UKBI), which draw on input from the wider breast cancer research community
- Engagement with multidisciplinary breast cancer colleagues to develop NeST - a multicentre audit to evaluate current practice in the use of neoadjuvant systemic therapies to treat breast cancer: http://reconstructivesurgerytrials.net/clinical-trials/nest
- The UK PRIMETIME study has been highlighted by the NCRI as an example of excellent consumer involvement http://www.ncri.org.uk/case-study/identifying-more-harm-than-good-the-primetime-breast-cancer-study/and this was achieved via input from EDS members
- Continued engagement with Clinical and Translational Radiotherapy (CTRad) Research Working Group to develop a national breast proton research proposal in collaboration with European partners is currently ongoing with update at CTRad proton research meeting in May 2018

Improve trials methodology & clinical utility

The Early Disease Subgroup has collaborated with the other subgroups and NIHR Clinical Research Network Breast subspecialty group to establish a trainee breast cancer research initiative. An inaugural national meeting in May 2018 will bring together cross-specialty oncology trainees with mentors to develop new simple, pragmatic research proposals: https://www.rcr.ac.uk/meeting/launch-meeting-breast-cancer-trainees-research-collaborative-group

Early Disease Subgroup members, including patient advocate members, have contributed to designing a study within a study (SWAT) investigating patient decisional conflict study within PRIMETIME. This study is now open and it is anticipated that this novel approach will bring added value to an existing portfolio trial.

Symptom Management Subgroup (Co-Chairs, Professor Debbie Fenlon, outgoing chair and Dr Adrienne Morgan)

Raise increased awareness of hot flush and night sweats workstream

The Symptom Management Subgroup continues to promote and develop research into symptoms and symptom support after breast cancer across the range of symptoms, with a main focus on menopausal issues, such as hot flushes and vaginal problems. Two surveys and two studies on sexuality and vaginal problems after breast cancer are in development. Studies include those that address the causes, underlying biology and physiology of symptoms as well as developing supportive interventions for people experiencing symptoms.

We are making links with the wider research establishment (non-cancer) in order to bring together new teams into this area. We have also led a symposium this year at the European Menopause and Andropause Society Meeting in Amsterdam, to continue to raise the debate in this area.

The group is kindly hosted by Baroness Delyth Morgan, Chief Executive of Breast Cancer Now, who also provides refreshments and secretarial support.

Support the development of current interventions to manage hot flush related issues

The FOAM study investigating the utility of folic acid for relief from hot flushes is promoted and supported by the group. Workstreams to review and disseminate data on the safety of progestins for management of hot flushes are currently in place

Support the development of new interventions

Understanding the biology of menopausal or endocrine therapy induced hot flushes are supported with aim of identifying therapies that can be evaluated for symptomatic relief.

Translational & Imaging Subgroup (Chair, Professor Iain Lyburn)

Support the community in the development and delivery of studies in advanced disease.

A UK group with a special interest in Inflammatory Breast Cancer (IBC) based at The University of Birmingham has been formed. The chair of the Breast Cancer CSG, Professor Dan Rea, and Professor Iain Lyburn are members. Preliminary teleconferences were held in 2017. The intention is for the group to initially manage patients with IBC from the Birmingham and adjacent areas; the aim is for subsequent exploration of the feasibility of further roll out across the UK. Initially this will involve data collation – clinical, imaging and pathological with a view to undertaking analysis, which may provide prognostic information. The strategic aim is for this to generate a network through which national multicentre trials can be developed encompassing clinical and translational aspects.

Explore opportunities for identifying cross-cutting translational themes across the portfolio

In addition to liaison with other subgroups of the Breast Cancer CSG, Professors Rea and Lyburn had a teleconference with Dr Christine Campbell, outgoing Chair of the Primary Care CSG Screening Subgroup who had previously undertaken a scoping exercise about exploring potential trials and data analysis in a personalized risk-based screening programme. Discussion involved incorporating parameters such as breast density, parity, body mass index and genetics.

Mr Stuart McIntosh, Dr Nisha Sharma and Professor Iain Lyburn have been involved in the development of the SMALL trial proposal.

The membership of the Subgroup has been grown and includes: Mr Stuart McIntosh, Consultant Surgeon and Dr Nisha Sharma, Consultant Radiologist. Professor Keith Rodgers of the Cranfield Forensic Institute, Cranfield University and Professor Nick Stone, lead of the Biomedical Spectroscopy Unit at Exeter University have kindly agreed to be available for discussion on specialist basic science applications.

Identify future translational opportunities for inclusion within portfolio studies

There is an increasing importance of imaging complementary biomarkers. Professor Lyburn and Professor Fiona Gilbert have been writing guidelines for magnetic resonance imaging of High Risk screening in the NHS BSP to be published later in 2018. This will facilitate consistency different centres allowing more valid comparison and thus incorporation into sub-studies of portfolio trials.

Members of the translational subgroup and main CSG were involved in setting up PRECISION – the CRUK Grand Challenge awarded for an international collaboration with teams from The Netherlands, USA and UK evaluating various aspects of DCIS. This project has major basic science translational components.

4. Task groups/Working parties

The Breast Cancer CSG had no task groups or working parties during the reporting year.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
None				
November 2017				
Validation of an autoantibody blood test for the detection of early breast cancer (BC), particularly hormone receptor positive BC	Biomarker Project Award (Full Application)	Professor John Robertson	Not Supported	Supported
POETIC-2: An innovative umbrella trial aiming to match molecular signatures with targeted agents against endocrine resistance in early breast cancer	Experimental Medicine Award (Full Application)	Professor Judith Bliss	Not Supported	Extensive development through close association with CSG with CSG member representation on Trial development group. Revised design in preparation.
ImproveMet: Liquid biopsies to improve metastatic breast cancer outcomes	Experimental Medicine Award (Full Application)	Professor Carlos Caldas	Not Supported	Developed with input from CSG members
SMARTer Trials: Systematic BioMARker Linked Bayesian Adaptive Randomised Phase II Trials of novel treatment combinations in extended adjuvant treatment of triple negative breast cancer (TNBC) and high grade serous ovarian cancer	Experimental Medicine Award (Outline)	Dr James Brenton	Invited to Full	Presented to CSG and developed by CSG members

(HGSOC) for patients with detectable disease by ctDNA for mutated TP53				
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**
SMALL	NIHR HTA	Mr Stuart McIntosh	Supported	Major involvement

6. Consumer involvement

The main Breast Cancer CSG has two consumer representatives, Lesley Stephen and Hilary Stobart. A number of additional consumers, including Elizabeth Benns, Mairead McKenzie, Lesley Turner, and Dr Adrienne Morgan are also involved in putting forward the views and needs of patients on each of its subgroups. In addition, Dr Adrienne Morgan, co-chairs the Symptom Management Subgroup. Excellent engagement and collaboration at strategy days, in research design, development and trial management occurs between the consumers and health professionals within the CSG, its subgroups and beyond in the UK and sometimes abroad. Representation occurs and is heard at each meeting and mentoring support is available where needed. Communication with a wider network of consumers, in particular from Independent Cancer Patients' Voice (ICPV) assists all the NCRI consumers in delivering the level of involvement needed. 2017 saw NCRI Breast Cancer consumers get involved in a wide variety of projects and studies within and outside the NCRI, although always with a clear focus on representing the needs of breast cancer patients.

Lesley Stephen

Some of these activities have included for Lesley Stephen, campaigning for Kadcyla to be funded in Scotland, supporting the Marks & Spencer Breast Cancer Awareness campaign to raise significant funds for Breast Cancer Now, sitting on the BCN Tissue Bank Operational Review Committee and taking part in a BBC Scotland documentary about the Beatson Cancer hospital and its research portfolio. Lesley has also helped to champion a focus on research into treatment for brain metastases, an area of need.

Hilary Stobart

Hilary Stobart has been co-author for a consumer poster for the PRECISION CRUK Grand Challenge, accepted for presentation at the San Antonio Breast Cancer Symposium in Dec 17. She has had ongoing involvement with a NICE technology review and assessed funding applications as part of the Breast Cancer Now Catalyst award and an NIHR RFPB funding panel. She also visited the Dept. of Radiotherapy, UZ Gent, Jun 2017 to discuss a Susan Komen project on prone radiotherapy and presented to the department on patient involvement in the UK.

Other consumer highlights include

- Being members, and sometimes co-applicants, of TMG/TSG/protocol working groups including: C-TRAK, REQUITE, PRIMETIME, UNIRAD, OPTIMA, OPTIMAM2, VOXTOX, 100,000 Genome Project – Breast GeCIP, PIONEER, MENOS4, Add Aspirin and ROSCO, CRUK PRECISION Grand Challenge

- Hilary Stobart and Lesley Turner (both TMG members for PRIMETIME) have partnered with Dr Coles (CI) to write a case study of impact of patient involvement in PRIMETIME for CTRad and for the RCR website.

- Consumers presented at the NCRI Brain Metastases Workshop and will be co-respondents applicants on two new brain metastases studies

- They will also be co-leading a new piece of research, surveying metastatic patients to understand their awareness and experience of clinical research opportunities

7. Priorities and challenges for the forthcoming year

Priority 1

Early disease: Submit funding application for HER-2 platform study

A meeting of key stake holders and the study research team was carried in June 2018 to discuss the most appropriate pathway for funding given that this is a complex platform study proposal and may require assistance from more than one funding body.

Priority 2

Collect data to understand the resource constraints that are restricting the number of breast cancer studies that can be supported by many hospitals, better understand and identify solutions to very slow set up times at local level. The Group are receiving feedback from researchers that trusts are finding resource constraints which delay study set up times and are increasingly cited as reasons for non-participation in multicentre studies. Understanding the detail behind this change has proven challenging.

Priority 3

Launch the Breast Cancer Trainees Research Collaborative Group and hold an inaugural meeting and select a range of deliverable projects that will engage trainees and provide unique publishable outputs.

Challenge 1

Use data from priority 1 to lobby for appropriate solutions to obstacles. In a severely resource challenged environment we need to identify mechanisms for streamlining processes and improving efficiency.

Challenge 2

Identify how to access and use routinely collected NHS data to support research data collection. This is important in conducting phase IV real world experience research and in long term follow-up in early breast cancer where treatment effects may take 10 years or more to mature and long-term toxicity out to 20 years or longer are important but often poorly documented aspects of clinical trials. Our experience to date shows that more work in this area is needed to understand all the data quality issues with routine data capture.

Challenge 3

With withdrawal from the European Union imminent we need to become more visible within the international community as a research group. We have representation within the Breast International Group (BIG) and are active participants in BIG studies but need to raise our profile within BIG. International collaboration is increasingly important in answering important academic questions but the organisation needed to run international trials is more onerous and more expensive. The funding streams for International research are similarly unfamiliar and often through multiple funding sources.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG Strategy
B – Advanced Disease Subgroup Strategy
C – Early Disease Subgroup Strategy
D – Symptom Management Subgroup Strategy
E – Translational & Imaging Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Professor Daniel Rea (Breast Cancer CSG Chair)

Appendix 1

Membership of the Breast Cancer CSG

Name	Specialism	Location
Dr Sheeba Irshad Kanth*	Clinical Lecturer	London
Dr Charlotte Coles	Clinical Oncologist	Cambridge
Dr Carolyn Taylor	Clinical Oncologist	Oxford
Dr Duncan Wheatley	Clinical Oncologist	Cornwall
Ms Lesley Stephen	Consumer	Edinburgh
Mrs Hilary Stobart	Consumer	Nottingham
Dr Jean Abraham	Medical Oncologist	Cambridge
Professor Janet Brown	Medical Oncologist	Sheffield
Professor David Cameron	Medical Oncologist	Edinburgh
Dr Ellen Copson	Medical Oncologist	Southampton
Dr Iain MacPherson	Medical Oncologist	Glasgow
Professor Carlo Palmieri	Medical Oncologist	Edinburgh
Professor Daniel Rea (Chair)	Medical Oncologist	Birmingham
Dr Nicholas Turner	Medical Oncologist	London
Professor Andrew Wardley	Medical Oncologist	Manchester
Dr Simon Vincent	Observer	London
Dr Elizabeth Mallon	Pathologist	Glasgow
Professor Emad Rakha	Pathologist	Nottingham
Professor Janet Dunn	Professor of Clinical Trials	Warwick
Professor Debbie Fenlon	Professor of Nursing	Swansea
Professor Iain Lyburn	Radiologist	Cheltenham
Dr Muthyala Sreenivas	Radiologist	Coventry
Professor Judith Bliss	Statistician	London
Mr Ramsey Cutress	Surgeon	Southampton
Ms Cliona Kirwan	Surgeon	Manchester
Mr Stuart McIntosh	Surgeon	Belfast
Mrs Jagdeep Singh*	Surgeon	Oxfordshire

* denotes trainee member

Membership of the Subgroups

Advanced Disease Subgroup		
Name	**Specialism**	**Location**
Dr Sheeba Irshad Kanth*	Clinical Lecturer	London
Dr Mark Beresford	Clinical Oncologist	Bristol
Dr Adrian Harnett	Clinical Oncologist	Norfolk
Dr Andreas Makris	Clinical Oncologist	Middlesex
Dr Duncan Wheatley	Clinical Oncologist	Cornwall
Ms Elizabeth Benns	Consumer	Letchworth
Ms Mairead MacKenzie	Consumer	London
Ms Lesley Stephen	Consumer	Edinburgh
Dr Anne Armstrong	Medical Oncologist	Manchester
Professor Robert Coleman**	Medical Oncologist	Sheffield
Dr Catherine Harper-Wynne	Medical Oncologist	London
Professor Carlo Palmieri (Chair)	Medical Oncologist	Liverpool
Dr Rebecca Roylance**	Medical Oncologist	London
Professor Peter Schmid	Medical Oncologist	Brighton
Dr Nicholas Turner**	Medical Oncologist	London

Early Disease Subgroup		
Name	**Specialism**	**Location**
Dr Charlotte Coles (Chair)	Clinical Oncologist	Cambridge
Professor Andrew Tutt	Clinical Oncologist	London
Ms Mairead MacKenzie	Consumer	London
Mrs Hilary Stobart	Consumer	Nottingham
Professor Andrew Wardley	Medical Oncologist	Manchester
Professor Judith Bliss	Statistician	London
Ms Cliona Kirwan	Surgeon	Manchester
Mr Stuart McIntosh	Surgeon	Belfast
Mrs Jagdeep Singh*	Surgeon	Oxfordshire

Symptom Management Subgroup		
Name	**Specialism**	**Location**
Dr Adrienne Morgan (Co-Chair)	Consumer	London
Dr Carolyn Morris	Consumer	Lewes
Mrs Lesley Turner	Consumer	Southampton
Dr Jenifer Sassarini	Clinical Lecturer	Glasgow
Dr Mei-Lin Ah-See	Clinical Oncologist	Middlesex
Professor Myra Hunter	Clinical Psychologist	London
Dr Anne Armstrong	Medical Oncologist	Manchester
Professor Debbie Fenlon (Co-Chair)	Professor of Nursing	Swansea
Dr Melanie Flint	Senior Lecturer in Immunopharmacology	Brighton
Professor Janet Dunn	Statistician	Warwick

Translational & Imaging Subgroup		
Name	**Specialism**	**Location**
Mrs Hilary Stobart	Consumer	Nottingham
Professor Rob Stein	Medical Oncologist	London
Dr Stuart Griffiths	NCRI Programme Manager	London
Professor John Bartlett**	Pathologist	Ontario
Professor Sarah Pinder	Pathologist	London
Dr Colin Purdie	Pathologist	Dundee
Professor Emad Rakha	Pathologist	Nottingham
Professor Valerie Speirs	Pathologist	Leeds
Professor Iain Lyburn (Chair)	Radiologist	Cheltenham
Dr Nisha Sharma	Radiologist	Leeds
Mr Stuart McIntosh	Surgeon	Belfast
Professor Keith Rodgers	Scientist	Cranfield
Professor Nick Stone	Scientist	Exeter
Professor Janet Dunn	Statistician	Warwick
Professor Alastair Thompson**	Surgeon	USA

* denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Overall strategy aim

Improve the outcomes and experience of breast cancer patients and those at risk of developing breast cancer.

Aims

1. Ensure that all breast cancer patients have the opportunity to take part in research with access to a wide range of studies.
2. Increase patient expectation of being involved in a clinical trial.
3. Ensure equality of access for all patients through developing appropriate referral pathways and extended PIC sites for complex studies.
4. Embed a research culture across the entire patient pathway within all healthcare professionals and in all institutions providing breast cancer services.
5. Optimise trial design to adequately answer specific questions within the confines of the current and future health care environment.
6. Empower and educate patients and the public to drive a research oriented culture within the provision of routine care.
7. Increase the number of local PIs participating in clinical trials.
8. Increase the level of access to and use of tissue from all patients throughout the patient pathway.
9. Educate all healthcare professionals on the advantages of recruiting patients to trials.
10. Maintain international collaboration where appropriate and key to the success of a trial.
11. Strengthen links with other NCRI CSGs, HCIS and Advisory Groups.
12. Strengthen links with groups and alliances which impact on the ability to deliver trials.
13. Ensure a balanced portfolio of clinical trials with appropriate mix of complexity to allow full exploitation of clinical trial expertise and capacity.
14. Encourage the documentation of research initiatives, research competencies and achievements of all breast cancer clinicians.
15. Further develop the interaction with the CSG and the CLRN subspecialty research leads.
16. Extend trainee collaborative to oncologists, radiologists and pathologist.
17. Integrate Annual Trials day activities into the new multi-professional biannual breast cancer research meeting.
18. Deliver the commercial and non-commercial portfolio.

B – Advanced Disease Subgroup Strategy

Strategic objective	Activity	CSG Lead	Date
1a. Portfolio development (general)	To horizon scan the portfolio to identify future gaps & to develop trial concepts for discussion within such areas To design and deliver trials embracing the concept of personalised medicine; explore targeted treatments in molecularly defined subgroups; modulate extent of treatment according to risk Explore opportunities for identifying cross cutting themes across the portfolio & for coupling / decoupling studies where appropriate	Subgroup	Ongoing
1b. Portfolio development (local therapy)	Explore opportunities for Surgery / RT technology evaluation • new technologies • extent of treatment • need for treatment • Refinement of screening	CC PB / AS / CK CH/DR /SM	Primtime open Nostra prelim to open 2017 Risk adapted screening platform application 2018
1c. Portfolio development (systemic therapies)	To promote concept of trial platforms / multi stage trials to test modulation of treatment according to risk & likely benefit To promote use of informative experimental models including focussing novel treatment evaluation to those with residual – assessable - disease • post neoadjuvant – macroscopic / microscopic (ctDNA) • adjuvant – microscopic (ctDNA) • window of opportunity – biological endpoints • Metastatic disease – plasma detectable ctDNA; disease accessible for biopsy To promote development of pragmatic trials to test residual unanswered treatment questions within context of contemporary trial design (exploring alternative routes for collecting follow up data – see below, incorporating PROMS collected digitally (e.g. via Web, App), serial monitoring for micrometastatic disease), e.g. • Choice of regimen (efficacy vs tolerability) • Duration • Sequencing of treatments	AT – PHOENIX – post neoadjuvant residual disease wop platform AW – her2+ modulating treatment according to risk JMB / DC / AR – pragmatic CT trials	HER-2 platform funding application 2018 Phoenix open 2018 Ct-RACK Funding application 2017 And Ongoing

Strategic objective	Activity	CSG Lead	Date
1d Portfolio development integrated (translational research)	Promote expectations for integrating translational research into all trials where possible (patient acceptability / cost considerations) • Biomarker evaluation to identify sensitive subgroups • Serial (plasma) monitoring for micrometastatic disease • Mutation testing in residual disease Develop virtual Biobank (guided by Translational subgroup) • cross talk between those holding samples • agreement about how material is collected, stored and shared • common expectations for generic consent, sharing etc. • SOPs for collections etc.	NT AT AW	HER-2 platform funding application 2018 Phoenix open 2018 Ct-RACK Funding application 2017
2 Collaborative approach to trial development & participation	Engage with breast cancer clinical research community to develop and deliver high quality internationally competitive studies • National Breast Trialists Day (now biannual) • National multiprofessional breast cancer reserach meeting • UK Breast Intergroup meetings 2x/year • UK Breast Intergroup Feasibility & interest surveys Harnessing expertise and linking people with related ideas (UKBI) – to maximise efficiency & quality to trials Promote integration of PPI involvement in discussions of both concepts and generic considerations (eg multiple biopsies) • Arrange forums for discussion • Ensure PPI representation at meetings • Aim to optimise efficiency in and minimise inconvenience to PPI representatives in relation to workload management Engage with Royal College of Surgeons and Association of Breast Surgery and to support initiatives to increase the number of surgical trainees involved in clinical trials research Link with CTRad to expand RT studies Maximise opportunities for international collaboration • BIG – UK a participant group • BIG – UK a lead group • Unilateral national collaborative groups (NSABP, NCIC, UNICANCER, ANZBCG)	All KR MM All CC JB DR DC	

Strategic objective	Activity	CSG Lead	Date
3. Improving trials methodology & clinical utility	Endeavour to identify new predictors of risk and outcome intermediate endpoints • aimed at being true surrogates of long term disease outcomes (DFS, OS) • able to identify/predict patients with residual disease risk Collaborate with NCIN (inc Breast SSCRG) and CRS to validate completeness and accuracy of data acquired from routine data sources with a view to replacing hospital based follow up for disease outcome Engage with trials methodologists for optimising trial designs efficiently – multiple questions within 1 trials (couple / decouple studies).	NT - Post neoadjuvant ctDNA mutation identification & monitoring for disease risk JB JD JD	CtTRACK And successor studies Ongoing Ongoing Ongoing

PB Peter Barry
JB Judith Bliss
DC David Cameron
CC Charlotte Coles
DF Debbie Fenlon
CK Cliona Kirwan
KR Kat Randle
AR Alistair Ring
AS Anthony Skene
NT Nick Turner
AT Andrew Tutt
AW Andrew Wardley

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C – Early Disease Subgroup Strategy

Strategic objective	Activity	CSG Lead	Date
1a. Portfolio development (general)	To horizon scan the portfolio to identify future gaps & to develop trial concepts for discussion within such areas To design and deliver trials embracing the concept of personalised medicine; explore targeted treatments in molecularly defined subgroups; modulate extent of treatment according to risk Explore opportunities for identifying cross cutting themes across the portfolio & for coupling / decoupling studies where appropriate	Subgroup	Ongoing
1b. Portfolio development (local therapy)	Explore opportunities for Surgery / RT technology evaluation • new technologies • extent of treatment • need for treatment • Refinement of screening	Local therapy leads	Primetime open Nostra prelim to open 2017 SMALL proposal to apply for funding 2018
1c. Portfolio development (systemic therapies)	To promote concept of trial platforms / multi stage trials to test modulation of treatment according to risk & likely benefit To promote use of informative experimental models including focussing novel treatment evaluation to those with residual – assessable - disease • post neoadjuvant – macroscopic / microscopic (ctDNA) • adjuvant – microscopic (ctDNA) • window of opportunity – biological endpoints • Metastatic disease – plasma detectable ctDNA; disease accessible for biopsy To promote development of pragmatic trials to test residual unanswered treatment questions within context of contemporary trial design (exploring alternative routes for collecting follow up data – see below, incorporating PROMS collected digitally (e.g. via Web, App), serial monitoring for micrometastatic disease), e.g. • Choice of regimen (efficacy vs tolerability) • Duration • Sequencing of treatments	AT – PHOENIX – post neoadjuvant residual disease wop platform AW – her2+ modulating treatment according to risk JMB / DC / AR – pragmatic CT trials	HER-2 platform funding application 2018/19 Phoenix open 2018 Ct-RACK Funding application 2017 And Ongoing

Strategic objective	Activity	CSG Lead	Date
1d Portfolio development integrated (translational research)	Promote expectations for integrating translational research into all trials where possible (patient acceptability / cost considerations) • Biomarker evaluation to identify sensitive subgroups • Serial (plasma) monitoring for micrometastatic disease • Mutation testing in residual disease Develop virtual Biobank (guided by Translational subgroup) • cross talk between those holding samples • agreement about how material is collected, stored and shared • common expectations for generic consent, sharing etc. • SOPs for collections etc.	NT AT AW	HER-2 platform funding application 2018/9 Phoenix open 2018 Ct-RACK Funding application 2017
2 Collaborative approach to trial development & participation	Engage with breast cancer clinical research community to develop and deliver high quality internationally competitive studies • National Breast Trialists Day (now biannual) • National multiprofessional breast cancer reserach meeting • UK Breast Intergroup meetings 2x/year • UK Breast Intergroup Feasibility & interest surveys Harnessing expertise and linking people with related ideas (UKBI) – to maximise efficiency & quality to trials Promote integration of PPI involvement in discussions of both concepts and generic considerations (eg multiple biopsies) • Arrange forums for discussion • Ensure PPI representation at meetings • Aim to optimise efficiency in and minimise inconvenience to PPI representatives in relation to workload management Engage with Royal College of Surgeons and Association of Breast Surgery and to support initiatives to increase the number of surgical trainees involved in clinical trials research Link with CTRad to expand RT studies Maximise opportunities for international collaboration • BIG – UK a participant group • BIG – UK a lead group • Unilateral national collaborative groups (NSABP, NCIC, UNICANCER, ANZBCG)	All MM, HS All CC JB DR DC	

Strategic objective	Activity	CSG Lead	Date
3. Improving trials methodology & clinical utility	Endeavour to identify new predictors of risk and outcome intermediate endpoints • aimed at being true surrogates of long term disease outcomes (DFS, OS) • able to identify/predict patients with residual disease risk Collaborate with NCIN (inc Breast SSCRG) and CRS to validate completeness and accuracy of data acquired from routine data sources with a view to replacing hospital based follow up for disease outcome Engage with trials methodologists for optimising trial designs efficiently – multiple questions within 1 trials (couple / decouple studies).	NT - Post neoadjuvant ctDNA mutation identification & monitoring for disease risk JB JD JD	CtTRACK And successor studies Ongoing Ongoing Ongoing

JB Judith Bliss
DC David Cameron
CC Charlotte Coles
CK Cliona Kirwan
MM Mairead MacKenzie
SM Stuart McIntosh
AR Alistair Ring
AS Anthony Skene
HS Hilary Stobart
NT Nick Turner
AT Andrew Tutt
AW Andrew Wardley

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D – Symptom Management Subgroup Strategy

Hot flush and night sweats workstream	Outputs
1. Raising awareness of the issue	• Undertaken rapid surveys into current knowledge and management of hot flushes with patients, primary and secondary care health professionals. • Acted as consultants to NICE guidance on menopause management, to ensure that management of menopause after breast cancer was included. • Presented eight posters and fifteen oral presentations at national and international conferences. • Presented a symposium on breast cancer at the European Menopause and Andropause Society conference 2015 and secured a further symposium for EMAS 2017. • Written five papers for publication. • Developing a brief guide for menopause management after breast cancer in conjunction with Macmillan.
2. Supporting the development of current interventions to manage hot flush related problems	• Currently have four funded studies (MENOS4, green pessaries, PIONEER, fMRI). • FOAM is also on the NCRI portfolio (folic acid for menopausal symptoms). • Two further studies currently shortlisted. • Two studies have been presented and supported at Group meetings. • Currently supporting the development of studies into acupuncture, CBT, adherence to hormone therapy and megace.
3. Supporting the development of new interventions.	• The group have identified researchers into the biology of oestrogen deprivation and new researchers in this area who will pursue this avenue for future research. A review of the current state of research has been undertaken and several studies are currently in development.

Our ongoing strategy is now to broaden out to include other symptoms. In the first instance we will focus on sexual difficulties as a consequence of treatment for breast cancer. The same strategy that was used for hot flushes and night sweats will be used to develop three streams of work: raising awareness of the issue, supporting the development of current interventions to manage hot flush related problems and supporting the development of new interventions. We will liaise with other CSGs where appropriate to ensure that research into other symptoms related to breast cancer is being supported in the most relevant CSG.

E – Translational & Imaging Subgroup Strategy

Strategic objective	Activity	CSG Lead	Date
1a. Portfolio development (general)	To identify future translational opportunities for inclusion within portfolio studies To work with the early and late subgroups to design and deliver trials embracing the concept of personalised medicine; explore targeted treatments in molecularly defined subgroups; modulate extent of treatment according to risk in early disease . Explore opportunities for identifying cross cutting translational themes across the portfolio & for coupling / decoupling studies where appropriate Encourage a uniform minimum standards across all MDTs for the extent and timing of pathological information including standard mutational analysis and biomarker evaluation through guideline and position paper publications Encourage uniform minimum standards for reporting and decision making within MDTs based on comprehensive and timely imaging and biomarker information including a requirement to identify and record potential trial eligibility	All AS SP	Ongoing
1b. Portfolio development imaging	Ensure /advise on appropriate protocols for imaging in portfolio studies identify opportunities for assessment of novel imaging research	IL/FG	PROSPECTS TRIAL to open 2017/18 Ongoing
1c. Portfolio development (systemic therapies)	To promote concept of trial platforms / multi stage trials to test modulation of treatment according to risk & likely benefit To promote use of informative experimental models including focussing novel treatment evaluation to those with residual – assessable - disease • post neoadjuvant – macroscopic / microscopic (ctDNA) • adjuvant – microscopic (ctDNA) • window of opportunity – biological endpoints • Metastatic disease – plasma detectable ctDNA; disease accessible for biopsy		Plasma Match recruiting 2017 cTRAC full application 2017 Phoenix First patient in 2018

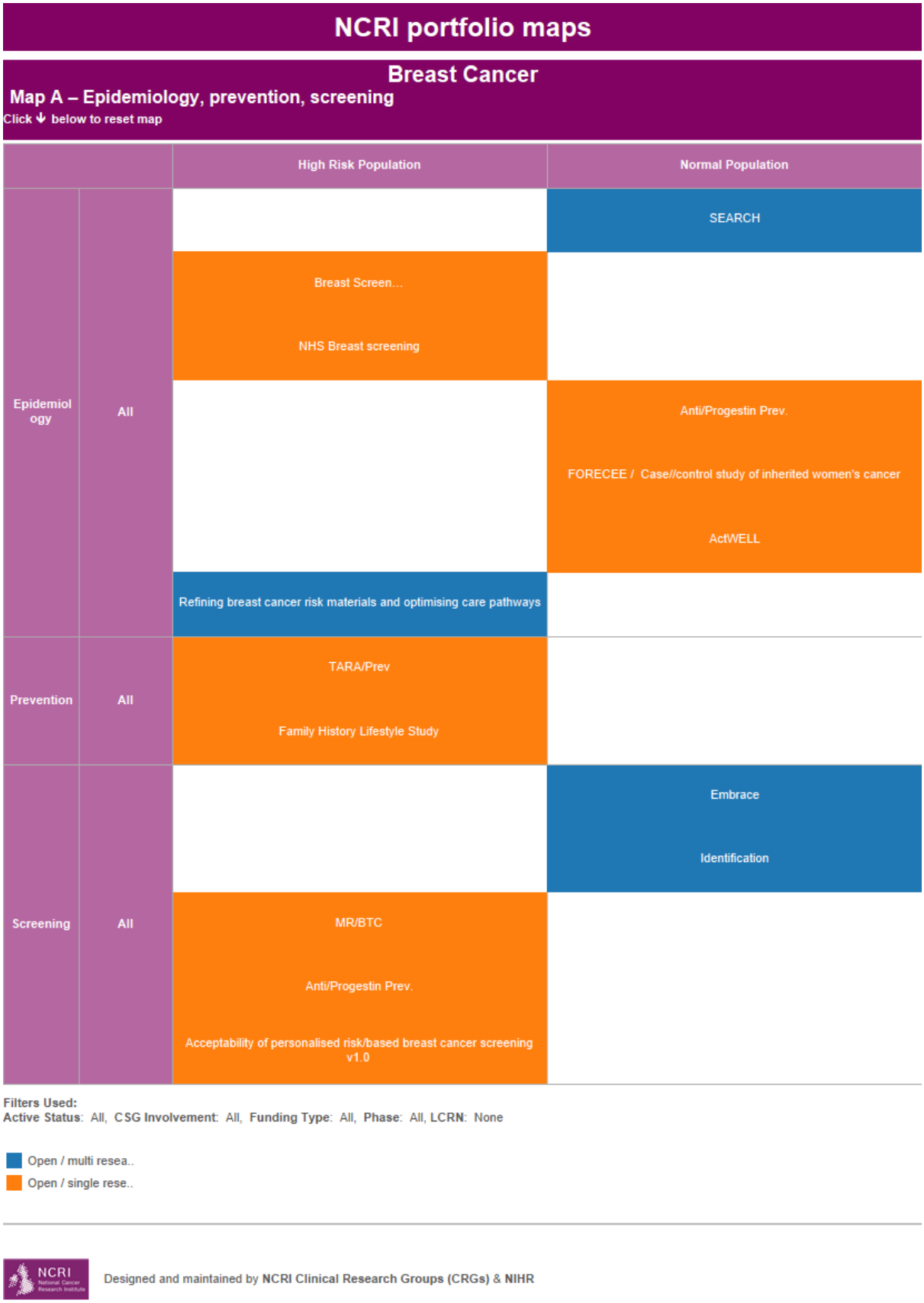
Strategic objective	Activity	CSG Lead	Date
1d integrated Imaging and translational research within the breast portfolio	Promote and advise on the integration translational and imaging research into all trials where possible to include • Biomarker evaluation to identify sensitive subgroups • Serial (plasma) monitoring for micrometastatic disease • Mutation testing in residual disease • Appropriate imaging modalities for all trials • Novel imaging (as subprotocol if appropriate) in clinical trials Develop virtual Biobank through cross talk between those holding samples • agreement about how material is collected, stored and shared • common expectations for generic consent, sharing etc. • SOPs for collections etc	NT	
2 Collaborative approach to developmentt of translational research	Engage with breast cancer clinical research community to develop and deliver high quality internationally competitive translational elements to portfolio studies Harnessing expertise and linking people with related skills to maximise & quality of translational input to trials Promote integration of PPI involvement in discussions of both concepts and generic considerations (e.g. genomic information multiple biopsies data protection) • Arrange forums for discussion • Ensure PPI representation at meetings Engage with Royal College of Surgeons and Association of Breast Surgery (via Adele Francis) and to support initiatives to increase the number of surgical trainees involved in clinical trials research Maximise opportunities for international translational collaboration • BIG – UK a participant group • BIG – UK a lead group • Unilateral national collaborative groups (NSABP, NCIC, UNICANCER, ANZBCG)	All HS All AS DR DC JB	Ongoing

Strategic objective	Activity	CSG Lead	Date
3. Improving trials methodology & clinical utility	Endeavour to identify new predictors of risk and outcome. • able to identify/predict patients with residual disease risk • Able to predict sensitivity/insensitivity to therapeutic intervention Engage with trials methodologists and bioinformaticians to ensure trials are designed so that translational data is exploited effectively and fully	NT AS/JB	Ongoing

PB	Rob Stein
JB	John Bartlett
FG	Fiona Gilbert
IL	Iain Lyburn
SP	Sarah Pinder
CP	Colin Purdie
ER	Emad Rakha
AS	Abeer Shaaban
VS	Val Spiers
JD	Janet Dunn
AT	Alistair Thompson
AF	Adele Francis
HS	Hillary Stobart

Appendix 3

Portfolio maps



NCRI portfolio maps

Breast Cancer

Map B – Diagnosis, Imaging

Click ↓ below to reset map

		Imaging	Non-imaging diagnostic/ assessment techniques
Intraoperative assessment	All	GE/137 fluor imaging	
		Outcomes following Cerenkov Luminescence	
Long term follow up	All	MAMMO /50	
Monitoring disease/ tumour response to treatment	All		
		FABB study SPECIALS CHERNAC	
		Baronet	Baronet
Monitoring treatment side effects	All		
		NICaS device in Herceptin patients / PHASE I	
Pre-diagnosis assessment / S..	All	MR/BTC CONTEND Study	
			cfDNA copy number instability as a diagnostic for Breast Neoplasia
		PROSPECTS	
			BREVERAT BREAST BIOPSY SYSTEM
			SMART STUDY : Version 6 dated 27th January 2016
		Phase-insensitive Ultrasonic Computed Tomography of the Breast	

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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NCRI National Cancer Research Institute

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NCRI portfolio maps

Breast Cancer

Map C – Neoadjuvant, perioperative, surgery

Click ↓ below to reset map

		Neoadjuvant	Peri-operative / window of opportunity	Surgery
Invasion	All	affect breast cancer neoadjuvant chemothera		
	ER-, Her2- and 3-ve		vivo study in breast cancer and sentinel lymph	
				POSNOC
		neoadj chemo SPECIALS ROSCO		
			ARP	
				Intraop' Marginprobe
		CHERNAC		
			TIP Study	
		PARTNER		
				Outcomes following Cerenkov Luminescence
		reoperative immunotherapy comb		immunotherapy combinations in b
	ER-, Her2+		vivo study in breast cancer and sentinel lymph	
				POSNOC
		neoadj chemo SPECIALS		
		ROSCO		
				Intraop' Marginprobe
		CHERNAC		
			TIP Study	
				Outcomes following Cerenkov Luminescence
	ER+, Her2+			POSNOC
		neoadj chemo SPECIALS ROSCO		
			ARP	
				Intraop' Marginprobe
		CHERNAC Baronet		
				Outcomes following Cerenkov Luminescence
			EMERALD	
	ER+,Her2-			POSNOC
		neoadj chemo SPECIALS		
		PALLET ROSCO		
			ARP	
				Intraop' Marginprobe
		CHERNAC Baronet		
				Outcomes following Cerenkov Luminescence
			EMERALD	
		Neo-RT		
			PEARL	
Other e.g. ILC	All			ST/ Novilase Breast Laser Ablation vs Surgery
				MOLL trial
Pre-invasion	All pre-invasion			LORIS Intraop' Marginprobe
	ER+,Her2-		The PIONEER Study	

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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Open / multi resea.. Suspended / singl..

NCRI National Cancer Research Institute

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NCRI portfolio maps

Breast Cancer

Map D – Adjuvant

Click ↓ below to reset map

		Local therapy (Radiotherapy)	Systemic Therapy
Invasive (receptor status unspecifi..	ER-, Her2- and 3-ve	FAST/Forward TARGIT-B Trial of radiotherapy in higher risk breast cancer patients POSNOC SuPPORT 4 All Clinical Feasibility Trial	CAVA OLYMPIA Add/Aspirin C-3475 + Chemotherapy as Neoadjuvant and Adjuvant therapy for TNI Cardiac CARE IMPassion30
	ER-, Her2+	FAST/Forward TARGIT-B Trial of radiotherapy in higher risk breast cancer patients POSNOC SuPPORT 4 All Clinical Feasibility Trial	CAVA Add/Aspirin Cardiac CARE LATTE
	ER+, Her2+	FAST/Forward TARGIT-B Trial of radiotherapy in higher risk breast cancer patients POSNOC SuPPORT 4 All Clinical Feasibility Trial	CAVA Add/Aspirin Cardiac CARE LATTE
	ER+,Her2-	FAST/Forward TARGIT-B Trial of radiotherapy in higher risk breast cancer patients POSNOC PRIMETIME SuPPORT 4 All Clinical Feasibility Trial	OPTIMA CAVA UNIRAD Add/Aspirin CBYL719X2402 PALbociclib CoLlaborative Adjuvant Study Cardiac CARE
Other e.g. ILC	All	FAST/Forward TARGIT-B Trial of radiotherapy in higher risk breast cancer patients POSNOC SuPPORT 4 All Clinical Feasibility Trial	LATTE UNIRAD Add/Aspirin Cardiac CARE
	ER+,Her2-		OPTIMA ROLo
Pre-invasive	All		CAVA

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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In Setup / single re..
Open / single rese..

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NCRI portfolio maps

Breast Cancer

Map E – Metastatic

Click ↓ below to reset map

		a) Metastatic-1st line	b) Metastatic-2nd line	c) Metastatic-3rd line, etc
BRCA	All	CORE Trial		AT13148 Phase I
ER+	All	FABB study CAVA FAKTION MBC / disease registry POSEIDON CANC - 4839 monarcHER: CANC - 4799 CORE Trial Nektar214 ombination with fulvestrant in subjects with ER - A study of Ipatasertib with Paclitaxel in Breas	POSEIDON	AT13148 Phase I
ER+ HER2-	All	PARSIFAL 1 CARBON in the Treatment and Evaluation of Metastatic I3Y-MC-JPCF CORE Trial Estrogen Receptor Positive Breast Cancer		
HER2-	All	Breast cancer-3652/0002-G1 Therapeutics, Inc CORE Trial MP0274-CP101 LUCY 21 - AZD9496 VS Fulvestrant in Primary Breas		AT13148 Phase I
HER2+/ lother	All	NCRN / 3159 CONCEPT FURVA, Version CANC 5244 monarcHER: CANC - 4799 DC-0077 for PIK3CA-mutant solid tumours / b B9991025 PROCLAIM-CX-2009 ib ravtansine thorough ECG and drug interacti 0456/0112 - Regeneron-R3767-ONC-1613 - A study of Ipatasertib with Paclitaxel in Breas , Multipart, Multiarm, FTiH, Open-label study o l Cancer Vaccine study in Patients with Advan AZD1775 Continued Access tudy of ADCT-502 in patients with advanced so	NCRN / 3159 Margetux + Chemo vs Trastuzumab HER2CLIMB	AT13148 Phase I
Triple negative	All	l Study of Pembrolizumab + Chemotherapy in mbrolizumab in Patients with Previously Treate CORE Trial dy for triple negatve breast cancer patients wi) and Eribulin in patients with advanced breast IMpassion 131 - A study of Ipatasertib with Paclitaxel in Breas ImmunoBC udy in Metastatic Triple Negative Breast Canc RochePh1btriplenegBC IMpassion 132		AT13148 Phase I

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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In Setup / single re.. Open / single rese..

NCRI National Cancer Research Institute

Designed and maintained by **NCRI Clinical Research Groups (CRGs)** & **NIHR**

NCRI portfolio maps

Breast Cancer

Map F – Supportive care

Click ↓ below to reset map

		During treatment	Late Effects / survivorship
Supportive care - All	Decision making	A Multi/centred/study of the effectiveness of PEGASUS	
		Proxy decision making for older women with breast cancer	
	Lifestyle, diet, exercise		
		B/AHEAD3	
		Abreast of Health: Phase 1 - v1.0	
		Abreast of Health: Phase 2 - v1.0	
	Research methods	Bridging the Age Gap	
		CCRN 2949 (Breast reconstruction)	
		4Ps Study	
	Side effects		
			ACUFOCIN
			FOAM Trial
		eSMART: Randomi	
		HORIZONS	HORIZONS
		MENOS 4	
			Preventing Cardiotoxicity in Breast Cancer Patients: PROACT
	Treatment management	CAVA	
		NICaS device in Herceptin patients / PHASE I	

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

Null

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Open / single rese..

NCRI National Cancer Research Institute

Designed and maintained by **NCRI Clinical Research Groups (CRGs)** & **NIHR**

NCRI portfolio maps

Breast Cancer

Map G – Translational

Click ↓ below to reset map

		Disease process	Side Effects	Treatment/Pharmacology
a) Invasion	ER-, Her2-	Existing Breast Cubbs BC Subtypes SPECIALS The BeGIN study TNBC in D&G AURORA REVEAL version 1 plasmaMATCH Personalised Breast Cancer Program c-TRAK TN	RAPPER RTGene	
	ER-, Her2+	DETECT Existing Breast Cubbs BC Subtypes SPECIALS The BeGIN study AURORA REVEAL version 1 plasmaMATCH Personalised Breast Cancer Program	RAPPER RTGene	
	ER+, Her2+	DETECT Existing Breast Cubbs BC Subtypes SPECIALS The BeGIN study AURORA plasmaMATCH Personalised Breast Cancer Program	RAPPER RTGene	
	ER+,Her2-	DETECT Existing Breast Cubbs BC Subtypes SPECIALS The BeGIN study AURORA plasmaMATCH Personalised Breast Cancer Program	RAPPER Lymphocyte prod. The BeGIN study RTGene	
b) Pre-invasion	All	Cubbs BC Subtypes The BeGIN study plasmaMATCH 3D scanning of lymphoedema arms Personalised Breast Cancer Program	The BeGIN study RTGene	
c) ILC	All	CTCF & BORIS BM Existing Breast VERB Study Cubbs BC Subtypes SPECIALS The BeGIN study AURORA REVEAL version 1 Personalised Breast Cancer Program The ZOLMENO study	RTGene	
d) Normal tissue/ other	All	Tumour Angiogen Existing Breast Body Composition In Breast Cancer Tissue Stresses of Cancer		AZD1775 Food Effects

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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Open / multi resea.. Suspended / singl..

NCRI National Cancer Research Institute

Designed and maintained by **NCRI Clinical Research Groups (CRGs)** & **NIHR**

Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Carboplatin in BRCA1/2-mutated and triple-negative breast cancer BRCAness subgroups: the TNT Trial. Tutt A et al Nat Med. 2018 2018 May;24(5):628-637	The TNT trial is one of a small number of contemporary, rare phase III academic studies in advanced breast cancer. It has demonstrated similar response to carboplatin and docetaxel as first line chemotherapy in unselected triple negative disease.	Developed by the CSG
2. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. Copson E et al Lancet Oncol. 2018 Feb;19(2):169-180.	The key output from this report is the finding that survival in germline BRCA associated breast cancers are the same as non BRCA associated cancer. This data is critical to discussions in determining treatment and in particular in considering the role and timing of prophylactic preventative surgery. This data will undoubtedly impact on decisions made by women diagnosed with BRCA associated cancer.	Developed by the CSG

3. Addition of gemcitabine to paclitaxel, epirubicin, and cyclophosphamide adjuvant chemotherapy for women with early-stage breast cancer (tAnGo): final 10-year follow-up of an open-label, randomised, phase 3 trial. Earl HM et al, Lancet Oncol. 2017 Jun;18(6):755-769.	The study was negative and similar overseas trials and the neoadjuvant counterpart to this Trial Neotango have confirmed this result. As a negative study it is not practice changing but is an important contemporary reminder that extrapolating data in the advanced disease setting to the early disease setting is unreliable.	Developed by the CSG
4. Disease-free and overall survival at 3.5 years for neoadjuvant bevacizumab added to docetaxel followed by fluorouracil, epirubicin and cyclophosphamide, for women with HER2 negative early breast cancer: ARTemis Trial. Earl HM et al, Ann Oncol. 2017 Aug 1;28(8):1817-1824	This study which has previously reported increased pCR after neoadjuvant chemotherapy including the antiangiogenic agent bevacisumab has in this publication showed no improvement in long term outcome and has in conjunction with other similar studies clearly demonstrated a disconnect between the impact of antiangiogenic agents on primary breast cancer and micrometastatic	Developed by the CSG
5. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Lancet Oncol. 2018 (17)27-39	This publication provided unique data generated from worldwide collaboration with hundreds of collaborators and individual trials including all relevant NCRI portfolio studies.	

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Breast Cancer CSG portfolio, 41 trials closed to recruitment and 43 opened.

Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	12148	5973	4642	5888	9.5	12.0
2014/2015	11417	5109	6042	3146	12.3	6.4
2015/2016	4065	4540	1654	2572	3.38	5.25
2016/2017	2882	7744	1300	5212	2.65	10.64
2017/2018	3124	9617	846	6559	1.73	13.39