NCRI
National
Cancer
Research
Institute

NCRI Gynaecological Cancer Clinical Studies Group

Annual Report 2015-16

Partners in cancer research

NCRI Gynaecological Cancer CSG
Annual Report 2015-16

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

The NCRI Gynaecological Cancer Clinical Studies Group has a long history of leading and recruiting to academically-driven trials that have changed practice. We currently lead flagship international studies in all three major gynaecological disease areas.

Highlights of this year included the opening of ICON8B, a large phase III trial exploring whether dose-dense weekly chemotherapy and bevacizumab can be combined to improve outcomes in first line poor-prognosis ovarian cancer. We are also now running two subtype specific ovarian cancer trials, NiCCC (clear cell) and LOGS (low grade serous carcinoma), the latter in collaboration with the US Gynecologic Oncology Group. We lead INTERLACE, an international trial in cervical cancer, providing an opportunity to improve outcome in this disease not only by introducing a new treatment, but also through better quality control of radiotherapy. The CSG also participates in SHAPE, a trial of simple versus radical surgery in early cervix cancer. The CSG is due to open STATEC, a new international surgical trial in endometrial cancer, in 2016. Thus, with large-scale studies in each major disease area, we will remain an internationally competitive group.

In the past twelve months, we have had significant publications, with both the CHORUS and ICON6 trials appearing in the *Lancet*, and CIRCCA and updated data from Study 19 in *Lancet Oncology*. The ARIEL2 study featured as an oral presentation at both ASCO and ESMO in 2015, whilst PETROC and further data from Study 19 will be presented as oral abstracts at ASCO 2016. CSG members are also invited speakers at ASCO and ESMO in 2016.

2. Structure of the Group

The main structure of the Group has not altered with three Subgroups (ovary, endometrium and cervix/vulva) based upon primary disease site. Dr Ros Glasspool and Professor Richard Edmondson remain Chairs of the ovary and endometrium subgroups respectively. Dr Emma Hudson took over from Professor Nick Reed as chair of the Cervix/Vulva Subgroup. The CSG would like to express its thanks to Nick Reed for his sterling service to the CSG over many years.

Subgroups continue to meet two/three times per year, usually once or twice face-to-face. The endometrium and cervix subgroups held a second joint meeting in April 2016, and the Ovary Subgroup continues to have its annual meeting with the Scottish Gynaecological Cancer Group in

Glasgow in February. There was a second and successful CSG clinical trials meeting in London in December 2015.

The first two trainee members of the Gynaecological CSG, Debra Josephs and Michelle Mackintosh, will complete their two year terms in mid-2016, and there was an impressive list of applicants to replace them, again suggesting a wide enthusiasm for clinical trials amongst trainees in the three main specialties (medical oncology, clinical oncology, gynaecological oncology).

3. CSG & Subgroup strategies

Main CSG

The over-arching and unchanging strategy of the Gynaecological CSG is to co-ordinate a portfolio of clinical trials that will collectively permit innovative and practice-changing research in gynaecological cancers. These trials will cover the spectrum of gynaecological malignancies and will be available to women throughout the UK. The three key priorities for the coming five years were outlined in the strategy document of 2015:

The first is to maximise recruitment, especially in centres that are currently under-recruiting. Liaison with the Gynaecological Cancer Leads in the fifteen Clinical Research Network regions remains challenging, with variable enthusiasm and engagement around the country. This strategy will also require that clinical trials be opened in as many centres as possible, rather than only in centres that have traditionally recruited. The ovary subgroup in particular is seeking to work co-operatively with industry partners to ensure that this happens. Innovative trial designs, such as umbrella studies, will reduce downtime between trials, thereby improving overall recruitment.

The second is to broaden the portfolio. In particular this will involve collaboration with other CSG in the areas of prevention (most pressingly in obesity-induced endometrial cancer), survivorship and supportive and palliative care.

Finally, through the NCRI and ECMC networks, the CSG has a unique opportunity to lead stratified, biomarker-driven trials in gynaecological cancers, with associated translational research. TR-ICON7 and TR-ICON8/8B have ensured that multiple biological specimens (for example tumour, germline DNA, circulating tumour DNA) have been collected, which will facilitate multiple translational research projects.

Already, plans are being developed for a biomarker-drive trial in first-line high grade serous ovarian cancer. Imaginative partnership with industry as well as international collaboration will be required to ensure the success of such studies.

Cervix/Vulva Subgroup (Chair, Dr Emma Hudson)

A successful Subgroup workshop was held on 22 April 2016 in conjunction with the Endometrial Subgroup. Although not as well attended in 2015, the format of the meeting facilitated interesting and lively discussions. A further combined meeting is planned for December 2016.

In October 2015, the CIRCCA trial was published in the *Lancet Oncology* concluding that cedarinib, in combination with standard chemotherapy, has significant activity in metastatic cervical cancer, and highlighted the rationale for further trials of antiangiogenic agents for this disease.

Although the flagship trial INTERLACE continues to recruit more slowly than predicted accrual has increased recently with international collaboration. The trial is open in Mexico and several sites are in set up in Norway. Significant discrepancies in recruitment rates across the UK persist, which are being addressed by personal correspondence to all PI's of the trial.

SHAPE, which investigates the feasibility of less radical surgery in early cervical cancer, opened last year and is recruiting across the UK.

Comice is a new initiative in collaboration with AZ which investigates the role of maintenance cedarinib and olaparib after chemotherapy for advanced/ recurrent cervical cancer. This trial is in development.

The phase III trial of dose escalation IMRT, Depict, has completed recruitment and the phase III is planned.

There are several initiatives being developed in both vulval cancer and VIN using agents dependent on the aetiological cause of the disease, vaccines for HPV related disease, steroids for lichen sclerosis and immunomodulators. Collaboration with the colorectal CSG to develop a trial in HPV-associated cancers of the vulva, cervix and anus is ongoing.

Endometrial Subgroup (Chair, Professor Richard Edmondson)

The Subgroup met twice in the past 12 months, in London in December 2015 and in Manchester in 2016. The latter was an open workshop format organised jointly with the Cervix/Vulva Subgroup, a format which continues to be popular.

The endometrial portfolio has continued to grow over the last year and now has trials covering prevention, first line treatment, and management of recurrent and metastatic disease. The development of a trial for the latter (COPELIA) is a major step as this has been an area lacking in trials for some time.

The imminent opening of the STATEC study will represent a big challenge for the endometrial subgroup over the coming years in terms of recruitment but also represents a unique opportunity to 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 lacking.

The endometrial subgroup has also provided support for the newly formed Surgical Gynaeoncology Research Network, a consortium of trainees who have already carried out a national audit and submitted their first trial grant application.

Finally the inclusion of endometrial cancer in the second wave of cancer sites to participate in the 100,000 genome project is welcomed as this will provide a platform for future clinical and translational studies.

Ovarian Subgroup (Chair, Dr Ros Glasspool)

The Subgroup had face-to-face meetings in September 2015 and February 2016, the latter a joint meeting with the SGCTG. Once again, meetings were well attended with 39 and 53 attendees respectively. Following the strategy meeting, three working groups have been established to develop proposals for biomarker directed trials, trials in elderly women and surgical trials. The biomarker group met in February with follow up teleconferences and a proposal for an investigator led study has been submitted to AstraZeneca. Several surgical studies are also in development.

Key successes include opening of ICON8B, which is recruiting ahead of schedule, and OCTOPUS, as well as successful funding applications for ICON9 and TRICON8B. In early phase studies, HIPROC opened, the phase I component of PISARRO completed and PRIMROSE was funded by

CRUK's New Agents' Committee. Encouragingly, recruitment to both TRIOC and NiCCC, which had previously been of concern, has improved considerably.

A lack of recruitment to observational and screening/prevention studies has been a recurring theme in previous feedback reports to the CSG. However, in the past 12 months, the FORECEE project and a programme developing risk prediction models led by Antonis Antoniou have been funded. ROCKETS and SOCQER-2, evaluating pathways to diagnosis and quality of life following major surgery respectively, have opened with an application for a ROCKETS translational study in development.

One board remaining concern is the time it is taking to for sites to open to recruitment, which is affecting study timelines and recruitment. The CSG will continue to work with sites and sponsors to address this.

4. Task groups/Working parties

In response to the challenge posed by rare gynaecological cancers, a working group, led by Dr Marcia Hall, Professor Glenn McCluggage and Dr Lynn Hirschowitz (Chair of the British Association of Gynaecological Pathologists), have developed RaNGO – Rare Neoplasms of Gynaecological Origin. This is a translational study to ensure that tissue and germline DNA are collected from women with specified rare gynaecological cancers, along with clinical and treatment details. This is intended to act as a platform for translational research studies as well as helping to define standards of care in the UK.

As detailed above, there are also working groups within the ovarian subgroup developing trials in specific areas, including biomarker-directed studies and surgical trials.

5. Patient recruitment summary for last 5 years

Recruitment to Gynaecological CSG trials continues to be adequate. The percentage of patients entering interventional trials increased to 6% in 2015 – 16. As previously, single very large trials dominate recruitment. In 2016 – 17, the major trials will be ICON8B (ovarian cancer), INTERLACE (cervix cancer) and STATEC (endometrial cancer). It is vital that these trials recruit rapidly in as many centres as possible – ICON8B is considerably ahead of its recruitment target demonstrating that it is possible for gynaecological cancer trials to recruit rapidly.

Two clear features of recruitment persist. The first is that ovarian cancer currently dominates. In 2015 – 16, over half of recruitment (55%: 1375/2451) into trials of patients known to have a gynaecological malignancy involved ovarian cancer. There have been large endometrial cancer trials (PORTEC3, ASTEC) previously, demonstrating that broad recruitment need not be limited to ovarian cancer studies. Trials in which surgery or radiotherapy are the dominant treatment modalities continue to pose challenges: SHAPE (simple vs radical hysterectomy in early stage cervix cancer) is recruiting slowly in the UK. More positively, INTERLACE, previously of grave concern, has responded to significant effort with considerably improved recruitment over the past 12 months, partially due to increased UK recruitment and partially due to international recruitment (Mexico). INTERLACE particularly highlighted the challenges of ensuring Quality Control and consistent radiotherapy planning, especially of Intensity Modulated Radiotherapy (IMRT).

The second clear feature is geographical variation in recruitment. The charity Target Ovarian Cancer previously undertook a major piece of work in ovarian cancer, mapping regional differences

in recruitment – the data are illuminating, with an eight-fold difference between the top and bottom quartiles of recruitment by CRN. The CSG has attempted to engage with the new gynaecological leads from the fifteen Clinical Research Networks, with varying degrees of success. The roles and responsibilities of the CRN gynae cancer leads still remains unclear.

In the Gynaecological Cancer CSG portfolio, 10 no. of trials closed to recruitment and 19 opened.

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

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	4763	597	4389	597	28.6	3.9

Table 2 Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	335	10750	183	754	1.0	4.3
2013/2014	1809	823	1628	823	9.3	4.7
2014/2015	899	891	705	869	4.0	5.0
2015/2016	1441	1022	1173	975	6.70	5.57

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

The Gynaecological CSG has a prominent international outlook. There are two international consortia to which the CSG contributes strongly, GCIG (the Gynecologic Cancer InterGroup) and ENGOT (European Network of Gynaecological Oncology Trials). The CSG sends four members (and the MRC two) to these meetings. CSG members hold prominent positions of leadership in both organisations: Professor Jonathan Ledermann is co-chair of the Rare Tumour Subgroup at GCIG, whilst Professor McNeish is chair of the translational committee of ENGOT. In addition, the CSG sends two members (Susana Banerjee and Alex Taylor) to the ENGOT Gynaecological Cancer Academy from 2015 - 2017. This group seeks to develop the next generation of leaders in Gynaecological Cancer in Europe, and meets three times per year with workshops and networking events. The CSG was also well represented at the 5th Ovarian Cancer Consensus Conference in Toyko in November 2015. Members of the CSG self-fund travel to these meetings and the MRC pays the annual subscription to the GCIG.

Links to other CSG are evolving. A joint proposal (with the colorectal CSG) for a study in HPV-positive vulval and anal cancer is being developed. In addition, the Gynae CSG will participate in the HORIZONS study looking at long term recovery in patients with cancer, run by the Macmillan and the Survivorship Research Group at the University of Southampton. Dr Emma Crosbie is particularly active in primary prevention studies in endometrial cancer.

The issues relating to the CRN network gynaecological cancer leads are described above.

7. Funding applications in last year

The CSG has had another successful year, with full funding of ICON9 and TRICON8B (sample collection from participants in ICON8B) from Cancer Research UK's Clinical Research Committee. In addition, the New Agents' Committee also funded PRIMROSE, a phase I/II combination study in collaboration with Clovis Oncology and Verastem.

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
ICON 9: An international phase 3 randomised trial of cediranib and olaparib maintenance in patients with relapsed platinum sensitive ovarian cancer	Full application	Dr Shibani Nicum	Funded
TRICON8: Sample collection of ovarian cancer tissues and blood for translational research from patients participating in the Cancer Research UK MRC ICON8 trial (extension for ICON8B)	Sample collection *Extension*	Dr James Brenton	Funded
December 2015			
Development of a highly accurate DNA methylation classifier for prevalent and incident cervical pre-cancer	Full application	Professor Attila Lorincz	Funded
TransSOCQER2: The generation of a contemporaneous tissue collection from patients undergoing surgery for advanced ovarian cancer	Sample Collection application	Professor Richard Edmondson	Not funded
May 2016			
transPORTEC: Developing and validating prognostic and predictive biomarkers in high risk endometrial cancer	Full application	Professor Richard Edmondson	Not funded
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
PRIMROSE	New Agents' Committee - phase I/II trial grant	Dr Yvette Drew	Funded

8. Collaborative partnership studies with industry

The CSG has a history of a successful collaboration with industry partners such as Roche, AstraZeneca, GSK, Clovis Oncology and Boehringer Ingelheim, who have all supported trials in gynaecological cancer. The models of support have varied and include CTAAC or ECMC Alliance (NAC) funding, full industry support for investigator-initiated trials or hybrid funding. These arrangements are complex and rely greatly of the negotiations between the Clinical Trials Unit developing the trial, Industry and the Chief Investigator. Encouragingly, new proposals have been developed by and with the CSG during 2015–16. These include TAX-TORC2, a randomised phase II trial of AZD2014 and paclitaxel in platinum-resistant ovarian cancer, which has just opened. This will be the first arm of OCTOPUS (Ovarian Cancer Trials of Paclitaxel – Umbrella Study), which will be a rolling trial for women with platinum-resistant ovarian cancer with weekly paclitaxel as the control arm, to which arms containing novel agents can be added, either as single agent or in combination with the paclitaxel. Weekly paclitaxel is the agreed first-choice regime for women with

platinum-resistant ovarian cancer, and the SaPPrOC study demonstrated that there is enthusiasm for recruiting into trials with this as control arm. Another weekly paclitaxel-based trial is HIPROC, a phase I study developed with the CRUK Centre for Drug Development and Eli Lilly.

ICON9 and OCTOVA are new studies in platinum-sensitive and BRCA-mutated ovarian cancer respectively, both of which are due to open in late 2016 in partnership with AZ.

The number of commercial studies on the portfolio continues to rise, both in absolute numbers and proportion of the overall portfolio. The CSG is enthusiastic about collaboration with industry – however, there needs to be vigilance to ensure that commercial studies are not adopted onto the portfolio where there is a direct clash with academic studies and also to encourage industry to open studies beyond a narrow range of sites. The CSG, in particular the Ovary Subgroup, has developed lists of new centres with experience in large studies such as ICON8, which are keen to participate in industry studies.

9. Impact of CSG activities

The Group has led several practice changing trials over the last five years, with an excellent record of presentation at international meetings and publication in high-impact journals. The key results are:
The ICON 7 trial of bevacizumab in front-line treatment of ovarian cancer was key in assisting clinicians with decision-making about selecting the most appropriate patients for therapy. This was not evident in the data submitted for licensing. Also, the dose used was 50% of the licensed dose. However, this dose and the identification of the group most likely to benefit from the drug have been instrumental in guiding the Cancer Drug Fund process for approval. The Scottish Medicines Consortium has now approved routine use of bevacizumab in women with stage 4 disease, partially based upon ICON7 data.

The Group developed and led CHORUS, a trial comparing primary (neoadjuvant) chemotherapy with primary surgery followed by chemotherapy, and also contributed to an earlier study, EORTC 55971, with a very similar design. The EORTC trial has led to a significant change in practice, confirming the absence of detriment in survival by delaying surgery in a group of women who present with advanced disease. CHORUS (published in 2015) has shown similar results and, as a result UK, European and to some extent US practice has changed, and thus a significant proportion of patients now have primary chemotherapy. CHORUS has also shown that postoperative hospital stay is reduced in those undergoing delayed surgery.

The CSG also contributed to critical studies of the PARP inhibitors olaparib and rucaparib. Critical to this was Study 19, which showed that maintenance olaparib following response to platinum-based chemotherapy in relapsed ovarian cancer, led to dramatic increases in progression-free survival, especially in those patients with germline or somatic mutations in *BRCA1* or *BRCA2*. These data led to the European licensing of olaparib in 2015. In addition, the CSG contributed to ARIEL2 and Ariel3 using rucaparib in relapsed ovarian cancer: positive data from ARIEL2 led to FDA Breakthrough Therapy designation for rucaparib in May 2015.

Finally, data from CSG clinical trials, as well as expert input from CSG members, has led to widespread availability of germline *BRCA1* and *BRCA2* mutation testing for women with ovarian cancer in the UK. Availability remains variable, but knowledge of germline mutation status is increasingly used as a stratification factor in clinical trials.

10. Consumer involvement

The Gynae CSG has two consumer representatives. The CSG wishes to express its thanks and gratitude to Hilary Stobart who left the CSG in 2015 after four years of valuable work. We welcome Beryl Elledge who joined the Group in 2015 and joins Angela Stagg who joined in 2014.

Mrs Stagg attended the full CSG meeting December 2015 and joint Endometrium Cervix/Vulval Subgroup meeting in April 2016, and is a member of the INTERLACE TMG. She has provided consumer feedback on patient information sheet and consent form within protocol for the RANGO proposal; produced summary patient information text, and participated in Womb Alliance priority setting survey. In addition she has continued to liaise with consumer colleagues on trial matters. Mrs Stagg is a regular member of People's Health in the West of England (PHWE) Strategy group; as and allocated Core Partner public contributor at Executive Group meetings (Bristol Health Partners: BHP), she has contributed to BHP's Strategy review public consultations, etc. and its Health Integration Team progress update meetings.

Mrs Elledge also attended the full CSG meeting in December 2015, has joined the cervix subgroup and brings extensive experience from her time as co-chair of South East London Consumer Research Panel (CRP) for Cancer, a collaborative project between Guy's and St Thomas' NHS Foundation trust. The main aim of the CRP is to increase the engagement of patients /carers in the whole research process – from generation of research questions, through protocol development and advice on issues such as ethics and patient recruitment. In addition, the CRP acts as the voice in the development of lay summary and patient information sheets to aid recruitment of patients in clinical trials. Mrs Elledge is also a member of the Cecily Saunders Institute patient public involvement committee, and the patient representative on the Genomics England 100,000 genomes project at Guys and St Thomas'. Her main activities in the last year have included attending the two day NCRI Consumer induction training, attendance at the National Consent Model workshop and the Primary Care and Cancer Screening research day. She has also had input into the INTERLACE and STATEC trials for the CSG.

Both consumer members have mentors from the CSG – it is clear that mentoring arrangements are vital to ensure that the consumer members fully understand the groups' activities and strategy, as well as have an understanding of gynaecological cancer management. One immediately helpful action has been the generation of a Gynaecological CSG acronym buster, but it is apparent that the mentoring requires more intensive input. This is an area in which the CSG will develop in the next 12 months.

11. Open meetings/annual trials days/strategy days

The second Gynaecological CSG trials meeting took place at the Royal College of Physicians in London on Thursday 10 December 2015. The overall aim of the day was to celebrate the successes of the CSG and its trials since 2013, to express thanks to sites for their continue recruitment, and to present results of CSG portfolio trials to those unable to the large international meetings where they were first presented. There were 150 registrants, similar to 2013. Feedback was very positive. However, several attendees noted that the programme was heavily biased towards ovarian cancer. This largely reflects the portfolio in recent years. However, the next meeting in 2017 will have an increased number of non-ovarian trial presentation – for example PORTEC3 will have reported its initial results by then.

12. Priorities and challenges for the forthcoming year

In February 2015, the CSG set out its strategy for 2015–18. The priorities and challenges in the coming year, set against the strategic goals, as follows:

1. Core trials role - ICON9, the new flagship trial in platinum-sensitive relapsed ovarian cancer, needs to open in the first quarter of 2017. STATEC, a critical trial in endometrial cancer, needs to launch in 2016. A new trial in relapsed cervix cancer needs to be developed, and a study in vulval cancer remains a critical requirement. Work towards our long term goal of a biomarker-directed first-line trial in high grade serous ovarian cancer continues. A proposal for trial of radiotherapy in first line clear cell ovarian cancer is being developed through GCIG.
2. Trial recruitment - The trials that are open simply need to recruit to time and to target. ICON8B is doing so. INTERLACE is improving. Others are doing less well. Similarly, recruitment nationally is uneven – the CSG will continue to engage with the gynae cancer leads in the fifteen Clinical Research Networks to maximize recruitment opportunities.
3. Diversity of membership - The CSG now includes a dedicated space for a gynae-pathologist (usually the Chair of the British Association of Gynae Pathologists). In the 2016 round of applications, the CSG Chair will actively encourage applications from clinical nurse specialists and radiologists to ensure that there is a good representation from all specialties. Applications from clinical oncologists have declined in recent years, and care will be taken to ensure that this critical specialty remains represented on the Group.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
- A – Main CSG Strategy
- B – Cervix/Vulva Subgroup Strategy
- C – Endometrial Subgroup Strategy
- D – Ovarian Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Professor Iain McNeish (Gynaecological Cancer CSG Chair)

Appendix 1

Membership of the Gynaecological Cancer CSG

Name	Specialism	Location
Ms Emma Hudson	Clinical Oncologist	Cardiff
Dr Melanie Powell	Clinical Oncologist	London
Professor Nicholas Reed	Clinical Oncologist	Glasgow
Dr Alexandra Taylor	Clinical Oncologist	London
Ms Beryl Elledge	Consumer	Winchester
Mrs Angela Stagg	Consumer	Bristol
Dr Emma Crosbie	Gynaecological Oncologist	Manchester
Professor Richard Edmondson	Gynaecological Oncologist	Manchester
Dr Christina Fotopoulou	Gynaecological Oncologist	London
Dr Maria Kyrgiou	Gynaecological Oncologist	London
Dr Michelle MacKintosh*	Gynaecological Oncologist	Manchester
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 Debra Josephs*	Medical Oncologist	London
Professor Jonathan Ledermann	Medical Oncologist	London
Dr Michelle Lockley	Medical Oncologist	London
Dr Rosemary Lord	Medical Oncologist	Merseyside
Professor Iain McNeish (Chair)	Medical Oncologist	Glasgow
Dr Agnieszka Michael	Medical Oncologist	Guildford
Dr Shibani Nicum	Medical Oncologist	Oxford
Dr Lynn Hirschowitz	Pathologist	Birmingham
Mr Jim Paul	Statistician	Glasgow

*denotes trainee member

Membership of the Subgroups

Ovarian Subgroup		
Name	**Specialism**	**Location**
Dr Sanjiv Manek	Consultant Pathologist	Oxford
Mrs Sundha Sundar	Gynaecological Oncologist	Birmingham
Dr Ros Glasspool (Chair)	Medical Oncologist	Glasgow
Dr Susie Banerjee	Medical Oncologist	London
Professor Jonathan Ledermann	Medical Oncologist	London
Dr Rosemary Lord	Medical Oncologist	Merseyside
Professor Iain McNeish	Medical Oncologist	Glasgow
Dr Shibani Nicum	Medical Oncologist	Oxford
Dr Sarah Williams	Medical Oncologist	Birmingham
Dr Nafisa Wilkinson	Pathologist	Leeds

Endometrial Subgroup		
Name	**Specialism**	**Location**
Dr Jane Orton	Clinical Oncologist	Leeds
Dr Melanie Powell	Clinical Oncologist	London
Dr Nick Reed	Clinical Oncologist	Glasgow
Dr Alex Taylor	Clinical Oncologist	London
Dr Emma Crosbie	Gynaecological Oncologist	Manchester
Professor Richard Edmondson (Chair)	Gynaecological Oncologist	Manchester
Dr Andrew Clamp	Medical Oncologist	Manchester
Dr Rebecca Kristeleit	Medical Oncologist	London
Professor Jonathan Ledermann	Medical Oncologist	London
Dr Axel Walther	Medical Oncologist	Bristol
Dr Raji Ganesan	Pathologist	Birmingham
Dr Naveena Singh	Pathologist	London

Cervix/Vulva Subgroup		
Name	**Specialism**	**Location**
Ms Emma Hudson (Chair)	Clinical Oncologist	Cardiff
Dr Jackie Martin	Clinical Oncologist	Sheffield
Professor Nick Reed	Clinical Oncologist	Glasgow
Dr Alexandra Taylor	Clinical Oncologist	London
Dr Tara Barwick	Consultant Radiologist	London
Dr Jenny Forrest	Gynaecological Oncologist	Devon
Mr Jeremy Twigg	Gynaecological Oncologist	Stockton-on-Tees
Dr Faruqi Asma	Histopathologist	London
Dr Susana Banerjee	Medical Oncologist	London
Dr Rosemary Lord	Medical Oncologist	Merseyside
Professor John Tidy	Surgeon	Sheffield

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

- Application to be sought from radiologist and CNS at next round of advertisements. Progress – at least two CNS have applied to join the CSG in the spring 2016 application round.
- Develop a more formal and transparent process for Subgroup approval. Progress – all three subgroups have developed clearer criteria for formal subgroup approval of trial ideas.
- New Cervix Subgroup Chair position. Progress – Emma Hudson commenced as subgroup chair in January 2016.
- Active mentoring, greater education, earlier involvement for consumer representatives. Progress – Mentors named for both consumer representatives.
- Improved recruitment in currently low recruiting networks by end 2016. Progress – this continues to be a challenge; more targeted contact with network leads in poorly recruiting networks to be instigated.
- Increase Gynaecological CSG applications to NIHR and MRC funding schemes over next three years. Progress – one successful NIHR application (MROC, Professor Andrea Rockall), and further applications in progress (e.g. PRESS-GO, Dr Michelle Mackintosh, application to RfPB). Those presenting new trial ideas to Subgroups will be actively encouraged to seek funding from other sources as well as CRUK Clinical Research Committee.
- To ensure that translational sample collection embedded in all trial designs at first draft. Progress – this is now routine in all new trial proposals from the CSG.

B – Cervix/Vulva Subgroup Strategy

- New trial in relapsed disease. Progress – COMICE study proposal being developed by the Subgroup.
- New trial targeting HPV disease, possibly in conjunction with anal cancer (Colorectal CSG). Progress – Preliminary discussions have taken place but no firm trial idea yet in place.
- One therapy trial in relapsed vulva cancer with associated tissue collection. Progress – This remains a critical goal for the CSG.

C – Endometrial Subgroup Strategy

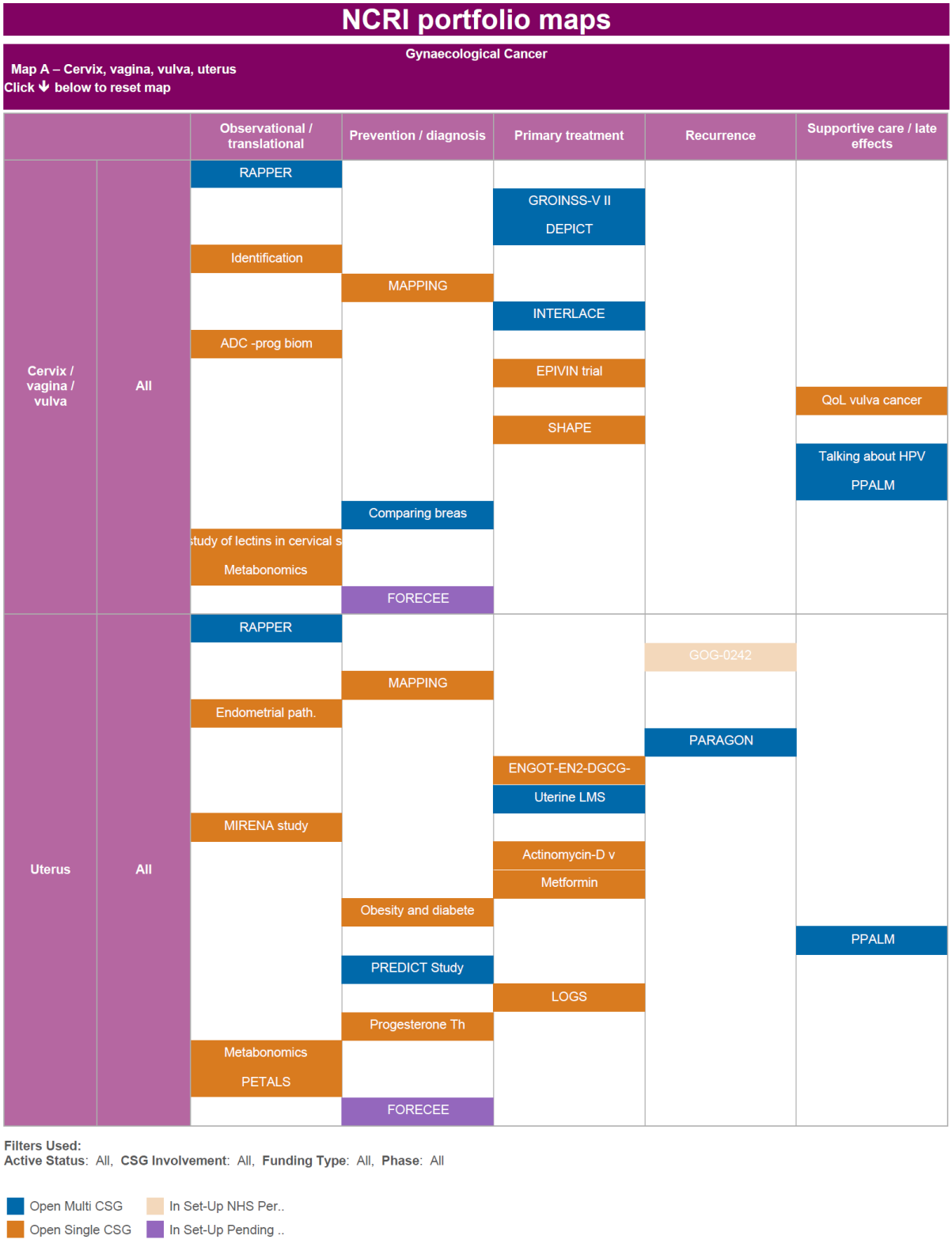
- New first-line biomarker-driven study. Progress - PORTEC4 design now radically revised to incorporate new biomarker ideas, especially importance of *POLE* mutation group.
- To launch new study of primary prevention of endometrial cancer within three years. Progress – series of preliminary trials in primary prevention being run via Manchester with the aim of establishing large primary prevention trial application in 2018.

D – Ovarian Subgroup Strategy

- New trials in elderly patients. Progress – Working Group established.
- Development of first-line biomarker-driven study. Progress – Working Group established and new proposal being developed for CRUK Experimental Medicine Programme grant call.

Appendix 3

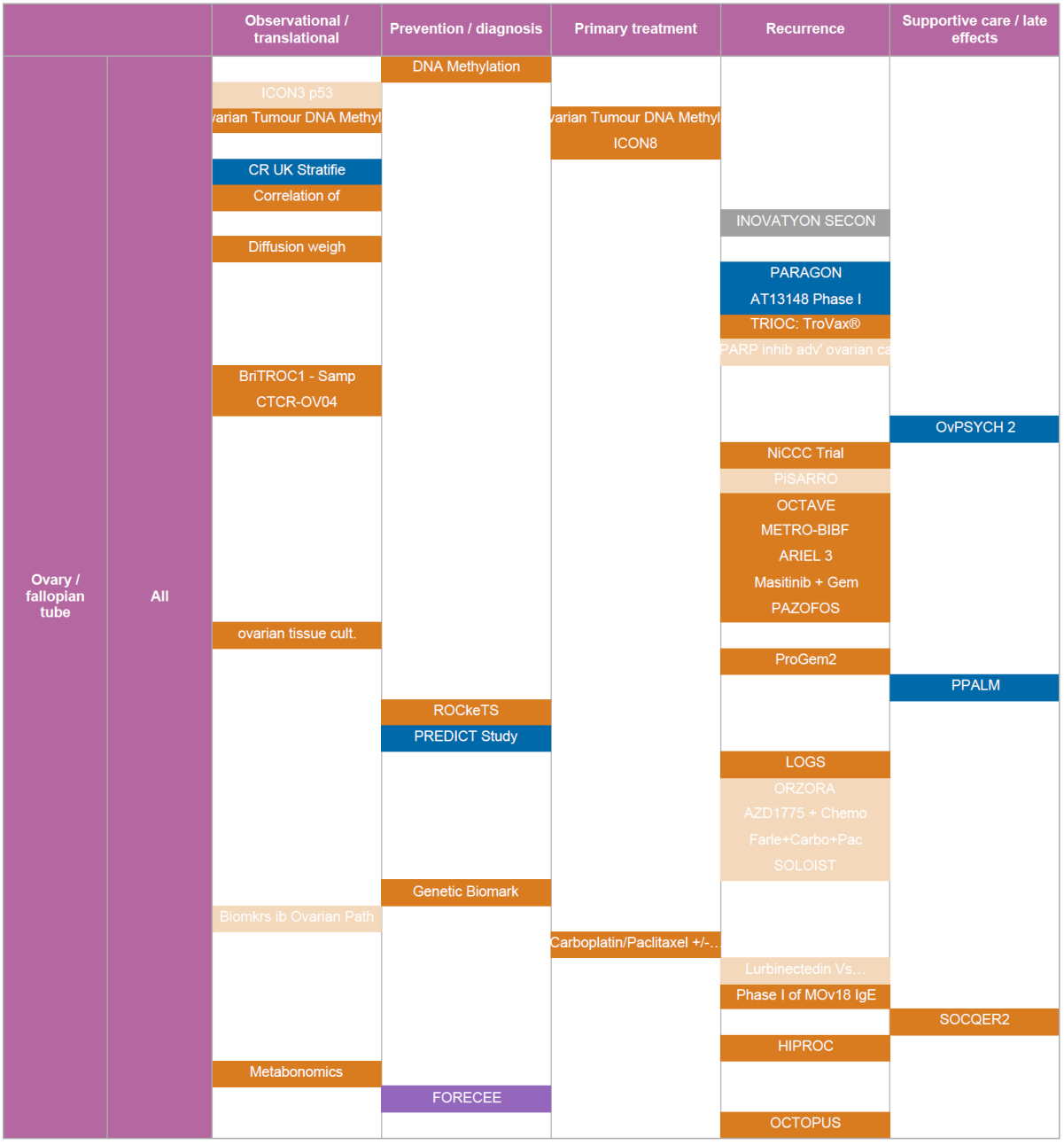
Portfolio maps



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

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

Appendix 4

Publications in the reporting year

ICON6

Ledermann JA, Embleton AC, Raja F, Perren TJ, Jayson GC, Rustin GJ, Kaye SB, Hirte H, Eisenhauer E, Vaughan M, Friedlander M, Gonzalez-Martin A, Stark D, Clark E, Farrelly L, Swart AM, Cook A, Kaplan RS, Parmar MK. Cediranib in patients with relapsed platinum-sensitive ovarian cancer (ICON6): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2016;387(10023):1066-74.

CHORUS

Kehoe S, Hook J, Nankivell M, Jayson GC, Kitchener H, Lopes T, Luesley D, Perren T, Bannoo S, Mascarenhas M, Dobbs S, Essapen S, Twigg J, Herod J, McCluggage G, Parmar M, Swart AM. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. Lancet 2015;386(9990):249-57.

ICON7 final results

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Appendix 5

Major international presentations in the reporting year

Ariel2 - ASCO June 2015

McNeish IA, Oza AM, Coleman RL, Scott CL, Konecny GE, Tinker A, O'Malley DM, Brenton J, Kristeleit RS, Bell-McGuinn K, Oaknin A, Leary A, Lin K, Raponi M, Giordano H, Goble S, Rolfe L, Yelensky R, Allen AR, Swisher EM (2015). Results of ARIEL2: A Phase 2 trial to prospectively identify ovarian cancer patients likely to respond to rucaparib using tumor genetic analysis. J Clin Oncol. 33(15).

Ariel2 – ESMO Sept 2015

Kristeleit RS, Swisher EM, Oza AM, Coleman RL, Scott CL, Konecny GE, Tinker A, O'Malley DM, Brenton J, Bell-McGuinn K, Oaknin A, Leary A, Lin KK, Raponi M, Giordano H, Maloney L, Goble S, Yelensky R, McNeish IA (2015). Final Results of ARIEL2 (Part 1): A phase 2 trial to prospectively identify ovarian cancer (OC) responders to rucaparib using tumor genetic analysis. Eur. J. Cancer. 51:S531:2700.

Lin KK, Sun J, Maloney L, Goble S, Oza AM, Kristeleit RS, Coleman RL, Scott CL, Robillard L, Mann E, Isaacson J, Harding T, Giordano H, Rolfe L, McNeish I, Swisher EM, Yelensky R, Allen A, Raponi M (2015). Quantification of genomic loss of heterozygosity enables prospective selection of ovarian cancer patients who may derive benefit from the PARP inhibitor rucaparib. Eur. J. Cancer. 51:S531:2701.