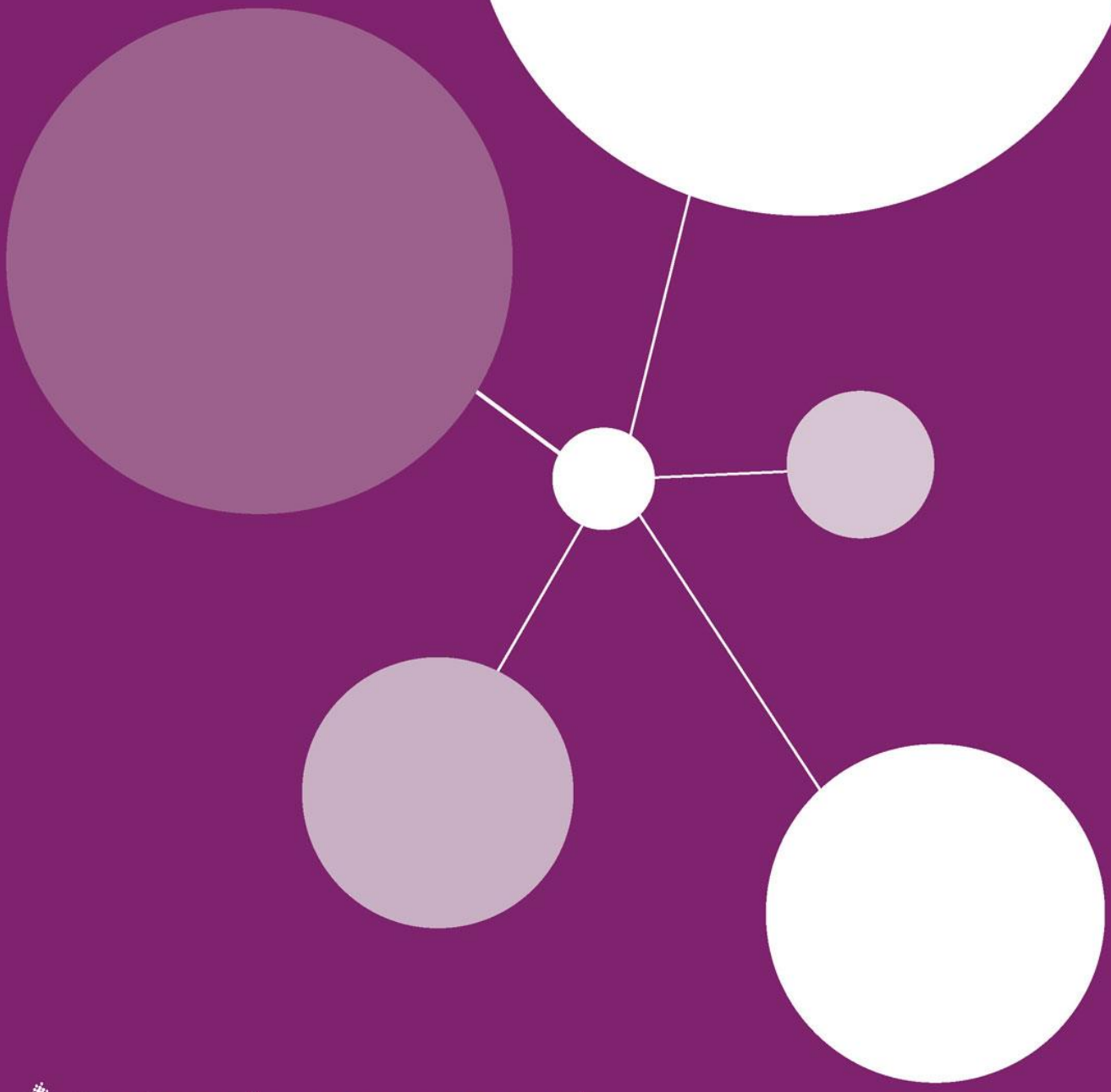
NCRI
National
Cancer
Research
Institute

NCRI Breast Cancer Clinical Studies Group

Annual Report 2015-16



Partners in cancer research

NCRI Breast Cancer CSG Annual Report 2015-16

1. Executive Summary (including top 3 achievements in the year)

In this reporting year we have seen 31 trials closing balanced by the opening of 30 new studies. The numbers of patients recruited into studies appears to have dropped in 2015/16 compared to previous years. This has been anticipated as several studies with broad inclusion criteria have closed and replacement. New studies in many instances now need to fragment breast cancer into subgroups defined by molecular or other sub-classification often with smaller sample size and frequently more complex in design. There has been a response to the need to develop large studies Recently opened or opening imminently are studies with broad inclusion criteria such as the Add Aspirin N=2000, OPTIMA N=4000 and ROSCO N= 1040 will result in improved overall recruitment as the number of open and participating sites increases over 2016/17. The ongoing need to design and successfully fund more studies with broad eligibility and attractive to a broad range of NHS sites is an ongoing challenge and a discussion topic at CSG Strategy and new trial development discussions. The importance of new and innovative trials utilising cutting edge technology and concepts are critically important. The portfolio contains such trials with recent success in funding new innovative studies. The portfolio in development remains diverse but a reverse in the decline in recruitment requires close working with the CSG and breast subspecialty local leads.

Output successes from clinical trials this year include the presentation of significant findings from:

- The IMPORT LOW study demonstrating he safety of partial breast radiotherapy.
- The IBIS II study demonstrating activity of anastrazole after surgery for DCIS.
- The NEOEXEL trial demonstrating that clinical response to neoadjuvant endocrine therapy is significantly increased with the addition of the COXII inhibitor celecoxib.
- The OPTIMA prelim study demonstrating the feasibility of multiparametric testing to select patients for adjuvant chemotherapy in a randomised setting leading to a full phase III trial of 400 patients.
- The EPHOS B study demonstrating that dual targeted anti HER-2 therapy as neoadjuvant treatment in the absence of chemotherapy can induce pathological complete responses within a matter of days.

2. Structure of the Group

The CSG structure comprises of the main CSG with Subgroups for advanced disease, early disease, translational and imaging and symptom management.

The future structure has been discussed while the current structure is thought to work productively. The Translational and Imaging Subgroup may no longer be needed. The potential formation of an immunotherapy subgroup or working party is been considered and a working party to develop a platform on which to structure a suite of trials for optimisation of screening is planned.

There has been stability in membership with a number of successful reapplications for a second terms within the main CSG.

3. CSG & Subgroup strategies

Main CSG

The strategy for the CSG defined in the 2014-15 report continues to evolve we have been able to develop and roll out trials of new technology and also deliver on the availability of trials that are suitable for all breast units to contribute to. For some trials the use of central testing facilitates both of these objectives. For the next year a key new strategic aim is to unite the considerable UK breast cancer screening expertise and explore research methods to underpin a rationale for redesign of the breast screening programme to include captures a range of diverse factors that inform risk and allow a risk adapted approach to screening.

Translational & Imaging Subgroup (Chair, Dr Abeer Shaaban)

The Translational and Imaging Subgroup reviewed and provided feedback on trials with translational component and also on relevant Registration of Concept studies. The Subgroup continued to produce thoughtful position papers on relevant topics for both clinical trials and NHS service delivery. Key workstreams, many with published outputs (see appendix), include:

- Timely availability of molecular markers at the time of MDT Ki67 standardisation within the context of clinical trial and also for standard laboratory testing.
- Guidance on neoadjuvant chemotherapy specimen handling and reporting for routine and trial purposes.
- Recruitment of two eminent breast radiologists has prompted initiatives to address standardization of breast MR imaging pathology.
- Digital pathology in supporting translational research and analysis in the context of clinical trials.
- Subgroup representation (A Shaaban, V Speirs) on the new CM-Path initiative supported by the NRCI Executive.

Early Disease Subgroup (UK Breast Intergroup) (Chair, Professor Judith Bliss)

The Early Disease Subgroup has broad multi-disciplinary membership and aims to support the research community in the development and prioritisation of trial concepts. In addition the group has been proactive in identifying areas where there is a gap on the portfolio and again considering priorities for questions arising in those areas. One example of such, is work ongoing to design a multi-am, response driven platform trial for patients with Her2+ early breast cancer

with the aim of modulating treatment according to a patients initial response to anti-HER2 therapy – escalating treatment for those whose disease does not seem to exhibit early evidence of response and shortening treatment for those whose disease appears exquisitely sensitive to anti Her2 treatment.

The Subgroup engages actively with the wider research community via the UK Breast Intergroup, hosted by the Early Disease Subgroup, which meets twice a year and where any investigator can propose a new trial concept and receive structured feedback to enable revisions to be made prior to submission to a funding committee. This has led to successful funding outcomes for several trials in the last year including NOSTRA a study to determine the feasibility of randomising women with ER negative HER-2 positive women to radiotherapy alone vs the inclusion of standard surgery after apparent pCR in response to neoadjuvant dual targeted anti HER-2 agents with chemotherapy. The c-TRAK TN (ctDNA mutation positive driven intervention).

The Subgroup will continue to work with the breast GECIP to ensure that genomic profiling from multiple projects including the 100,000 genome project can be used to inform the design of future early breast cancer trials. We are in discussion with Genomics England to identify appropriate clinical trials where suitable samples already exist or can be collected during recruitment where a whole genome sequencing approach my provide added value to the trial and simultaneously fit the broader aims of Genomics England.

Advanced Disease Subgroup (Chair, Dr Alastair Ring)

The Advanced Disease Subgroup oversees a large portfolio of therapeutic interventional trials. Key achievements of the Subgroup include:

1. Delivery of a large trial portfolio (36 trials currently open or in the process of opening S metastatic (ref: portfolio map). This portfolio is well balanced with good representation of trials in all disease subgroups (defined by ER status, HER-2 status and BRCA mutation status). This maximises the likelihood that patients with advanced disease will be potentially eligible for a clinical trial.
2. A number of academic studies have been funded and are underway or in set-up. These include trials of ctDNA directed therapy (plasma-MATCH), studies addressing unmet needs such as systemic therapy for brain metastases (BLUEBELL and CiPHER) and trials of novel agents (FURVA, CONCEPT and POSEIDON).
3. UK investigators continue to contribute at an international level to industry sponsored studies.

Symptom Management Subgroup (Co-chairs, Dr Deborah Fenlon and Dr Adrienne Morgan)

This Subgroup was initiated as a working party in 2013 by patient advocate members of the main CSG. As such, the Subgroup is a response to a patient identified need for more research to be instigated into symptoms and symptom management that affect people with breast cancer. We believe that the patient driven aspect of this group is of fundamental significance and patient advocates are an inherent part of the Subgroup. To capitalise on this, we have co-opted members from the charities Independent Cancer Patients' Voice, Breast Cancer Care and Breast Cancer Now to support our work. Three core members of the Group are patient advocates and the group is co-chaired by a health professional (Dr Deborah Fenlon) and a patient (Dr Adrienne Morgan).

This Subgroup was established with a remit to support the development of research into symptoms that affect women with breast cancer. The original remit was to focus on hot flushes and night sweats (HFNS); this is now to broaden out to include other symptoms. In the first instance, the strategy will be to 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:

1. Raising awareness of the issue
2. Supporting the development of current interventions to manage sexual related problems
3. Supporting the development of new interventions.

Two new members with expertise in psychosexual issues have been invited to the group to help develop this stream of work. We are currently developing surveys to establish current practice in the UK.

Where we have capacity, we will explore other issues that arise and continue to liaise with other CSGs and Subgroups to ensure that research into problems relevant to people with breast cancer is being addressed and supported by the most appropriate group. The Subgroup is kindly hosted by Baroness Delyth Morgan, Chief Executive of Breast Cancer Now, at the House of Lords, who also provides refreshments and secretarial support.

4. Task groups/Working parties

The Breast Cancer CSG currently has no task groups or working parties.

5. Patient recruitment summary for last 5 years

In the Breast Cancer CSG portfolio, 32 no. of trials closed to recruitment and 31 opened.

Table 1 Summary of patient recruitment by RCT/Non-RCT

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	33914	5483	8428	4772	19.6	11.1

Table 2 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
2012/2013	20257	11940	7154	6594	14.6	13.5
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

6. Links to other CSGs, international groups and network subspecialty leads

The CSG is represented at the Breast International Group (BIG) which is the primary route to international collaboration multiple BIG studies are in set up open or in follow including UK led international studies. The BIG scientific director Theodora Giuliotti spoke at our Annual Trials meeting and attended a CSG meeting as an observer.

The CSG has close links with The Association of Breast Surgeons Research committee. Links exist with the Supportive and Palliative Care CSG, Primary Care CSG, Imaging Subgroups and SPED Advisory Group.

The Symptom Management Subgroup has formal links with the Psychosocial Oncology and Survivorship CSG with the Chair (Dr Jo Armes) as a co-opted member and with the Supportive and Palliative Care CSG with Lesley Turner as a member of both CSGs.

7. Funding applications in last year

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
A Window of opportunity study to assess the biological effects of Enobosarm (Gtx024) in estrogen receptor positive, androgen receptor positive early breast cancer	Feasibility application	Professor Carlo Palmieri	Funded
December 2015			
ImproveMet: Liquid biopsies to improve metastatic breast cancer outcomes		Professor Carlos Caldas, Dr Nicholas Turner & Dr Richard Baird	Scored as Preliminary - invited to resubmit
Assay development to determine breast cancer biomarker candidate distribution in nipple aspirate	Feasibility application	Dr Chris Sutton	Not funded
A Phase 2 Single-Arm Study of Combination Therapy with the Immunological Breast Cancer Vaccine Nelipepimut-S/rhGM-CSF (NEUVAX) Plus Pembrolizumab (KEYTRUDA) in Patients with Advanced Breast Cancer		Dr Mary O'Brien	Scored as Preliminary - invited to resubmit
PARTNER Sample Collection: Platinum and PARP inhibitor for Neoadjuvant treatment of Triple NEgative and/or BRCA positive breast cancer	Sample Collection	Dr Jean Abraham	Funded
May 2016			
Improving survival in high risk early triple negative breast cancer with intervention targeted to patients with minimal residual disease – phase II study with pembrolizumab	Full application	Dr Nicholas Turner & Professor Judith Bliss	Endorsed
A non-randomised Feasibility Study to assess if patients with residual cancer following dual targeted neoadjuvant treatment for ER-negative	Full application	Dr Adele Francis & Dr Daniel Rea	Endorsed

HER2-positive early breast cancer can be identified by multiple Ultrasound Scan (USS)-directed tumour-bed biopsies? All patients will undergo surgery.			
NEOTYPE (Neo21-RS): A phase II randomised study of the cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with oestrogen suppression therapy versus oestrogen suppression therapy alone as neoadjuvant therapy in ER-positive intermediate recurrence score primary breast cancer	Full application	Professor Carlo Palmieri	Not endorsed
A Phase 2 Single-Arm Study of Combination Therapy with the Immunological Breast Cancer Vaccine Nelipepimut-S/rhGM-CSF (NEUVAX) Plus Pembrolizumab (KEYTRUDA) in Patients with Advanced Breast Cancer	Full application	Dr Mary O'Brien	Not funded
PHOENIX: A preoperative "window of opportunity" phase IIa biomarker endpoint trial of FAK or P13K/MTORC1/2 inhibition in patients with post-neoadjuvant chemotherapy resistant residual triple-negative breast cancer (TNBC)	Full application	Professor Andrew Tutt and Professor Judith Bliss	Not funded due to budget constraints
ImproveMet: Liquid biopsies to improve metastatic breast cancer Outcomes	Full application	Professor Carlos Caldas, Dr Nick Turner and Dr Richard Baird	Not funded
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
fMRI to predict treatment outcome of flushes in women with breast cancer using tamoxifen	NHSGGC Endowment fund	Dr Jenifer Sassarini	Funded
PIONEER: A Pre-operative wIndOw study of letrozole plus PR agonist [Megace] versus letrozole aloNE in post-menopausal patients with ER-positive breast cancer	Anti-Cancer Fund	Dr Richard Baird	Funded
MENOS4: 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	Breast Cancer Now	Dr Deborah Fenlon	Funded
Improving adherence to adjuvant endocrine therapy in women with breast cancer: a feasibility trial of a community pharmacy intervention	Breast Cancer Now	Prof Eila Watson	Shortlisted
Investigating the Aetiology of Hot Flush Mechanisms during Oestrogen Deprivation Therapy using cell lines in vitro	Breast Cancer Now	Dr Melanie Flint	Not funded
Exercise for hot flushes	Breast Cancer Now	Dr Helen Jones	Not funded

8. Collaborative partnership studies with industry

The Astra Zeneca Alliance partnership continues to provide study opportunities in breast cancer The STAKT study

Two new initiatives from Pfizer present new opportunities a new alliance partnership and an access programme supported through Breast Cancer Now to provide access to Pfizer pipeline drugs for use in translational studies.

The portfolio comprises a heathy mixture of industry studies academic partnership studies and exclusively academic studies. The CSG particularly the metastatic subgroup is closely involved in the planning of studies to minimise overlap and ensure that gaps in the portfolio are identified and studies sought or developed to maximise opportunities when they present. A number of industry studies overlap but it is unusual to have competing studies open at sites where the sites with large populations are able to run overlapping studies but even within the overlapping inclusion criteria are usually able to identify patient centred factors.

9. Impact of CSG activities

- The adjuvant Bisphosponate metanalysis has clearly demonstrated the clinical argument for introduction of adjuvant bisphosphonate therapy in post-menopausal women this is being introduced at local level in an increasing number of localities. A national policy from NHS England is awaited.
- The recent metanalysis analysis of aromatase inhibitors the recent data on endocrine therapy fin premenopausal women (SOFT and TEXT studies) and the data on extended adjuvant tamoxifen provides the evidence base for refinement in adjuvant endocrine therapy.
- The CSG provides commentary to all breast cancer applications to CRUK funding committees
- NICE appraisals for cancer drugs are of increasing importance with the reconfiguration of the Cancer Drugs fund. Appraisals of neoadjuvant pertuzumab and upcoming reappraisals of a number of breast cancer drugs are impacted by submissions and representation on panels by CSG members.
- The Symptom Management Subgroup had representation on the NICE menopause guidelines and altered the remit to include recommendations for people with breast cancer.

10. Consumer involvement

Excellent engagement and collaboration occurs between the consumers and health professionals across the CSG, all Subgroups and beyond in the UK and sometimes abroad. Representation occurs and is heard at each meeting and support is available where needed.

The Breast research community values consumer involvement at all levels of research design and delivery. Working and communicating with a network of consumers, especially from Independent Cancer Patient's Voice, assists the NCRI consumers in delivering the level of

involvement needed, keeping the patient at the heart of research, and having a holistic view across the wide range from translation to advanced disease.

In addition strong consumer representation continues to be a key driving force behind the Symptom Management Subgroup; initiated and co-chaired by a consumer, through individual membership, ICPV and Breast Cancer Care as co-opted members and Breast Cancer Now, who provide secretariat support and facilities for meetings including refreshments.

A few highlights from the individual activities of our NCRI consumers include:

- Members, and sometimes co-applicants, of various TMG/TSG/protocol working groups including C-TRAK, REQUITE, PRIMETIME, UNIRAD, OPTIMA, OPTIMAM2, VOXTOX, 100,000 Genome Project – Breast GeCIP, PIONEER, MENOS4.
- UK Breast Intergroup.
- RCR Breast Radiotherapy Consensus Guidelines, presented and part of core development group.
- Co-author of publication from the Breast CSG Translational subgroup in European Journal of Surgical Oncology.
- NIHR RFPB East of England Funding Board member.
- Chaired and presented at joint CRUK/CTRad/ICPV session at Britain Against Cancer in December 2015 on importance of data collection.
- Working to increase patient involvement in development of national data standards for pathology.
- Presented at European Commission on Breast Cancer Plenary in December 2015 on 'Involving Patients in Difficult Decisions'.
- Ran workshop on Embedding the MCA among Health and Social Care Practitioners - Supporting Decision Making and Advocacy (Sept 2015).
- Member of steering group for the UK Therapeutic Cancer Prevention Network (UKTCPN) – part of ECMC.

11. Open meetings/annual trials days/strategy days

The Annual Trials meeting was held on 6 March attended by over 250 researchers providing an opportunity showcase and discuss the immunotherapy and genomic aspects of UK breast cancer research and to present to investigators results from recently presented trials. The meeting incorporated investigator meetings for the EPOS-B and IMPORT LOW studies, where investigators were able to see data from these trials presented for the first time ahead of public presentation at the European Breast Cancer meeting. This aspect of the meeting is particularly appreciated and we intend to repeat this at future annual meetings where possible.

12. Priorities and challenges for the forthcoming year

Restoring recruitment to recently achieved levels is both a priority and a challenge for the CSG. This requires working with regional subspecialty leads (SSLs) to identify barriers to site set up and recruitment to open studies.

Maintain the momentum for developing surgical trials in breast cancer. We continue to encourage surgically led studies and actively promote a clinical trials culture within the surgical community.

Delivery on the breast component of the 100,000 genome project with the linking of GEL to a selected group of clinical trials. A process for considering clinical trials to be formally linked to GEL is underway

Establish a mechanism for a coordinated approach to evaluation of breast screening initiatives with the intent to demonstrate how to integrate novel Imaging Genetic and lifestyle information to improve screening without increasing harms through over-diagnosis.

Ensuring that the new NHS HRA trial approvals and set up procedure does not cause undue delay in trial set up: Inevitable teething issues are emerging with the NEW HRA process. There are currently significant backlogs in processing amendments. The CSG will share experience in navigation of the new approvals process and in collaboration with trials units guide researchers through the new arrangements.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
- A – Main CSG Strategy
- B – Translational & Imaging Subgroup Strategy
- C – Early Disease Subgroup Strategy
- D – Advanced Disease Subgroup Strategy
- E – Symptom Management Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Dr Daniel Rea (Breast Cancer CSG Chair)

Appendix 1

Membership of the Breast Cancer CSG

Name	Specialism	Location
Dr Deborah Fenlon	Associate Professor in Cancer Care	Southampton
Ms Shelley Potter*	Clinical Lecturer in General Surgery	Bristol
Professor David Cameron	Clinical Oncologist	Edinburgh
Dr Charlotte Coles	Clinical Oncologist	Cambridge
Dr Carolyn Taylor	Clinical Oncologist	Oxford
Mrs Katrina Randle	Consumer	Leeds
Mrs Hilary Stobart	Consumer	Nottingham
Dr Elizabeth Mallon	Histopathologist	Glasgow
Professor Janet Brown	Medical Oncologist	Sheffield
Dr Ellen Copson	Medical Oncologist	Southampton
Dr Helena Earl	Medical Oncologist	Cambridge
Dr Iain Macpherson	Medical Oncologist	Glasgow
Professor Carlo Palmieri	Medical Oncologist	Liverpool
Dr Daniel Rea (Chair)	Medical Oncologist	Birmingham
Dr Alistair Ring	Medical Oncologist	Brighton
Professor Peter Schmid	Medical Oncologist	Brighton
Dr Nicholas Turner	Medical Oncologist	London
Dr Andrew Wardley	Medical Oncologist	Manchester
Dr Abeer Shaaban	Pathologist	Birmingham
Professor Janet Dunn	Professor of Clinical Trials	Warwick
Dr Emma Harris	Radiologist	London
Professor Iain Lyburn	Radiologist	Cheltenham
Dr Ciara O'Brien*	Specialist Registrar Medical Oncology	Manchester
Professor Judith Bliss	Statistician	London
Ms Adele Francis	Surgeon	Birmingham
Professor Chris Holcombe	Surgeon	Liverpool
Mr Stuart McIntosh	Surgeon	Belfast
Professor Arnie Purushotham	Surgeon	London

*denotes trainee member

Membership of the Subgroups

Translational & Imaging Subgroup		
Name	**Specialism**	**Location**
Mrs Hilary Stobart	Consumer	Nottingham
Dr Rob Stein	Medical Oncologist	London
Professor John Bartlett**	Pathologist	Ontario
Professor Iain Lyburn	Radiologist	Cheltenham
Professor Sarah Pinder	Pathologist	London
Dr Colin Purdie	Pathologist	Dundee
Dr Emad Rakha	Pathologist	Nottingham
Dr Abeer Shaaban (Chair)	Pathologist	Birmingham
Dr Val Speirs	Pathologist	Leeds
Professor Janet Dunn	Statistician	Warwick
Ms Adele Francis	Surgeon	Birmingham
Professor Alastair Thompson**	Surgeon	USA

Advanced Disease Subgroup		
Name	**Specialism**	**Location**
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	Guildford
Mrs Katrina Randle	Consumer	Leeds
Dr Anne Armstrong	Medical Oncologist	Manchester
Professor Rob Coleman	Medical Oncologist	Sheffield
Dr Alistair Ring (Chair)	Medical Oncologist	Birmingham
Dr Rebecca Roylance**	Medical Oncologist	London
Professor Peter Schmid	Medical Oncologist	Brighton
Dr Nick Turner**	Medical Oncologist	London
Dr Cath Harper-Wynne	Medical Oncologist	London

Symptom Management Subgroup		
Name	**Specialism**	**Location**
Dr Debbie Fenlon (co-chair)	Associate Professor	London
Dr Adrienne Morgan (co-chair)	Consumer	Southampton
Dr Carolyn Morris	Consumer	Lewes
Mrs Lesley Turner	Consumer	Southampton
Dr Jenifer Sassarini	Clinical Lecturer	Glasgow
Dr Andreia Fernandes	Clinical Nurse Specialist	London
Dr Mei-Lin Ah-See	Clinical Oncologist	Middlesex
Professor Myra Hunter	Clinical Psychologist	London
Dr Melanie Flint	Senior Lecturer in Immunopharmacology	Brighton
Professor Janet Dunn	Statistician	Warwick

Early Disease Subgroup (UK Breast Intergroup)		
Name	**Specialism**	**Location**
Dr Deborah Fenlon	Associate Professor	Southampton
Dr Charlotte Coles	Clinical Oncologist	Cambridge
Professor Andrew Tutt	Clinical Oncologist	London
Mrs Katrina Randle	Consumer	Leeds
Mrs Hilary Stobart	Consumer	Nottingham
Dr Andrew Wardley	Medical Oncologist	Manchester
Professor Judith Bliss (Chair)	Statistician	London
Mr Peter Barry	Surgeon	London
Dr Cliona Kirwan	Surgeon	Manchester
Mr Anthony Skene	Surgeon	Bournemouth

*denotes trainee member
**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Overall aim: Improve the outcomes and experience of breast cancer patients and those at risk of developing breast cancer

The CSG strategy is described in hierarchical strata with 17 overarching aims which underpin the strategic aims of the Breast CSG expanded in detail within descriptions of translational advanced and early disease domains.

Aims:

1. Ensure that all breast cancer patients have 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. Improve International collaboration where appropriate and key to the success of a trial.
11. Strengthen links with other NCRI CSGs, HCIS, advisory groups and CTRad.
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 and research competencies and achievements of all breast cancer clinicians.
15. Disseminate trials information and availability through regional subspecialty leads to enhance recruitment.
16. Deliver the commercial and non-commercial portfolio.
17. Review configuration of subgroups.

B – 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 AF/SP	Ongoing Position paper publications 2016
1b. Portfolio development imaging	Ensure /advise on appropriate protocols for imaging in portfolio studies identify opportunities for assessment of novel imaging research. (See early disease section for screening strategy)	IL/FG	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		Ongoing

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 Link appropriate clinical trials to 100,000 genome project WGS	NT	Ongoing 2016

Strategic objective	Activity	CSG Lead	Date
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	All	
	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	HS	
	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 AS DR DC JB	

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

C – Early Disease Subgroup (UK Breast Intergroup) 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	CC / AT PB / AS / CK/AF	Ongoing With new funding proposals for 2017
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	post neoadjuvant residual diseaseplatform HER2+ modulating treatment according to risk/response JMB / DC / AR /NT pragmatic CT trials	Ist early disease Trial open 2017 Metatsatic disease trial end 2016 HER-2 Trial submission 2016/17

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	Ongoing
1d Portfolio development Screening and prevention	Convene a group of specialists with expertise relevant to genetics epidemiology lifestyle and imaging technology and screening implementation to explore a comprehensive approach to screening research	DR	2016

Strategic objective	Activity	CSG Lead	Date
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 • UK Breast Intergroup meetings 2x/year • UK Breast Intergroup Feasibility & interest surveys	All	ongoing
	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	KR MM	
	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	All	
	Link with CTRad to expand RT studies	CC	
	Maximise opportunities for international collaboration • BIG – UK a participant group • BIG – UK a lead group • Unilateral national collaborative groups (NSABP, NCIC, UNICANCER, ANZBCG)	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 – NCIN Validation project / with breast SSCRG	annual

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
AF	Adele Francis
DR	Daniel Rea

D – Advanced Disease Subgroup Strategy

Aims:

1. Circulating tumour DNA-driven studies - With the funding by CRUK (in collaboration with commercial partners) of the plasma-MATCH study, and the proposal of IMPROVEmet (Liquid biopsies to improve metastatic breast cancer outcomes) we believe that this area is a key UK strength. We will encourage the development of studies using this technology as a means to identify patients for trials of novel therapies, and also for disease monitoring whilst on therapy.
2. Collaboration with industry - The Subgroup has a good history of collaboration with pharmaceutical partners, in particular AZ through the alliance strategy. With similar initiatives from other partners established/in development, the Advanced Disease Subgroup needs to capitalise on these.
3. Genomic profiling - The Subgroup will continue to work with the breast GECIP to ensure that genomic profiling can be used to inform the design of future advanced breast cancer trials. A number of members of the Subgroup are also members of the breast GECIP, and Dr Nick Turner leads the breast GECIP.
4. Portfolio management - It remains a challenge to deliver the commercial trial portfolio whilst maintaining the presence of academic studies. Commercial trials are adopted onto the metastatic portfolio assuming they achieve minimal criteria and this can mean that there are fewer sites available to undertake academic studies, which themselves are associated with less funding. The Advanced Disease Subgroup needs to actively promote the academic portfolio in the UK. The Subgroup would also be keen to be more involved in distribution of commercial studies, to ensure better access for patients to clinical trial opportunities. This is particularly important with the partitioning of breast cancer into smaller target groups (e.g. BRCA associated cancers) and studies using agents with toxicities which sites may be less familiar with (e.g. immunotherapy). Our patient members are very active in supporting the work of the Group by attending conferences, giving presentations and exhibiting posters and by stimulating thoughts around the development of new work in this field.

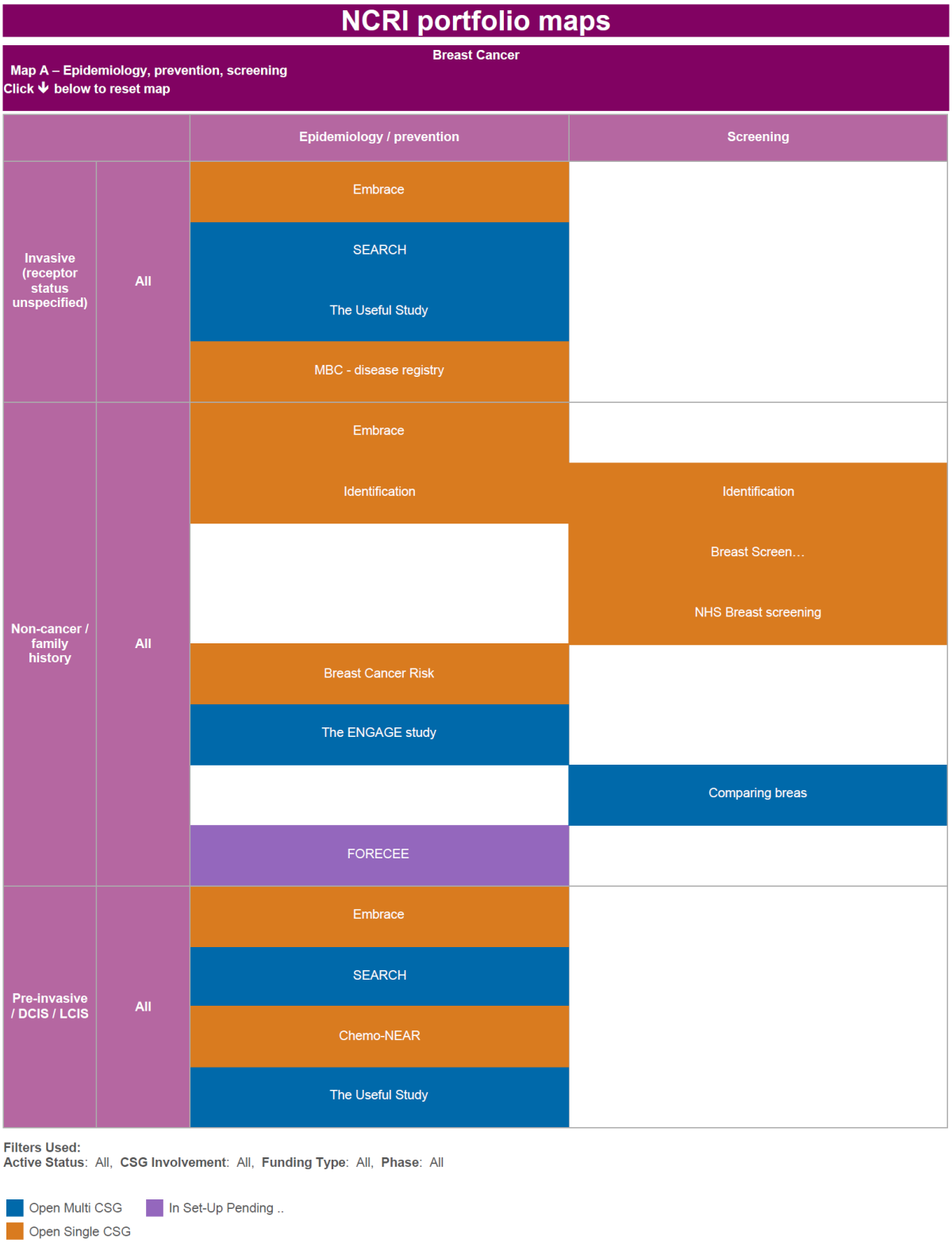
E – Symptom Management Subgroup Strategy

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.

Appendix 3

Portfolio maps



NCRI portfolio maps

Map B – Diagnosis, Imaging
Click ↓ below to reset map

Breast Cancer

		Diagnosis / imaging
ER-HER2+	All	
ER-HER2+ (includes triple negative)	All	
ER+ HER2+	All	
Invasive (receptor status unspecified)	All	COPE Digital breast MagSNOLL MIMIC Cerenkov Lum
		GE-137 fluor imaging
		CONTEND Study
		CIST full study CHERNAC
Non-cancer / family history	All	Digital breast
		MAMMO -50
		SPECIALS
		GeMCaS
		MR-BTC
Pre-invasive / DCIS / LCIS	All	COPE Digital breast FABB study
		TPI - in vivo s
		FAB-IE
		MIMIC EBLIS POPPET
		Digital breast

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG Suspended Single ..
Open Multi CSG

NCRI portfolio maps

Breast Cancer

Map C – Neoadjuvant, perioperative, surgery
Click ↓ below to reset map

		Neoadjuvant	Perioperative	Surgery
ER-HER2+ (includes triple negative)	All	carboplatin		
ER+ HER2+	All	Neoadjuvant Letrozole PALLET		
Invasive (receptor status unspecified)	All	neoadj chemo RIO ROSCO	AZD9496vFulvestrant TIP Study	ExAblate POSNOC ARP Intraop' Marginprobe
Pre-invasive / dcis / lcis	All			LORIS PREHEAT Tria

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG
Open Multi CSG In Set-Up NHS Per..

NCRI portfolio maps

Breast Cancer

Map D – Adjuvant
Click ⬇ below to reset map

		Adjuvant - radiotherapy	Adjuvant – systemic treatment
ER-HER2+	All		SOLAR-1
ER-HER2+ (includes triple negative)	All		EORTC 90091-10093 OLYMPIA
ER+ HER2+	All		OPTIMA EORTC 90091-10093 UNIRAD EORTC 75111
Invasive (receptor status unspecified)	All		LATTE
		FAST-Forward TARGIT-B Trial POSNOC	
Pre-invasive / dcis / lcis	All	Add-Aspirin	
			The use of a pr

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG
Open Multi CSG Suspended Single ..

NCRI portfolio maps

Breast Cancer

Map E – Metastatic
Click ↓ below to reset map

		Metastatic-1st line	Metastatic-2nd line	Metastatic-3rd line, etc
BRCA	All			AT13148 Phase I
			BravO	BravO
		BMN 673	BMN 673	
		Veliparib		
ER+	All		NCRN279	
				AT13148 Phase I
				BELLE 3
		FINESSE	FINESSE	
		MANTA	MANTA	
		FAKTION		
		exemestane + everol.	exemestane + everol.	
		LEE011 + BYL719 + Letro	LEE011 + BYL719 + Letro	
		LEE011 with everolimus and exemestane	LEE011 with everolimus and exemestane	
		NCRN - 3156	NCRN - 3156	
		CANC - 3548	CANC - 3548	
		BOADICEA	BOADICEA	
		POSEIDON	POSEIDON	
		Monaleesa 3	Monaleesa 3	
ER+ HER2+	All	ALTERNATIVE		
		BOADICEA	BOADICEA	
		Neratinib		
HER2+	All			AT13148 Phase I
				NALA
			Enzal+Trastuz	Enzal+Trastuz
HER2+/other	All			AT13148 Phase I
			FGFR Study	FGFR Study
			BravO	BravO
		BI 836845		
			CiPHER	CiPHER
		NCRN - 3156	NCRN - 3156	
		NCRN - 3159	NCRN - 3159	
		CANC - 3548	CANC - 3548	
		CONCEPT		
		FURVA, Version		
			Herceptin + Perjeta +Docetaxel	Herceptin + Perjeta +Docetaxel
		Monaleesa 3	Monaleesa 3	
		3223 + paclitaxel in cancer subjects with bon		
Triple negative	All			AT13148 Phase I
			PARP inhibitor adv' breast ca	PARP inhibitor adv' breast ca
		CheckMate032		
		MEDI4736		
		PAKT		
			BMN 673 in BRCA	
		COBIMETINIB+PACLIT		
		ANTI-PD-L1 Ab+/- NAB PACLIT		
		GTx-024		GTx-024
		Pembrolizumab		
		METRIC		

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG
Open Multi CSG

NCRI portfolio maps

Map F – Supportive care
Click ↓ below to reset map

Breast Cancer

		Supportive care/late effects/end of life care
Lifestyle interventions, diet and excercise	All	Multifrequency PLACE Physical activ.
		B-AHEAD3 FOAM Trial
		LivingWELL - A app for exercises post BC surgery
Psychological analysis	All	
Psychotherapy	All	
Research method validation	All	Breast Recon. QoL
		PICTURE BREAST PICTURE BREAST
		4Ps Study
Side effects management and pain	All	RELATED
		POBRAD-M LOTUS
		ACUFOCIN eSMART: Randomi PLACE PROSPER
Treatment choice	All	Bridging the Age Gap Investigating how women with breast cancer view Tamoxifen
		YoDA BRCA: Gene A multi-centred-study of the effectiveness of PEGASUS
Treatment management	All	CAVA
		use of Seri

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG In Set-Up Pending ..
Open Multi CSG

NCRI portfolio maps

Map G – Translational
Click ↓ below to reset map

Breast Cancer

		Translational
ER-HER2+	All	Genome Profilin
ER-HER2+ (includes triple negati..	All	Genome Profilin
		TNBC in D&G
ER+ HER2+	All	VERB Study
		STAKT study
		IBIS 3 Feasibility version 1.0
		YAP1
Invasive (receptor status unspecified)	All	RAPPER
		DETECT EORTC 10085 CHAMPion
		CR UK Stratifie
		Analysis of pre [18F]ICMT11 - changes
		Cubbs BC Subtypes EBLIS
		Lymphocyte prod. REQUITE
		pericytes in BC
		AURORA Xray Diffraction of breast cancers
Non-cancer / family history	All	SPECIALS The BeGIN study
		Anti-Progestin Prev.
Pre-invasive / DCIS / LCIS	All	
		RAPPER
		SIBS
		CTCF & BORIS BM Tumour Angiogen
		DETECT CHAMPion
		CR UK Stratifie
		Existing Breast

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG In Set-Up NHS Per..
Open Multi CSG Null Suspended Single ..

Appendix 4

Publications in the reporting year

OPTIMA trial

Stein RC, Marshall A, Hall PS, Bartlett JMS, Rooshenas L, Campbell A, Cameron DA, Rea D, Macpherson I, Earl HM, Poole CJ, Francis A, Morgan A, Harmer V, Pinder SE, Stallard N, Donovan J, Hulme C, McCabe C, Hughes-Davies L, Makris A, Dunn JA. OPTIMA (optimal personalised treatment of early breast cancer using multi-parameter analysis), a prospective trial to validate the predictive utility and cost-effectiveness of gene expression test-directed chemotherapy decisions. Cancer Research 2016; 76:4s (abstr OT3-02-12)

Dunn J, Marshall A, Campbell A, Cameron D, Earl H, Macpherson I, Poole C, Rea D, Francis A, Harmer V, Morgan A, Stallard N, Makris A, Hughes-Davies L, Stein R. Practicalities of using an adaptive design for decision making within the optima trial: optimal personalized treatment of early breast cancer using multi-parameter tests. Trials 2015; 16(Suppl 2):P212

Stein RC, Dunn JA, Bartlett JM, Campbell AF, Marshall A, Hall P, Rooshenas L, Morgan A, Poole C, Pinder SE, Cameron DA, Stallard N, Donovan JL, McCabe C, Hughes-Davies L, Makris A. OPTIMA prelim: randomised feasibility study of personalised care in the treatment of women with early breast cancer. Health Technol Assess. 2016 Feb;20(10):1-202. doi: 10.3310/hta20100.

Stein RC, Makris A, Hughes-Davies L, Bartlett, JMS, Marshall A, Hall PS, Campbell A, Pinder SE, Cameron DA, Rea D, Earl H, Macpherson I, Poole C, Canney P, Francis A, Morgan A, Stallard N, Hulme C, McCabe C, Dunn JA. Results of the OPTIMA (Optimal Personalized Treatment of early breast cancer using Multi-parameter Analysis) prelim study. European Journal of Cancer 2015; 51, S268 (abstr 1809)

Comparing breast cancer multi-parameter tests in the OPTIMA prelim trial: No test is more equal than the others. *JNCI* (Accepted February 2016)

Stein, RC, Makris, A, Hughes-Davies, L, Bartlett, JMS, Marshall, A, Hall, PS, Campbell, A, Pinder, SE, Cameron, DA, Rea, D, Earl, H, Macpherson, I, Poole, C, Canney, P, Francis, A, Morgan, A, Stallard, N, Hulme, C, Mccabe, C & Dunn, JA. 1809: Results of the OPTIMA (Optimal Personalized Treatment of early breast cancer uslng Multi-parameter Analysis) prelim study. The European Cancer Congress 2015 *European Journal of Cancer* 2015; 51S268.

POETIC Trial

Bliss J, Gillman A, Kilburn L, Morden J, Sidhu K, Wilcox M, Evans A, Holcombe C, Horgan K, Skene A, Vidya R, Robertson J, Dowsett M, Smith I, Trialists P. A POETIC story: lessons learnt from the world's largest breast cancer window of opportunity study. Meeting Abstract: Trials 16(Suppl 2):P83

Gellert P, Segal CV, Gao Q, Li T, Miller CA, Mardis E, Martin L-A, Holcombe C, Skene A, Bliss J, Robertson J, Smith I, Dowsett M, Group PTM, Trialists. Exome sequencing of post-menopausal ER+ breast cancer (BC) treated pre-surgically with aromatase inhibitors (AIs) in the POETIC trial (CRUK/07/015) Meeting Abstract: Cancer Res 75(Suppl 9):S1-04

FAST Forward Trial

Brunt AM, Sydenham M, Yarnold J, Wheatley D, Somaiah N, Kelly S, Harnett A, Coles C, Goodman A, Zotova R, Griffin C, Morden J, Bliss J. Acute skin toxicity reported in the FAST-Forward trial (HTA 09/01/47): a phase III randomised trial of 1-week whole breast radiotherapy compared to standard 3 weeks in patients with early breast cancer. Meeting Abstract: UKRO Coventry 7-9 June 2015 18 #P46

Zotova R, Yarnold J, Wheatley D, Griffin C, Brunt AM. Interim analysis of the radiotherapy quality assurance programme for the FAST-Forward breast trial. Meeting Abstract: Rad Oncol115(Suppl 1):S209 #PD-)430

EPHOS B Trial

Bundred N, Cameron D, Kalaitzaki E, Morley R, Cramer A, Webster-Smith M, Narayanan S, Brunt AM, Horgan K, Hanby A, Ooi J, Hong A, Naik J, Evans A, Shaaban A, Bliss J. Effects of perioperative lapatinib in early HER2+ breast cancer - the UK EPHOS-B trial (CRUK/08/002). Meeting Abstract: Proceeds of San Antonio Breast Cancer Symposium 2015 #PD5-06

TACT2 Trial

Chapman H, Bloomfield D, Cameron D, Bliss J, Barrett-Lee P, Canney P, Morden J, Velikova G, Hall P, on behalf of the TACT2 Trial Management Group. Cost-effectiveness analysis of the use of pegfilgrastim to enable accelerated adjuvant chemotherapy in the TACT2 trial (CRUK/05/019) Meeting Abstract: Eur J Cancer 51(Suppl 3):S183 #1231

Morden J, Bliss J, Bayani J, Laing R, Agrawal R, Thomas J, Goodman A, Loo V, Clark P, Canney P, Barrett-Lee P, Bartlett J, Cameron D. Intrinsic subtypes and BCL2 as predictive and prognostic biomarkers in the TACT2 trial (CRUK/05/019) Meeting Abstract: Canc Res 75(Suppl 9):P4-11-04

Velikova G, Morden J, Barret-Lee P, Bloomfield D, Brunt AM, Canney P, Coleman R, Sergenson N, Verrill M, Wardley A, Bliss J, Cameron D, on behalf of the TACT2 Trial Management Group. Quality of life (QOL) results of the UK TACT2 Trial: more intensive chemotherapy for early breast cancer (EBC) has a measurable impact on patient-reported symptoms and functioning (CRUK/05/019) Meeting Abstract: Qual Life Res 24(Suppl 1):91 #1085

Bayani J, Morden J, Skaria S, Bliss P, Grieve R, Harnett A, Bradley C, Ritchie D, Barrett-Lee P, Canney P, Cameron D, Bliss J, Bartlett J. Androgen receptor expression is an independent marker of lower residual risk in the TACT2 trial (CRUK/05/019). Meeting Abstract: Canc Res 75(Suppl 9):#P4-11-03

TNT Trial

Cheang M, Bliss J, Dowsett M, Kilburn L, Grigoriadis A, Gillett C, Pinder S, Gazinska P, Haynes B, Kernaghan S, Tovey H, Owen J, Harries M, Ellis P, Tutt A, Group obotTTM. Concordance of intrinsic subtyping and risk of recurrence (ROR) scores between matched primary and metastatic tissue from triple negative breast cancer trial (TNT) Meeting Abstract: J Clin Oncol 33(Suppl):#1019

Tovey H, Bliss J, Tutt A, Morden J, Jarman K, Martin S, Kernaghan S, Toms C, Kilburn L, investigators T. Managing non-proportionality of hazards (PH) within TNT: a randomised phase III trial of carboplatin compared to docetaxel for patients with metastatic or recurrent locally advanced triple negative (TN) or brca1/2 breast cancer (BC). Meeting Abstract: Trials 16 (Suppl

2):P150

Tutt A, Ellis P, Kilburn L, Gilett C, Pinder S, Abraham J, Barrett S, Barrett-Lee P, Chan S, Cheang M, Dowsett M, Fox L, Gazinska P, Grigoriadis A, Gutin A, Harper-Wynne C, Hatton M, Kernaghan S, Lanchbury J, Morden J, Owen J, Parikh J, Parker P, Rahman N, Roylance R, Shaw A, Smith I, Thompson R, Timms K, Tovey H, Wardley A, Wilson G, Harries M, Bliss J. The TNT trial: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). Meeting Abstract: Canc Res 75(Suppl 9):S3-01

TACT Trial

Jamal-Hanjani M, A'Hern R, Birkbak NJ, Gorman P, Gronroos E, Ngang S, Nicola P, Rahman L, Thanopoulou E, Kelly G, Ellis P, Barrett-Lee P, Johnston SR, Bliss J, Roylance R, Swanton C. Extreme chromosomal instability forecasts improved outcome in ER-negative breast cancer: a prospective validation cohort study from the TACT trial. Peer-reviewed Article: Ann Oncol 26(7):1340-6

Garcia-Saenz, J.A., Bermejo, B., Estevez, L.G., Palomo, A.G., Gonzalez-Farre, X., Margeli, M., Pernas, S., Servitja, S., Rodriguez, C.A., Ciruelos, E. SEOM clinical guidelines in early-stage breast cancer 2015 2015 Clinical and Translational Oncology

Senkus, E., Kyriakides, S., Ohno, S., Penault-Llorca, F., Poortmans, P., Rutgers, E., Zackrisson, S., Cardoso, F. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up 2015 Annals of Oncology

Coates, A.S., Winer, E.P., Goldhirsch, A., Gelber, R.D., Gnant, M., Piccart-Gebhart, M.J., Thürlimann, B., Senn, H.-J., André, F., Baselga, J., Bergh, J., Bonnefoi, H., Burstein, H., Cardoso, F., Castiglione-Gertsch, M., Colleoni, M., Curigliano, G., Davidson, N.E., Leo, A.D., Ejlertsen, B., Forbes, J.F., Galimberti, V., Goodwin, P., Harbeck, N., Hayes, D.F., Huober, J., Hudis, C.A., Ingle, J.N., Jassem, J., Jiang, Z., Karlsson, P., Morrow, M., Orecchia, R., Kent Osborne, C., Partridge, A.H., de la Peña, L., Pritchard, K.I., Rutgers, E.J.T., Sedlmayer, F., Semiglazov, V., Shao, Z.-M., Smith, I., Toi, M., Tutt, A., Viale, G., von Minckwitz, G., Watanabe, T., Whelan, T., Xu, B. Tailoring therapies-improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015 2015 Annals of Oncology

MAPLE Trial

Leary A, Evans A, Johnston SR, A'Hern R, Bliss JM, Sahoo R, Detre S, Haynes BP, Hills M, Harper-Wynne C, Bundred N, Coombes G, Smith I, Dowsett M. Antiproliferative Effect of Lapatinib in HER2-Positive and HER2-Negative/HER3-High Breast Cancer: Results of the Presurgical Randomized MAPLE Trial (CRUK E/06/039) Peer-reviewed Article: Clin Cancer Res 21(16):OF1-9

IMPORT Trial

Tsang Y, Ciurlionis L, Kirby A, Locke I, Venables K, Yarnold J, Titley J, Bliss J, Coles C, on behalf of the IMPORT Trial Management Group. Clinical impact of IMPORT HIGH trial (CRUK/06/003) on breast radiotherapy practices in the United Kingdom. Meeting Abstract: Br J Radiol 88(1056):20150453

A multicentre study of the evidence for customized margins in photon breast boost radiotherapy. Emma J Harris, Mukesh B Mukesh, Ellen M Donovan, Anna M Kirby, Joanne S Haviland, R A Jena, John Yarnold, Angela Baker, June Dean, Sally Eagle, Helen Mayles, Clare Griffin, Rosalind Perry, Andrew Poynter, Charlotte E Coles, Philip M Evans, and On behalf of the IMPORT high trialists BJR 89, June 2015

Clinical Impact of IMPORT HIGH trial (CRUK/06/003) on breast radiotherapy practices in the United Kingdom. Y Tsang, L Ciurlionis, A Kirby, I Locke, J Yarnold, J Titley, J Bliss, C Coles and on behalf of the IMPORT trial management group. BJR accepted for publication November 2015

START Trial

Yarnold J, Somaiah N, Bliss JM. Hypofractionated radiotherapy in early breast cancer: Clinical, dosimetric and radio-genomic issues. Meeting Abstract: The Breast 24(Suppl 2):S108-S13

POSH: Prospective Study of Outcomes of Sporadic versus Hereditary Breast Cancer

Eccles DM, Li N, Handwerker R, Maishman T, Copson ER, Durcan LT, Gerty SM, Jones L, Evans DG, Haywood L, Campbell I. Genetic testing in a cohort of young patients with HER2-amplified breast cancer. Ann Oncol. 2016 Mar;27(3):467-73. doi: 10.1093/annonc/mdv592. Epub 2015, Dec 17

Eccles BK, Copson ER, Cutress RI, Maishman T, Altman DG, Simmonds P, Gerty SM, Durcan L, Stanton L, Eccles DM; POSH Study Steering Group. Family history and outcome of young patients with breast cancer in the UK (POSH study). Br J Surg. 2015 Jul;102(8):924-35. doi: 10.1002/bjs.9816. Epub 2015, May 2

The LORIS trial

Francis A, Thomas J, Fallowfield L, Wallis M, Bartlett JM, Brookes C, Roberts T, Pirrie S, Gaunt C, Young J, Billingham L, Dodwell D, Hanby A, Pinder SE, Evans A, Reed M, Jenkins V, Matthews L, Wilcox M, Fairbrother P, Bowden S, Rea D. Addressing overtreatment of screen detected DCIS. Eur J Cancer. 2015 Nov;51(16):2296-303. doi: 10.1016/j.ejca.2015.07.017.

AZURE trial

Westbrook JA, Cairns DA, Peng J, Speirs V, Hanby AM, Holen I, Wood SL, Ottewell PD, Marshall H, Banks RE, Selby PJ, Coleman RE, Brown JE. CAPG and GIPC1: Breast Cancer Biomarkers for Bone Metastasis Development and Treatment. J Natl Cancer Inst. 2016 Jan 12;108(4). pii: djv360. doi: 10.1093/jnci/djv360. Print 2016 Apr. Erratum in: J Natl Cancer Inst. 2016 Apr;108(4). pii: djw017. doi: 10.1093/jnci/djw017. PubMed PMID: 26757732.

Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. *Early Breast Cancer Trialists' Collaborative Group (EBCTCG)* Lancet 2015; 386: 1353–61*

PathIES trial

Speirs V, Viale G, Mousa K, Palmieri C, Reed SN, Nicholas H, Cheang M, Jassem J, Lønning PE, Kalaitzaki E, van de Velde CJ, Rasmussen BB, Verhoeven DM, Shaaban AM, Bartlett JM, Bliss JM, Coombes RC; PathIES Sub-Committee. Prognostic and predictive value of ERβ1 and ERβ2 in the Intergroup Exemestane Study (IES)-first results from PathIES. Ann Oncol. 2015 Sep;26(9):1890-7. doi: 10.1093/annonc/mdv242. Epub 2015 May 22. PubMed PMID: 26002610

Phase II Randomized Preoperative Window-of-Opportunity Study of the PI3K Inhibitor Pictilisib Plus Anastrozole Compared With Anastrozole Alone in Patients With Estrogen Receptor–Positive Breast Cancer

Peter Schmid, Sarah E. Pinder, Duncan Wheatley, Jane Macaskill, Charles Zammit, Jennifer Hu, Robert Price, Nigel Bundred, Sirwan Hadad, Alice Shia, Shah-Jalal Sarker, Louise Lim, Patrycja Gazinska, Natalie Woodman, Darren Korbie,Matt Trau, PaulMainwaring, Steven Gendreau,Mark R. Lackner,MikaDerynck, Timothy R.Wilson, Hannah Butler, Gemma Earl, Peter Parker, Arnie Purushotham, and Alastair Thompson. Published Ahead of Print on March 14, 2016 as 10.1200/JCO.2015.63.9179.

Macroscopic handling and reporting of breast cancer specimens pre- and post-neoadjuvant chemotherapy treatment: review of pathological issues and suggested approaches

Pinder, S. E.Rakha, E. A., Purdie, C. A., Bartlett, J. M., Francis, A., Stein, R. C., Thompson, A. M., Shaaban, A. M. On behalf of the Translational Subgroup of the NCRI Breast Clinical Studies Group. Histopathology 2015: 67(3), p279-93

Availability of oestrogen receptor and HER2 status for the breast multidisciplinary meeting discussion; time to get it right

Adele Francis, John Bartlett, Dan Rea, Sarah E Pinder, Robert C Stein, Hilary Stobart, Colin A Purdie, , Emad Rakha, Alastair Thompson, Abeer M Shaaban. On behalf of the Translational Subgroup of the NCRI Breast Clinical Studies Group. *EJSO, in press* DOI: http://dx.doi.org/10.1016/j.ejso.2016.02.015

Overtreatment of Low-Grade Ductal Carcinoma In Situ

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ARTemis

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Factors Associated with Intentional and Unintentional Non-adherence to Adjuvant Endocrine Therapy Following Breast Cancer
Brett et al. European Journal of Cancer Care, 2016 (in press)

Helping Patients to Help Themselves Following Breast Cancer Treatment
Fenlon, D. Khambaita, P. Hunter, M. 2015. Clinical Oncology 27: 640-646

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Appendix 5

Major international presentations in the reporting year

POSH: Prospective Study of Outcomes of Sporadic versus Hereditary Breast Cancer
Eccles DM, Li N, Handwerker R, Maishman T, Copson ER, Durcan LT, Gerty SM, Jones L, Evans DG, Haywood L, Campbell I. Genetic testing in a cohort of young patients with HER2-amplified breast cancer. Ann Oncol. 2016 Mar;27(3):467-73. doi: 10.1093/annonc/mdv592. Epub 2015, Dec 17

Characterization of male breast cancer: First results of the EORTC10085 / TBCRC / BIG / NABCG International Male BC Program
Cardoso F, Bartlett J, Slaets L, van Deurzen C, van Leeuwen-Stok E, Porter P, Linderholm B, Hedenfalk I, Schröder C, Martens J, Bayani J, van Asperen C, Murray M, Hudis C, Middleton L, Vermeij J, Peeters S, Fraser J, Nowaczyk M, Rubio IT, Aebi S, Kelly C, Ruddy K, Winer E, Nisson C, Dal Lago L, Korde L, Benstead K, Van Den Weyngaert D, Bogler O, Goulioti T, Dif N, Messina C, Tryfonidis K, Bogaerts J, Giordano S. The 2014 San Antonio Breast Cancer Symposium (San Antonio, TX, December 9-13, 2014) *Cancer Research* May 2015;75(9_Supplement):S6-05

OPTIMA
Stein R, Marshall A, Hall P, Bartlett J, Rooshenas L, Campbell A, Cameron D, Rea D, MacPherson I, Earl H, Poole C, Francis A, Morgan A, Harmer V, Pinder S, Stallard N, Donovan J, Hulme C, McCabe C, Hughes-Davies L, Makris A, Dunn J. OPTIMA (Optimal Personalised Treatment of early breast cancer uslng Multi-parameter Analysis), a prospective trial to validate the predictive utility and cost-effectiveness of gene expression test-directed chemotherapy decisions. The 2015 San Antonio Breast Cancer Symposium (San Antonio, TX, December 8-12, 2015)

NEO-EXCEL: Neoadjuvant trial of pre-operative exemestane or letrozole +/- celecoxib in the treatment of ER positive postmenopaual early breast cancer; A prospective phase III multicentre double blind placebo randomised controlled trial
Adele Francis, Christopher Poole, Cassandra L. Brookes, Robert Stein, John M.S. Bartlett, Janet Dunn, Peter Canney, Richard Sutton, Raouf Daoud, Mike Hallissey, Raj Achuthan, Margaret Grant, Jaspreet Babrah, Simon Smith, Judith Fraser, Anil Desai, Muhamed Al Dubaisi, Ashraf Patel, James Bristol, Sankaran Chandrasekharan, Catherine Prest, Alan Jewkes, Daniel Rea. The 2015 San Antonio Breast Cancer Symposium (San Antonio, TX, December 8-12, 2015)

The UK EPHOS-B Trial
Nigel Bundred, David Cameron, Eleftheria Kalaitzaki, Rachael Morley, Angela Cramer, Mark Webster-Smith, Sankaran Narayanan, Murray Brunt, Kieran Horgan, Andrew Hanby, Jane Ooi, Anne Hong, Jay Naik, Abigail Evans, Abeer Shaaban and Judith Bliss. Effects of perioperative antiHER-2 lapatinib in early breast cancer - the UK EPHOS-B Trial (CRUK/08/002) Late breaking abstract presentation at EBCC, 09/03/2016, Amsterdam.

Partial breast radiotherapy for women with early breast cancer: first results of local recurrence data for IMPORT LOW
C Coles, R Agrawal, ML Ah-See, H Algurafi, A Alhasso, AM Brunt, C Chan, C Griffin, A Harnett, P Hopwood, A Kirby, E Sawyer, I Syndikus, J Titley, Y Tsang, D Wheatley, M Wilcox, J Yarnold, JM

Bliss and on behalf of the IMPORT TMG (CRUK/06/003). Late breaking abstract presentation at EBCC, 09/03/2016, Amsterdam.

Exploring adherence to adjuvant endocrine therapy (AET) following treatment for breast cancer
Brett, Jo, Watson, Eila, Boulton, Mary, Fenlon, Debbie, Hulbert Williams, Nick, Donnelly, Peter, Walter, Fiona, Lavary, Bernadette, Morgan, Adrienne and Morris, Carolyn. British Psychosocial Oncology Society 2016 Annual Conference

Invited Opening Address "Is it me or is it hot in here?"
Morgan, A. Breast Cancer Care Nurses Conference, 6 November 2015

Management of hot flushes in UK breast cancer patients: Comparing the clinician and patient perspective. NCRI Breast CSG Working Party on Symptom Management
Fenlon, D. Armes, J. Dunn, J. Filshie, Hunter, M. Ah-See, M.L. Morgan, A. Khambaita, P. Pennery, E. sassarini, J. Young, A. Fernandes, A. Noble, J. Stanway, S. Balmer, C. Lumsden, MA. Morris, C. Turner, L. European Menopause and Andropause Society Conference, Madrid 2015

The impact of hot flushes on women who have had breast cancer
Morgan and Fenlon. European Menopause and Andropause Society Conference, Madrid 2015

Current management of hot flushes after breast cancer
Ah--See, M.L. European Menopause and Andropause Society Conference, Madrid 2015

Non pharmacological management options for hot flushes after breast cancer
Hunter, M. European Menopause and Andropause Society Conference, Madrid 2015

Management of symptoms following breast cancer
Fenlon, D. Royal College of Radiologists, London