NCRI
National
Cancer
Research
Institute

NCRI Gynaecological Cancer Clinical Studies Group

Annual Report 2017-18

Partners in cancer research

NCRI Gynaecological Cancer CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

The first achievement is the impact of our trials on the management of women with gynaecological cancers. Data from portfolio trials, including ARIEL2, Study 10 and SOLO2, have led to the approval of two PARP inhibitors (olaparib and rucaparib) in the EU and USA for the treatment of relapsed ovarian cancer. Results of major trials have been published in high impact journals, including ARIEL3 (Lancet), ARIEL2 and PORTEC3 (both Lancet Oncology), and PETROC (Annals of Oncology), whilst the primary analysis of ICON8 was presented as an oral presentation at ESMO 2017. These trials will have major influences upon clinical management.

Achievement 2

The second achievement is the breadth of our portfolio. In addition to major phase III trials in the first line treatment of all three major gynaecological cancers and multiple studies of novel therapies in recurrent disease, the portfolio includes studies of multi-parametric MRI in advanced ovarian cancer staging, primary prevention of endometrial cancer in women at high risk, IMRT in locally advanced cervical cancer, improved diagnostic test accuracy in ovarian cancer and elemental feeding patients with bowel obstruction, as well as highly translational science-driven studies. We have surgical studies (SHAPE and TRUST) investigating the optimum surgical management of gynaecological cancers, and we are collaborating with Macmillan Survivorship Research Group in the HORIZONS study of health and well-being of adults diagnosed with cancer. Finally, we will open RANGO, our rare pan-gynaecological cancer study in 2018, and we continue to recruit to our studies in specific rare tumours, including NiCCC (clear cell carcinoma) and LOGS (low grade serous ovarian cancer).

Achievement 3

The third achievement is our international influence. Through GCIG (Gynaecologic Cancer Intergroup) and ENGOT (European Network of Gynaecological Oncology Trial groups), in which CSG members have key leadership roles, we operate on an international stage. Examples of recent international trials led or co-led by the CSG include ICON8, ICON8B, PETROC, PORTEC3, ARIEL2, ARIEL3 and STATEC. Furthermore, ICON9 and ATHENA will open in 2018, ensuring that our trials continue to influence the management of gynaecological cancers throughout the world.

2. Structure of the Group

The main structure of the Group has not altered, with three subgroups (Ovarian, Endometrial and Cervix/Vulva) based upon primary disease site. Two of the Subgroup Chairs, Dr Ros Glasspool (Ovarian), and Dr Emma Hudson (Cervix/Vulva) remain unchanged, but Dr Emma Crosbie from University of Manchester has taken over from Professor Richard Edmondson as Chair of the Endometrial Subgroup.

Professor Jonathan Ledermann (past CSG Chair), Professor Edmondson (past Endometrial Subgroup Chair) and Dr Alex Taylor left the group in the past year. We thank them for their work, especially Professors Ledermann and Edmondson, who have both been stalwarts of the CSG for many years. We welcomed two new clinical oncologists, Dr Azmat Sadozye and Dr Gemma Eminowicz, onto the group, and we have also been pleased to welcome a radiologist, Professor Evis Sala from Cambridge. Recruitment of a radiologist was a key aim from last year's recruitment round. The main CSG continues to reserve a space for a gynaecological pathologist (currently Dr Naveena Singh), but further widening of the membership, in particular at subgroup level, remains a key strategic objective of the group.

The second pair of trainee members, Dr Kezia Gaitskell and Dr Sarah Kitson, completed with two-year membership of CSG in 2018, and we look forward to appointing further trainee members. Overall, the Gynaecological CSG remains an enthusiastic supporter of the trainee member programme

The main CSG structure is changing, and will comprise a small executive group, with the responsibilities of developing studies devolved to the subgroups, which become 'workstreams'. This change emerged from the recent CSG strategy and is supported by the NCRI, increased support for the expanded role of subgroups has been acknowledged.

3. CSG & Subgroup strategies

Main CSG

The CSG held a one-day strategy meeting on 16th March 2018 – the full strategy document is presented in Appendix 2. Although many of the key strategic aims of the group remain unchanged from the 2014 review, a series of specific new goals were enunciated and these will be enacted in the next 2-3 years. The key strategic elements for the whole CSG (as opposed to the disease-specific subgroups) are as follows:

Overall trials strategy

The core mission of the CSG remains to develop and conduct high quality trials in gynaecological cancer. Within this aim, several important points were identified

- There should be a CSG-led phase III trial in first line management for each of the main three gynaecological cancers (ovary, endometrium, cervix) open at all times. Currently, these are ICON8B, STATEC and INTERLACE, respectively. The subgroups should continue to develop follow-up studies to ensure seamless transition from one trial to the next.
- Risk and prevention are two areas that have been under-represented in the portfolio. There is considerable expertise in risk stratification and gynae cancer prevention in the CSG and more widely in the UK. The CSG will develop at least one national study in either primary prevention or risk stratification within the next two years.
- Imaging is another area of considerable strength, and the MROC study of multi-parametric MRI is already open across the UK. It was agreed that incorporation of novel imaging modalities and novel imaging endpoints into clinical trials was vital. A strategic aim of incorporation of novel imaging analysis as co-primary or secondary endpoint in phase II or phase III trial by 2020 was agreed.

Membership

Current CSG membership remains dominated by medical oncologists, and also has a bias to those from South East of England. Although the proportion of medical oncologists appointed reflects the proportions within applications for membership, there has been some success in recent years in diversification, with the appointment of two new clinical oncologists in 2018, a radiologist and a Health Services researcher in 2017, as well as *ex officio* CSG membership for the President of the British Association of Gynae Pathologists. In 2018-2020, we will seek to appoint at least one new clinical oncologist and a Clinical Nurse Specialist. Involvement of basic and translational scientists at subgroup level is also an important aim.

Subgroups

The strategy meeting felt strongly that there should still be three subgroups. However, joint meetings between the endometrium and cervix/vulva subgroups should take place twice per year, given the overlap in clinical teams that treat these diseases. It was also felt that this would maximise attendance and involvement. The subgroups were felt to be strong, especially the ovarian subgroup, and should remain the engine for new trials development. The

consumer members felt that their input would be more valuable in the subgroups than main CSG.

It was also felt that the practice of the Ovarian Subgroup to have large open meetings should be encouraged, again to maximise trial participation and trial ownership by the UK gynaecological cancer community.

Subspecialty leads and regional recruitment

The disparity in recruitment rates between the best and worst-recruiting networks has been highlighted in recent years, especially in ovarian cancer trials. The appointment of new oncologists with an interest in gynaecological cancer has had a noticeable positive effect on recruitment in several centres. Several network Subspecialty Leads (SSLs) attended the Strategy Day and it was agreed that communication between the CSG and the network leads needs to improve. A new procedure was developed whereby communication, about site selection in particular, will be channelled via the SSLs and the Subgroup Chairs. Given the open nature of subgroup meetings in gynae cancer, it was agreed that SSLs would routinely be invited to subgroup meetings.

Consumers and charity partners

It was agreed that the subgroups were a far more effective forum for consumer input than the bi-annual main CSG meetings. In the Gynae CSG, trials are developed and discussed at subgroup meetings, with the main CSG largely having an oversight and management role. A key strategic aim for 2018 onwards is that consumer members will attend subgroup meetings as their key priority.

There are several very strong and effective gynaecological cancer charities, and representatives of these charities are regular attenders at ovarian subgroup meetings. It was felt strongly that this was highly effective as a mechanism for disseminating information about clinical trials. A key strategy is to extended invitations to other charity partners to attend the endometrial and cervix/vulval subgroups in future.

Cervix/Vulva Subgroup (Chair, Dr Emma Hudson)

Recruitment to the flagship first-line trial INTERLACE has improved with international collaboration enabling sites in Mexico and Italy to open; in addition, sites in India are due to open in Summer 2018. A revised recruitment target of 500 has been approved, with the aim that recruitment will complete in December 2019. With more than 300 patients now recruited, this target seems very feasible.

In addition, the ENGOT CX-8 first line trial of tisotumab vedotin alone or in combination with pembrolizumab or carboplatin will open in late 2018, as will MaRuC, which looks at the role of maintenance rucaparib for patients with locally advanced cervical cancer.

The SHAPE study of simple versus radical hysterectomy in early stage cervix cancer continues – after a slow start, recruitment both in the UK and internationally is improving. The UK is the 4th largest recruiting country.

Finally, trials of radiotherapy in cervix cancer remain of great importance – DEPICT has completed recruitment (dose-escalated IMRT in locally advanced cervix cancer) and a funding decision on REGENCY (stereotactic boost and IMRT in recurrent endometrial and cervical cancers) is awaited.

Vulval cancer remains a work in progress. Unfortunately, it has not been possible to develop a joint trial with the anorectal subgroup of the colorectal CSG for HPV-positive anal and vulval cancers. However, the strategy day reaffirmed the CSG's determination to develop a trial in vulval cancer, as detailed below.

Key strategic aims

Open new trials in relapsed disease The CSG has developed COMICE, which investigates maintenance cedarinib and olaparib following chemotherapy for advanced or recurrent cervical cancer. COMICE has been developed in collaboration with AstraZeneca and is due to open in May 2018 and is open to all centres in the UK.
Develop a therapy trial in relapsed vulva cancer with associated tissue collection. Developing a trial in relapsed vulval cancer with associated tissue collection remains a key strategic aim for the CSG. At the strategy meeting in March 2018, this was reiterated. There is strong scientific rationale for combining radiotherapy with immunotherapy in vulval cancer; thus, a trial evaluating radiotherapy with a checkpoint inhibitor in recurrent or locally advanced vulval cancer is being developed. Given the rarity of this disease, this trial will require international collaboration, most probably via ENGOT.

Endometrial Subgroup (Chair, Dr Emma Crosbie)

The endometrial cancer portfolio has continued to grow over the last 12 months, and now has trials covering prevention, first line treatment, survivorship and management of recurrent and metastatic disease. The recent CSG strategy day highlighted the importance of screening, prevention and early detection trials to clinicians, consumers and charity representatives, and these are undergoing development. There will be two endometrial subgroup meetings in 2018 (June and December) held in conjunction with the Cervix/Vulva Subgroup.

STATEC, an international surgical endometrial trial developed in the UK, has now opened. It will provide important answers related to the role of lymphadenectomy and adjuvant therapy in endometrial cancer, as well as to allow the development of sentinel node techniques, an area in which the UK is lagging internationally. The trial has already opened in a small number of UK and international sites, with more in set up phase, although recruitment is likely to be a significant challenge in view of the numbers of recruits needed.

COPELIA, a trial of cediranib and olaparib in relapsed and metastatic disease, will open imminently and brings trials of new targeted therapies to endometrial cancer for the first time in an investigator-led study developed through the Subgroup.

Key strategic aims

Launch a new study of primary prevention of endometrial cancer in high risk women The portfolio of pilot studies assessing prevention interventions for obesity-related endometrial cancer have completed and their results will inform a large multicentre RCT. This will be developed and submitted for funding in 2018-19.
Test a new endometrial cancer detection tool in symptomatic women A simple, easy to administer, non-invasive endometrial cancer detection tool could enable the effective triage of symptomatic women for diagnostic testing. The Gynae CSG strategy day highlighted the importance of research in this area, which ranked second most important research priority in the recently completed James Lind Womb Cancer Alliance. An accurate detection tool could also be used for screening asymptomatic women at high risk of endometrial cancer, thus enabling early detection and improved outcomes from endometrial cancer.
Test non-surgical treatments in early stage and pre-invasive disease A significant proportion of younger women with endometrial cancer wish to avoid hysterectomy in order to preserve fertility, whilst many others are not fit for surgery due to obesity and associated co-morbidities. A strategic aim of the endometrial subgroup is to develop weight loss interventions for obesity-associated endometrial cancer and atypical hyperplasia. The subgroup aims to develop a new protocol within the next 18 months.

Ovarian Subgroup (Chair, Dr Ros Glasspool)

The Ovarian Subgroup continues to maintain a portfolio of trials across all aspects of ovarian cancer management. We have academic trials in first line chemotherapy (ICON8b), recurrent disease (ICON9, OCTOPUS, DICE and CENTURION) and rare tumours (LOGS, NiCCC, RANGO), all of which have embedded translational sample collection. We also have risk prediction (OCTAGON), risk reduction (PROTECTOR), diagnostic algorithm (ROCKETS), imaging (MROC) and supportive care trials (HORIZONS, OVPSYCH2). The subgroup participates in many commercial trials (PRIMA, NOVA, JAVELIN 100 and 200, SOLO1), which will increase through membership of ENGOT. The CSG will lead ATHENA and participate in OREO and FIRST, all of which are commercially-sponsored ENGOT trials. In addition, we will recruit to academic ENGOT studies (e.g. EORTC 1508, NSGO umbrella study) whilst ENGOT groups are participating in ICON8B, ICON9 and NiCCC. We have had new trial proposals in early diagnosis (Loyalty Card Study, EDBOC), surgery (OVHIPEC), rare/early phase (ATARI, low grade serous hormone trial, PROMPT) and phase IV (MONITOR).

The subgroup meetings continue to be very well attended with many of the SSLs now also attending. The meetings provide a format to discuss new ideas, highlight trials with problems or new issues, foster collaborations and mentor new investigators. The SSLs have also been actively involved in identifying sites for first line trials of PARP inhibitor/immune checkpoint inhibitor

combinations. As well assisting in feasibility assessment, this process has also given sites that have not previously been approached for commercial studies the opportunity to participate, thereby improving access to clinical trials across the country.

The Ovarian Subgroup continues to lead our international collaborations via GCIG (Professor Jonathan Ledermann, Chair of rare tumour group; Professor Charlie Gourley, Chair of translational group; Dr Ros Glasspool, Chair of meta-analysis group) and ENGOT (Dr Marcia Hall and Dr Glasspool, rare tumour group; Dr Glasspool and Dr Susana Banerjee, phase I/II group [Dr Glasspool co-chair]).

Key strategic aims

Trials in the frail/elderly

Dr Banerjee has submitted the FAIR-O Study to Wellbeing of Woman for funding. This is a prospective multicentre study evaluating feasibility and value of geriatric assessment and intervention in epithelial ovarian cancer patients. It will also investigate sarcopaenia as a predictive marker of survival and tolerance of chemotherapy. Dr Agnieszka Michael is investigating the use of an electronic Frailty Index (eFI) in routine practice and will develop a specific trial proposal in 2018-9.

Biomarker stratification trials

The BriTROC consortium (led by Iain McNeish and Dr James Brenton) has identified novel, prognostic copy number signatures that may decode the extreme copy number abnormalities found in ovarian high grade serous carcinoma that have prevented biomarker development and may identify targetable drivers of the disease. Validation on trial cohorts including ICON8 is planned for 2018-9. The STRATROC consortium (led by Professor Bob Brown) was invited to submit a full application to the MRC Stratified Medicine bid, but ultimately was not funded. However, it brought together a multi-disciplinary team from across the country committed to development of biomarkers particularly focussing on guiding surgical management. It is hoped that this group will continue to work on new proposals. The SMARTER trial (led by Professor Helena Earl and Dr James Brenton) has been invited to submit a full application for a CRUK Experimental Cancer Medicine programme. In addition, the MOC1 trial (Professor Gordon Jayson), a prospective validation of pTie2 as a response marker for bevacizumab, has been submitted to NIHR EME.

Surgical trials

The surgical group has opened a number of trials including TRUST, PROMISE, SIGNPOST and PROTECTOR. The amount of residual disease at the end of debulking surgery for ovarian cancer is a strong predictor of outcome. However, undertaking clinical trials to address the question of how extensive surgery should be remains very challenging, and there remains vigorous debate as to the appropriateness of primary vs interval surgery. The SOCQER2 trial is an observational trial of patient reported outcomes following ovarian cancer surgery. It recruited above its original target and included patients from Australia and India. It has tackled many of the challenges of mapping disease and recording surgical procedures. It also highlighted the importance of having the full population data as the denominator in any non-randomised trials. The initial data are being analysed and a follow-on study as well as a sub-

study investigating acute kidney injury are being developed. This may be performed in conjunction with the national ovarian cancer audit being led by the RCOG and the British Gynaecological Cancer Society.

4. Task groups/Working parties

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

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
Development of more accurate screening tests for the early detection of ovarian cancer	Full application	Dr John Timms	Not supported	Minimal
CEBOC: Evaluation of the safety of CEdiranib in the prevention of subacute Bowel obstruction in platinum-resistant Ovarian Cancer	Full application	Professor Gordon Jayson	Not supported	Developed by CSG
COPELIA: A 3-Arm Randomised Phase II Evaluation of Cediranib in Combination with Weekly Paclitaxel or Olaparib Versus Weekly Paclitaxel Chemotherapy as Second-Line Therapy for Advanced/ Metastatic Endometrial Carcinoma or for disease relapse within 12 months of adjuvant carboplatin-paclitaxel chemo	Full application (Endorsement)	Dr Andrew Clamp	Endorsement not supported	Developed by CSG
CeNturIOn: An open-label, randomised, phase II trial of ruCaparib combined with Nivolumab +/- Ipilimumab to augment response in homologous repair deficient patients with relapsed Ovarian cancer	Outline application (Endorsement)	Dr Marcia Hall	Invited to full	Developed by CSG
REGENCY: Stereotactic radiotherapy for recurrent gynaecological cancer	Outline application (Endorsement)	Dr Alexandra Taylor	Invited to full	Developed by CSG

Nonavalent HPV vaccine after local conservative treatment for cervical pre-invasive disease: a randomised controlled trial	Outline application	Dr Maria Kyrgiou	Not invited to full	Discussed with CSG and approved
PREDICTION - Predictive biomarkers to improve chemotherapy response in ovarian high grade serous carcinoma	Outline application	Professor Iain McNeish	Not invited to full	Developed by CSG
TRIOC: A Randomised Parallel Group Double-Blind Phase II Study to Assess the Activity of TroVax® (MVA-5T4) Versus Placebo in Patients with Relapsed Asymptomatic Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer	Full application (no-cost amendment)	Dr Agniezska Michael	Supported	Developed by CSG
November 2017				
ROCTEST: Rapid Ovarian Cancer TESTing	Biomarker Project Award	Dr Emmanouil Karteris		Discussed with CSG and approved
Risk stratification of Human Papillomavirus infection using a multiplex chemokine assay for the improved diagnosis of cervical disease and cancer	Biomarker Project Award (Full Application)	Dr Kate Cuschieri	Preliminary	Discussed with CSG and approved
CeNturIOn: An open-label, randomised, phase II trial of ruCaparib combined with Nivolumab +/- Ipilimumab to augment response in homologous repair deficient patients with relapsed Ovarian cancer	Early Phase & Feasibility Study Endorsement	Dr Marcia Hall	Supported	Developed by CSG

A randomised double blind placebo controlled Phase II clinical trial of Cediranib and Olaparib maintenance in advanced recurrent Cervical Cancer	Early Phase & Feasibility Study Endorsement	Dr Rosemary Lord	Supported	Developed by CSG
PORTEC-4: Randomised phase III trial of molecular profile-based versus standard recommendations for adjuvant radiotherapy for women with early stage endometrial cancer	Late Phase Study (Full Application)	Dr Melanie Powell	Not Supported	Developed by CSG
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**
STRATROC	MRC Stratified Medicine	Professor Bob Brown	Invited to full but not funded	Developed by CSG
FAIR-O	Wellbeing of Women	Dr Susie Banerjee	Pending	Developed by CSG

6. Consumer involvement

Beryl Elledge

I have attended and contributed at the CSG strategy day held in March 2018, thus giving a patient/carer overview for the strategic direction of the group for 2018-2022. I also attend the main Gynaecological CSG meetings. I feel the engagement of consumers within the clinical studies meetings allows the consumers voice to be heard in the development, monitoring and evaluation of cancer research. Consumer members have on-going training and are provided with an individual mentor for support.

I contribute to the broader consumer involvement in the following groups:

- Macmillan Horizons programme-understanding the impact of diagnosis and treatment on everyday life. The research is being set up to follow gynaecological cancers from their diagnosis for five years.
- Co-chair of South East London Consumer Research Panel for Cancer. This panel is a collaborative project between the Guy's and St Thomas' NHS Foundation Trust and Kings College London Biomedical Research Centre. The panel's aim is to support the consumer involvement needs of both organisations.
  - Since October 2010 the panel has been asked to review numerous patient information materials for research studies.
  - Members of the panel include patient/carers, Senior Lecturer at King's College, Head of Biobanking for King's College and overseen by Research Manager for the Cancer Centre, Kings Health Partners Cancer Centre.
- I am also an active member of the independent Cancer Patients Voice "Use My Data" group.

Julia Tugwell

I joined the Gynae CSG and NCRI in July 2017. At the most recent meeting I was assigned to the Cervical/Vulval Subgroup (I think this title should have vagina tacked on to it too). Since then, I have been serving my apprenticeship in the world of gynae cancer research and the NCRI Consumer Forum. I have attended one Gynae CSG meeting, the Gynae CSG Annual Trials Meeting (December 2017) and the Gynae CSG Strategy Day in March 2018. I also attended the NCRI Conference in Liverpool, the Britain Against Cancer conference, two Consumer Forum meetings and most recently have joined the NCRI JLA LWBC Steering Group. I have made suggestions to CSG that the distribution of funding both across the gynae cancer types and across the cancer pathway are unequal and that this need rectifying. I see this as an absolute priority. I have forged relationships with members of the other CSGs (Primary Care, SPED, Head and Neck and Psycho social CSG's). I continue being involved with gynae relevant cancer charities, suggesting their inclusion at the CSG Strategy Day. Currently I am an advocate for The Eve Appeal as they launch their Get Lippy campaign. An initial research idea has been broached across the relevant CSGs and I have yet to hear back from members of the Gynae CSG. I continue to take up any opportunity offered within NCRI to learn more and will be attending the Proton Beam Workshop at the Christie and the PHE conference in June.

7. Priorities and challenges for the forthcoming year

Priority 1

It is essential that we maintain recruitment to time and target in all our trials. This is particularly important for the flagship studies, including ICON8B, STATEC, ICON9, INTERLACE and ATHENA. Our strategy for maintaining recruitment includes ensuring that trials are available in as many centres as possible, regular meetings with investigators to identify barriers to recruitment and encouraging Chief Investigators to interact with recruiting sites. In addition, we are working with the network subspecialty leads to ensure that we reach sites that have not previously participated in commercial studies.

Priority 2

The CSG has previously had few trials in relapsed cervix and endometrial cancer. Thus, opening and running COMICE and COPELIA in these indications is a key priority for 2018-19. There is increasing interest in both these cancer types from the pharmaceutical industry, and demonstration that we are able to run successful trials in relapsed disease will be important for future trial prospects.

Priority 3

A medium-term priority is the development of new trials in novel areas, including prevention and risk, as well as therapeutic trials in vulval and vaginal cancers. This will require exploration of alternative funding sources, working with new collaborators and different trial designs from our usual therapeutic studies. In addition, we wish to explore studies of early/rapid diagnosis with the primary care CSG, which again will require new trial models.

Challenge 1

Recruitment remains our key challenge as well as our top priority. There are multiple factors that contribute to recruitment challenge, including competing trials, investigator fatigue and limited resources at sites. In first-line ovarian cancer, there are potentially 5 commercial trials that could compete with ICON8B – the CSG is actively managing the number of commercial studies that will open and is marshalling sites to ensure that there is good distribution across the country. INTERLACE has demonstrated that poor recruitment can be reversed with concentrated effort, opening of new sites and active management. STATEC will pose specific challenges in endometrial cancer – it will answer a critical question, but faces polarised surgical opinion that will require very active management from the CSG, Chief Investigator and Trials Unit.

Challenge 2

The current funding environment is challenging. CSG members and investigators are aware that applications should be made to funding streams beyond CRUK Clinical Research Committee, e.g. to NIHR and MRC DPFS – for example, MROC is funded by NIHR and the MOC1 study has been submitted to the NIHR EME stream. In addition, close working with industry remains essential, and we will need to continue to work with pharmaceutical

companies: for example, ATHENA is an industry-sponsored study but was developed with significant academic input from the CSG. Dr Rebecca Kristeleit is the Co-Chief Investigator and Iain McNeish is the translational lead. Many pharma companies automatically approach ENGOT if they wish to run a multi-centre European trial in gynaecological cancers, and thus closer working with ENGOT is essential.

Challenge 3

Optimal use of consumer members. The CSG is fully committed to patient and public involvement in its activities – consumer members attend all CSG meetings, are invited to join one of the subgroups and are allocated a mentor to provide support and education. However, there is some frustration, both from the consumers and the Chair, that the consumer members could be more effectively deployed. This reflects the operation of the Gynae CSG, with trial design and key decision-making delegated to the subgroups. An important solution to this challenge is to embed the consumers within the subgroup structure and to emphasise the importance of the subgroups as the forum for trial development where consumer input will be most influential.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
A – Main CSG & Subgroup Strategies

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

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

Professor Iain McNeish (Gynaecological Cancer CSG Chair)

Appendix 1

Membership of the Gynaecological Cancer CSG

Name	Specialism	Location
Dr Gemma Eminowicz	Clinical Oncologist	London
Dr Emma Hudson	Clinical Oncologist	Cardiff
Dr Susan Lalondrelle	Clinical Oncologist	London
Dr Azmat Sadozye	Clinical Oncologist	Glasgow
Ms Beryl Elledge	Consumer	Winchester
Miss Julia Tugwell	Consumer	Exeter
Dr Emma Crosbie	Gynaecological Oncologist (Surgeon)	Manchester
Professor Christina Fotopoulou	Gynaecological Oncologist (Surgeon)	London
Dr Sarah Kitson*	Gynaecological Oncologist (Surgeon)	Manchester
Dr Maria Kyrgiou	Gynaecological Oncologist (Surgeon)	London
Dr Susana Banerjee	Medical Oncologist	London
Dr Rebecca Bowen	Medical Oncologist	Bath
Dr Ros Glasspool	Medical Oncologist	Glasgow
Dr Marcia Hall	Medical Oncologist	Middlesex
Dr Michelle Lockley	Medical Oncologist	London
Dr Rosemary Lord	Medical Oncologist	Merseyside
Professor Iain McNeish (Chair)	Medical Oncologist	London
Dr Agnieszka Michael	Medical Oncologist	Guildford
Dr Shibani Nicum	Medical Oncologist	Oxford
Dr Kezia Gaitskell*	Pathologist	London
Dr Naveena Singh	Pathologist	London
Professor Kinta Beaver	Professor of Cancer Nursing/Health Services Researcher	Lancashire
Professor Evis Sala	Radiologist	Cambridge
Mr Jim Paul	Statistician	Glasgow

* denotes trainee member

Membership of the Subgroups

Cervix/Vulva Subgroup		
Name	**Specialism**	**Location**
Ms Emma Hudson (Chair)	Clinical Oncologist	Cardiff
Professor Nick Reed	Clinical Oncologist	Glasgow
Dr Tara Barwick	Consultant Radiologist	London
Miss Julia Tugwell	Consumer	Exeter
Dr Jenny Forrest	Gynaecological Oncologist	Devon
Mr Jeremy Twigg	Gynaecological Oncologist	Stockton-on-Tees
Professor John Tidy	Gynaecological Oncologist	Sheffield
Dr Susana Banerjee	Medical Oncologist	London
Dr Rosemary Lord	Medical Oncologist	Merseyside
Dr Asma Faruqi	Pathologist	London
Dr Lynn Hirschowitz	Pathologist	Birmingham
Dr Jackie Martin	Clinical Oncologist	Sheffield

Endometrial Subgroup		
Name	**Specialism**	**Location**
Dr Melanie Powell	Clinical Oncologist	London
Dr Andrew Clamp	Medical Oncologist	Manchester
Dr Rosemary Lord	Medical Oncologist	Merseyside
Dr Axel Walther	Medical Oncologist	Bristol
Dr Naveena Singh	Pathologist	London
Dr Emma Crosbie (Chair)	Gynaecological Oncologist	Manchester
Dr Sarah Kitson*	Gynaecological Oncologist	Manchester
Dr Maria Kyrgiou	Gynaecological Oncologist	London

Ovarian Subgroup		
Name	**Specialism**	**Location**
Dr Sarah Williams	Clinical Oncologist	Birmingham
Dr Sadaf Ghaem-Maghami	Gynaecological Oncologist	London
Mrs Sundha Sundar	Gynaecological Oncologist	Birmingham
Dr Susana Banerjee	Medical Oncologist	London
Dr Ros Glasspool (Chair)	Medical Oncologist	Glasgow
Professor Jonathan Ledermann**	Medical Oncologist	London
Dr Rosemary Lord	Medical Oncologist	Merseyside
Professor Iain McNeish**	Medical Oncologist	London
Dr Shibani Nicum	Medical Oncologist	Oxford
Dr Axel Walther	Medical Oncologist	Bristol
Dr Sanjiv Manek	Pathologist	Oxford
Dr Nafsia Wilkinson	Pathologist	Leeds

* denotes trainee member

**denotes non-core member

Appendix 2

A – CSG & Subgroup Strategies 2018-2022

Gynaecological Cancer CSG Strategy

This strategy timeline has been produced to define the Gynaecological Cancer Research Strategy Plan and its implementation and will be reviewed and updated at each CSG meeting (supported by All)
The document is composed of the following:

Page : NCRI Gynaecological Cancer CSG Strategy: plan of implementation, containing agreed strategic objectives (1- 6), specific actions, CSG leads and proposed deadlines.

Gynaecological CSG members	Responsibility
Professor Kinta Beaver (KB)	**Professor of Cancer Nursing, Lancashire**
Dr Rebecca Bowen (RB)	Consultant Medical Oncologist, Bath
Dr Emma Crosbie (EC)	Clinical Senior Lecturer, Manchester
Ms Beryl Elledge (BE)	Consumer
Dr Ros Glasspool (RMG)	Consultant Medical Oncologist, Glasgow
Dr Emma Hudson (EH)	Consultant Oncologist, Cardiff
Dr Susan Lalondrelle (SL)	Consultant Clinical Oncologist, London (Royal Marsden)
Dr Michelle Lockley (ML)	Reader in Medical Oncology, London (Barts and UCH)
Professor Iain McNeish (IMcN)	Professor of Oncology, London (Imperial)
Dr Agnieszka Michael (AM)	Consultant Medical Oncologist, Surrey
Mr Jim Paul (JP)	Senior Research Fellow, Glasgow
Professor Evis Sala (ES)	Professor of Oncology Imaging, Cambridge
Ms Julia Tugwell (JT)	Consumer
Ms Laura Chambers (NCRI)	Administration Manager
Ms Nicola Keat (NCRI)	Head of Research Groups
Ms Aifric Müller (NCRI)	CSG Coordinator

Strategic objective	Action	CSG Lead	Date	Outcomes
1. Current CSG membership 1a – to widen diversity of specialties	Active encouragement of applications from clinical oncology, nursing, virology and epidemiology. Not possible to restrict geographical applications but active encouragement of applications from all of UK	IMcN	Dec 2018	Two more clinical oncology members; one more nurse member
1b – Re-organisation	Given the diverse nature of gynae cancers, aim to discuss with NCRI Central possibility of reducing overall CSG membership (e.g. to 10) to make the main CSG a strategic/oversight body, with much greater delegated to the subgroups as the decision-making forum for the CSG. This would allow an increase in the number of core sub-group members (e.g. 14 per subgroup) and increase the input from consumers.	IMcN	By time of next formal CSG review	Reduction in CSG membership; increased membership of subgroups

Strategic objective	Action	CSG Lead	Date	Outcomes
2. Subgroups 2a - Subgroup numbers	Subgroup meetings to remain the critical forum for trial and protocol development. To continue with three subgroups (ovary, endometrial, cervix/vulva)	EC, EH, RG, IMcN	On-going	CSG to continue to have three subgroups
2b - Subgroup meetings	Joint endometrial and cervix/vulva meetings to take place twice per year	EC, EH,	Mar 2019	Two face-to-face meetings of endometrial and cervix/vulva subgroups to have taken place by April 2019
2c - Subgroup chairs	Time as subgroup chair not to count in 3+3 year membership of CSG – vital to gain necessary experience prior to becoming subgroup chair.	IMcN	Dec 2018	Subgroup chairs to be allowed to continue beyond 3+3 year membership of CSG
2d - Subgroup membership	To widen membership, especially if numbers of subgroup members can increase. Increased participation/membership from basic scientists and charity representatives, especially in cervix/vulva subgroup	EC, EH, RG, IMcN	Mar 2019	At least one charity representative to be invited to cervix/vulva subgroup; invitation for basic scientists with interest in translational research to attend subgroup meetings

Strategic objective	Action	CSG Lead	Date	Outcomes
3.Subspecialty leads interactions 3a - Full list of SSL	NIHR central to provide accurate and up to date list of Gynae SSL	PW	Jul 2018	Accurate and up to date SSL list
3b - Improved dialogue between SSL and CSG	Subgroup chairs to liaise with SSL rather than individual sites for site selection	EC, EH, RG	On-going	Site identification to be devolved to SSL

Strategic objective	Action	CSG Lead	Date	Outcomes
4. Consumers and charity partners 4a - Consumer role	Consumer members to be embedded within subgroups rather than main CSG	EC, EH, RG, IMcN	Dec 2018	Consumer members to attend subgroup meetings rather than main CSG meetings
4b - Charity partners	Patient organisation/charities to be regularly invited to attend endometrial and cervix/vulva subgroup meetings – already attending ovarian subgroup meetings	EC, EH	Mar 2019	Eve Appeal, Jo's Trust,

Strategic objective	Action	CSG Lead	Date	Outcomes
5. Overall trials strategy 5a - First line intervention trials	The CSG should aim to have a first line trial in all three common gynaecological cancers – endometrium, ovary, cervix – and aim to have future trials in planning at time of opening of current trial	All	On-going	A major phase III first-line intervention trial open at all times for all three common gynaecological cancers
5b - Risk/prevention studies	To expand CSG-led studies that address identification of high risk patients prior to diagnosis of cancer and/or studies addressing prevention of gynaecological cancer	All	Jun 2019	One national risk/prevention study led by the CSG funded/ approved
5c - Early diagnosis/ rapid diagnosis	Develop a trial/protocol with primary care CSG to improve speed of diagnosis in ovarian cancer	All	Jun 2020	
5d - Imaging studies	RECIST has multiple flaws as a reporting tool, particularly in ovarian cancer. Action to incorporate novel imaging endpoints into future phase III trials	All	Jun 2021	Incorporation of novel imaging analysis as co-primary or secondary endpoint in phase II or phase III trial.

Strategic objective	Action	CSG Lead	Date	Outcomes
6.1.Disease-specific research: Vulva Cancer 6.1a - First line trial in locally advanced vulval cancer	Develop a first line trial in locally advanced/recurrent vulval cancer – combination of radiotherapy and immune checkpoint inhibition deemed most likely to be funded. Consider IRCI badging given the rarity of vulval cancer	EH, SL	Jun 2020	Funding or industry support for trial
6.1b - Joint HPV-positive study	Aim to develop joint protocols for HPV-positive cancers within gynae tumours and to include anal cancer subgroup +/- head and neck CSG	EH, IMcN	Jun 2020	Joint protocol for HPV positive gynae/ anal malignancies funded/supported by industry
6.2 Disease-specific research: Ovarian cancer 6.2a - Ovarian cancer in the frail/elderly	Development of trial evaluating geriatric assessment tool and chemotherapy treatment in the frail/elderly	AM, SB, RMG IMcN	Jun 2020	One new trial in which geriatric assessment tool is utilised and/or that evaluates chemotherapy specifically in the frail/elderly

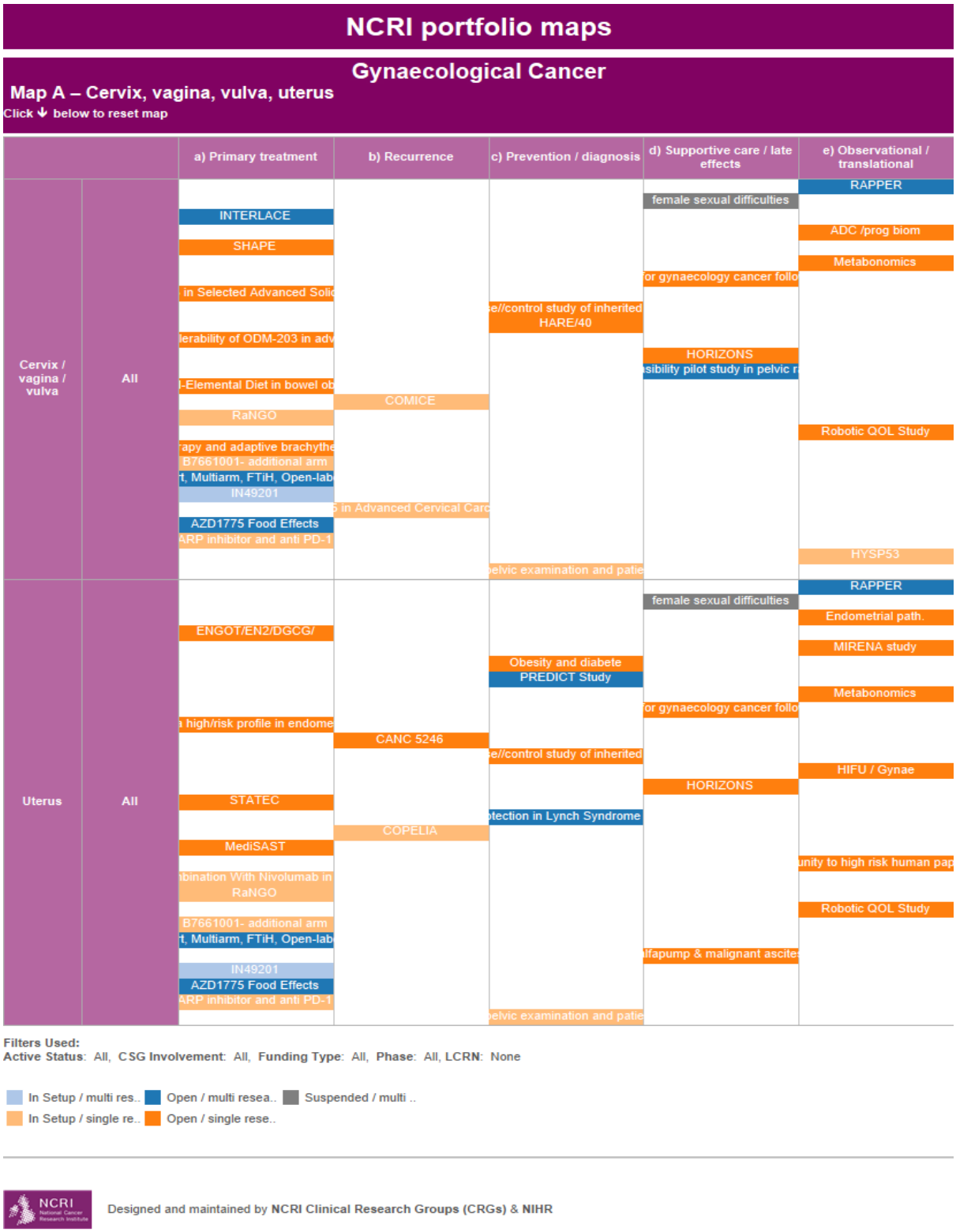
Strategic objective	Action	CSG Lead	Date	Outcomes
6.2b - Molecular stratification	Urgent need to develop trial in which patients with newly diagnosed ovarian cancer are stratified according to molecular classifiers	All	Jun 2020	First line trial in which molecular stratification is an integral component to be
6.2c -Surgical trial	There is still robust debate as to which patients gain benefit from primary surgery vs interval debulking, and which patients may not benefit from surgery at all. Action to develop study in which surgical decision algorithm is integral to study design	All	Jun 2021	First line trial in which surgical decision algorithm is integral to stratification and/or treatment allocation
6.2c Screening	Following failure of UKCTOCS, there remains a need to screening study in ovarian cancer, both for high risk populations and unselected population. Such a study would have to incorporate molecular markers and improved imaging.	All	Jun 2022	Development of pilot protocol for screening study with stage shift as primary endpoint.
6.2d - Platinum-resistant trials	Outcomes for women with platinum-resistant disease remain very poor. CSG needs to have a portfolio of trials for women with resistant disease, including those who have had multiple prior lines of therapy	All	On-going	At least two trials open at all times for women with platinum-resistant disease

Strategic objective	Action	CSG Lead	Date	Outcomes
6.3 Disease-specific research: Endometrial cancer 6.3a - Prevention	Significant strength in endometrial cancer prevention within CSG. National primary prevention study women at high risk of developing endometrial cancer required	EC	Jun 2020	National primary prevention study in high risk women to be funded/supported by industry
6.3b Survivorship	Outcome for women with endometrial cancer is good. Need to develop protocols to minimise hospital visits and maximise QoL for women treated for endometrial cancer	KB	Jun 2020	Multi-centre study investigating survivorship in early stage endometrial cancer
6.3c- Recurrent endometrial cancer	Although overall prognosis for endometrial cancer is good, prognosis for those with relapsed disease is very poor with no licensed new drugs. CSG needs to develop portfolio of trials in relapsed endometrial cancer	All	Jun 2019	At least one national trial open in relapsed endometrial cancer

Strategic objective	Action	CSG Lead	Date	Outcomes
6.3d Molecular stratification	Recent advances in the understanding of endometrial cancer biology means that stratification by molecular subtype should be incorporated into first line endometrial cancer trials	All	Jun 2020	Molecular stratification to be incorporated into next first line intervention trial in newly-diagnosed endometrial cancer
6.4 Disease-specific research: Cervical cancer 6.4a - Screening	Uptake of cervical cancer screening remains low. Studies required to assess methods to increase screening uptake in partnership with primary care CSG	All	Jun 2020	Study addressing interventions to increase cervical screening uptake funded
6.4b Recurrent disease	Prognosis for recurrent cervix cancer is very poor. CSG needs to ensure that there are studies open for women with recurrent disease	All	Jun 2019	At least one multi-centre study open in recurrent cervical cancer.

Appendix 3

Portfolio maps

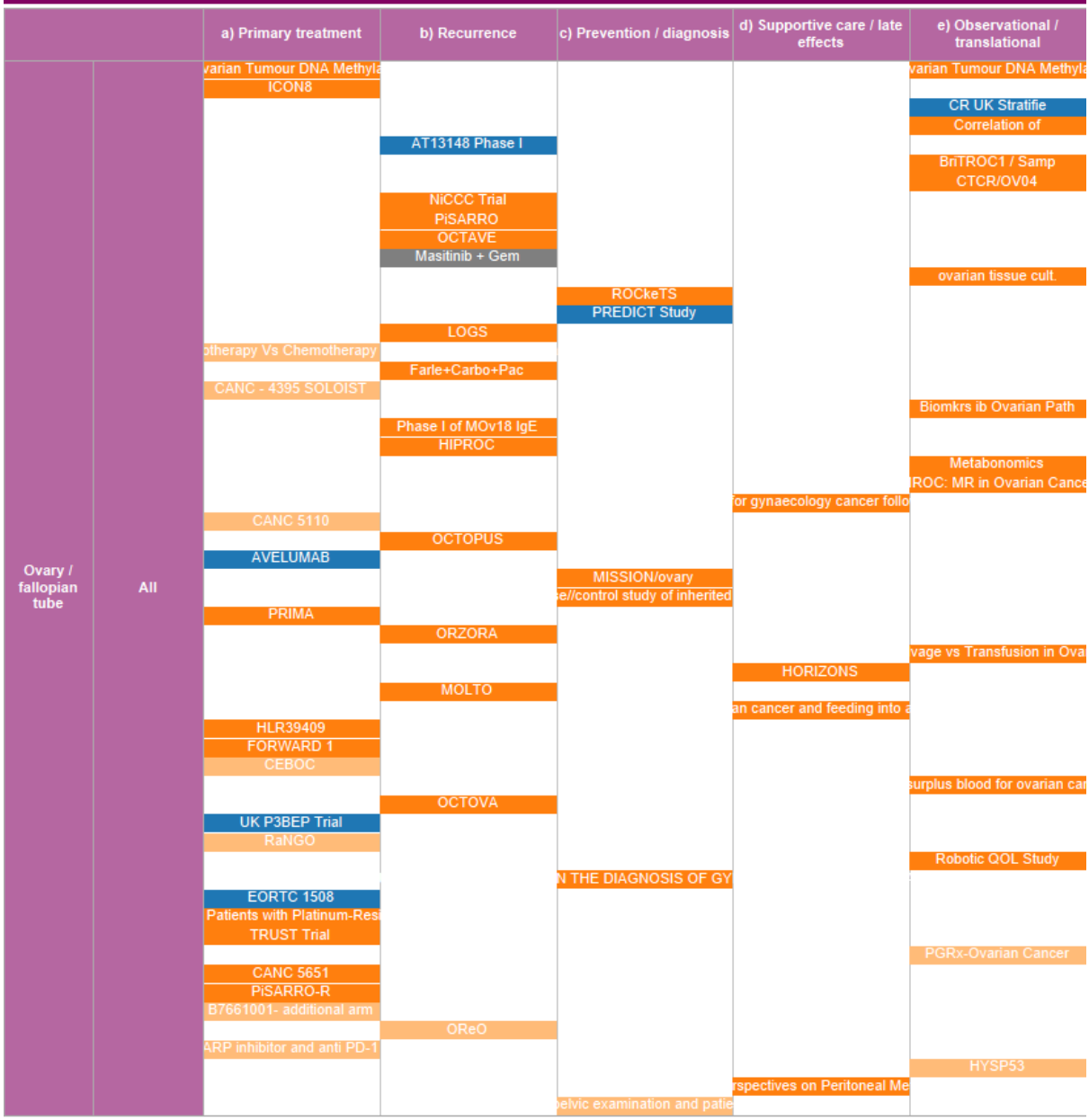


NCRI portfolio maps

Gynaecological Cancer

Map B – Ovary, fallopian tube

Click ↓ below to reset map



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

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

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

Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a randomised, double-blind, placebo-controlled, phase 3 trial. Coleman, R et al. Lancet 390(10106): 1949-1961.	ARIEL3 demonstrated that maintenance rucaparib following platinum chemotherapy very significnatly extended progression-free survival in high grade ovarian cancer in both BRCA1/2 mutated and non-mutated patients. The positive outcome of this trial has led to the applications for licencing of rucaparib in the USA by the FDA for the maintenance treatment of relapsed ovarian cancer.	ARIEL3 was a portfolio study developed by CSG members in conjuction with Clovis Oncology and the Gynecologic Oncology Group in the US, with Jonathan Ledermann as co-chief investigator.
2. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. M. E. Powell et al. Lancet Oncol 2018. 19(3): 295-309.	PORTEC3 will change practice internationally - it demonstrated that the addition of chemotherapy to adjuvant radiotherapy treatment of high risk early stage endometrial cancer did not improve progression-free survival overall, but did have a significant effect in patients with stage III disease and did improve overall failure-free survival.	PORTEC3 was a joint trial from the Dutch Gynaecological Oncology Group and the CSG. Melanie Powell, former CSG member, was UK PI, and the UK was the leading country for recruitment.
3. Antitumor activity and safety of the PARP inhibitor rucaparib in patients with high-grade ovarian carcinoma and a germline or somatic BRCA1 or	These two studies investigated rucaparib in relapsed high grade ovarian cancer, with ARIEL2 recruiting patients both with and without germline *BRCA1/2* mutations, and	ARIEL2 and Study 10, which were both developed by the CSG in conjunction with Clovis

	BRCA2 mutation: Integrated analysis of data from Study 10 and ARIEL2. Oza, A et. Gynecol Oncol 2018 147(2): 267-275.	Study 10 recruiting only those with germline *BRCA1/2* mutations. The response rates and duration of response to single-agent rucaparib were sufficiently impressive that it has now been licenced both in the US (FDA) and EU (EMA) as treatment for women with relapsed platinum-sensitive high grade ovarian cancer with germline or somatic mutations in *BRCA1/2*.	Oncology. Iain McNeish was co-chief investigator on ARIEL2.
4.	Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomised, placebo-controlled, phase 3 trial. Pujade-Lauraine E et al, Lancet Oncol 201718(9): 1274-1284.	SOLO2 was a randomised portfolio phase III trial of maintenance olaparib in women with germline or somatic mutations in *BRCA1/2* who had responded to platinum chemotherapy in the relapse setting, The data were very strongly positive, and resulted in FDA and EMA approval of olaparib in this setting. An application to NICE will be considered in summer 2018.	SOLO2 was a portfolio study supported by the CSG with major recruitment from CSG members and former members, including Jonathan Ledermann and Charlie Gourley.
5.	OV21/PETROC: a randomized Gynecologic Cancer Intergroup phase II study of intraperitoneal versus intravenous chemotherapy following neoadjuvant chemotherapy and optimal debulking surgery in epithelial ovarian cancer. Provencher, D. M et al. Ann Oncol 2018 29(2): 431-438.	PETROC was the first trial of intraperitoneal chemotherapy in the UK, and the first trial of intra-peritoneal chemotherapy following interval debulking surgery. It showed that three cycles of intra-peritoneal carboplatin and paclitaxel was superior to three cycles of conventional intra-venous chemotherapy. Intra-peritoneal chemotherapy remains deeply controversion in the management of ovarian cancer, but PETROC demonstrated that it can be given	Developed by the CSG in conjuction the Canadian NCIC

	across multiple UK centres safely and effectively.	

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Gynaecological Cancer CSG portfolio, 19 trials closed to recruitment and 22 opened.

Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	1809	823	1628	823	9.3	4.7
2014/2015	899	891	705	869	4.0	5.0
2015/2016	930	1312	883	1058	5.04	6.04
2016/2017	1053	2297	953	1100	5.44	6.28
2017/2018	878	3192	773	1087	4.42	6.21