NCRI
National
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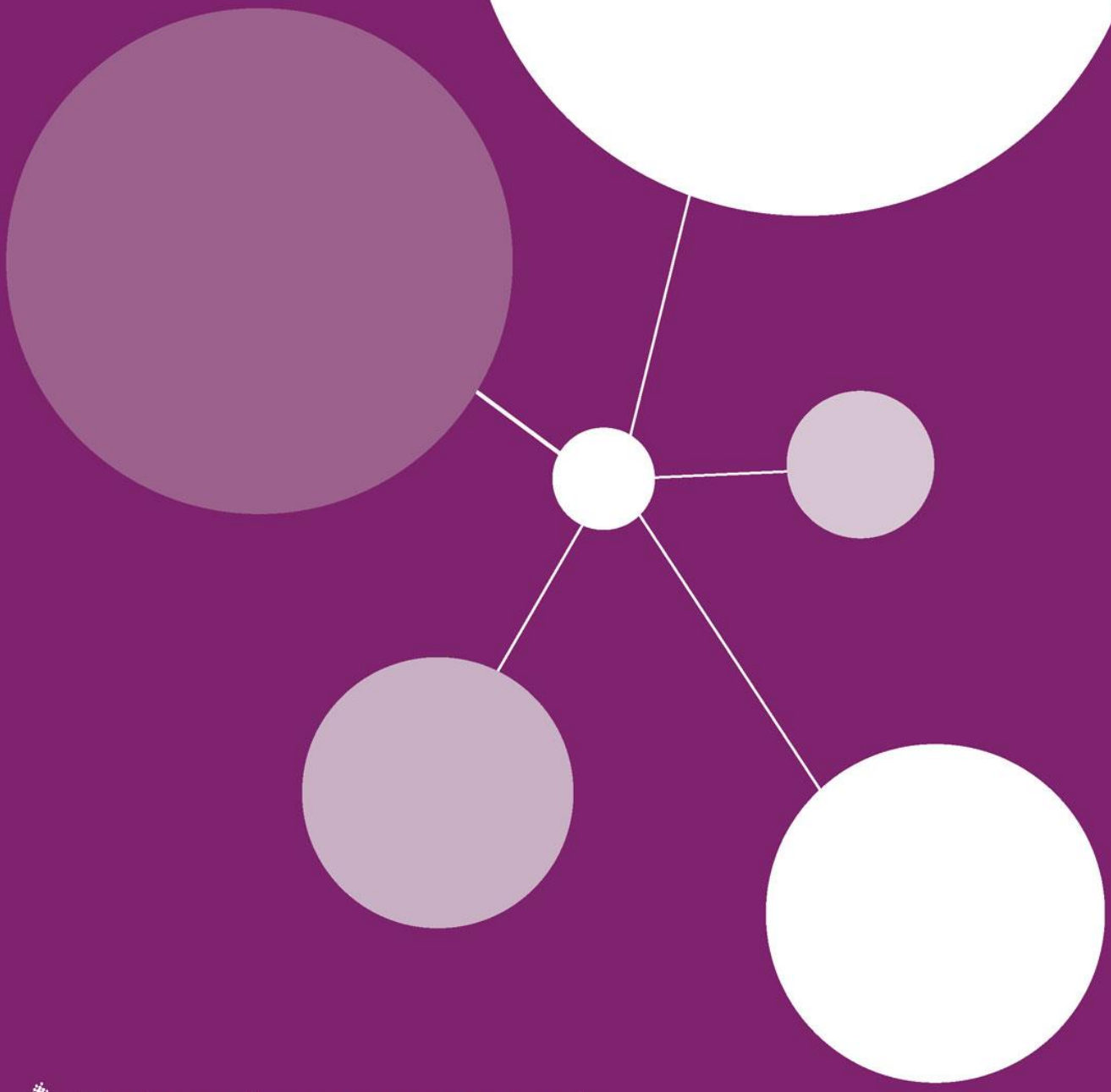
NCRI Colorectal Cancer Clinical Studies Group

Annual Report 2015-16



Partners in cancer research

NCRI Colorectal Cancer CSG Annual Report 2015-16

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

In 2015-16, the Colorectal CSG had a successful progress review by an international panel (see Appendix 6), refined its strategy, grown the portfolio and extended our interactions with other CSGs, particularly the cross-cutting CSGs Supportive and Palliative Care, Psychosocial Oncology & Survivorship CSGs and Primary Care and also the Upper GI CSG.

Our main challenges this year have again been around declining overall recruitment, gaps in our trials portfolio despite repeated attempts to attain funding for trials in these areas, and increasing capacity blocks and obstacles to clinical research in the highly pressurised service environments across all four devolved UK nations. The changes to the Cancer Drugs Fund in England have had a negative impact on our studies. Recruitment to our (and other CSG) studies has continued to be challenging not only because of the restructuring of the NIHR and funding committees and NHS pressures, but also because the move to personalised medicine and 'niche' trials. FOCUS4 exemplifies some of these issues, with a complex, adaptive trial design with biomarker defined cohorts that are not all simultaneously open. During this year, one cohort has stayed open (FOCUS4-N), one has closed (FOCUS4-D), one has opened (FOCUS4-B), one cohort is agreed and will open in late 2016 (FOCUS4-C), two cohorts are in very advanced stages of negotiation (FOCUS4-A and FOCUS4-E) and one is in earlier stages of negotiation (FOCUS4-F). There is a real need to understand why colorectal cancers do not respond to the current immune checkpoint inhibitors so that we can design studies using rationale combinations and biomarkers to exploit these agents and deliver meaningful impact on outcomes such as those increasingly seen in other solid tumours.

The top three achievements of the Colorectal CSG in 2015-16 were:

1. Successful review by our International Panel with very helpful guidance to both our CSG, and also to NCRI. The discussions have been particularly useful in further increasing our international collaborations.
2. Opening of the Add-Aspirin trial in the adjuvant treatment of stage II and III colorectal cancer in October 2015 and having 120 patients registered and 58 randomised over the subsequent six months, meeting our recruitment targets.
3. FOCUS4 progressing with 88 UK sites open, 432 patients registered, and 116 patients randomised. The rapid completion of the FOCUS4-D study constituted an important milestone for the FOCUS4 trial programme because although there was a disappointing lack of benefit from Her-1, 2, 3 inhibition in 'all wild type' CRC, it means we have quickly

and efficiently answered one of the compelling questions posed at the outset of the trial and can now investigate an alternate therapeutic approach in this cohort.

2. Structure of the Group

The Colorectal CSG has not changed its structure over the last few years and continues the same leadership team of the main CSG (Chaired by Professor Richard Wilson), the Adjuvant & Advanced Disease Subgroup (Chaired by Professor Anne Thomas), the Anorectal Subgroup (chaired by Dr Richard Adams), the Screening & Prevention Subgroup (Chaired by Professor Mark Hull) and the Surgical Subgroup (Chaired by Mr Simon Bach). There are currently 24 members on the Colorectal CSG (see Appendix 1). Of these, 20 are clinical/scientific members, two are consumer representatives and two are trainee members. Our membership represents a broad balance of specialties with five medical oncologists, five surgeons, four clinical oncologists, two pathologists, two radiologists, a specialist nurse, a geneticist, a gastroenterologist and a statistician. We also have representation from all four UK devolved nations.

There is a policy of regular rotation of membership and the choice of new members is based on their record of involvement with colorectal cancer research and on the need to maintain a balance of expertise, career stage, gender and geographical representation. There have been changes in membership over the last year and we said farewell and thanked our consumers Alison Allam and Ann Russell, Drs Vanessa Potter and Dawn Storey, Ms Katharine Williams, Mr Paul Ziprin and Professor Dion Morton. In particular, we wished Professor Will Steward a happy retirement and thanked him for his many years of outstanding contribution including successfully Chairing our CSG. We welcomed the new members Professor Gina Brown, Ms Susan Moug, Dr Nick West, Ms Jane Winter and our two new consumer members Dr Sandra Irvine and Ms Monica Jefford. We have greatly enjoyed and gained from the contributions of our inaugural trainee members Dr Jenny Seligmann and Mr Angus McNair and look forward to continuing work with them in other roles as they rotate off and are replaced by two new trainees.

3. CSG & Subgroup strategies

Main CSG

Our 2014-19 strategy was developed at a strategy meeting in November 2013 and has since been refined following significant changes in our CSG and Subgroup leadership, through discussions prior to and following our International Progress Review in April 2015 and at our main CSG and Subgroup meetings.

We have increased our interactions and collaborations with:

- The ECMCs and ECMC Network through FOCUS4 and the ECMC Combinations Alliance.
- The Supportive & Palliative Care CSG and the Psychosocial Oncology and Survivorship CSG through presentations and attendance at main CSG and subgroup meetings.
- CTRad through interaction on specific trials but also methodologies.
- The Upper GI CSG on studies in CRC liver metastases and small bowel cancer.
- Our aim of international collaborative working to facilitate delivery of practice changing studies in rare cancers, such as anal cancer and small bowel cancer, has been achieved with ongoing recruitment to INTERAACT and the opening of the BALLAD trial and recruitment to it in the UK and France.
- We have increased our involvement with early career researchers and clinical trainees

through CSG and Subgroup membership and with the very successful surgical trainee trial networks.

- The very challenging area of post mortem studies has been sensitively and successfully initiated with the ground-breaking GIFT study in Leeds, with its initial results submitted for publication.
- The opening of the Add-Aspirin trial has aided our strategic aim of providing pragmatic studies as a balance to our complex 'niche' studies in order to maintain high recruitment and provide trial access to all recruiting sites.
- Under Professor Mark Hull's leadership, there has been a clear expansion of research activities in screening, prevention and early diagnosis.
- The strategy of the Adjuvant & Advanced Disease Subgroup is to ensure that our trial portfolio is of an international standard from early phase studies to large biomarker-driven phase III studies encompassing qualitative research where appropriate to improve the lives of patients with colorectal cancer.
- Our strategy of identifying clinical and translational 'research gaps' in CRC is underway with a very productive series of meetings of eight workstreams which started this year. Many CSG and Subgroup members are working with the charity Bowel Cancer UK on this project and there will be both a report and a scientific publication emanating from this project. The programme has already highlighted areas of unmet need, and one of the major challenges will be designing studies with the appropriate methodology to address the questions that arise.
- The S-CORT stratified research programme on colorectal cancer biology is investigating our current and historical portfolio clinical trials and translational studies to improve our understanding of the molecular subtypes within CRC, develop biomarker stratifications that predict outcomes from current and novel therapies and enable personalised treatments that improve outcomes in early and late stage CRC.

4. Task groups/Working parties

We have set up a Task Group in conjunction with the Upper GI CSG on colorectal liver metastases. This has representation from both CSGs and includes expertise in liver surgery, systemic therapy and interventional oncology including SIRT and SABR. This group met for the first time after our recent Annual Trials Meeting and a further meeting is planned in September 2016. This will result in better co-ordination of clinical and translational research activity, and will also enhance our ability to specifically develop studies around the treatment of colorectal liver metastases and to compete successfully for trial grants in this field.

5. Patient recruitment summary for last 5 years

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	8855	2560	7767	2560	22.6	7.4

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	4690	6416	3433	3151	8.5	7.8
2013/2014	3276	4432	1908	1924	4.7	4.8
2014/2015	4825	1081	4728	1020	11.7	2.5
2015/2016	4872	1995	4842	1346	11.99	3.33

In the Colorectal Cancer CSG portfolio, 16 trials closed to recruitment and 13 opened during 2015-16. There are currently 66 trials open and eight in set-up encompassing both interventional and non-interventional studies and academic and commercial studies, and spread across adjuvant and advanced disease, surgery, anorectal and screening and prevention categories. The Group feels its portfolio is reasonably broad and can include the majority of patients seen with colorectal cancer, although there are still some very significant gaps that we are trying to fill.

Since 2011-12, there has been a fall in recruitment to interventional studies, but we were very pleased to see this trend being reversed (albeit by small numbers) in 2015-16. While the figures for trials opening are encouraging, these are lower than in previous years, and many of the trials opening will recruit relatively small numbers and only from a small selection of our centres. There is also a continuing excess of observational over interventional trials. We are trying very hard to develop and obtain funding for large, pragmatic interventional trials as well as personalised medicine studies in both early and advanced disease settings. The opening of additional centres and new cohorts in FOCUS4 and the rapid roll-out of Add-Aspirin will significantly improve accrual to interventional trials.

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

We have made significant headway in enhancing our involvement with the Supportive & Palliative Care CSG and the Psychosocial Oncology & Survivorship CSG particularly, and to a lesser extent with the Primary Care CSG. This has included invitations to both our CSG and Annual Trials meetings and several dedicated teleconferences. We anticipate significant outputs from the much more mutually informed and collegiate working relationships that we now have. A more coordinated approach to working with the Upper GI CSG on colorectal liver metastases has been addressed by both Groups, and there is now the above mentioned Task Group, as well as increased cross-representation on the appropriate Subgroups of both CSGs.

We continue to have very good joint working around the International Rare Cancers Initiative (IRCI) with colleagues from the NCI, Canadian Cancer Trials Group, EORTC, INCA, Australia and Japan. Several CSG members continue their work in the Anal Cancer and the Small Bowel Adenocarcinoma Working Groups, with recruitment to the InterAACT relapsed/metastatic anal cancer trial being highest of any IRCI trial. The adjuvant BALLAD trial in SBA has now opened in the UK and France with six patients recruited, and the trial has been submitted for funding in Japan, the Netherlands and Belgium. A parallel trial in advanced SBA exploring use of a PD-1 inhibitor is in final negotiation.

Agreement has been reached with the Canadian Cancer Trials Group to extend FOCUS4 to Canada

which will help with recruitment but also allow development of new biomarker-stratified cohorts and access to further novel agents.

Unfortunately, our successful first joint meeting between the leadership of the Colorectal and Upper GI CSGs and the GI Cancer NIHR Cancer Network Subspecialty Leads last year has not yet been repeated. We aim to have our next joint meeting in autumn 2016.

7. Funding applications in last year

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
April 2015 (Population Research Committee)			
CHALLENGE UK: A UK arm of the Colon Health And LifeLong Exercise chaNGE trial.	Full application	Dr Vicky Coyle	Funded
July 2015 (CTAAC)			
OCTOPUS: An adaptive randomised factorial phase III trial of FOLFOX +/- Irinotecan +/- Bevacizumab in patients with liver only metastases from colorectal cancer	Outline application	Professor John Primrose	Full application not invited
December 2015			
A Revolutionary Approach for Enumeration and Characterisation of Circulating Tumour Cells in Metastatic Colorectal Cancer	Feasibility application	Dr Nicholas Bryan & Dr Thomas Hanna	Not funded
European phase III study comparing in association with neoadjuvant chemoradiotherapy, a radiation dose escalation using 2 different approaches	Feasibility application	Professor Arthur Sun Myint	Not funded
FOxTROT2: A randomised controlled trial aiming to establish whether giving 6 weeks of combination chemotherapy prior to surgery improves the probability of cure for patients with operable colon cancers compared to surgery alone	Feasibility application	Professor Dion Morton	Not funded
CREATE: Chemotherapy for Rectal cancer before or After local TrEatment. A UK led international phase III randomised trial comparing 12 weeks of chemotherapy either before or after standard local pelvic treatment in MRI defined operable cancer at high risk of metastatic relapse	Outline application	Dr Simon Gollins	Invited to submit a full application
QUICKSTEP: A window of opportunity study platform to allow investigation of the modulation of the tumour microenvironment in colorectal cancer	Outline application	Professor Gary Middleton	Invited to submit a full application
May 2016			
CREATE: Chemotherapy for Rectal cancer before or After local TrEatment. A UK led international phase III randomised trial comparing 12 weeks of chemotherapy either before or after standard local pelvic treatment in MRI defined operable cancer at high risk of metastatic relapse	Full application	Dr Simon Gollins, Professor David Sebag-Montefiore & Mr Simon Bach	Not funded
Screening for colorectal cancer using the volatile faecal metabolome and SIFT-MS	Full application	Dr Claire Turner & Professor John Hunter	Not funded

Validation of POLE proofreading domain mutation as a biomarker in colorectal and uterine cancers	Full application	Dr David Church	Not funded
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
Prepare-ABC – prehabillitation for colorectal cancer patients	HTA – Full application	Mr James Hernon	Funded
Lilly cdc7 inhibitor phase I/II trial with an expansion cohort in metastatic CRC	CRUK New Agents Committee	Professor Richard Wilson	Funded
Parastomal hernia commissioned call	HTA – Full application	Neil Smart and Tom Pinkney	Not funded
CREST 2	HTA – Full application	Mr Jim Hill	Decision awaited
CoSINe European colorectal trials network for surgery	H2020 - Full application	Mr Simon Bach	Not funded
HiP - Surgical technique for frail patients with rectal cancer	BDRF - Full application	Mr Dale Vimalchandran	Funded
Granule – Undergraduate training workshops for participation in RCT's	BDRF - Full application	Mr Aneel Bhangu, Mr Simon Bach	Funded

On behalf of the CSG, Professor Sebag-Montefiore drew up a discussion document reviewing our funding and strategy to improve this. The key points from it are highlighted below:

- In comparison to other CSGs dealing with common solid tumours, our Group was not found to be faring worse on funding applications.
- We must avoid competing applications from within and outside our CSG and Subgroups (e.g. liver metastases).
- We must identify portfolio gaps.
- Applicants need to circulate the application to the full CSG membership for comments
- We should use the full range of expertise of the CSG including patient and PPI involvement.
- We must better record CSG member feedback in minutes from Subgroups.
- We should engage and develop academic trainees.
- Applications must be circulated broadly in both outline and near-final form in good time before submission.

8. Collaborative partnership studies with industry

There were eight industry trials in our portfolio this year that have been adopted by the NIHR. These studies can be problematic for our CSG both because of competition with our CSG-developed academic studies (e.g. MODUL and IMPALA with FOCUS4) and poor information received about the progress of these trials for which we are meant to have an oversight role.

The FOCUS4 trial has involved ongoing very close working with a number of both small and large pharmaceutical companies. Some agents are licensed already in other indications, but others (e.g. AZD1775 WEE1 inhibitor) have only been used in relatively small numbers of patients and a recommended phase II dose only recently determined. Hence, discussions, agreement and protocol development for FOCUS4 biomarker-stratified cohorts using these agents are both complex and very time-consuming.

A recurrent feature of collaboration with industry is late withdrawal from studies by companies with

limited or no warning or compensation. Some of these had full regulatory and ethical approvals and all involved considerable, time and resource from CTUs, the CSG and investigators.

We continue to have very positive engagement with pharmaceutical companies through the ECMC Combinations Alliance, with a variety of phase I/II trials in development which will have expansion cohorts targeting metastatic colorectal cancer.

9. Impact of CSG activities

The FOCUS4 trial continues to bring together our two cancer research networks (the ECMC network for early phase trials and the four UK devolved NCRNs for late phase trials). This enhanced understanding and collaborative working will be very beneficial for future precision medicine studies both from our and other CSGs.

Members contribute significantly to NICE and HTA appraisals and to NICE guidelines. Dr Potter was the coordinator for NCRI/RCP/RCR/ACP/JCCO and produced our contribution to the Multiple Technology Appraisal (MTA) of Cetuximab (review of TA176) and panitumumab (partial review of TA240) for the first line treatment of metastatic colorectal cancer with this activity lasting all of this reporting year.

Our collaboration with the two national UK colorectal cancer charities continues to grow. Beating Bowel Cancer and Bowel Cancer UK are both full partners in the S-CORT stratified medicine programme. Bowel Cancer UK are leading on and partnering with multiple CSG and Subgroup members on the critical research gaps analysis project for colorectal cancer under co-Chairs Professors Ian Tomlinson and Richard Wilson. There have been meetings of most of the eight workstream groups, and the report and commissioned publication in Gut from this work should both be published in the next reporting year. The identification of these gaps will allow a targeted programme of future grant applications in areas of unmet need.

The Surgical Subgroup continues its exemplary work in successful engagement of recently appointed consultants, trainees and now medical students in trial design, set-up and delivery with glowing results. The Surgical Subgroup continue its very successful collaboration with subspecialty associations (such as ACPGBI and ESCP), charities and consumers, NIHR and the RCS. As a result of a succession of themed trials days at the RCS to develop RCS/ACPGBI research initiatives through a Delphi research exercise (led by Ms Nicola Fearnhead), a series of national research priorities in colorectal surgery were agreed and funding applications are under development, primarily with the BDRF through commissioned calls.

10. Consumer involvement

Our consumer representatives have provided outstanding support and input into all facets of working of the Colorectal Cancer CSG, both at the main CSG and Subgroup meetings. These members provide written comments on an increasing volume of documents circulated for discussion. Mentorship for our consumer members is an important component of their success. Mrs Ann Russell and Ms Alison Allam both stepped down this year and were replaced by Dr Sandra Irvine and Mrs Monica Jefford. Although Ann has stepped down formally from the CSG, she is still very involved with us through her roles in SPADE (the NIHR Strategic PPI Advice, Delivery and Evaluation panel), and the TREC, FOCUS4, ADD-ASPIRIN TRIAL and CHALLENGE UK trials and provides a

link with the Primary Care CSG of which she now sits on as a member.

Sandra Irvine is a member of the Northern Ireland Cancer Research Consumer Forum and its Bowel Cancer Interest Subgroup, Communication & Awareness Subgroup and Forum Training & Evaluation Subgroup. She is also the PPI representative for the S-CORT Belfast centre and the DMEC for our CSG study exploring Vitamin D in colorectal cancer. She has reviewed grants for the CSG for CTAAC/CRC and provided input to a fellowship submission by a researcher in Southampton to develop a physical activity intervention for colorectal cancer survivors by email, telephone interview and review of documents). She attended the NCRI Consumer Forum in London in March 2016 and the inaugural S-CORT Scientific meeting in London. She has a key role in planning and the forthcoming PPI event and meeting for S-CORT in Belfast.

Monica Jefford is a volunteer for Bowel Cancer UK, a Patient Advisory Group member volunteer for the London Research Design Service, a NCRI Consumer Research Forum (CRFO) member, an invited attendee at the NIHR CRN South London Partnership Board Meetings, a member of the National Research Ethics Committee (REC) in London Hampstead, a member of the South East London Cancer Help Centre Bowel Cancer Support group and a member of the SELRN Consumer Research Panel. She is a PPI advisor for the Royal Marsden NHS Foundation Trust (TRM) Institute of Cancer Research (ICR), a member of Clinical Research Facility Management Strategy Group for the Biomedical Research Centre and a member of the Patient and Carer Research Review Panel. At a trial level, she is a member of the TRACC TMG. She was also a speaker/participant at the PPI in Research Macmillan Cancer Research and TRM in October 2015, the ICR BRC meeting in April 2016, the Clinical Trials TRM, ICR BRC meeting, the Bowel Cancer UK presentation to deaf forum and the Patient experience presentation for Imperial College medical students as part of their primary care module.

11. Open meetings/annual trials days/strategy days

Our 2016 Annual Trials Meeting took place in, what for many of us, was a new venue of the Cavendish Conference Centre. It was over-subscribed and had a large audience from a wide range of disciplines and backgrounds who interacted freely throughout.

Mr John Scholefield Chaired the screening session with superb talks on FIT; new opportunities and challenges by Professor Stephen Halloran; optimising screening uptake by Dr Christian von Wagner and high quality colonoscopy by Dr Colin Rees. Dr Mark Harrison and Professor Maria Hawkins updated us on stereotactic radiotherapy and its role in liver/lung metastases and pelvic nodal relapse. Mr Simon Bach discussed research on post-operative pain following bowel surgery and Dr Matt Wilson introduced us to the UK perioperative medicine clinical trials network and described their new research initiatives and opportunities for collaboration with us. Professor Kerry Courneya from the University of Alberta, Edmonton, Canada gave an outstanding keynote lecture on Physical Activity and Cancer. This set the scene well for descriptions by Dr Vicky Coyle on CHALLENGE UK and Mr James Hernon on the PREPARE-ABC trial. We then heard updates from our trainee member Dr Jenny Seligmann on the FOCUS4 trial, Professor Tim Maughan on S-CORT, Professor Ruth Langley on Add-Aspirin, Mr Joim Hill on CREST and CREST-2 and finally Subgroup reports from Professors Mark Hull and Anne Thomas, Dr Richard Adams and Mr Simon Bach.

In our feedback, 67 of 72 responders rated the meeting as good or excellent; 67 of 72 said it was mostly or highly relevant to their CPD needs; 69 of 72 felt the meeting was of the right length and all found the content of the presentations good or excellent. The free text comments were mostly very

positive and sometimes very amusing and as always will be used to help us refine the programme and format for next year's meeting.

12. Priorities and challenges for the forthcoming year

The three top priorities for the Colorectal CSG for 2016-17 are:

1. To complete our critical research gaps analysis with Bowel Cancer UK and use this to guide our future grant applications and trial development.
2. To increase the number of, and accrual to, our portfolio studies, particularly our interventional trials.
3. To increase our collaborations with other CSGs and relevant research groups within the UK and also with our international colorectal cancer research partners.

The three main challenges for the Colorectal CSG for 2016-17 are depressingly similar to those of last year and are:

1. Delivery of increasingly complex trials across all four UK nations in a time of increasing NHS capacity blocks, limited time for NHS consultant involvement and severe financial pressures.
2. How to deal with the problems of equitable, reasonable and consistent access to new drugs, procedures and devices across the four UK devolved nations and with a changing and currently undefined 'new' Cancer Drugs Fund.
3. How to promote, undertake and complete in timely fashion clinical and translational colorectal cancer research with reduced support from our reconfigured clinical research networks particularly in England and Wales and increased emphasis on other disease areas.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

- A – Main CSG Strategy
- B – Surgical Subgroup Strategy
- C – Anorectal Subgroup Strategy
- D – Screening & Prevention Subgroup Strategy
- E – Adjuvant & Advanced Disease Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Appendix 6 – Strengths & Weaknesses from the Colorectal Cancer CSG 2015 Progress Review

Dr Richard Wilson (Colorectal Cancer CSG Chair)

Appendix 1

Membership of the Colorectal Cancer CSG

Name	Specialism	Location
Professor Diana Eccles	Clinical Geneticist	Southampton
Dr Richard Adams	Clinical Oncologist	Cardiff
Dr Mark Saunders	Clinical Oncologist	Manchester
Professor David Sebag-Montefiore	Clinical Oncologist	Leeds
Dr Ricky Sharma	Clinical Oncologist	Oxford
Professor Richard Wilson (Chair)	Clinical Oncologist	Belfast
Dr Alexandra Irvine	Consumer	Belfast
Ms Monica Jefford	Consumer	Surrey
Professor Mark Hull	Gastroenterologist	Leeds
Dr Jane Winter	GI Cancer Nurse	Southampton
Dr Janet Graham	Medical Oncologist	Glasgow
Dr Sheela Rao	Medical Oncologist	London
Dr Jenny Seligmann*	Medical Oncologist	Leeds
Professor Anne Thomas	Medical Oncologist	Leicester
Dr Nick West	Pathologist	Leeds
Professor Manuel Salto-Téllez	Pathologist	Belfast
Professor Gina Brown	Radiologist	London
Dr Rohit Kochhar	Radiologist	Manchester
Dr Louise Brown	Statistician	London
Mr Simon Bach	Surgeon	Birmingham
Mr James Hernon	Surgeon	Norwich
Mr James Hill	Surgeon	Manchester
Mr Angus McNair*	Surgeon	Bristol
Ms Suan Moug	Surgeon	Glasgow

*denotes trainee member

Membership of the Subgroups

Surgical Subgroup		
Name	**Specialism**	**Location**
Mr Angus Mcnair**	Clinical Lecturer in Academic Surgery	Bristol
Mrs Ann Russell	Consumer	St Neots
Mr Simon Bach (Chair)	Surgeon	Birmingham
Mr Aneel Bhangu*	Surgeon	Birmingham
Mrs Julie Cornish*	Surgeon	Oxford
Mr James Hernon	Surgeon	Norwich
Mr James Hill	Surgeon	Manchester
Miss Nicola Fearnhead	Surgeon	Cambridge
Professor Dion Morton**	Surgeon	Birmingham
Mr Tom Pinkney**	Surgeon	Birmingham
Mr Jared Torkington	Surgeon	Cardiff
Mr Dale Vimalachandran	Surgeon	Chester
Mr Paul Ziprin	Surgeon	London

Screening & Prevention Subgroup		
Name	**Specialism**	**Location**
Professor Diana Eccles**	Clinical Geneticist	Southampton
Mrs Lindy Berkman	Consumer	London
Dr Ann Mackie	Director, PHE Screening	London
Professor Wendy Atkin	Epidemiologist	London
Professor Roger Blanks	Epidemiologist	Oxford
Professor John Burn	Epidemiologist	Newcastle
Dr Christian von Wagner	Epidemiologist	London
Professor Mark Hull (Chair)	Gastroenterologist	Leeds
Professor Colin Rees	Gastroenterologist	Newcastle
Professor Annie Anderson	Nutritionist & Dietician	Dundee
Professor John Saxton	Physiologist	East Anglia
Mr Simon Bach**	Surgeon	Birmingham
Professor Bob Steele	Surgeon	Dundee

Anorectal Subgroup		
Name	**Specialism**	**Location**
Dr Richard Adams (Chair)	Clinical Oncologist	Cardiff
Dr Duncan Gilbert	Clinical Oncologist	Brighton
Dr Simon Gollins	Clinical Oncologist	Denbighshire
Dr Mark Harrison	Clinical Oncologist	Watford
Dr Leslie Samuel	Clinical Oncologist	Aberdeen
Professor David Sebag-Montefiore	Clinical Oncologist	Leeds
Mr Alf Oliver	Consumer	Hull
Dr Sheela Rao	Medical Oncologist	London
Professor Phil Quirke	Pathologist	Leeds
Dr Gina Brown	Radiologist	London
Mr Andrew Renehan	Surgeon	Manchester

Adjuvant & Advanced Disease Subgroup		
Name	**Specialism**	**Location**
Dr Leslie Samuel	Clinical Oncologist	Aberdeen
Dr Mark Saunders	Clinical Oncologist	Manchester
Professor Richard Wilson	Clinical Oncologist	Belfast
Mrs Ann Russell	Consumer	St Neots
Dr John Bridgewater	Medical Oncologist	London
Dr Ian Chau	Medical Oncologist	London
Dr Janet Graham	Medical Oncologist	Glasgow
Dr Tim Iveson**	Medical Oncologist	Southampton
Professor Gary Middleton**	Medical Oncologist	Birmingham
Dr Paul Ross**	Medical Oncologist	London
Professor Anne Thomas (Chair)	Medical Oncologist	Leicester
Professor Phillip Quirke	Pathologist	Leeds
Professor John Primrose	Surgeon	Southampton

*denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

- Extend and formalise our interactions and collaborations with a number of groups including:
    - ECMCs and ECMC Network
    - Supportive & Palliative Care CSG
    - Psychosocial Oncology and Survivorship CSG
    - Biomarkers & Imaging CSG
    - CTRad
    - Upper GI CSG on studies in CRC liver metastases, peritoneal malignancies and small bowel cancer
- Work collaboratively on an international scale to facilitate delivery of practice changing studies in the fields of colorectal cancer, anal cancer, small bowel cancer and peritoneal malignancies, particularly in rare cancers and in rare subgroups of more common cancers.
- Increase our engagement with:
    - consumers
    - early career researchers and clinical trainees
    - CIs of UKCRN Cancer portfolio trials who do not currently liaise with the Colorectal CSG
- Maintain excellent imaging, surgery, pathology and radiotherapy QA in all our clinical trials through active engagement with:
    - diagnostic radiology
    - pathology
    - imaging and biomarkers expertise
    - CTRad
- Move forward a stratified medicine approach to research across prevention, adjuvant and advanced disease settings through:
    - increasing the use of biomarkers in trials
    - increasing the number of biomarker-driven trials in the portfolio
- Systematically collect germline and tumour DNA, normal and tumour tissue throughout the disease pathway including investigation of post mortem studies.
- Develop a comprehensive tissue access policy which includes access to venous blood, normal and tumour tissue and extracted nucleic acids where there no longer exists a functioning TMG/TSC for the individual trial.
- Develop a data access policy which covers access to both historical and prospective clinicopathological and outcome datasets.
- Regularly review our membership to ensure:
    - appropriate statistical, GI and molecular pathology, imaging and other specialist expertise on the main group with equitable rotation
    - appropriate Subgroup membership (from both members and non-members of the main CSG) and equitable rotation
- Develop and promote pragmatic studies as a balance to our ‘niche’ studies in order to maintain high levels of recruitment and trial access to all recruiting sites.
- Expand our research activities in screening, prevention and early diagnosis.

- Expand the range and number of funding bodies to which our funding submissions are made and improve their likelihood of funding success.
- Increase our work in the field of survivorship.
- Review our and others clinical and translational research portfolio to identify 'research gaps' in CRC and ensure a comprehensive, balanced and innovative study portfolio.
- Develop a research programme on colorectal cancer biology using our current and historical portfolio clinical trials and translational studies to improve our understanding of the molecular subtypes within CRC.
- Develop biomarker stratifications that predict outcomes from current and novel therapies and enable personalised therapy to improve outcomes in early and late stage CRC.

B – Surgical Subgroup Strategy

- Enhance the portfolio of surgical trials including the development of two new surgical trials by the end of 2015.
- Develop a study for patient optimisation prior to surgery.
- Develop a new study in organ preservation.
- Set up new studies on the role of surgery in advanced disease.
- Develop device studies.
- Include biomarker validation within our RCTs.
- Increase the number of surgical consultants across the UK involved in research.
- Integrate surgical trainees into the work of the Subgroup.

C – Anorectal Subgroup Strategy

- Develop a seamless portfolio of trials that allow timely follow-on with no significant gaps between trials.
- Use complex design in the delivery of future trials, e.g. MAMS design, umbrella trials.
- Develop and get funded a phase III trial for anal cancer.
- Develop trials for organ preservation in rectal cancer.
- Develop trials which test the effectiveness of systemic treatments replacing resection in resectable rectal cancer.
- Explore the options for a trial in synchronous resectable metastatic disease from rectal cancer.
- Develop a study which focuses on improving toxicity and PROM assessment.
- Continue to develop combination trials of radiotherapy and novel agents.
- Link with other CSGs on understanding the biology of and advancing trial development in HPV-driven cancers.

D – Screening & Prevention Subgroup Strategy

- Increase the Subgroup membership to include more members of the CSG and a wider UK representation.
- Expand the trial portfolio to include more UK wide trials.
- Enhance research links with the four UK national bowel cancer screening programmes; the Screening and Prevention Sub-group of the Primary Care CSG; the ECMC UK Therapeutic Cancer Prevention Network (UK-TCPN); the National Awareness and Early Diagnosis Initiative (NAEDI) and with the UK Screening, Prevention and Early Diagnosis Advisory Group (SPED).

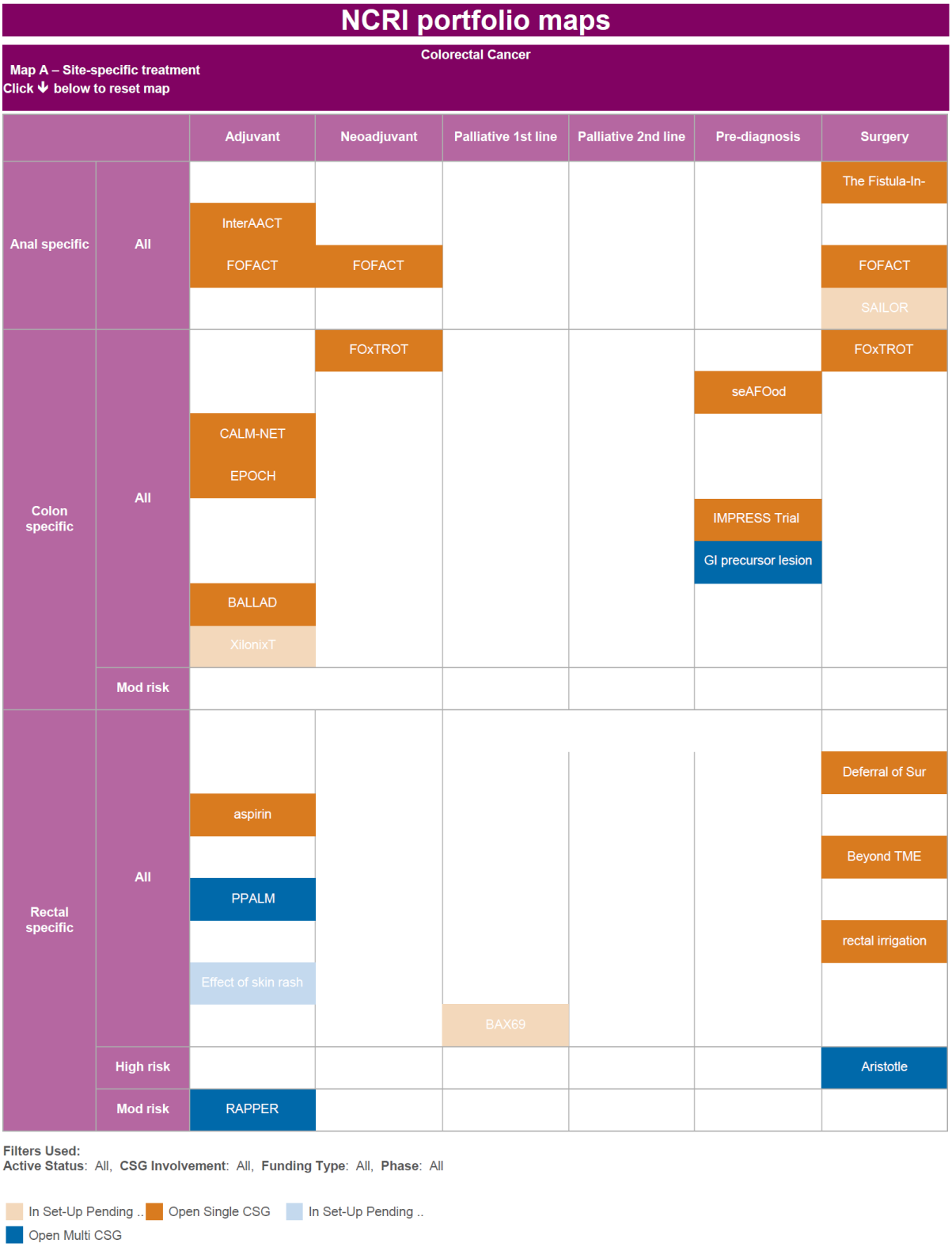
- Develop strategies to increase participation in screening and prevention studies and programmes, particularly from 'hard to reach' populations.
- Develop more lifestyle studies in primary and secondary prevention of CRC.
- Develop more biology-based chemoprevention studies.
- Encourage a seamless transition from screening to studies of novel treatment for early stage disease.
- Encourage and support studies of 'generic' prevention agents including 're-purposed' drugs.

E – Adjuvant & Advance Disease Subgroup Strategy

- Continue to develop early phase studies to feed through to our future phase II and III RCTs.
- Extend our links with the ECMC network and with the pharmaceutical and biotechnology industries to increase the number of early phase trials in our portfolio.
- Ensure close working relationships with the Upper GI CSG with respect to CRC liver metastases, peritoneal malignancies and small bowel cancer studies.
- Collaborate with the Psychosocial Oncology and Survivorship, Supportive & Palliative Care and Primary Care CSGs to ensure appropriate input into our and their colorectal cancer studies and, where appropriate, develop joint studies.
- Standardise our approach to measuring late effects.
- Set up a post mortem tumour heterogeneity study.
- Explore the development of studies for different subgroups of patients and at different stages of the patient journey.
- Develop studies on biomarkers that will help us to define which patients do and do not benefit from therapy in the neo-adjuvant, adjuvant and advanced disease settings.
- Increase work in the field of survivorship (in particular as regards lifestyle issues) in both the adjuvant and advanced disease settings.
- Develop trials to cover all our disease settings, and in particular:
    - a large pragmatic adjuvant study (in addition to Add-Aspirin)
    - a large pragmatic 1st line study (in addition to FOCUS4)
    - studies in second-line, third-line and beyond third-line metastatic disease
    - studies on tissue/tumour heterogeneity
- Develop our biological research and trials in tumour immunology in CRC.

Appendix 3

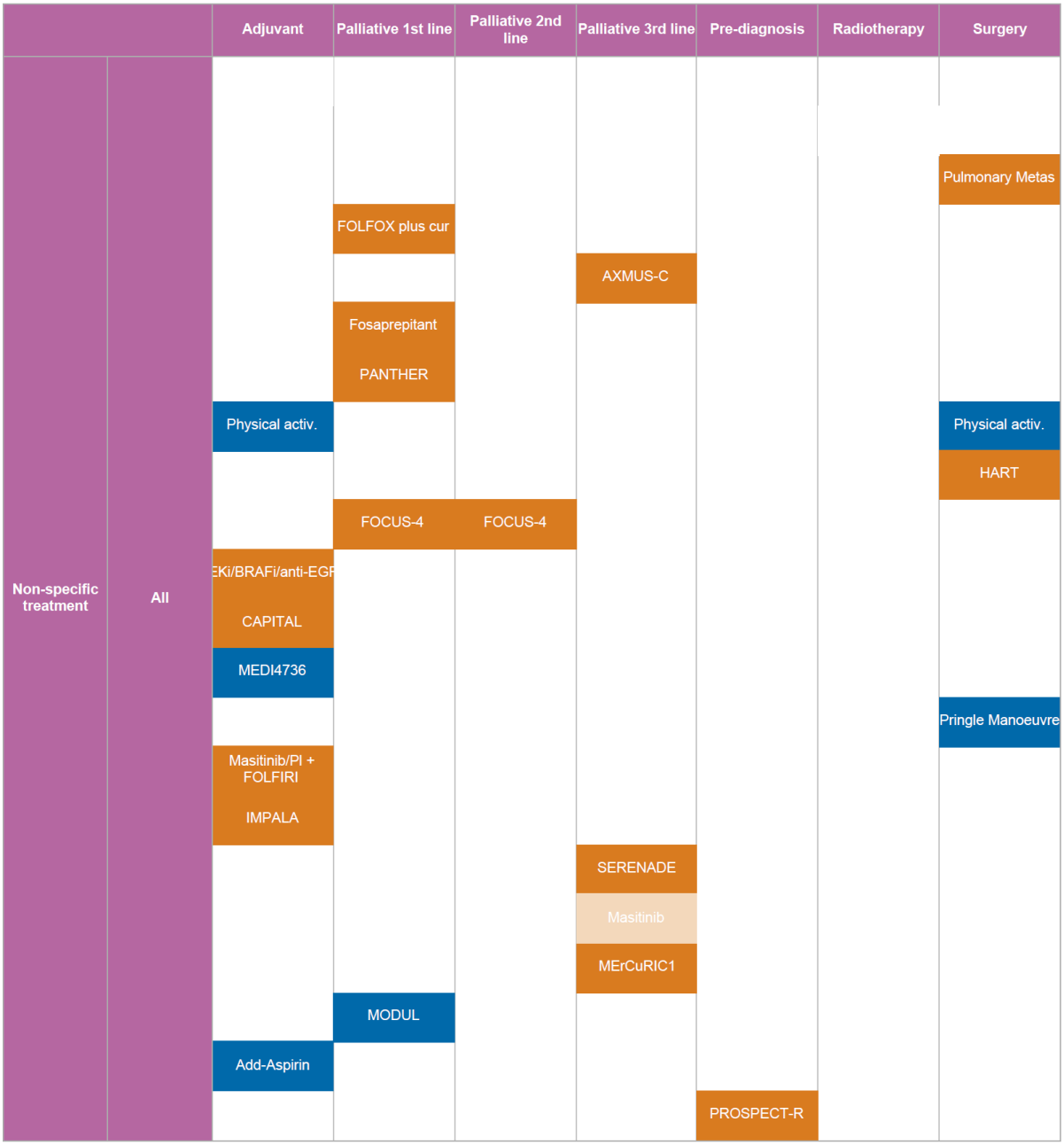
Portfolio maps



NCRI portfolio maps

Colorectal Cancer

Map B – Non-specific treatment
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 Null
Open Multi CSG

NCRI portfolio maps

Colorectal Cancer

Map C – Non-treatment, translational
Click ↓ below to reset map

		Adjuvant	Diagnosis / screening / prevention	Neoadjuvant	Palliative 1st line	Pre-diagnosis	Surgery	Therapeutic
Biomarkers	**All**	Functionality Tumour Angiogen	Functionality Tumour Angiogen DWIBS ctDNA v6.0 TRACCr	Functionality Tumour Angiogen	Functionality Tumour Angiogen	Functionality Tumour Angiogen cteria in colorectal nel lymph node biop	Functionality Tumour Angiogen	Functionality Tumour Angiogen
Diagnostics / imaging	**All**	Raman colon dia CR UK Stratifie	Raman colon dia CR UK Stratifie Streamline C MARVEL Lactate Imaging DWIBS sigmoidoscopy FIT test CONSCOP Study Of PRolif	Raman colon dia CR UK Stratifie	Raman colon dia CR UK Stratifie	Raman colon dia CR UK Stratifie MAGENTA MINSTREL	Raman colon dia CR UK Stratifie MARVEL mp. Robotic surgery	Raman colon dia CR UK Stratifie
Genetics / mechanisms	**All**	NSCCG Functionality Molecular patho PRESENT role of STAT1	Functionality PRESENT	NSCCG Functionality Molecular patho PRESENT	NSCCG Functionality Molecular patho PRESENT	Functionality CORGI COGS2 PRESENT Pop. DNA collxns SOCCS3 Vitamin D and C Targeting microRNA N-WASP HPV epidemiolog JAM-A RAFV600E immunc	NSCCG Functionality Molecular patho PRESENT Measurement of	NSCCG Functionality Molecular patho PRESENT EpiMET

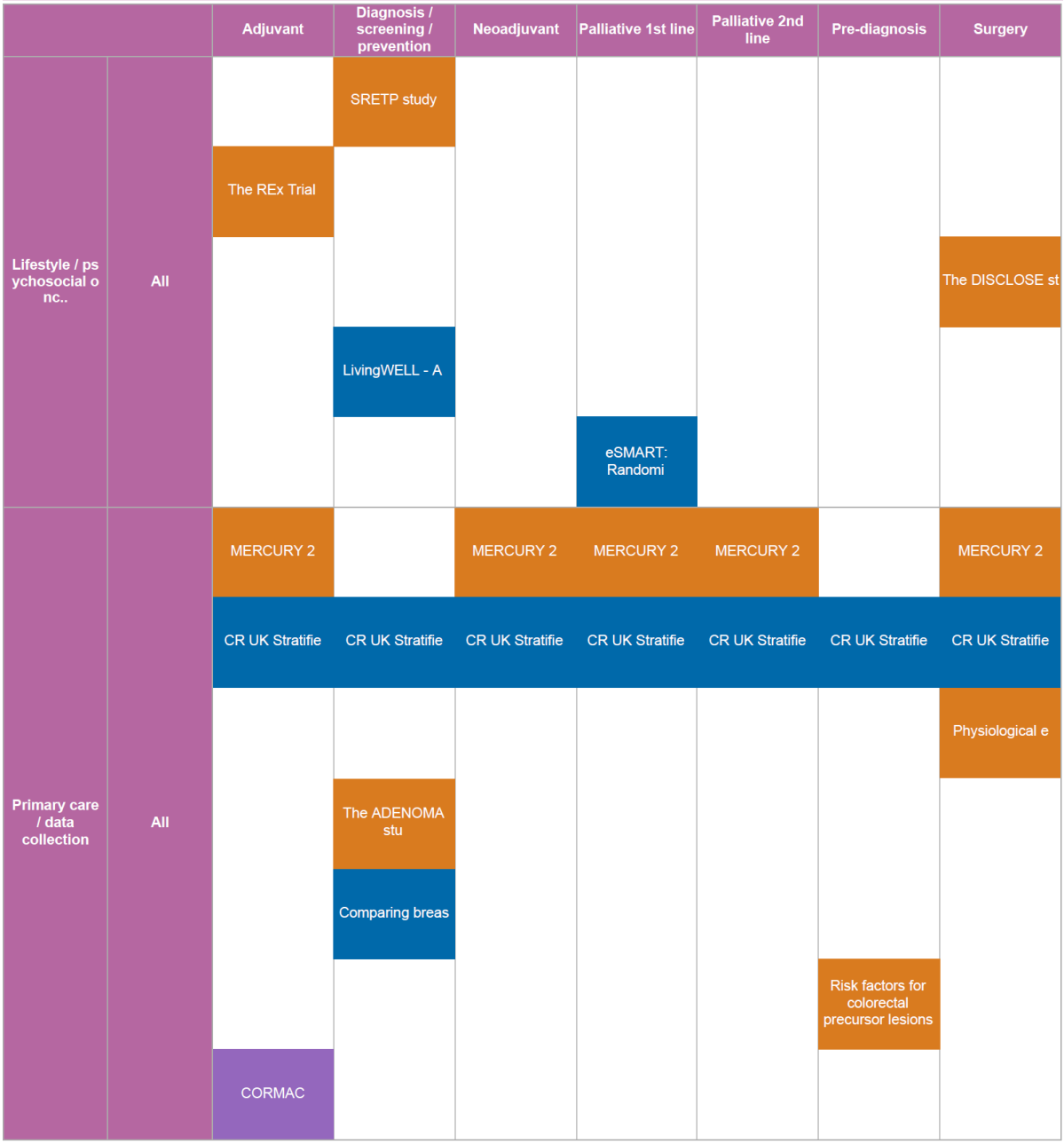
Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

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

NCRI portfolio maps

Colorectal Cancer

Map D – Non-treatment, supportive care, primary care
Click ↓ below to reset map



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

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

Appendix 4

Publications in the reporting year

ACT I and II

Downing A, Morris EJ, Aravani A, Finan PJ, Lawton S, Thomas JD, Sebag-Montefiore D. The Effect of the UK Coordinating Centre for Cancer Research Anal Cancer Trial (ACT1) on Population-based Treatment and Survival for Squamous Cell Cancer of the Anus. Clin Oncol (R Coll Radiol). 2015 Dec;27(12):708-12

Gilbert A, Francischetto EO, Blazeby J, Holch P, Davidson S, Sebag-Montefiore D, Velikova G. Choice of a patient-reported outcome measure for patients with anal cancer for use in cancer clinical trials and routine clinical practice: a mixed methods approach. Lancet. 2015 Feb 26; 385 Suppl 1:S38. doi: 10.1016/S0140-6736(15)60353-1.

BACCHUS

Glynne-Jones R, Hava N, Goh V, Bosompem S, Bridgewater J, Chau I, Gaya A, Wasan H, Moran B, Melcher L, MacDonald A, Osborne M, Beare S, Jitlal M, Lopes A, Hall M, West N, Quirke P, Wong WL, Harrison M; Bacchus investigators. Bevacizumab and Combination Chemotherapy in rectal cancer Until Surgery (BACCHUS): a phase II, multicentre, open-label, randomised study of neoadjuvant chemotherapy alone in patients with high-risk cancer of the rectum. *BMC Cancer* 15: 764, 2015

BEWEL

Anderson AS, Caswell S, Macleod M, Craigie AM, Stead M and Steele RJC (2015). Awareness of lifestyle and colorectal cancer risk – findings from the BeWEL study. *Biomed Res Int* Article ID 871613, doi:10.1155/2015/871613

Stead M, Craigie AM. Macleod M, McKells J Caswell S Steele RJC Anderson AS (2015) Why are some people more successful at lifestyle change than others? Factors associated with successful weight loss in the BeWEL randomised controlled trial of adults at risk of colorectal cancer *Int J Beh Nutr Phys Act* 12:87

Steele RJ, Anderson AS, Macleod M, Craigie AM, Caswell S, Belch J, Treweek S; The BeWEL team (2015) Colorectal adenomas and diabetes : implications for disease prevention *Colorectal Dis*. Jul;17(7):589-944

CAPP2

Movahedi M, Bishop DT, Macrae F et al. Obesity, Aspirin, and Risk of Colorectal Cancer in Carriers of Hereditary Colorectal Cancer: A Prospective Investigation in the CAPP2 Study. J Clin Oncol. 2015 Nov 1;33(31):3591-7. doi: 10.1200/JCO.2014.58.9952.

COIN and COIN-B

Al-Tassan NA, Whiffin N, Hosking FJ et al. A new GWAS and meta-analysis with 1000 Genomes imputation identifies novel risk variants for colorectal cancer. Sci Rep. 2015 May 20;5:10442. doi: 10.1038/srep10442.

Grenader T, Nash S, Adams R, Kaplan R, Fisher D, Maughan T, Bridgewater J. Derived neutrophil lymphocyte ratio is predictive of survival from intermittent therapy in advanced colorectal cancer: a post hoc analysis of the MRC COIN study. Br J Cancer. 2016 Mar 15;114(6):612-5.

Jarvis D, Mitchell JS, Law PJ et al. Mendelian randomisation analysis strongly implicates adiposity with risk of developing colorectal cancer. British Journal of Cancer (2016 In Press).

Orlando G, Law PJ, Palin K, et al. Variation at 2q35 (PNKD and TMBIM1) influences colorectal cancer risk and identifies a pleiotropic effect with inflammatory bowel disease. Hum Mol Genet. 2016 Mar 22. pii: ddw087.

Phipps AI, Passarelli MN, Chan AT, et al. Common genetic variation and survival after colorectal cancer diagnosis: a genome-wide analysis. Carcinogenesis. 2016 Jan;37(1):87-95.

Renfro LA, Loupakis F, Adams RA, Seymour MT, Heinemann V, Schmoll HJ, Douillard JY, Hurwitz H, Fuchs CS, Diaz-Rubio E, Porschen R, Tournigand C, Chibaudel B, Falcone A, Tebbutt NC, Punt CJ, Hecht JR, Bokemeyer C, Van Cutsem E, Goldberg RM, Saltz LB, de Gramont A, Sargent DJ, Lenz HJ. Body Mass Index Is Prognostic in Metastatic Colorectal Cancer: Pooled Analysis of Patients From First-Line Clinical Trials in the ARCAD Database. J Clin Oncol. 2016 Jan 10;34(2):144-50.

Shi Q, de Gramont A, Grothey A, Zalcberg J, Chibaudel B, Schmoll HJ, Seymour MT, Adams R, Saltz L, Goldberg RM, Punt CJ, Douillard JY, Hoff PM, Hecht JR, Hurwitz H, Díaz-Rubio E, Porschen R, Tebbutt NC, Fuchs C, Souglakos J, Falcone A, Tournigand C, Kabbinavar FF, Heinemann V, Van Cutsem E, Bokemeyer C, Buyse M, Sargent DJ. Individual patient data analysis of progression-free survival versus overall survival as a first-line end point for metastatic colorectal cancer in modern randomized trials: findings from the analysis and research in cancers of the digestive system database. J Clin Oncol. 2015 Jan 1;33(1):22-8.

CUFOX

Irving GR, Iwuji CO, Morgan B, Berry DP, Steward WP, Thomas A, Brown K & Howells LM (2015) Combining curcumin (C3-complex, Sabinsa) with standard care FOLFOX chemotherapy in patients with inoperable colorectal cancer (CUFOX): study protocol for a randomised control trial. Trials. 2015; 16:110. doi: 10.1186/s13063-015-0641-1.

James MI, Iwuji C, Irving G, Karmokar A, Higgins JA, Griffin-Teal N, Thomas A, Greaves P, Cai H, Patel SR, Morgan B, Dennison A, Metcalfe M, Garcea G, Lloyd D, Berry DP, Steward WP, Howells LM, Brown K. Curcumin inhibits cancer stem cell phenotypes in ex vivo models of colorectal liver metastases, and is clinically safe and tolerable in combination with FOLFOX chemotherapy. Cancer Letters 2015 Aug 10; 364(2): 135-41.

E-SCOUT

Krebs MG, Renehan AG, Backen A, Gollins S, Chau I, Hasan J, Valle JW, Morris K, Beech J, Ashcroft L, Saunders MP, Dive C. Circulating Tumor Cell Enumeration in a Phase II Trial of a Four-Drug Regimen in Advanced Colorectal Cancer. Clin Colorectal Cancer. 2015 Jun;14(2):115-22.

EXPERT-C

Sclafani F, Chau I, Cunningham D, et al. Prognostic role of the LCS6 KRAS variant in locally advanced rectal cancer: results of the EXPERT-C trial. Ann Oncol. 2015 Sep;26(9):1936-41.

Sclafani F, Peckitt C, Cunningham D et al. Short- and Long-Term Quality of Life and Bowel Function in Patients With MRI-Defined, High-Risk, Locally Advanced Rectal Cancer Treated With an Intensified Neoadjuvant Strategy in the Randomized Phase 2 EXPERT-C Trial. Int J Radiat Oncol Biol Phys. 2015 Oct 1;93(2):303-12.

FACS

Pugh SA, Shinkins B, Fuller A, Mellor J, Mant D, Primrose JN. Site and Stage of Colorectal Cancer Influence the Likelihood and Distribution of Disease Recurrence and Postrecurrence Survival: Data From the FACS Randomized Controlled Trial. Ann Surg. (2016 In Press).

FOCUS, PICCOLO and QUASAR

Richman SD, Southward K, Chambers P, Cross D, Barrett J, Hemmings G, Taylor M, Wood H, Hutchins G, Foster JM, Oumie A, Spink KG, Brown SR, Jones M, Kerr D, Handley K, Gray R, Seymour M, Quirke P. HER2 overexpression and amplification as a potential therapeutic target in colorectal cancer: analysis of 3256 patients enrolled in the QUASAR, FOCUS and PICCOLO colorectal cancer trials. J Pathol. 2016 Mar;238(4):562-70.

FOCUS4

Lawler M, Kaplan RS, Wilson RH, Maughan TS. Changing the paradigm – multi-stage multiarm randomised trials and stratified cancer medicine. Oncologist August 2015; 20 (8): 849-851.

Richman SD, Adams R, Quirke P, Butler R, Hemmings G, Chambers P, Roberts H, James MD, Wozniak S, Bathia R, Pugh C, Maughan T, Jasani B; FOCUS4 Trial Management Group. Pre-trial inter-laboratory analytical validation of the FOCUS4 personalised therapy trial. J Clin Pathol. 2016 Jan;69(1):35-41.

MERCURY II

Battersby NJ, How P, Moran B, Stelzner S, West NP, Branagan G, Strassburg J, Quirke P, Tekkis P, Pedersen BG, Gudgeon M, Heald B, Brown G; MERCURY II Study Group. Prospective Validation of a Low Rectal Cancer Magnetic Resonance Imaging Staging System and Development of a Local Recurrence Risk Stratification Model: The MERCURY II Study. Ann Surg. 2015 Mar 27. [Epub ahead of print].

PICCOLO

Seligmann JF, Elliott F, Richman SD, Jacobs B, Hemmings G, Brown S, Barrett JH, Tejpar S, Quirke P, Seymour MT. Combined Epiregulin and Amphiregulin Expression Levels as a Predictive Biomarker for Panitumumab Therapy Benefit or Lack of Benefit in Patients With RAS Wild-Type Advanced Colorectal Cancer. JAMA Oncol. 2016 Feb 11. doi: 10.1001/jamaoncol.2015.6065**SIGGAR**

Halligan S, Dadswell E, Wooldrage K, Wardle J, von Wagner C, Lilford R, Yao GL, Zhu S, Atkin W. Computed tomographic colonography compared with colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicentre randomised trials with economic evaluation (the SIGGAR trials). Health Technol Assess. 2015 Jul;19(54):1-134.

SONATINA

Hill EJ, Roberts C, Franklin JM, Enescu M, West N, MacGregor TP, Chu KY, Boyle L, Blesing C, Wang LM, Mukherjee S, Anderson EM, Brown G, Dutton S, Love SB, Schnabel JA, Quirke P, Muschel R,

McKenna WG, Partridge M, Sharma RA. Clinical Trial of Oral Nelfinavir before and during Radiation Therapy for Advanced Rectal Cancer. Clin Cancer Res. 2016; 22(8): 1922-31.

OTHER

Gilbert A, Ziegler L, Martland M, Davidson S, Efficace F, Sebag-Montefiore D, Velikova G. Systematic Review of Radiation Therapy Toxicity Reporting in Randomized Controlled Trials of Rectal Cancer: A Comparison of Patient-Reported Outcomes and Clinician Toxicity Reporting.
Int J Radiat Oncol Biol Phys. 2015 Jul1;92(3):555-67.
Greenhalgh TA, Dearman C, Sharma RA. Combination of Novel Agents with Radiotherapy to Treat Rectal Cancer. Clin Oncol (R Coll Radiol). 2016 Feb; 28(2):116-39. doi: 10.1016/j.clon.2015.11.002.

Morris EJ, Penegar S, Whiffin N, Broderick P, Bishop DT, Northwood E, Quirke P, Finan P, Houlston RS. A retrospective observational study of the relationship between single nucleotide polymorphisms associated with the risk of developing colorectal cancer and survival. PLoS One. 2015 Feb 24;10(2):e0117816. doi: 10.1371/journal.pone.0117816. eCollection 2015.

Sclafani F, Kim TY, Cunningham D et al. A Randomized Phase II/III Study of Dalotuzumab in Combination With Cetuximab and Irinotecan in Chemorefractory, KRAS Wild-Type, Metastatic Colorectal Cancer. J Natl Cancer Inst. 2015 Sep 23;107(12):djv258. doi: 10.1093/jnci/djv258.

Wardle J, von Wagner C, Kralj-Hans I, Halloran SP, Smith SG, McGregor LM, Vart G, Howe R, Snowball J, Handley G, Logan RF, Rainbow S, Smith S, Thomas MC, Counsell N, Morris S, Duffy SW, Hackshaw A, Moss S, Atkin W, Raine R. Effects of evidence-based strategies to reduce the socioeconomic gradient of uptake in the English NHS Bowel Cancer Screening Programme (ASCEND): four cluster-randomised controlled trials. Lancet. 2016 Feb 20;387(10020):751-9

Appendix 5

Major international presentations in the reporting year

ACT II

Robert Glynne-Jones, Helen Margaret Meadows, Andre Lopes, Richard A. Adams, David Sebag-Montefiore Compliance to chemoradiation (CRT) using mitomycin (MMC) or cisplatin (CisP), with or without maintenance 5FU/CisP chemotherapy (CT) in squamous cell carcinoma of the anus (SCCA) according to radiotherapy (RT) dose, overall treatment time (OTT) and chemotherapy (CT) and their impact on long-term outcome: Results of ACT II. J Clin Oncol 33, 2015 (suppl; abstr 3518). ASCO Annual Meeting, 2015.

BALLAD

Evans J, Aparicio T, Le Malicot K, Nakamura K, Honma Y, McWilliams RR, ten Tije AJ, Anthoney A, Boyd R, Dixon-Hughes J, Graham J, Iveson T, Nicoll J, Paul J, Salto-Tellez M, Starling N, Ueno M, Yim K, Bridgewater J, Wilson RH. GLOBAL BALLAD: An International Rare Cancers Initiative trial to evaluate the potential Benefit of Adjuvant chemotherapy for smaLL bowel Adenocarcinoma (IRCI 002). ASCO Annual Meeting, 2016.

COIN, FOCUS AND PICCOLO

Jenny F. Seligmann, David Fisher, Christopher G. Smith, Faye Elliott, Susan Richman, Philip Quirke, Tim Maughan, Jeremy Cheadle, Richard A. Adams, Matthew T. Seymour, Gary William Middleton. Exploring outcomes of RAS-mutant advanced colorectal cancer treated with chemotherapy: Analysis from 2254 patients (pts) in randomised clinical trials. ASCO Annual Meeting, 2016.

EASI-SWITCH

Forde C, McMullan R, Clarke M, Wilson RH, Plummer ER, Thomas AL, Barnes RA, Adams RA, Chau I, Grayson M, McDowell C, Agus A, Brown E, Storey DJ, McAuley D, Coyle V. The EASI-SWITCH Trial – Early switch to oral antibiotic therapy in patients with low risk neutropenic sepsis. ASCO Annual Meeting, 2016.

MERCURIC

Van Schaeybroeck S, Rolfo CD, Élez E, Kelly S, Houlden J, Collins L, Love S, Andre T, Lawler M, Di Nicolantonio F, Grayson M, Popovici VC, Bardelli A, Laurent-Puig P, Salto-Tellez M, Maughan T, Tabernero J, Peeters M, Wilson RH, Middleton MR. MErCuRIC1: A Phase I study of MEK1/2 inhibitor PD-0325901 with cMET inhibitor crizotinib in RASMT and RASWT (with aberrant c-MET) Metastatic Colorectal Cancer Patients. ASCO Annual Meeting, 2015.

Maxwell P, del Favero J, Fuchs M-A, Tabernero J, Maughan T, Middleton M, Adams R, Rolfo C, Hennessy B, Laurent-Puig P, Bardelli A, Andre T, Popovici V, Johnston P, Wilson R, Lawler M, Van Schaeybroeck S, Salto-Tellez M on behalf of the MErCuRIC consortium. Validation of a MEK/MET-specific NGS panel for early phase trial interrogation. American Association of Cancer Research Annual Meeting, 2016.

Appendix 6

Strengths & weaknesses from the Colorectal Cancer CSG 2015 Progress Review

The panel identified a number of strengths which for ease of reference are listed as bullet points below:-

- A highly successful group with a strong international presence and reputation.
- A clear subgroup structure which is working well.
- The Chair and subgroup chairs are dynamic, cohesive and work well as a team.
- Strong commitment to making the Group successful.
- Membership is strong, comprehensive and includes a number of hard hitters.
- Excellent and innovative approaches to developing future researchers, including involvement of medical students in some projects.
- Consumer involvement which is respected and well supported by the Group, with innovative involvement in priority setting.
- A large broad portfolio of international standard containing some cutting edge trials particularly in biomarker driven stratified medicine and surgery.
- Strong translational work.
- A common sense approach to the complexity and breadth of early diagnosis work.
- The number of publications in high impact journals.
- Active participation in the International Rare Cancers Initiative (IRCI), including leading on two trials.
- Highly successful annual trials meetings which are well received by the research community.

The panel felt that although the Group are very successful there is scope for improvement if the Group and NCRI addressed a number of areas as listed below:-

For the CSG

- Developing a clearer more focussed strategy for the CSG itself with clear bullet points, which will help guide the continued development of the research portfolio with the Group, as well as sell the Group more easily to the research community and funders.
- Having a clearer overall strategy for the Group's translational work which currently appears to be done on a study by study basis.
- Thinking through the Group's approach to genomics so that the available resources are best used.
- Exploring the possibility of developing immunological studies.
- Developing a matrix of themes which run across all the Group's work.
- Developing networks of researchers modelled on the surgical network in all of the subgroups.
- Continuing to develop working relationships with the newly emerging subspecialty leads across the research networks in the UK to maximise recruitment.
- Being more creative as to how involvement in subgroups can be extended to more researchers.
- Providing more focussed reports in the future.

For the NCRI

- Engaging with the university sector and NHS trusts to ensure that clinical research though the development and successful completion of clinical trials and related studies gains appropriate recognition. Participation in CSG and related national activities is a critically important field of

activity that deserves to be more highly valued in both academic and service spheres. Staff involved in this work need better support from their parent organisations to enable their participation in this type of research.

- Engaging with funding bodies other than CRUK to ensure CSG input into their thinking about the nature and methods of research in colorectal cancer and hence their consideration of funding submissions.