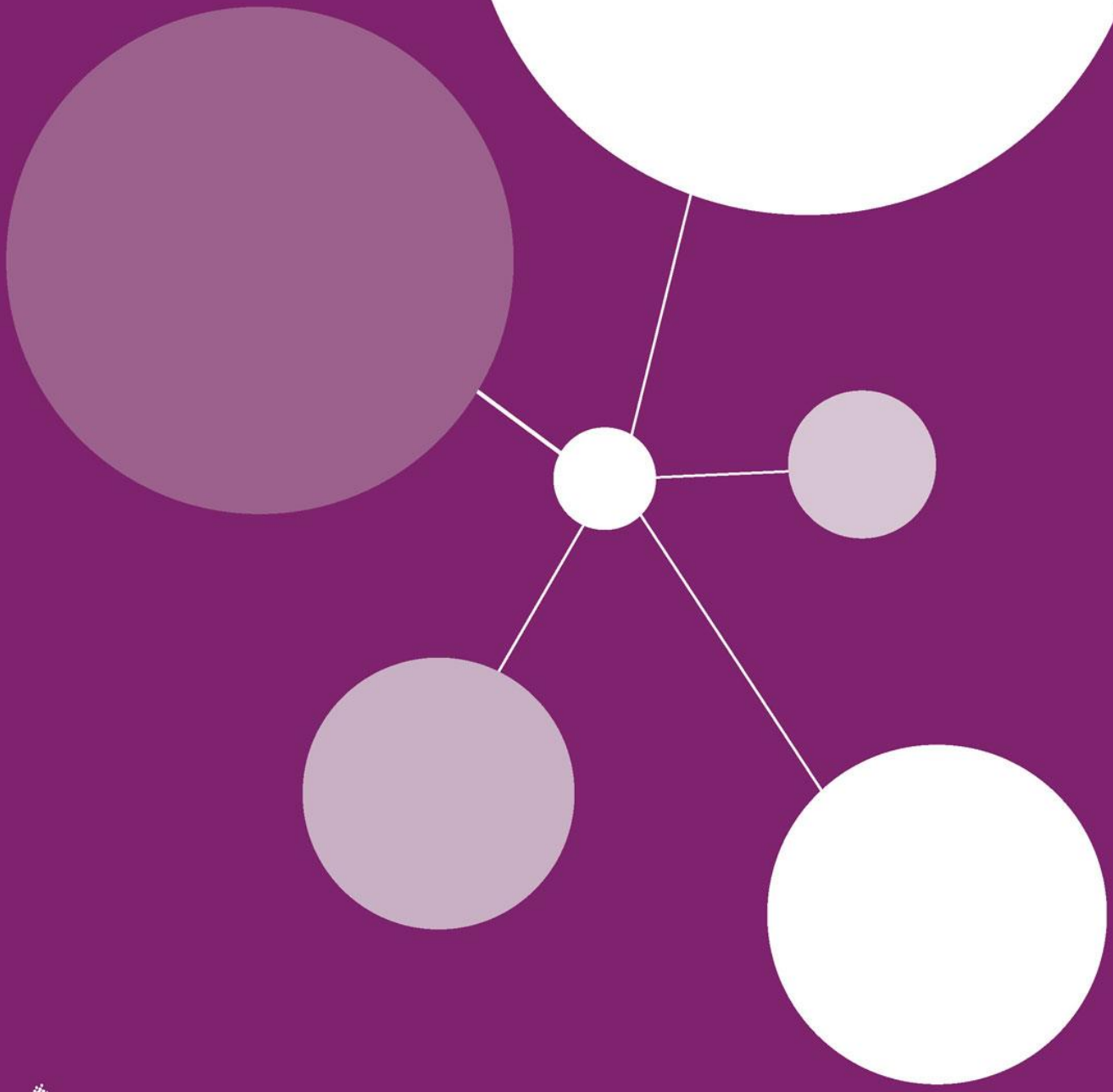
NCRI
National
Cancer
Research
Institute

NCRI Breast Group

Annual Report 2018-19



Partners in cancer research

NCRI Breast Group Annual Report 2018-19

1. Top 3 achievements in the reporting year

Achievement 1

High profile presentations at International meetings

World class NCRI supported studies presented by UK investigators continue to be a consistent feature at International scientific meetings

ASCO 2018

Persephone trial results (Earl *et al)*

Persephone randomised 4088 patients with HER-2 positive early breast cancer to 6 or 12 months of adjuvant/neoadjuvant trastuzumab . The primary endpoint of non inferiority was met 4-year DFS rates were 89·4% (95%CI, 87·9-90·7) in the 6-month group and 89·8% (95%CI 88·3-91·1) in the 12-month group (Hazard Ratio 1·07; 90%CI 0·93–1·24, non-inferiority p=0·01), demonstrating non-inferiority of 6-months trastuzumab. Congruent results were found for overall survival (OS) (non-inferiority p=0·001). The trial is already influencing practice with many patients lower risk patients now terminating trastuzumab after 6 months. There are some unexpected but non-significant trends in subgroups that warrant further consideration and while Persephone is the largest of the reduced duration studies it is the only one to show non inferiority so a patient level metanalysis of all trials is planned. The primary manuscript is in press. Persephone is an HTA funded academic study developed within the NCRI CSG

ESMO 2018: Presentation of primary analysis of the Impassion 130 study (Schmidt et al)

SABCS 2018: PALLET trial results presented (Dowsett et al)

EBCTCG metanalysis of survival after regional radiotherapy (Gray et al)

IMPORT High 3 year toxicity outcomes (Coles *et al*)

Achievement 2

Major publications

Publication of of the PALLET trial results Johnson et al JCO

The PALLET study has a complex mutiarm study exploring the combination of aromatase inhibition and CDK4/6 inhibition but is in essence a comparison of 12- 14 weeks neoadjuvant letrozole/placebo vs letrozole/palbociclib with an inbuilt 2 week window study of combination and monotherapies. The study has reported a non significant increase in clinical response from 49.5% to 54.4% but a highly significant reduction in proliferation measured by Ki67 staining (log-fold change -2.2 to -4.1 p<0.0001 or -88.5% vs 97.4% and an increase in the number of tumours undergoing cell cycle arrest from 59 to 90% This study has led to a phase III study design where only cancers not showing adequate Ki67 response are randomised to the addition of a CDK4/6 inhibitor or placebo.

Impassion 130 Schmidt et al NEJM 2018

In this study patients with unselected triple negative advanced breast cancer were randomised to nab paclitaxel and placebo or the anti PDL1 antibody atezolizumab. The study reported an overall improvement in median RFS from 5.5 to 7.2 months (HR0.80 p0.0025). In the 40% of tumours PDL1 positive cases (40%) RFS improved from 5.0 to 7.5 months (HR 0.62 p0.0001)

This landmark study is the first phase III study in breast cancer to show a clear benefit from immune checkpoint inhibitor therapy and is the basis for a first marketing authorisation of immunotherapy in triple negative PDL1 positive breast cancer.

The Impassion 130 study is a NCRI badged industry sponsored International study The chief Investigator Peter Schmidt is a recent CSG member. This achievement demonstrates the ability of the UK academic clinicians to work with industry to design and deliver practice changing clinical trials.

Achievement 3

Establishment of a trainee collaborative for trainees in clinical oncology medical oncology pathology and radiology

This trainee collaborative has been formed under the guidance of Ellen Copson and many other CSG members. A 'sandpit' brainstorming workshop to consider and select a first round of trainee projects was held in 2018 the collaborative will hold an inaugural National meeting in October 2019. The collaborative will allow trainees to participate in a research active peer group environment, provide opportunities for participation and leadership in clinical research. The collaborative is chaired by Adam Heetun who is a current CSG trainee representative. A manuscript describing the formation and potential has been accepted (Heetun et al Clinical Oncology in press) the collaborative has three projects in progress.

2. Structure of the Group

The group structure is largely unchanged, but the activity has shifted with subgroups playing a more substantial role in detailed trial development. The frequency of main CSG meetings has been reduced from 3 times per year to twice per year

Trainee members are attached to both main CSG and to a subgroup

The mechanism for providing evaluation of new study proposals by first presenting at the Breast Intergroup meeting is now working smoothly. This process ensures that there is a single portal through which all studies are considered the open nature of this process gives the wider research community to understand what new proposals are in progress and also provides an opportunity to provide a brief update on studies in development set and recruitment. Proposals that require more detailed discussion are channelled to the main CSG or to an appropriate subgroup for more detailed review and refinement.

3. Breast Group & Subgroup strategies

Breast Group Strategy

Increase patient expectation of being involved in a clinical trial This is an ongoing activity taken forward by our consumer members and the message cascaded through local patient support groups. Also discussed at length at professional meetings including Association of Breast Surgeons and our own Breast Trials Meeting.
BFurther the develop the Breast Cancer portfolio This very generic strategic goal is a persistent theme within the entire CSG
Collaborative approach to trial development & participation The CSG operates an open door approach to potential researchers wishing to develop a clinical study. We accept all proposals for initial presentation to the UK BIG Breast Intergroup meeting This is held 2 times per year and provides an open platform to bring new proposals to the CSG and wider research community and patient advocates. The proposals are presented and discussed in open forum prior to a formal written feedback to investigators after discussion with the appropriate subgroup. This year at the biannual Breast Trials Meeting, the Chair presented an outline of the pathway for both established and emerging researchers to help them navigate the pathway through the various CSG mechanisms of designing and successfully funding deliverable studies of the highest clinical and scientific value.
Improve trials methodology & clinical utility Our trials portfolio includes both conventional design studies and an increasing number of novel design studies. The use of novel methodology and statistics is frequently included in discussions within the CSG and with researchers presenting studies to the CSG. The main CSG has two senior trials unit methodologists who are very keen to advise and work with researchers in exploring the potential novel clinical trial designs. While in many cases the basic clinical trial designs are appropriately standard, it is the norm for translational opportunities to be integrated into the design of most clinical trials
Embed a research culture across the entire patient pathway within all healthcare professionals and in all institutions, provide breast cancer services We continually promote the concept of a clinical trial based approach to standard practice within breast cancer services. This is reinforced through presentations at professional meetings. We are supporting regional clinical trial roadshows the first of these held in Manchester hosted by the Association of Breast Surgeons. This first roadshow inspired by and modelled on the success of the lower GI CSG roadshows provides an educational forum for local research teams to learn about research activity and to meet Chief investigators in an interactive and constructive environment where locality issues can be explored.
Empower and educate patients and the public to drive research-oriented culture within the provision of routine care The inclusion of consumer representatives in all levels of CSG activity arms them with the knowledge to promote a research ethos to the general public and to existing patients.

Increase the number of local PIs participating in clinical trials

The open nature of our structure is intended to attract new investigators providing opportunities for networking at UK Breast Intergroup meetings.

We have in particular been making persistent efforts in collaboration with the Association of Breast Surgeons to encourage surgeons not previously research active to become new Principal investigators and have been expanding the surgical research portfolio as part of the overall CSG strategy to increase interest and opportunities for surgeons to participate in multicentre studies. Surgical studies coming on stream or in development such as Nostra Feasibility determining the ability of protocolised radiologically guided biopsies to predict pathological complete response, the SMALL trial of radiological excision of small indolent cancers and the ATNEC study of postneoadjuvant axillary management will maintain interest and momentum

The development within ABS of 'no innovation without evaluation' is bringing a variety of studies to evaluate new surgical techniques through the Breast Intergroup.

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

The variability in willingness to release samples for research remains a challenge to some studies the translational subgroup works with pathologists to encourage sharing of routinely collected tissue fro research. We have encountered a trend towards a more restrictive approach in some hospitals as more indications for biomarker testing in breast cancer become routine requiring tissue retention at site or provision of a trusted and robust real time service for tissue sample return from research collections. This issue is planned as a topic for discussion at the Birmingham pathology course in November 2019.

Understand the issues and pressures encountered at sites to inform researchers of potential challenges in local delivery

We have conducted a site questionnaire to explore barriers to research participation the survey results have been shared at the CSG/ Clinical trials unit forum. They demonstrate patchy access to various elements of infrastructure to open and conduct clinical studies. Most notable is the difficulty in accessing pathology and imaging support to research.

Screening

A strategic goal of the CSG has been to encourage collaboration and generation of studies to validate the utility of risk adapted breast screening and to evaluate new imaging modalities this has resulted in successful funding and setting up of risk adapted screening study. Patients attending first round screening will be allocated to personalised screening using a combination of genetic risk profiling breast density lifestyle and breast density to determine individual risk and allocation to multiple imaging modalities and screening frequency.

Advanced Disease Subgroup (Chair, Professor Carlo Palmieri)

The Advanced Disease Subgroup has multi-disciplinary membership and aims to support the community in the development and delivery of studies in advanced disease. The group also takes a proactive approach in identifying areas where there are gaps or issues in relation to the delivery of the portfolio. One recent example relates to the lack of studies for metastatic disease involving the CNS and the issues with delivering these studies when they are instigated. This is a current focus of the group.

The Subgroup engages actively with the wider research community via the twice-yearly UK Breast Intergroup meeting. UKBI provides an opportunity for new trial proposal to be presented and receive structured feedback. The group encourages all new proposals in the setting of advanced disease to be presented at this meeting. This along with the subgroup's own review and feedback, it is hoped ensures only well worked up proposals move forward to funding bodies.

The subgroup continues to deliver a broad trial portfolio, (based on both on phase and disease subgroup involved). There are currently: 20 trials open, in addition to 9 multi-CSG Phase I studies and 14 in the process of opening (ref: portfolio map, May 2019). The portfolio had broad representation of trials in all disease subgroups (defined by ER, PgR and HER2 status), and maximises the likelihood that patients with advanced disease will be potentially eligible for a clinical trial. UK investigators continue to contribute at an international level to industry-sponsored studies.

Early Disease Subgroup (Chair, Dr Charlotte Coles)

Develop Early Disease Subgroup portfolio

We have identified the following areas for development

Local therapy:

(i) *Can axillary treatment be safely de-escalated following complete pathological response to neo-adjuvant systemic therapy?*

Subgroup has supported chief investigator develop outline application for phase III randomised trial: provided written feedback following 2 UKBI meetings

Full application is now in progress

(ii) *Is there an identifiable group of patients with early breast cancer gaining substantial benefit from proton beam therapy (PBT)?*

Subgroup has developed multidisciplinary team; presented at 2 UKBI meeting

Study design improved considerably following participation in 2 PBT CTRad workshops

Radiotherapy planning studies and PPI focus groups in progress prior to funding submission

Systemic therapy:

Can HER2-directed therapy be safely de-escalated in selected patients with a complete molecular tumour response to neo-adjuvant therapy?

Subgroup in collaboration with other key UK researchers developing novel biomarker-directed non-randomised study design

Results from key trials reported in 2018 were required before progressing proposal

A Revised design was presented at UKBI and UK research community views surveyed prior to funding submission. The survey has established a keen interest in studying the question but in association with wider PPI consultation feedback indicates doubts remain about patients willingness to be randomised to current design and additional data is being generated to demonstrate the impact of presenting stage on outcome after pathological complete response. The additional complication is the recent NICE recommendation for neoadjuvant/ adjuvant dual targeted therapy to selected patients only. This however presents opportunities for an alternative de-escalation design. Considerable debate and discussion continues and through links with BIG and North American groups we working to establish that separate questions are addressed or collaborations established rather than duplication of effort. This may allow answers to be generated to a number of de-escalation questions rapidly through International collaboration. We have been deliberately cautious in bringing a funding proposal forward until a deliverable and hopefully future proof trial is developed.

Translational/ Personalised medicine

(iii) Can we design trials to further understanding of biological mechanisms of endocrine resistance?

- Subgroup has supported development of POETIC-A, builds on successful POETIC study
  Presented at UKBI and Breast CSG, feedback incorporated
  Submitted to CRUK for endorsement, outcome awaited

Adopt a collaborative approach to trial development

1. *Engaging with wider breast cancer community*
   - UKBI biannual meetings provide unique forum for researchers to present new proposals and obtain comments from wider community/key opinion leaders with written feedback
   - A UK-wide questionnaire regarding barriers to trial set-up/delivery circulated - findings suggest consistent resource constraints for pathology/imaging
   - Greater engagement with breast pathologists/radiologists via Imaging and Translational subgroup – deliberate overlap of subgroup membership

2. *Integrate PPI into all stages of trial development*
   - Numerous examples of PPI input changing/enhancing/supporting new trial designs, e.g. Phoenix, PRIMETIME, C-TRAK, SMALL, etc
   - Members of subgroup initiated a Lifetime Achievement Award on behalf of breast cancer research community at NCRI National Breast Clinical Trials meeting for Maggie Wilcox, former CSG member

3. *Engage with Association of Breast Surgery (ABS)*
   - Subgroup has deliberately recruited 2 active ABS members to:
     - Raise awareness of ABS-badged trials within surgical community to promote engagement/recruitment, e.g. PRIMETIME, SMALL, NOSTRA, LORIS
     - Engage with bra-net group (surgical techniques/devices); implement ABS "sandpit" sessions to support very early research ideas; published surgical research gap analysis – Lancet Oncology 2018

- CSG Collaboration with ABS for trials roadshow

4. *Engage with CTRad*
   - Current subgroup chair - senior author for CTRad-led practice changing RT trials review: Br J Cancer 2018
   - Representation on workstream 2 (early phase trials)
   - On-going engagement with Breast PBT proposal

Improve trials methodology & clinical utility

1. *Collaborate with Imaging and translational subgroup to explore and develop full potential of imaging as validated early biomarkers of response in early breast cancer/micrometastatic disease*
   - Outline paper on Imaging and Pathology correlation in HER2+ve disease: presentation and response to treatment – progressing in conjunction with the Imaging and Translational subgroup and deliberating linking with HER2+ve de-escalation study

2. *Collaborate with NIHR CRN Breast subspecialty group –bringing together cross-specialty oncology trainees with mentors to develop new simple, pragmatic research proposals*
   - Developed with subgroup input
     - 3 research initiatives on-going
     - Second national meeting September 2019
     - Editorial submitted to *Clinical Oncology* journal

Symptom Management Subgroup (Co-Chairs, Anne Armstrong and Adrienne Morgan)

To Identify gaps in current research in symptoms management in breast cancer

The Symptom Management Subgroup aims to both develop and promote research into symptoms after a diagnosis of breast cancer. Initial work of the subgroup focused on hot flushes, but with the success of a number of projects has more recently expanded to the management of urogenital atrophy and sexual health issues after a diagnosis of breast cancer. A survey of sexual issues in breast cancer survivors has had over 300 respondents. The results are currently being analysed for presentation and publication later this year. It is anticipated that this survey will be able to identify areas of unmet need to drive future research as well as highlighting gaps in care provision. A parallel survey has also been circulated to health professionals involved in the care of patients with breast cancer.

Support development of new research into identified gaps

The successful funding of the SWEET programme grant (2018, Co-applicant Lesley Turner; £2,487,452) will develop aids to encourage adherence to adjuvant endocrine therapy and includes a work package on adherence related to side effects from therapy.

The group has benefited from links with the wider (non-cancer) research establishment, which may lead to innovative management solutions. Dr Mel Flint (University of Brighton) is supervising a PhD student investigating heat sensitivity in female breast cancer survivors exercising during heat stress, with preliminary work presented at 2 recent conferences. The project developed in conjunction with active involvement of subgroup members.

Research is also being developed into urogenital atrophy. A study funded by Abertawe Bro Morgannwg University Health Board will investigate the incidence and management of vulvo-vaginal atrophy in the Welsh menopausal population by utilizing the Welsh SAIL database. Grant applications are also in development to look at 2 different interventions for the management of urogenital atrophy.

Support translation of research findings into practice

A key achievement of the work of the subgroup in hot flushes has been the completion of the MENOS4 study (PI D Fenlon), commissioned by Breast Cancer Now in response to the initial work of the subgroup. This multi-centre randomised phase II study investigated the use of breast care nurse delivered cognitive behavioural therapy to reduce the impact of hot flushes in women with breast cancer. The study has completed recruitment and will be presented at MASCC, June 2019. Having demonstrated the benefit of this approach the next step is to deliver training to breast cares nurses across the country. A patient driven initiative will then have achieved getting an intervention into standard clinical practice.

Another study, promoted and supported by the group, FOAM, investigating the use of folic acid supplements as a treatment for hot flushes has completed accrual.

The group continues to raise awareness of the burdens of treatment related symptoms in breast cancer survivors. A workshop is planned at UK Interdisciplinary Breast Cancer Symposium 2020.

Hunter MS, Nuttall J, Fenlon D 2019 A comparison of three outcome measures of the impact of vasomotor symptoms on women's lives. Climacteric 2019 22 41-23

Brett J, Boulton M, Fenlon D, Hulbert-Williams NJ, Walter FM, Donnelly P, Lavery BA, Morgan A, Morris C, Watson EK. 2018 Adjuvant endocrine therapy after breast cancer: a qualitative study of factors associated with adherence. 2018 Patient Prefer Adherence. 12 291-300

Brett J, Hulbert-Williams NJ, Fenlon F, Boulton M, Walter FM, Donnelly P, Lavery B, Morgan A, Morris C, Horne R, Watson E 2017. Psychometric properties of the Beliefs about Medicine Questionnaire- adjuvant endocrine therapy (BMQ-AET) for women taking AETS following early-stage breast cancer. 4(2):205510291774046., DOI:10.1177/2055102917740469

Fenlon, D., Nuttall, J., May, C., Raftery, J., Fields, J., Kirkpatrick, E., Abab, J., Ellis, M., Rose, T., Khambhaita, P. and Galanopoulou, A., 2018. MENOS4 trial: a multicentre randomised controlled trial (RCT) of a breast care nurse delivered cognitive behavioural therapy (CBT) intervention to reduce the impact of hot flushes in women with breast cancer: Study Protocol. BMC women's health, 18(1), p.63.

Translational & Imaging Subgroup (Chair, Professor Iain Lyburn)

-

Support the community in the development and delivery of studies across the portfolio

The subgroup impact is across the portfolio, incorporating screening, early and advanced disease with the aim of continuing to expand studies to incorporate more translational elements in this era of multifaceted personalised medicine.

Members of the translational and imaging subgroup were integral to development of and are collaborators on a number of studies including:

PRECISION – The CRUK Grand Challenge awarded for an international collaboration with teams from The Netherlands, USA and UK evaluating various aspects of DCIS. As part of Work Package 4, samples from the USA have been analysed (imaging characteristics, microstructure and fundamental chemistry of calcifications and adjacent tissues) at the University of Exeter and the University of Cranfield. Samples from 3 UK sites (Cambridge, Kings College, London and Gloucestershire) are also being collated to undergo analysis.

2 trials due to open later in 2019:
SMALL (evaluating vacuum-assisted excision of small, screen-detected breast cancers)
Experience from implementing ***LORIS*** (surgery versus active monitoring for low risk ductal carcinoma in situ) has been utilised to try and maximise potential recruitment from the outset.

BRAID (Breast Screening – Risk Adaptive Imaging for Density) is evaluating several breast imaging modalities which may provide personalised breast cancer screening to women with high density breast parenchymal patterns on mammography.

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

Development of collaboration with CM-Path

The chair of the subgroup attended a workshop to foster links – there is huge potential for symbiosis between biomedical imaging and pathology with investigations/tests often digitized which facilitates data collection and analysis in more robust reproducible manner.

Via organizations such as the British Society of Breast Radiology (BSBR) opportunities have been provided for clinicians to present upcoming studies to radiologists at a national level at the Scientific Meetings Research Workshops. In November 2018 short presentations on ***NOSTRA*** (A prospective non-randomised multi-centre feasibility study to assess if patients with residual cancer following dual-targeted neoadjuvant chemotherapy treatment for HER2-positive, ER-negative early breast cancer can be identified by multiple image guided tumour bed biopsies) and ***SMALL*** were delivered which engendered discussion and enthusiasm. At the

next meeting in November 2019 similarly an opportunity will be offered to trialists from ***BRAID*** and ***PHOENIX*** (A pre-surgical window of opportunity and post-surgical adjuvant biomarker study of DNA damage response inhibition and/or anti-PD-L1 immunotherapy in patients with neoadjuvant chemotherapy resistant residual triple negative breast cancer)
This has approach has fostered engagement within the wider community and triggered ideas about translational aspect incorporation in future studies.

Identify future translational opportunities for inclusion within portfolio studies
A longstanding theme is the gap between resource (often time) and the desire to deliver and participate in research for many 'jobbing' translational personnel, particularly pathologists and radiologists. Expectation and practical voids hamper opportunities. Translational aspects of studies need to have profiles enhanced. Subgroup members are galvanising support at local level to encourage participation in established trial protocols but also to develop ideas for translational sub studies.

Standardization (across sites and between episodes at the same site) remains an issue in complex imaging. Standardised guidelines are being collated. An example includes working with the TMG for PHEONIX to collate information via questionnaire and liaise directly with site imaging teams to facilitate the development/implementation of protocols in the most practicable way.

The group are looking at opportunities of exploring the utility of Artificial Intelligence (AI) and deep learning, which are likely to play major future roles in translational medicine.

Following on from the success of PRECISION, further MRC grants have been applied for *Breast Cancer: Early diagnosis using materials immortalisation.* Initial reviews were favourable; a final decision is awaited in the next 2 months.

4. Task groups/Working parties

The Breast Group 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**	**Funding amount**
May 2018					
HERDi PREDICT: Feasibility study to measure HER2-HER3 dimer expression in patients with HER-2 positive breast cancer receiving HER2 targeted therapies	Biomarker Project Award	Dr Gargi Patel	Not Supported	Presented at UK BIG meeting with constructive criticism	
November 2018					
A multi-cohort Phase Ib/expansion cohort study of the efficacy and safety of radiosurgery with durvalumab followed by durvalumab and standard of care systemic therapy in patients with brain metastases secondary to breast cancer	Clinical Trial Award	Professor Carlo Palmieri	Conditionally Supported	Developed within the advanced disease subgroup and at a cross cutting multi CSG workshop	
PRELIM: A Study to Evaluate the Effect of Zileuton, a leukotriene synthesis inhibitor, in Breast Cancer Participants with Persisting Circulating Tumour (ct)DNA The 'PRELIM' (prevention of leukotriene-induced metastatic risk) study	Experimental Medicine Award Outline	Professor Charles Coombes	Invited to full	Presented at UK BIG meeting and modifications to trial design suggested and incorporated	
Other committees					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**

ATNEC study	NIHR HTA	Amit Goyal	Invited to full application	CSG mechanisms used extensively for development	

6. Consumer involvement

The main Breast Cancer CSG has two consumer representatives, Lesley Stephen and Jan Rose. Jan Rose joined the group in September 2018 and is a member of the Early Disease Subgroup and the Symptom Management Subgroup. Lesley Stephen is a member of the Advanced Disease Subgroup which has a new member, Nicky Newman.

A number of additional consumers are also involved in putting forward the views and needs of patients on each of its subgroups. Dr Adrienne Morgan co-chairs the Symptom Management Subgroup and Lesley Turner is also a member. Hilary Stobart and Mairead McKenzie are members of the Early Disease 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. 2018 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

Lesley has also helped to champion a focus on research into treatment for brain metastases, an area of need. She is patient representative on the PRIMROSE study (a national prospective observational study in breast cancer patients with central nervous system involvement in the UK); she is also the patient representative on a study which will combine an Astra-Zeneca immunotherapy drug (Durvaluma) with targeted radiotherapy (SRS) to treat newly diagnosed brain metastases.

In addition she is co-leading a new piece of research, surveying metastatic patients to understand their awareness and experience of clinical research opportunities. This survey hopes to report during 2019 and to remove some of the barriers that limit MBC women from accessing clinical trials.

Jan Rose

Jan has been welcomed to the Breast Clinical Studies Group and has also joined the Early Diagnosis and the Symptom Management Subgroups. As well as being a patient representative on the National Audit for Breast Cancer in Older People Clinical Steering Group, current NCRI activities include:

Collaborator on POETIC-A(Pre-Operative Endocrine Therapy for Individualised Care with Abemaciclib

Co-applicant on ATNEC(Axillary management in T1-3N1NO breast cancer patients with FNA(Fine Needle Aspiration) or core biopsy proven nodal metastases at presentation after Neoadjuvant Chemotherapy) study

Co-applicant on SWEET (Improving outcomeS for Women diagnosed with early breast cancer through adherence to adjuvant Endocrine Therapy)

Support from the NCRI Consumer Forum is invaluable to support the Consumer Members' roles on the Breast Clinical Studies Group. Together with attending the NCRI Cancer Conference in 2018, this has contributed to the consumers' knowledge and development.

Other consumer highlights from CSG and subgroup members include:

- A talk at the Association of British Surgery conference in June 2018 on 'every patient deserves to be offered a clinical trial', and being a panel member at Symposium Mammographica, July 2018 discussing "Being on the Right side of the Law".
- Speaker at Breast Cancer Trainees Research Collaborative Group, May 2018
- involvement as representatives and TMG members in a number of trials, including C-Trak TN, PRIMETIME, SMALL etc
- involved as members of the Breast Cancer NOW – catalyst funding panel
- membership of the BCN Tissue Bank Operational Review Committee
- good patient engagement in the first UKIBCS in Manchester 2018 with a symptom management poster being presented
- involvement on the executive planning committee will ensure full patient engagement in the 2020 UKIBCS Birmingham meeting

7. Priorities and challenges for the forthcoming year

Priority 1

This priority is carried forward from last year to confirm the proposal for a HER-2 de escalation study in HER-2 positive cancer. Pathological complete response pCR after neoadjuvant therapy is associated with a good outcome compared to residual disease, a trial proposal to determine if it is safe to deescalate adjuvant treatment after pCR has been in discussion for a considerable time. The issues are described in the Early Disease Subgroup section.

Priority 2

Complete a gap analysis working in metastatic breast cancer

Last year a gap analysis in breast surgery was conducted and published (Cutress et al Lancet Oncology 2018). A similar approach will be used in the planned metastatic gap analysis as previous gap analyses are now out of date. This new gap analysis will be spearheaded by our trainee representatives supported by the Metastatic Subgroup Chair and interdisciplinary group of CSG members. This exercise will identify areas of opportunity in metastatic breast cancer research. Whilst providing a comprehensive review of knowledge gaps and research opportunities and we anticipate that this will provide the background to new proposals in areas such as treatment sequencing and in the management of oligometastatic disease.

Priority 3

Trainee collaborative

Build on the achievements of last year. The trainee collaborative is now established and functioning we need to ensure the momentum is maintained and that the trainee collaborative becomes an embedded part of trainee activity providing experience of research for juniors at different levels and we hope this will help embed a culture of research integrated into standard clinical practice and bring new young talent forward. The collaborative is recognised by the Association of Breast Physicians as an important component of research learning opportunities for trainees. New proposals will be considered at the trainee meeting in September.

Challenge 1

Maintain levels of clinical trial recruitment in a challenging service environment faced with both funding shortages but also staffing shortages at multiple levels in the research team this is particularly acute in breast radiology and pathology. A UK-wide questionnaire regarding barriers to trial set-up/delivery has been circulated via UKBI– initial findings suggest consistent resource constraints for pathology and imaging and inconsistent access to support for setting up and conducting research in general but in particular difficulty accessing imaging and pathology.

Challenge 2 Maintain the profile of research within hospitals faced with the difficulties outlined above alongside increasingly complex studies often requiring real time molecular diagnostic procedures and more complex imaging requirements or interventions.
Challenge 3 Ensuring that trials competing in the same population are brought on stream at the appropriate time to prevent problems from competition. This is particularly difficult as predicting the life cycle of large trials is very difficult. Both set up recruitment and timely data return can be slowed due to resource issues at sites or regulatory funding or organisational barriers. This requires close cooperation with individual trials management groups and is greatly aided by encouraging overlap of trial management groups and early engagement between these when potentially competing studies are being considered.

8. Collaborative partnership studies with industry

There are numerous studies within the portfolio that involve industry collaboration indeed the majority of metastatic studies are conducted in partnership with industry who provide novel agents and frequently full or partial funding to studies

Recent examples of industrial collaboration for trials in set up phase include Radiant B, a trial of immunotherapy (dervolimumab) in combination with stereotactic radiotherapy for breast cancer brain metastasis.
The poetic A study of adjuvant abemerciclib targeted to patients where window exposure to aromatase inhibition, demonstrates incomplete suppression of Ki67. The individual project progress are described elsewhere.

9. Appendices

Appendix 1 - Membership of Breast Group and subgroups

Appendix 2 – Breast Group and Subgroup strategies
- A – Breast Group 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 Group Chair)

Appendix 1

Membership of the Breast Group

Name	Specialism	Location
Dr Sheeba Irshad Kanth*	Clinical Lecturer	London
Dr Indrani Bhattacharya*	Clinical Oncologist	London
Dr Charlotte Coles	Clinical Oncologist	Cambridge
Dr Carolyn Taylor	Clinical Oncologist	Oxford
Dr Duncan Wheatley	Clinical Oncologist	Cornwall
Dr Adam Heetun*	Clinical Research Fellow	Southampton
Mrs Janice Rose	Consumer	Gloucester
Ms Lesley Stephen	Consumer	Edinburgh
Dr Jean Abraham	Medical Oncologist	Cambridge
Dr Anne Armstrong	Medical Oncologist	Manchester
Professor Janet Brown	Medical Oncologist	Sheffield
Dr Iain MacPherson	Medical Oncologist	Glasgow
Professor Carlo Palmieri	Medical Oncologist	Edinburgh
Professor Daniel Rea (Chair)	Medical Oncologist	Birmingham
Professor Andrew Wardley	Medical Oncologist	Manchester
Dr Simon Vincent	Observer	London
Dr Elizabeth Mallon	Pathologist	Glasgow
Professor Chris Lord	Professor of Cancer Genomics	London
Professor Janet Dunn	Professor of Clinical Trials	Warwick
Professor Iain Lyburn	Radiologist	Cheltenham
Dr Muthyala Sreenivas	Radiologist	Coventry
Mr Ramsey Cutress	Surgeon	Southampton
Ms Cliona Kirwan	Surgeon	Manchester
Mr Stuart McIntosh	Surgeon	Belfast
Ms Shelley Potter	Surgeon	Bristol

* 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 Indrani Bhattacharya*	Clinical Oncologist	London
Dr Duncan Wheatley	Clinical Oncologist	Cornwall
Dr Eileen Parks*	Clinical Research Fellow	
Ms Lesley Stephen	Consumer	Edinburgh
Mrs Julie Strelley-Jones	Consumer	
Dr Anne Armstrong	Medical Oncologist	Manchester
Dr Gianfilippo Bertelli	Medical Oncologist	Sussex
Dr Catherine Harper-Wynne	Medical Oncologist	London
Dr Iain MacPherson	Medical Oncologist	Glasgow
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 (UK Breast Intergroup)		
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 (Co-Chair)	Medical Oncologist	Manchester
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
Professor Alastair Thompson**	Surgeon	USA
Professor Janet Dunn	Statistician	Warwick

* denotes trainee member

**denotes non-core member

Appendix 2

Breast Group & Subgroup Strategies

A – Breast Group Strategy

Overall strategic 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 pathologists.
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 Now open Risk adapted screening trial in set up
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 now 2019/20 Phoenix open 2019 Ct-RACK In set up

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
.

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

.

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 now 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 Almost complete cTRAC full now recruiting Phoenix First patient in 2019

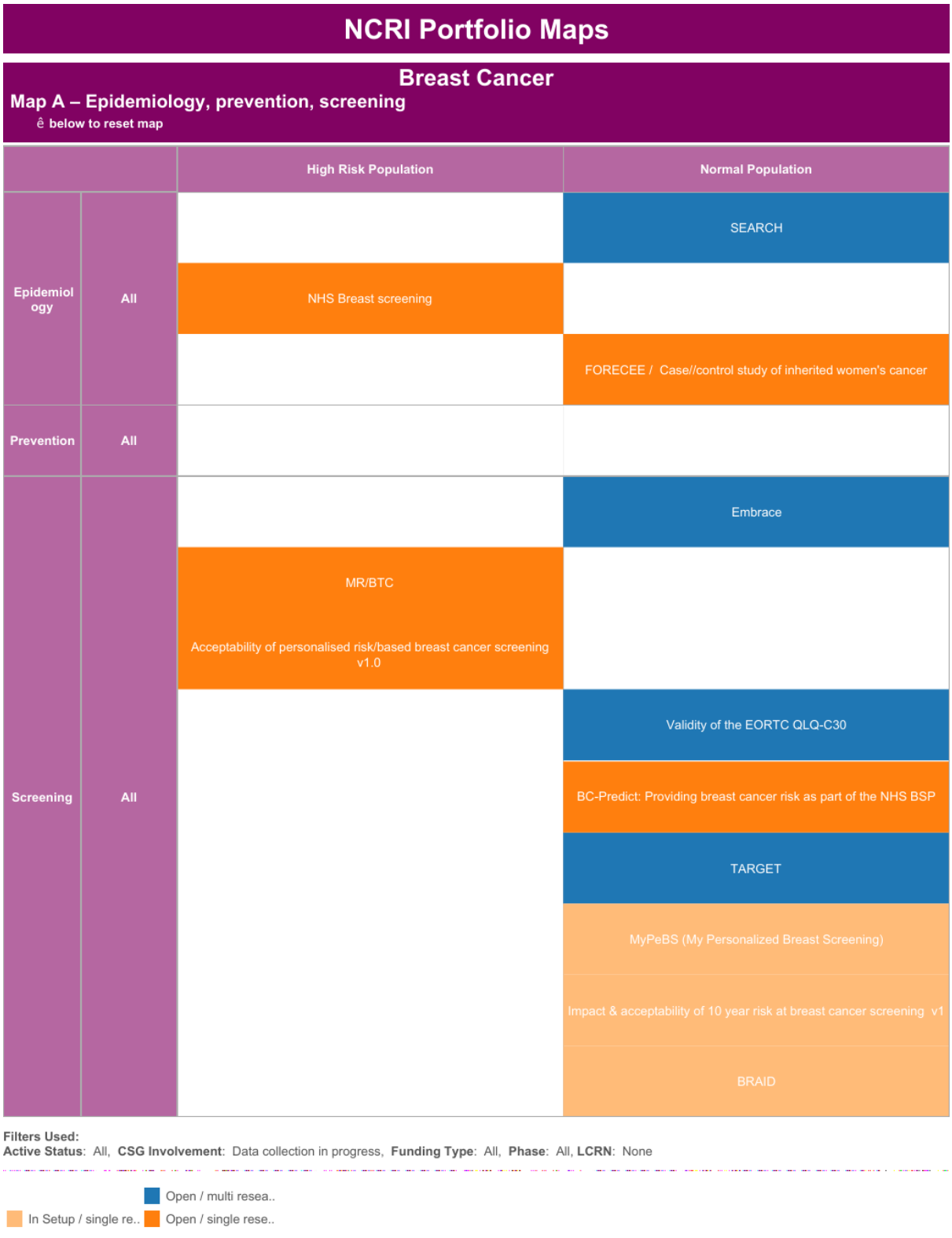
Strategic objective	Activity	CSG Lead	Date
1d integrated Imaging and translational research within the breast portfolio	Promote and advise on the integration translational and imaging research into all trials where possible to include • Biomarker evaluation to identify sensitive subgroups • Serial (plasma) 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

ê below to reset map

		Imaging	Non-imaging diagnostic/ assessment techniques
Intraoperative assessment	All	GE/137 fluor imaging	
Long term follow up	All		
Monitoring disease/ tumour response to treatment	All	Baronet	Baronet
		HERPET in Breast Cancer	
			Automated low dose risk assessment mammography
			Functional Assessment of Bone Metastases 2 (FABB2)
Monitoring treatment side effects	All		
		NICaS device in Herceptin patients / PHASE I	
Pre-diagnosis assessment / S..	All	MR/BTC	
			cfDNA copy number instability as a diagnostic for Breast Neoplasia
		PROSPECTS	
		CONTEST Study	
			Raman spectroscopy for rapid analysis of pathology of the breast.
			IDBC
			Fingertip smears for breast cancer diagnosis
		Deep learning in breast cancer screening	
			ENSEMBLE

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / single re.. Suspended / multi ..
In Setup / multi res.. Open / single rese.. Suspended / singl..

NCRI Portfolio Maps

Breast Cancer

Map C – Neoadjuvant, perioperative, surgery

ê below to reset map

		Neoadjuvant	Peri-operative / window of opportunity	Surgery
Invasion	All	affect breast cancer neoadjuvant chemothera Breast Cancer Her 2		The Pre-Bra Feasibility Study
	All pre-invas..	NEO21-RS Study		
	ER-, Her2- and 3-ve	neoadj chemo ROSCO PARTNER reoperative immunotherapy combinations in br BARBICAN	vivo study in breast cancer and sentinel lymph TIP Study immunotherapy combinations in br	POSNOC Intraop' Marginprobe
	ER-, Her2+	neoadj chemo ROSCO	vivo study in breast cancer and sentinel lymph TIP Study	POSNOC Intraop' Marginprobe
	ER+, Her2+	neoadj chemo ROSCO Baronet	EMERALD	POSNOC Intraop' Marginprobe
	ER+,Her2-	neoadj chemo ROSCO Baronet Neo-RT	EMERALD PEARL	POSNOC Intraop' Marginprobe
Other e.g. ILC	ER-, Her2+	NOSTRA-Feasibility Study, V1, 30/07/18		
	ER+,Her2-	PHERGain	The PIONEER Study	
Pre-invasion	All pre-invasion		Extended follow up of the TARGIT-A trial	LORIS Intraop' Marginprobe

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / single re.. Open / single rese..
Open / multi resea.. Suspended / singl..

NCRI Portfolio Maps

Breast Cancer

Map D – Adjuvant

ê below to reset map

		Local therapy (Radiotherapy)	Systemic Therapy
Invasive (receptor status unspecifi..	ER-, Her2- and 3-ve	TARGIT-B	
		POSNOC	
			Add/Aspirin
			Cardiac CARE
			IMPassion30
	ER-, Her2+	TARGIT-B	
		POSNOC	
			Add/Aspirin
			Cardiac CARE
	ER+, Her2+	TARGIT-B	
		POSNOC	
			Add/Aspirin
			Cardiac CARE
	ER+,Her2-		OPTIMA
		TARGIT-B	
		POSNOC	
			UNIRAD
			Add/Aspirin
			CBYL719X2402
		PRIMETIME	
			Cardiac CARE
			v Adjuvant TriAI with Ribociclib in HER2-negative and early breast car
Other e.g. ILC	All	TARGIT-B	
		POSNOC	
			UNIRAD
			Add/Aspirin
			Cardiac CARE
			Breast Cancer Her 2
	ER-, Her2- a..		c-TRAK TN
	ER+,Her2-		OPTIMA
		PHERGain	PHERGain
			ROLo
			TRANSLATE
Pre-invasive	All		
	ER-, Her2- a..		A-BRAVE Trial

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / single re.. Open / single rese..
In Setup / multi res.. Open / multi resea..

NCRI Portfolio Maps

Breast Cancer

Map E – Metastatic

ê below to reset map

		a) Metastatic-1st line	b) Metastatic-2nd line	c) Metastatic-3rd line, etc
BRCA	All	plasmaMATCH		
ER+	All	POSEIDON plasmaMATCH Nektar214 ombination with fulvestrant in subjects with ER - A study of Ipatasertib with Paclitaxel in Brea Debio 1347-201 - The FUZE Clinical Trial GDC-9545 for women with stage 1-3 operable	POSEIDON geRAD TED14856 MK7902-005 arib Monotherapy in HRRm or HRD Positive C	
ER+ HER2-	All	I3Y-MC-JPCF plasmaMATCH h everolimus/exemestane in PM women with H PYTHIA bel trial of H3B-6545 in HER2 negative breast EMERALD Disease Monitoring in Metastatic Breast Cance	D8530C00001 arib Monotherapy in HRRm or HRD Positive C Y ASSESSING ZN-C5 IN SUBJECTS WITH BF	
HER2-	All	Breast cancer-3652/0002-G1 Therapeutics, Inc plasmaMATCH MP0274-CP101 Patients with Locally Advanced or Metastatic B MORPHEUS-TNBC IPATunity250 l of Balixafortide in Patients with HER2 -ve Bre	fficacy of Venetoclax + Fulvestrant in ER+ MB arib Monotherapy in HRRm or HRD Positive C DS8201-A-U303, HER 2 - Low Breast Cancer	
HER2+/ lother	All	CONCEPT hemo vs Trastuzumab + Chemo in HER2+ Me plasmaMATCH DC-0077 for PIK3CA-mutant solid tumours / b B9991025 PROCLAIM-CX-2009 0456/0112 - Regeneron-R3767-ONC-1613 - A study of Ipatasertib with Paclitaxel in Brea , Multipart, Multiarm, FTiH, Open-label study o 1b study in patients with advanced or solid tu d Cancer Vaccine study in Patients with Advan la trial of BT1718 in patients with advanced so Hepatic Impairment Study in Patients with a S tory Study Novilase Ablation Malignant Breast BGB-290-103 A Phase 1b Study of BGB-290 ROIS DS8201-A-U301, HER2-Positive Breast cancer	HER2CLIMB arib Monotherapy in HRRm or HRD Positive C	DS8201-A-U302, HER2-Positive breast cancer
Triple negative	All	plasmaMATCH IMpassion 131 - A study of Ipatasertib with Paclitaxel in Brea udy in Metastatic Triple Negative Breast Canc RochePh1btriplenegBC IMpassion 132 y of LAG525 with PDR001 and carboplatin in a ase II study of oncology combinations in 1L S e 1b study of RO6870810 and Atezolizumab in Capivasertinib in mTNBC PHOENIX IMpALA in Triple -ve BC IPATunity170	arib Monotherapy in HRRm or HRD Positive C	

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / multi res.. Open / multi resea.. Suspended / singl..
In Setup / single re.. Open / single rese..

NCRI Portfolio Maps

Breast Cancer

Map F – Supportive care

ê below to reset map

		During treatment	Late Effects / survivorship
Supportive care - All	Lifestyle, diet, exercise	B/AHEAD3	
		ADAPT v1.0	
			The EMBRACE Study
	Pyschology / mental wellbeing	CPR Workstream 5: PROMs	
		Communication skills to prevent fear of cancer recurrence	
			Mini-AFTERc Intervention for Fear of Cancer Recurrence: Pilot Trial
	Research methods	CCRN 2949 (Breast reconstruction)	
		Personalisation in BC Medicine	
	Side effects	HORIZONS	HORIZONS
			Preventing Cardiotoxicity in Breast Cancer Patients: PROACT
		Mistletoe And Breast Cancer (MAB)	
	Treatment management	NICaS device in Herceptin patients / PHASE I	
		ePainQ: Feasibility study	
			e-path study
		Assessment of the MACPT tool to facilitate communication	
		Personalised Breast Cancer Program	
			Health Status of Women with Breast Cancer

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / multi resea.. Suspended / singl..
In Setup / single re.. Open / single rese..

NCRI Portfolio Maps

Breast Cancer

Map G – Translational

ê below to reset map

		Disease process	Side Effects	Treatment/Pharmacology
a) Invasion	All	IAMI - Safe Surgery for multiple breast cancer		S-986016 +/- BMS-936558 in Adv. Solid Tum mphoma and solid tumors-2252/0068-Five Prir Negative Pressure Wound Therapy system- CT NeoRay
	ER-, Her2-	Existing Breast BC Subtypes The BeGIN study TNBC in D&G AURORA REVEAL version 1	RAPPER	
	ER-, Her2+	DETECT Existing Breast BC Subtypes The BeGIN study AURORA REVEAL version 1	RAPPER	
	ER+, Her2+	DETECT Existing Breast BC Subtypes The BeGIN study AURORA	RAPPER	
	ER+,Her2-	DETECT Existing Breast BC Subtypes The BeGIN study AURORA	RAPPER Lymphocyte prod. The BeGIN study	Ribociclib Non-Interventional Study
b) Pre-invasion	All	BC Subtypes The BeGIN study 3D scanning of lymphoedema arms ating how platelets alter the genetics of breast	The BeGIN study	
	ER+, Her2+	Oncotype Dx node positive study		
	ER+,Her2-	Oncotype Dx node positive study		
c) ILC	All	Existing Breast VERB Study BC Subtypes The BeGIN study AURORA REVEAL version 1 The ZOLMENO study		
d) Normal tissue/ other	All	Tumour Angiogen Existing Breast Body Composition In Breast Cancer Tissue Stresses of Cancer DETACH V1.0		Safety profile of radium-223 dichloride e 2 Study of Neratinib in Patients With Solid T 8 in Solid Tumours with HER2 or HER3 Abnor

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / multi res.. Open / multi resea.. Suspended / multi ..
In Setup / single re.. Open / single rese.. Suspended / singl..

Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Short-term safety outcomes of mastectomy and immediate implant-based breast reconstruction with and without mesh (iBRA): a multicentre, prospective cohort study. Potter S et al; iBRA Steering Group; Breast Reconstruction Research Collaborative. Lancet Oncol. 2019 Feb;20(2):254-266. doi: 10.1016/S1470-2045(18)30781-2.	This study demonstrates the potential of the research trainee collaborative to formulate and deliver on research that provides unique insight into outcomes in UK surgical practice and provides the basis on which a variety of future breast reconstruction research studies.	The study was developed by CSG members and trainee members and demonstrates the productive nature of surgical research organised through the CSG.
2. Patient-Reported Outcomes Over 5 Years After Whole- or Partial-Breast Radiotherapy: Longitudinal Analysis of the IMPORT LOW (CRUK/06/003) Phase III Randomized Controlled Trial.Bhattacharya IS, Haviland JS, Kirby AM, Kirwan CC, Hopwood P, Yarnold JR, Bliss JM, **Coles CE**; IMPORT Trialists. J Clin Oncol. 2019	This study is an example of an exceptional sequence of radiotherapy trials developed by the CSG and predecessor groups stretching back more than 25 years that have had a major influence on both UK and International radiotherapy practice.	This study was fully developed by the CSG

Feb 1;37(4):305-317. doi: 10.1200/JCO.18.00982.		
3. Increasing the dose intensity of chemotherapy by more frequent administration or sequential scheduling: a patient-level meta-analysis of 37 298 women with early breast cancer in 26 randomised trials. Early Breast Cancer Trialists' Collaborative Group (**EBCTCG**).Lancet. 2019 Feb 7. pii: S0140-6736(18)33137-4. doi: 10.1016/S0140-6736(18)33137-4.		This metanalysis conducted by the Oxford group includes current and past CSG members and is CSG led.
4. Overall Survival with Palbociclib and Fulvestrant in Advanced Breast Cancer. Turner NC et al. N Engl J Med. 2018 Nov 15;379(20):1926-1936. doi: 10.1056/NEJMoa1810527.	The Chief Investigator Nick Turner was a CSG member during the conduct of this study which is an NCRI adopted study and has established UK investigators in the forefront of CDK4/6 inhibitors participation has been influential in placing the CSG in the position to conduct the academically led CDK 4/6 inhibitor studies PALETT and POETIC-A	CSG developed
5. Randomized Phase II Study Evaluating Palbociclib in Addition to Letrozole as Neoadjuvant Therapy in Estrogen Receptor-Positive Early Breast Cancer: PALLET Trial. Johnston S et al. J Clin	This study has led to a phase III study design where only cancers not showing adequate Ki67 response are randomised to the addition of a	CSG developed

Oncol. 2019 Jan 20;37(3):178-189. doi: 10.1200/JCO.18.01624.	CDK4/6 inhibitor or placebo as discussed in major achievements section	

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Breast Cancer Group portfolio, 45 trials closed to recruitment and 66 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
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
2018/2019	4575	9748	1714	7584	3.11	13.76