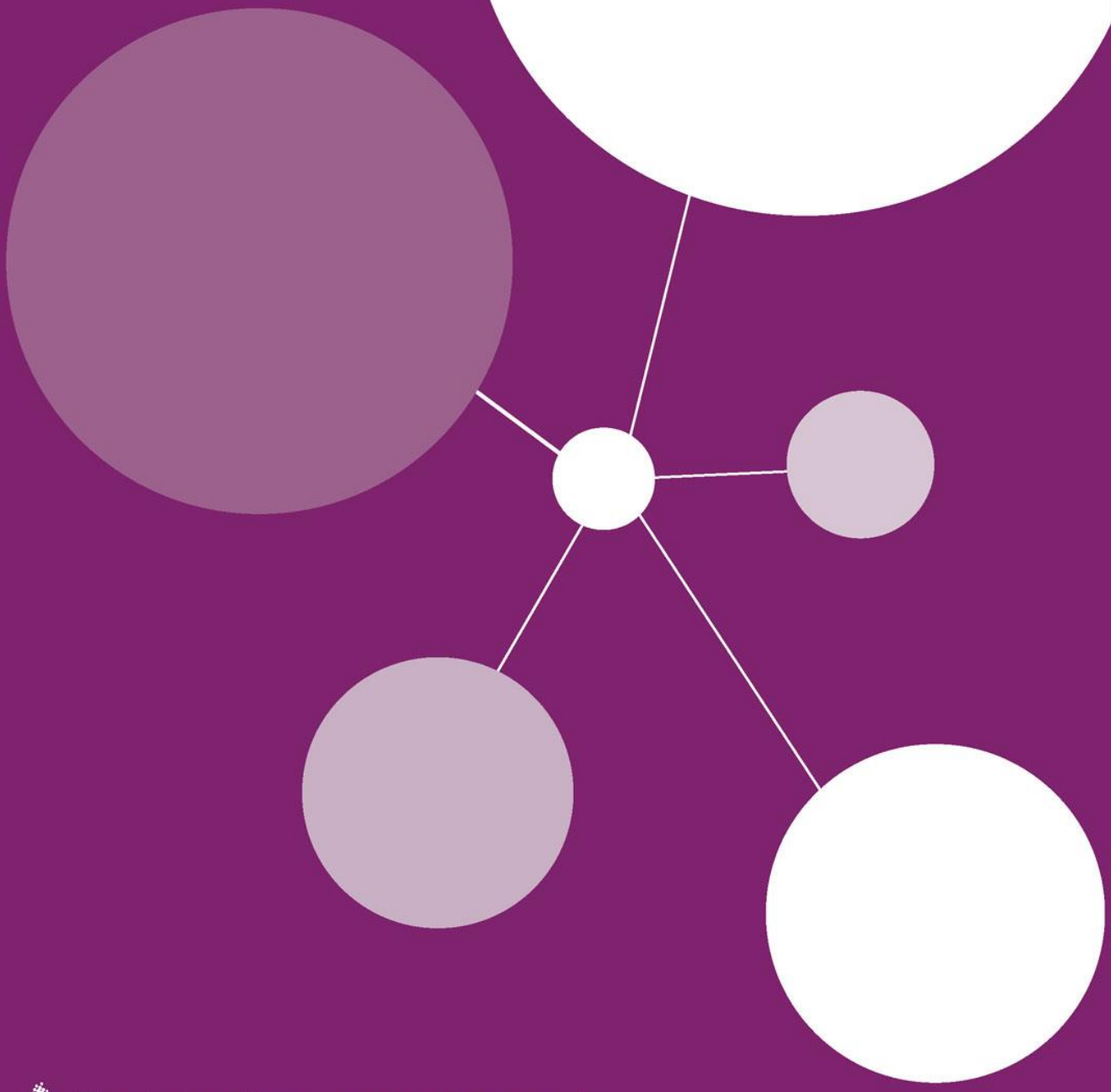
NCRI
National
Cancer
Research
Institute

NCRI Breast Cancer Clinical Studies Group

Annual Report 2016-17



Partners in cancer research

NCRI Breast Cancer CSG Annual Report 2016-17

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

The Breast Cancer CSG has continued with its primary function to develop and support recruitment to high quality clinical trials addressing clinically relevant issues. The portfolio continues to cover an extensive range of studies from screening, prevention, early and advanced disease incorporating surgery, radiotherapy and systemic treatment. The portfolio comprises a balance of complex and more straightforward pragmatic trials, allowing all breast units to contribute to the UK clinical trials programme.

The highlight output this year has been the publication of the practice changing IMPORT Low study of partial breast radiotherapy (Coles et al; Lancet Oncology). Other key outputs include the presentation of mature outcomes from the POSH study (Eccles et al; SABCS) and mature data from the ARTEMIS study (Earl et al; Lancet Oncology).

The OPTIMA trial has now opened and will determine the safely of targeting adjuvant chemotherapy to high risk cases defined by molecular profile. The plasmaMATCH study using circulating tumour DNA (ctDNA) to identify mutations suitable for targeted therapies has opened to recruitment The PHOENIX trial, using a window of opportunity after inadequate response to neoadjuvant chemotherapy, is now funded and will be opening to recruitment in the next reporting year. The CSG has made significant progress with the development of a proposal for a risk adapted screening trial incorporating family history lifestyle genomic profiling and breast density alongside tailored frequency and imaging modality.

The CSG has committed to build on the success of the surgical trainee collaborative by expanding this programme to incorporate medical oncology, clinical oncology, radiology and pathology trainees into a Pan Breast trainee collaborative. This will provide research opportunities for trainees to conduct research and gather accurate timely data on current practice to inform the design of new trials.

2. Structure of the Group

The Group structure has remained stable with the main CSG and three Subgroups mostly unchanged. Dr Charlotte Coles succeeds Professor Judith Bliss as Early Disease Subgroup Chair and Professor Carlo Palmieri succeeds Dr Alistair Ring as Advanced Disease Subgroup Chair. However, the process for developing new trials has been revised. New trial proposals will now be presented initially at the Breast Intergroup meetings where feedback will be provided. Detailed

aspects of promising proposals will then be supported as appropriate by the main CSG or relevant Subgroup. This structure will ensure there is wide dissemination of study proposals in development within the wider breast cancer research community. Collaboration of groups with common interests and similar proposals is strongly encouraged to maximise the pooling of expertise and to avoid duplication.

3. CSG & Subgroup strategies

Main CSG

The CSG has striven to maintain a balanced portfolio of internationally recognised, high quality clinical trials in an environment of increasingly complex subcategorisation of breast cancer. A broad range of trials are open to recruitment that require a variable level of technological coordination. On the high technology front, the plasmaMATCH study is now recruiting well and feeding into trials with for patients with defined druggable molecular targets. The PHOENIX window of opportunity study in poorly responding triple negative disease is funded and expected to open in the next reporting year. The cTRAC study, which will identify candidates with triple negative breast cancer for immunotherapy based on rising ctDNA titres, has been invited for full application to CRUK.

The Add Aspirin study and Mammo 50 studies are recruiting well and the PROSPECTS study will recruit 100,000 women invited for screening to conventional mammography vs tomosynthesis.

An area that has been a concern to the CSG is the comparatively small number of surgical studies and the incomplete engagement of the surgical community in participation. The CSG has worked with the Association of Breast Surgery (ABS) to formulate a national research strategy. A key aspect of this strategy is to include surgical research participation as a key performance indicator for breast surgery. Surgeons will be increasingly encouraged to take up PI roles in studies and a major expansion to the portfolio of surgically led clinical trials is planned. Progress has already been made with badging the PRIMETIME study: biomarker directed avoidance of radiotherapy as an ABS trial. The chief clinical co-ordinator of the study is a clinician scientist breast surgeon and surgeons are eligible to be PIs. Paradoxically, the breast surgical trainee collaborative has blossomed with the conduct iBra and MASDA studies. The CSG intends to build on this success with the formation of a trainee collaborative including pathology, radiology, medical and clinical oncology trainees.

This year we sadly report the death of Professor Adele Francis after a short illness. Professor Francis was a key member of the CSG and her pioneering research in the field of overtreatment was world leading. In her role as Royal College of Surgeons subspecialty lead for breast cancer research, she promoted the need to raise the profile of research within the surgical community and was the principal architect to formulating the current ABS research strategy. Her work in research engagement with patient advocates, surgical trainees and clinical nurse specialists was outstanding.

Translational & Imaging Subgroup (Chair, Dr Abeer Shaaban)

1. The Translational and Imaging Subgroup continued to review and provide feedback on submitted proposals with a translational component and Registration of Concept studies. The Subgroup members supported the set-up and delivery of high profile trials, presented their results in prestigious meetings and provided a healthy profile of publications (see

Appendix 4 for full list). The Subgroup is currently preparing a manuscript on the role of digital pathology in clinical trials with translational arm.

2. The imaging contribution of the Subgroup has been enhanced by the joining of two expert radiologists: Professors Iain Lyburn and Fiona Gilbert. They contributed to the MR Working Group of the British Society of Breast Radiologists (BSBR) to achieve harmonisation of MR imaging in the UK. Guidelines are being developed with the aim of harmonizing practice in an as practicably a way as possible so that uniformity may aid future collaborative research.
3. The current crises in diagnostic and academic pathology, recently highlighted by CRUK, hinders the pathologists' support and contribution to translational trials. The Subgroup has worked in partnership with the CM-Path initiative mapping the number and distribution of pathologists across different groups and subgroups and identified gap areas.
4. The Subgroup is addressing the issue of lack of Ki67 immunohistochemical standardisation. We are currently seeking funding to support the laboratory part of the programme.

Early Disease Subgroup (UK Breast Intergroup) (Chairs, Professor Judith Bliss and Dr Charlotte Coles)

The following specific examples of the Subgroup's achievements are listed under its three strategic objectives:

1. Portfolio development
    - Systemic therapy/translational (key research question identified) - understanding biological mechanisms of endocrine resistance. The Subgroup has contributed significantly to the trial design for POETIC 2 and this will be submitted for a full CRUK grant application in June.
    - Local therapy (key research question identified) – axillary treatment following neo-adjuvant systemic therapy. The Subgroup is assisting a surgical CI to build a strong national multidisciplinary research team working with the Imaging and Translational Subgroup to develop national guidelines for imaging in this setting.
2. Collaborative approach to trial development
    - Engage with the breast cancer research community – the Subgroup has given written feedback for nine trial proposals in the last year as an integral part of the UK Breast Intergroup meetings (UKBI). Development of the HER2+ platform trial proposal is ongoing and is complex and ambitious. Considerable progress was made via a dedicated half day meeting with both Early Disease Subgroup members and CSG members with particular expertise in this area and the design is in its final stages.
    - Promote PPI: secured PPI input for POETIC 2 through UKBI meetings and NCRI Dragon's Den - addressing perceived delay in surgery. Subgroup PPI is also facilitating a patient decisional conflict study within PRIMETIME.
    - Engage with Association of Breast Surgery and CTRad – PRIMETIME has been badged as surgical trial and Charlotte Coles chaired a UK breast radiotherapy proton research day on behalf of CTRad, with Subgroup representation
3. Improving trials methodology and clinical utility
    - New predictors of risk and outcome – OPTIMA (full study) and PRIMETIME are both open and will test the clinical utility of PAM50 and IHC4-C respectively in the

context of de-escalation of therapy.

- Collaborate NIHR CRN Breast subspecialty group – a trainee research initiative has been established, which will include a national meeting bringing together cross-specialty oncology trainees with mentors to develop new simple, pragmatic research proposals.

Advanced Disease Subgroup (Chairs, Dr Alastair Ring and 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 Subgroup 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 Subgroup.

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 Subgroup 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 both on phase and disease). There are currently 20 trials open, in addition to five multi-CSG Phase I studies and seven in set-up. The portfolio has a 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.

Symptom Management Subgroup (Co-Chair, Professor Debbie Fenlon, Dr Adrienne Morgan)

This Subgroup continues to promote awareness of research needs and to support the development of research into ongoing symptoms after breast cancer, particularly hot flushes and night sweats. We have now moved to incorporate other symptoms into the portfolio and are focusing on promoting research into sexual difficulties. Two national surveys will be conducted this year and will be presented in a symposium at the European Menopause and Andropause Society meeting. We have identified a wide range of scientists working in this area and influenced and stimulated new directions in research by bringing them together in this national forum. 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.

A series of new studies have been funded in the reporting year including one preclinical study and seven clinical studies with a wide range of approaches to tackling our understanding and ability to record and alleviate side effects of breast cancer treatments.

4. Task groups/Working parties

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

5. Patient recruitment summary for last 5 years

In the Breast Cancer CSG portfolio, 36 no. of trials closed to recruitment and 41 opened.

While there is a reasonable balance of studies opening and closing, there remains a trend for new studies to be smaller and focused on specific breast cancer subgroups but to some extent offset by the PROSPECTS tomosynthesis trial which will include very large numbers of women invited for screening (100,000).

Table 1 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
2016/2017	2882	7744	1300	5212	2.65	10.64

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

Links to other groups are as follows:

- The CSG Chair is a member of the Breast International Group (BIG).
- The Group is represented on CTRad by Charlotte Coles and the SPED Advisory Group by Cliona Kirwan.
- Links with the Supportive & Palliative Care and Primary Care CSGs are through nominated CSG members (Professors Palmieri and Wardley).
- A half day breast screening breakout session will be held at the SPED Genomic Risk Stratification Workshop on 15 May 2017.
- The Symptom Management Subgroup has formal links with the Psychosocial Oncology & Survivorship (POS) CSG (the Chair is a co-opted member) and the Supportive and Palliative Care CSG with Lesley Turner as a member of both.

7. 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**
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 (Feasibility Study)	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 HER2-positive early breast cancer can be identified	Full (Feasibility Study)	Dr Adele Francis & Dr Daniel Rea	Endorsed

by multiple Ultrasound Scan (USS)-directed tumour-bed biopsies? All patients will undergo surgery.			
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 (Feasibility Study)	Professor Carlo Palmieri	Not endorsed
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 (Feasibility Study)	Professor Andrew Tutt and Professor Judith Bliss	Not funded (due to budget constraints)
ImproveMet: Liquid biopsies to improve metastatic breast cancer Outcomes	Full (Feasibility Study)	Professor Carlos Caldas, Dr Nick Turner and Dr Richard Baird	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	Full (Feasibility Study)	Dr Mary O'Brien	Not funded
November 2016			
POETIC-2: An innovative umbrella trial aiming to match molecular signatures with targeted agents against endocrine resistance in early breast cancer	EMPA Outline	Professor Judith Bliss	Invited to full
Feasibility Study of Monotherapy with Disulfiram in Patients with known BRCA-defective Breast and Ovarian Tumours	Full (Feasibility Study)	Dr Shibani Nicum	Withdrawn
TransPOSNOC - individualised approach to treatment planning	Sample Collection	Mr Amit Goyal	Not Supported
PEARL Study: A window of opportunity study to assess the biological effects of progesterone in premenopausal ER-positive, PgR-positive early breast cancer	Full (Feasibility Study)	Professor Carlo Palmieri	Supported

8. Collaborative partnership studies with industry

There is extensive collaboration with Industry, predominantly at a trial specific level, and the Astra Zeneca alliance and Pfizer alliance have facilitated the development of several investigator initiated studies.

9. Impact of CSG activities

The CSG continues to impact on clinical practice with extended adjuvant endocrine therapy increasingly being adopted as a result of studies, e.g. the aTTom study demonstrating the

advantage of extended adjuvant tamoxifen. The results of the SOFT and TEXT studies have clarified the role of ovarian suppression, particularly in premenopausal women at high risk of recurrence. Axillary radiotherapy is becoming increasingly accepted and offered as an alternative to surgical clearance of the involved axilla based on the results of the AMAROS trial. This year has been most notable for the increased use of adjuvant bisphosphonates in postmenopausal women with early breast cancer based on the Oxford metanalysis of adjuvant bisphosphonate studies heavily influenced by the data from the UK AZURE trial. This is not yet universally adopted across the UK as local commissioning of adjuvant bisphosphonates is inconsistent but access has dramatically improved.

The CSG has successfully represented the case for access to neoadjuvant Pertuzumab to NICE. A positive NICE appraisal recommended use of up to four cycles of pertuzumab in combination with chemotherapy and trastuzumab. The Group has nominated clinical experts to multiple ongoing NICE appraisals in progress.

The CSG continues to provide assessment to the CRUK clinical trials and epidemiology population committee. The Group has provided support to the Industry alliance partnerships and Breast Cancer Now clinical trial applications, including the Pfizer initiative with Breast Cancer Now with several successful applications funded.

10. Consumer involvement

This year we say goodbye with grateful thanks to one of our consumer members, Katrina Randle, who has been very actively involved in many aspects of work of the main CSG and Subgroups over her five years of service. She has also contributed to a number of trials in various stages of development and will be continuing with this work in the future.

We also want to pay tribute to Professor Adele Francis who sadly passed away this year. She did so much to promote good public and patient involvement and to encourage and work with patient advocates.

We warmly welcome a new consumer member from Edinburgh, Lesley Stephen, who comes to join Hilary Stobart on the main CSG. She has experience of studies and treatment in metastatic breast cancer and has also campaigned for better access to drug treatments.

The breast research community values consumer involvement at all levels of research design and delivery and we have additional consumers actively involved in all of the CSG Subgroups, including Mairead MacKenzie, Elizabeth Benns, Lesley Turner, who also provides links to the Supportive and Palliative Care Subgroup, and Dr Adrienne Morgan. Working and communicating with a network of consumers, especially from Independent Cancer Patients' Voice (ICPV), assists all the NCRI consumers in delivering the level of involvement needed.

In addition, strong consumer representation continues to be a key driving force behind the Symptom Management Subgroup, which was initiated and is co-chaired by a consumer member (Dr Adrienne Morgan), through individual membership, ICPV and Breast Cancer Care as co-opted members. Breast Cancer Now also provide secretariat support and facilities for meetings including refreshments.

Our consumer members have contributed to many activities over the last year, some funded by NCRI but many by other organisations. Some highlights include:

- Being members, and sometimes co-applicants, of TMG/TSG/protocol working groups including: C-TRAK, REQUITE, PRIMETIME, UNIRAD, OPTIMA, OPTIMAM2, VOXTOX, 100,000 Genome Project – Breast GeCIP, PIONEER, MENOS4, Add Aspirin and ROSCO.
- NIHR RFPB East of England Funding Board member.
- Working with and raising the profile of the work of the NIHR Cancer and Nutrition Collaboration.
- Contributing to one of the successful CRUK Grand Challenge teams. The international PRECISION team aims to understand which women with DCIS will develop breast cancer.
- UK Therapeutic Cancer Prevention Network Conference (UKTCPN/ECMC) – "Patient and Public Involvement in Cancer Prevention" - July 2016.
- UK representative at the Novartis Global Advanced Breast Cancer Patient Advocate Advisory Board in Madrid - Oct 2016.
- Plenary meeting of European Initiative on Breast Cancer - Nov 2016.
- Gave the patient perspective at the West Midlands NHS Genomic Medicine Centre Meeting "The Future of Cancer Treatment: Can genetic science benefit patients?" - March 2017.

11. Open meetings/annual trials days/strategy days

The NCRI National Breast Trials Meeting held at the Royal College of Surgeons meeting was fully subscribed. This year particular the focus was on neoadjuvant treatments and novel radiotherapy concepts. The programme was modified to accommodate a tribute to Professor Francis from the CSG and ABS and ABS research committee chairs.

A one day meeting of CSG members and subgroup chairs with the LCRN Breast Subspecialty Leads was held in April. This meeting facilitated a dialogue and explored solutions to shared issues and to further develop strategy. The trainee collaborative expansion was a key output from this meeting as was the formation of a group under the leadership of Professor Holcombe to deliver well executed evaluation studies of new surgical technologies and devised in onco-plastic surgery.

12. Priorities and challenges for the forthcoming year

Priorities

1. Maintain the momentum in developing surgical trials and fostering a wider surgical research culture.
2. To progress the HER-2 platform trial from concept to funding proposal.
3. To progress the proposal for a risk adapted breast screening trial from concept to funding proposal.

Challenges

1. Recover levels of recruitment to clinical trials across the entire portfolio.
2. To ensure trials are internationally competitive without being too complex for an average NHS breast unit to contribute.
3. To ensure the portfolio is sufficiently broad that a clinical trial is available for most patients with breast cancer.

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 CSG

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

* denotes trainee member

Membership of the Subgroups

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
Professor Alastair Thompson**	Surgeon	USA

Advanced Disease Subgroup		
Name	**Specialism**	**Location**
Dr Sheeba Irshad Kanth*	Clinical Lecturer	London
Dr Mark Beresford	Clinical Oncologist	Bristol
Dr Adrian Harnett	Clinical Oncologist	Norfolk
Dr Andreas Makris	Clinical Oncologist	Middlesex
Dr Duncan Wheatley	Clinical Oncologist	Cornwall
Ms Elizabeth Benns	Consumer	Letchworth
Ms Mairead MacKenzie	Consumer	?
Ms Lesley Stephen	Consumer	Edinburgh
Dr Anne Armstrong	Medical Oncologist	Manchester
Professor Rob Coleman	Medical Oncologist	Sheffield
Professor Carlo Palmieri (Chair)	Medical Oncologist	Liverpool
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 Jacqueline Filshie	Anaesthetist	London
Professor Debbie Fenlon (Co-Chair)	Professor of Nursing	Swansea
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 Melanie Flint	Senior Lecturer in Immunopharmacology	Brighton
Professor Janet Dunn	Statistician	Warwick

Early Disease Subgroup (UK Breast Intergroup)		
Name	**Specialism**	**Location**
Dr Charlotte Coles	Clinical Oncologist	Cambridge
Professor Andrew Tutt	Clinical Oncologist	London
Mrs Hilary Stobart	Consumer	Nottingham
Dr Andrew Wardley	Medical Oncologist	Manchester
Dr Deborah Fenlon	Senior Research Fellow	Southampton
Mr Peter Barry	Surgeon	London
Dr Cliona Kirwan	Surgeon	Manchester
Mrs Jagdeep Singh*	Surgeon	Oxfordshire
Mr Anthony Skene	Surgeon	Bournemouth

*denotes trainee member
**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Overall strategy aim

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

Aims

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

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 SP	Ongoing
1b. Portfolio development imaging	Ensure /advise on appropriate protocols for imaging in portfolio studies identify opportunities for assessment of novel imaging research	IL/FG	PROSPECTS TRIAL to open 2017/18 Ongoing
1c. Portfolio development (systemic therapies)	To promote concept of trial platforms / multi stage trials to test modulation of treatment according to risk & likely benefit To promote use of informative experimental models including focussing novel treatment evaluation to those with residual – assessable - disease • post neoadjuvant – macroscopic / microscopic (ctDNA) • adjuvant – microscopic (ctDNA) • window of opportunity – biological endpoints • Metastatic disease – plasma detectable ctDNA; disease accessible for biopsy		Plasma Match recruiting 2017 cTRAC full application 2017 Phoenix First patient in 2018

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

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

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

C – Early Disease Subgroup Strategy

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

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

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

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

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D – Advanced Disease Subgroup Strategy

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

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

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

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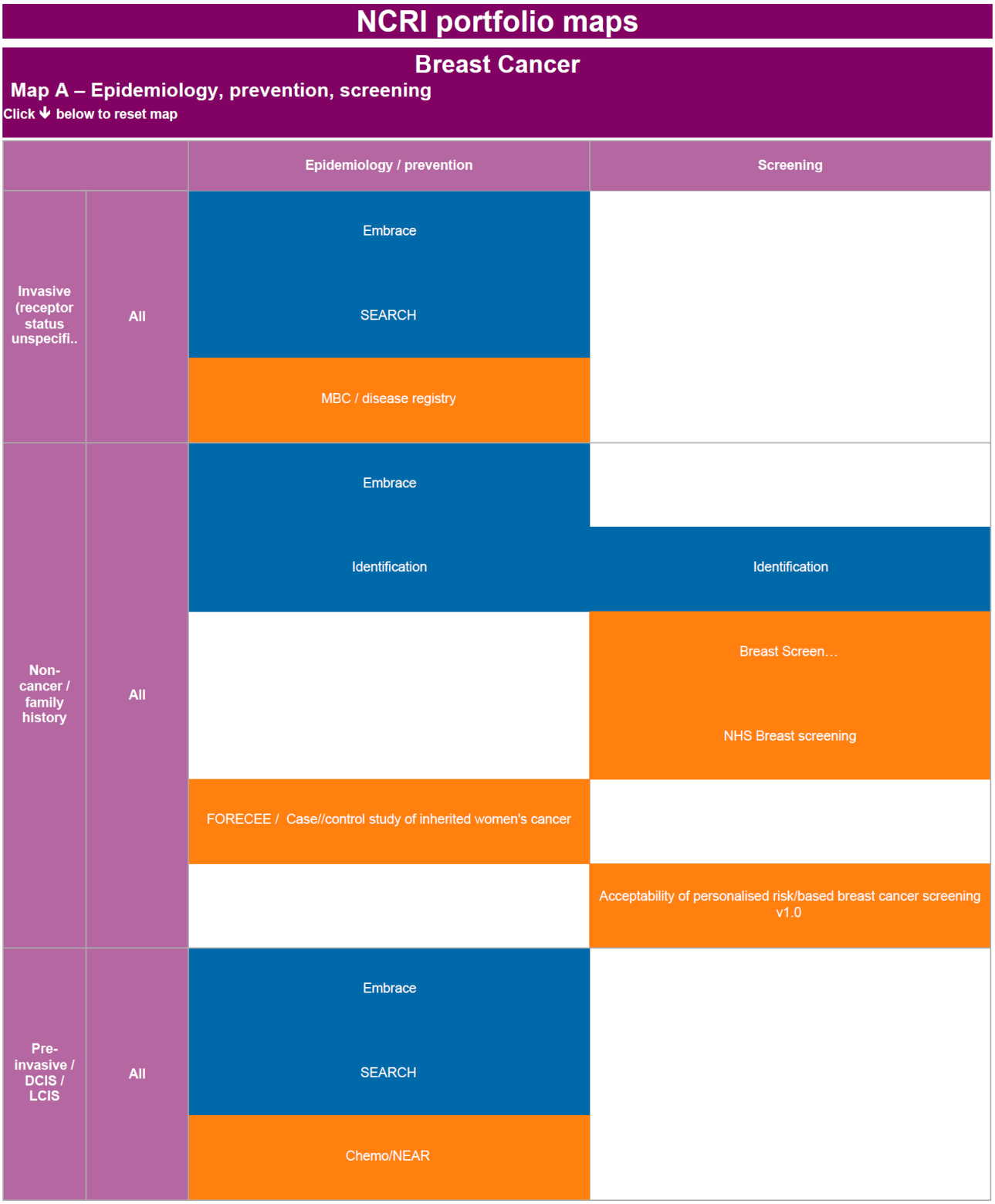
E – Symptom Management Subgroup Strategy

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

Breast Cancer

Map B – Diagnosis, Imaging

Click ↓ below to reset map

		Diagnosis / imaging
ER- HER2- (includes triple neg..	All	
ER- HER2+	All	
ER+ HER2-	All	
ER+ HER2+	All	
Invasive (receptor status unspecifi..	All	
		TPI - in vivo study in breast cancer and sentinel lymph nodes
		GE/137 fluor imaging
		CONTEND Study
		CIST full study
		CHERNAC
		NICaS device in Herceptin patients / PHASE I
		Outcomes following Cerenkov Luminescence
Non-cancer / family history	All	MAMMO /50
		SPECIALS
		GeMCaS
		MR/BTC
Pre-invasive / DCIS / LCIS	All	FABB study
		FAB/IE
		POPPET
		plasmaMATCH
		PROSPECTS
		SMART STUDY : Version 6 dated 27th January 2016

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

Open Multi CSG
Open Single CSG
Null
In Setup, HRA Ap..
In Setup, Waiting ..
In Setup, Waiting ..
Suspended Single..

NCRI portfolio maps

Breast Cancer

Map C – Neoadjuvant, perioperative, surgery

Click ↓ below to reset map

		Neoadjuvant	Perioperative	Surgery
ER-HER2- (includes triple neg..	All	MK-3475-522		
ER-HER2+	All	EMERALD		
ER+ HER2+	All	PALLET		
Invasive (receptor status unspecifi..	All			ExAblate
				POSNOC
		neoadj chemo		
		RIO		
		ROSCO		
				ARP
				Intraop' Marginprobe
			TIP Study	
		Baronet		
Pre-invasive / dcis / lcis	Null	PARTNER		
	All	OPTIMA		
				LORIS
				Magnetic Seed localisation of breast cancers Version 1
				BLAST/ Novilase Breast Laser Ablation vs Surgery Trial
		TARA/Prev		

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

Open Multi CSG
In Setup, Waiting ..
Open Single CSG

NCRI portfolio maps

Breast Cancer

Map D – Adjuvant

Click ↓ below to reset map

		Adjuvant - radiotherapy	Adjuvant – systemic treatment
ER- HER2- (includes triple negative)	All		OLYMPIA
		PALbociclib CoLlaborative Adjuvant Study	
			MK-3475 + Chemotherapy as Neoadjuvant and Adjuvant therapy for TNBC
ER+ HER2-	All		SOLAR/1 CompLEEment/1
ER+ HER2+	All		UNIRAD
Invasive (receptor status unspecifi..	All		
			LATTE
		FAST/Forward POSNOC CORE Trial	
		SuPPORT 4 All Clinical Feasibility Trial	
Pre-invasive / dcis / lcis	All	Add/Aspirin	

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

Open Multi CSG
Open Single CSG
Null
In Setup, Waiting ..

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	BMN 673 iparib (ABT-888) in Metastatic or LLA BRCA ENDEAR	BravO BMN 673	AT13148 Phase I BravO
ER+	All	FAKTION NCRN / 3156 POSEIDON ombination with fulvestrant in subjects with E	NCRN / 3156 POSEIDON GDC/0810 versus fulvestrant	AT13148 Phase I
ER+ HER2-	All	CARBON in the Treatment and Evaluation of Metastati I3Y-MC-JPCF Estrogen Receptor Positive Breast Cancer		
HER2-	All	BLUEBELL NELOPE/B / Protocol D Version 9 (09/FEB/20	KATE/2	AT13148 Phase I NALA
HER2+/ other	All	NCRN / 3156 NCRN / 3159 CONCEPT FURVA, Version DC-0077 for PIK3CA-mutant solid tumours / b	FGFR Study BravO CiPHER NCRN / 3156 NCRN / 3159 Margetux + Chemo vs Trastuzumab	AT13148 Phase I FGFR Study BravO CiPHER
Triple negative	All	NCRN628 / TNACITY CheckMate032 MEDI4736 PAKT ANTI/PD/L1 Ab+// NAB PACLIT Pembrolizumab METRIC MK/3475 in TNBC Study of Pembrolizumab + Chemotherapy in mbrolizumab in Patients with Previously Treat dy for triple negatve breast cancer patients w and Eribulin in patients with advanced breas IMpassion 131		AT13148 Phase I

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

Open Multi CSG
Open Single CSG
In Setup, HRA Ap..
In Setup, Waiting ..
In Setup, Waiting ..
Suspended Single..

NCRI portfolio maps

Breast Cancer

Map F – Supportive care

Click ↓ below to reset map

		Supportive care/late effects/end of life care
Lifestyle interventions, die..	All	PLACE
		B/AHEAD3
		FOAM Trial
		HORIZONS
Psychological analy..	All	
Psychotherapy	All	
		MENOS 4
Research method validation	All	
		4Ps Study
		Update of EORTC BR23 study: Phases I-III
Side effects management and ..	All	
		CCRN 2949 (Breast reconstruction)
		LOTUS
		ACUFOCIN
		eSMART: Randomi
		PROSPER
		ACTIVE
		Observational study exploring treatment for women with arm lymphoedema.
		3D scanning of lymphoedema arms
		Psychoeducational intervention for women prescribed tamoxifen
Treatment choice	All	Bridging the Age Gap
		A Multi/centred/study of the effectiveness of PEGASUS
		Nektar214
		Proxy decision making for older women with breast cancer
Treatment management	All	CAVA
		use of Seri

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

Open Multi CSG
Open Single CSG
Null
In Setup, HRA Ap..
In Setup, Waiting ..

NCRI portfolio maps

Breast Cancer

Map G – Translational

Click ↓ below to reset map

		Translational
ER-HER2+	All	Genome Profiling in ER Negative Breast Cancer
ER-HER2+ (includes triple negative)	All	Genome Profiling in ER Negative Breast Cancer
		TNBC in D&G
ER+ HER2+	All	IBIS 3 Feasibility version 1.0
Invasive (receptor status unspecifi..	All	RAPPER
		DETECT
		CHAMPion
		CR UK Stratifie
		VERB Study
		Cubbs
		BC Subtypes
		Lymphocyte prod.
		REQUITE
		pericytes in BC
		AURORA
		REVEAL version 1
		PRIMETIME
Non-cancer / family history	All	SPECIALS
		The BeGIN study
		Anti/Progestin Prev.
		Body Composition In Breast Cancer
		RTGene
		Personalised Breast Cancer Program
		Tissue Stresses of Cancer
Pre-invasive / DCIS / LCIS	All	
		RAPPER
		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

Open Multi CSG | Null | In Setup, Waiting ..
Open Single CSG | In Setup, HRA Ap.. | Suspended Single..

Appendix 4

Publications in the reporting year

Study	Reference
AZURE	Westbrook JA, Cairns DA, Peng J, Speirs V, Hanby AM, Holen I, Wood SL, Ottewell P, 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
	Kroep JR, Charehbili A, Coleman RE, Aft RL, Hasegawa Y,Winter MC, Weilbaecher K, Akazawa K, Hinsley S, Putter H, Liefers GJ, Nortier JWR, Kohno N. Effects of neoadjuvant chemotherapy with or without zoledronic acid on pathological response: a meta-analysis of randomized trials Eur J Cancer. 2016 Feb;54:57-63.
FAB-B	Azad GK, Cook GJ. Multi-technique imaging of bone metastases: spotlight on PET-CT. Clin Radiol. 2016;71:620-31.
	Cook GJ, Azad GK, Goh V. Imaging Bone Metastases in Breast Cancer: Staging and Response Assessment. J Nucl Med. 2016;57 Suppl 1:27S-33S.
	Azad GK, Taylor B, Rubello D, Colletti PM, Goh V, Cook GJ. Molecular and Functional Imaging of Bone Metastases in Breast and Prostate Cancers: An Overview. Clin Nucl Med. 2016;41:e44-50.
FAST-FORWARD	Brunt AM, Wheatley D, Yarnold J, Somaiah N, Kelly S, Harnett A, Coles C, Goodman A, Bahl A, Churn M, Zotova R, Sydenham M, Griffin C, Morden J Bliss J (2016). Acute skin toxicity associated with a 1-week schedule of whole breast radiotherapy compared with a standard 3 week-regimen delivered in the UK FAST-Forward Trial. Peer-reviewed Article: Radiother Oncol 120(1):114-118 doi.org/10.1016/j.radonc.2016.02.027
IBIS II	Forbes JF, Sestak I, Howell A, Bonanni B, Bundred N, Levy C, von Minckwitz G, Eiermann W, Neven P, Stierer M, Holcombe C, Coleman RE, Jones L, Ellis I, Cuzick J on behalf of the IBIS Investigators. Anastrazole versus tamoxifen for the prevention of locoregional and contralateral breast cancer in postmenopuasla women with locally excised ductal carcinoma in situ (IBIS-II): a double blind randomized controlled trial. Lancet 2016 Feb 27;387(10021):866-73
POETIC Trial	Gellert P, Segal CV, Gao Q, Lopez-Knowles E, Martin LA, Dodson A, Li T, Miller CA, Lu C, Mardis ER, Gillman A, Morden J, Graf M, Sidhu K, Evans A, Shere M, Holcombe C, McIntosh SA, Bundred N, Skene A, Maxwell W, Robertson J, Bliss J, Smith I, Dowsett M, Poetic Trial Management Group Trialists

	(2016). Impact of mutational profiles on response of primary oestrogen receptor-positive breast cancers to oestrogen deprivation. Peer-reviewed Article: Nat Commun 7:1-11 doi.org 10.1038/ncomms13294
	López-Knowles E, Gao Q, Cheang MCU, Morden J, Parker J, Martin L-A, Pinhel I, McNeill F, Hills M, Detre S, Afentakis M, Zabaglo L, Dodson A, Skene A, Holcombe C, Robertson J, Smith I, Bliss J, Dowsett M (2016). Heterogeneity in global gene expression profiles between biopsy specimens taken peri-surgically from primary ER-positive breast carcinomas. Peer-reviewed Article: Breast Cancer Res 18(1):1-10 doi.org/10.1186/s13058-016-0696-2
POSH:	Prospective Study of Outcomes of Sporadic versus Hereditary Breast Cancer. T. Maishman*1, R. I. Cutress*2, A. Hernandez1, S. Gerty1, E. R. Copson2, L. Durcan1, and D. M. Eccles1. Local-recurrence and breast oncological surgery in young women with breast cancer; the POSH study. Annals of Surgery 2016 (in press) doi: 10.1097/SLA.0000000000001930
PRIMETIME	Kirwan CC, Coles CE, Bliss J, Kirwan C, Kilburn L, Fox L, Cheang M, Griffin C, Francis A, Kirby A, Ah-See M, Sharma R, Mukesh M, Twyman N, Loane J, Dodson A, Provenzano E, Kunkler I, Yarnold J, Pharoah P, Caldas C, Stobart H, Turner L, Megias D, Bliss J, Coles CE (2016). It's PRIMETIME. Postoperative avoidance of radiotherapy: biomarker selection of women at very low risk of local recurrence. Peer-reviewed Article: Clin Oncol. 2016;28(9):594-6 doi.org/10.1016/j.clon.2016.06.007
QUEST	Bidad N, MacDonald L, Winters Z, Edwards S, Emson M, Bliss J, Griffin C, Horne R (2016). How informed is declared altruism in clinical trials? A qualitative interview study of patient decision-making about the QUEST trials (quality of life after mastectomy and breast reconstruction). Peer-reviewed Article: Trials 17(1) 1-10 doi.org/10.1186/s13063-016-1550-7
START	Haviland JS, Hopwood P, Mills J, Sydenham M, Bliss J, Yarnold JR, Start Trialists' Group (2016). Do patient-reported outcome measures agree with clinical and photographic assessments of normal tissue effects after breast radiotherapy? The experience of the standardisation of breast radiotherapy (START) trials in early breast cancer. Peer-reviewed Article: Clin Oncol (R Coll Radiol) 28(6):345-53 doi.org/10.1016/j.clon.2016.01.011
	Haviland J, Bentzen S, Bliss J, Yarnold J (2016). Prolongation of overall treatment time as a cause of treatment failure in early breast cancer: an analysis of the UK START (Standardisation of Breast Radiotherapy) trials of

	fractionation. Peer-reviewed Article: Radiother Oncol 121(3):420-423 doi.org/10.1016/j.radonc.2016.08.027
SOFEA	Fribbens C, O'Leary B, Kilburn L, Hrebien S, Garcia-Murillas I, Beaney M, Cristofanilli M, Andre F, Loi S, Loibl S, Jiang J, Bartlett CH, Koehler M, Dowsett M, Bliss J, Johnston SR, Turner NC (2016). Plasma ESR1 mutations and the treatment of estrogen receptor-positive advanced breast cancer. Peer-reviewed Article: J Clin Oncol 34(25):2961-8 doi.org/10.1200/JCO.2016.67.306
YoDA BRCA	FOSTER, C., RECIO-SAUCEDO, A., GRIMMETT, C., CUTRESS, R., ECCLES, D., ARMSTRONG, A., GERTY, S., TURNER, L., MASON, S., COPSON, E., ECCLES, B., EVANS, G. & AHMED, M. 2015. Webbased decision aids to support young women with breast cancer. Psycho-Oncology, 24, 4-5.
	GRIMMETT, C., BROOKS, C., RECIO-SAUCEDO, A., CUTRESS, R., COPSON, E., EVANS, G., GERTY, S., ARMSTRONG, A., TURNER, L., MASON, S., AHMED, M., ECCLES, B., ECCLES, D. & FOSTER, C. 2016. YoDA BRCA: views and experiences around genetic testing for young women with breast cancer: developing a decision aid. Psycho-Oncology, 25, 10-11.
	GRIMMETT, C., PICKETT, K., SHEPHERD, J., WELCH, K., ECIO-SAUCEDO, A., STREIT, E., SEERS, H., TURNER, L ARMSTRONG, A., CUTRESS, R I., EVANS, G D., COPSON, E., MEISER, B., ECCLES, D & FOSTER, C. Systematic review of the empirical investigation of resources to support decision making regarding BRCA1 and BRCA2 genetic testing at the time of breast cancer diagnosis. Under review Journal of Genetic Counselling April 2016.
New pathways in the treatment for menopausal hot flushes	Sassarini, Jenifer, and Richard A. Anderson. The Lancet (2017).
Neurokinin 3 receptor antagonism as a novel treatment for menopausal hot flushes	Prague, Julia K., Rachel E. Roberts, Alexander N. Comninos, Sophie Clarke, Channa N. Jayasena, Zachary Nash, Chedie Doyle et al. "Neurokinin 3 receptor antagonism as a novel treatment for menopausal hot flushes: a phase 2, randomised, double-blind, placebo-controlled trial." The Lancet(2017).
Factors related to the experience of menopausal symptoms in women prescribed tamoxifen	Moon, Zoe, Myra S. Hunter, Rona Moss-Morris, and Lyndsay Dawn Hughes. Journal of Psychosomatic Obstetrics & Gynecology (2016): 1-10.
Patient preference and adherence 11	Moon, Zoe, Rona Moss-Morris, Myra S. Hunter, Sophie Carlisle, and Lyndsay D. Hughes. "Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: a systematic review." (2017): 305.
MANAGING MENOPAUSE IN	Fenlon, Deborah. ASIA-PACIFIC JOURNAL OF CLINICAL

BREAST CANCER	ONCOLOGY. Vol. 12. 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY-BLACKWELL, 2016.
Exploring adherence to adjuvant endocrine therapy (AET) following treatment for breast cancer	Brett, Jo, et al. Psycho-Oncology 25 (2016): 6.
Factors associated with intentional and unintentional non-adherence to adjuvant endocrine therapy following breast cancer	Brett, Jo, D. Fenlon, Mary Boulton, Nicholas J. Hulbert-Williams, F. M. Walter, Peter Donnelly, Bernadette Lavery, Adrienne Morgan, Carolyn Morris, and Eila Watson. European Journal of Cancer Care (2016).
Roll the dice and it's a toss-up between quality of life and life	Brett, Jo, Debbie Fenlon, Mary Boulton, Nick Hulbert-Williams, Fiona Walter, Peter Donnelly, Nicola Stoner, Adrienne Morgan, and Carolyn Morris. "" Roll the dice and it's a toss-up between quality of life and life": a mixed methods study exploring adherence to adjuvant endocrine therapy and interventions to improve adherence." In PSYCHO-ONCOLOGY, vol. 25, no. SP. S 3, pp. 124-124. 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY-BLACKWELL, 2016.

Appendix 5

Major international presentations in the reporting year

Study	Conference details
IMPORT Low	Coles C, Griffin C, Kirby A, Titley J, Agrawal R, Alhasso A, Bhattacharya I, Brunt AM, Ciurlionis L, Chan C, Donovan E, Emson M, Harnett A, Haviland J, Hopwood P, Jefford M, Kaggwa R, Sawyer E, Syndikus I, Tsang Y, Wheatley D, Wilcox M, Yarnold J, Bliss J (2017). Partial breast radiotherapy after breast conservation surgery for early breast cancer: 5 year outcomes from the IMPORT LOW (CRUK/06/003) phase III randomised controlled trial. Meeting Abstract: ESTRO 2017 5-9 May 2017, Vienna
POETIC Trial	Tutt A, Cheang M, Kilburn L, Tovey H, Gillett C, Pinder S, Lanchbury J, Abraham J, Barret S, Barrett-Lee P, Chan S, Gazinska P, Grigoriadis A, Kernaghan S, Hoadley K, Gutin A, Harper-Wynne C, Hatton M, Owen J, Parker P, Roylance R, Shaw A, Smith I, Thompson R, Timms K, Wardley A, Wilson G, Harries M, Ellis P, Ashworth A, Perou C, Bliss J, Rahman N, Brown R, on behalf of the TNT Trial Management Group (2016). BRCA1 methylation status, silencing and treatment effect in the TNT trial: A randomized phase III trial of carboplatin compared with docetaxel for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). SABCS 2016 Meeting Abstract: Canc Res 77(Suppl 4):#S6-01
	Gao Q, Lopez-Knowles E, Cheang M, Morden J, Martin L, Sidhu K, Evans D, Martins V, Dodson A, Skene A, Holcombe C, Mallon E, Evans A, Bliss J, Robertson J, Smith I, Dowsett M. True effect of aromatase inhibitor (AI) treatment on global gene expression (expr) changes in postmenopausal ER+ breast cancer (BC) patients; a POETIC study (CRUK/07/015). Meeting Abstract: Canc Res 77(Suppl 4):#P02-09-02
	Cheang M, Morden J, Gao Q, Parker J, Lopez-Knowles E, Detre S, Hills M, Zabaglo L, Tomiczek M, Mallon E, Robertson J, Smith I, Bliss J, Dowsett M (2017). The impact of intrinsic subtypes and molecular features on aromatase inhibitor induced reduction of proliferation marker of Ki67 in primary ER+ breast cancer: a POETIC study (CRUK/07/015). Meeting Abstract: Canc Res 77(Suppl 4):#P2-10-02
	Bliss J, Morden J, Evans A, Holcombe C, Horgan K, Mallon E, Raghavan V, Skene A, Dodson A, Hills M, Detre S, Zabaglo L, Graf M, Banerji J, Gillman A, Robertson J, Dowsett M, Smith I, on behalf of the POETIC Trialists (2017). Clinico-pathological relationships with Ki67 POETIC (CRUK/07/015) - critical lessons for assessing Ki 67 for prognosis and as a

	pharmacodynamic marker. Meeting Abstract: Canc Res 77(Suppl 4):#P2-05-1
SOFEA:	O'Leary B, Fribbens C, Kilburn L, Hrebien S, Garcia-Murillas I, Beaney M, Cristofanilli M, Andre F, Loi S, Loibl S, Jiang J, Bartlett CH, Koehler A, Dowsett M, Bliss J, Johnston S, Turner N. ESR1 mutations in circulating tumour DNA predict outcome to endocrine treatment in patients with estrogen receptor positive advanced breast cancer; analysis of 521 patients in the SoFEA and PALOMA3 trials. Meeting Abstract: Canc Res 76(Suppl 14):#LB-069
START	Griffin C, Porta N, Snape J, Bliss J, Yarnold J (2017) Patient reported outcomes following lymphatic radiotherapy: Results from the UK START (Standardisation of Breast Radiotherapy) trials. Presented on behalf of the START Trial Management Group. Meeting Abstract: Eur J Canc 72(suppl 1):S5 #3BA doi: 10.1016/S0959-8049(17)30100-4
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