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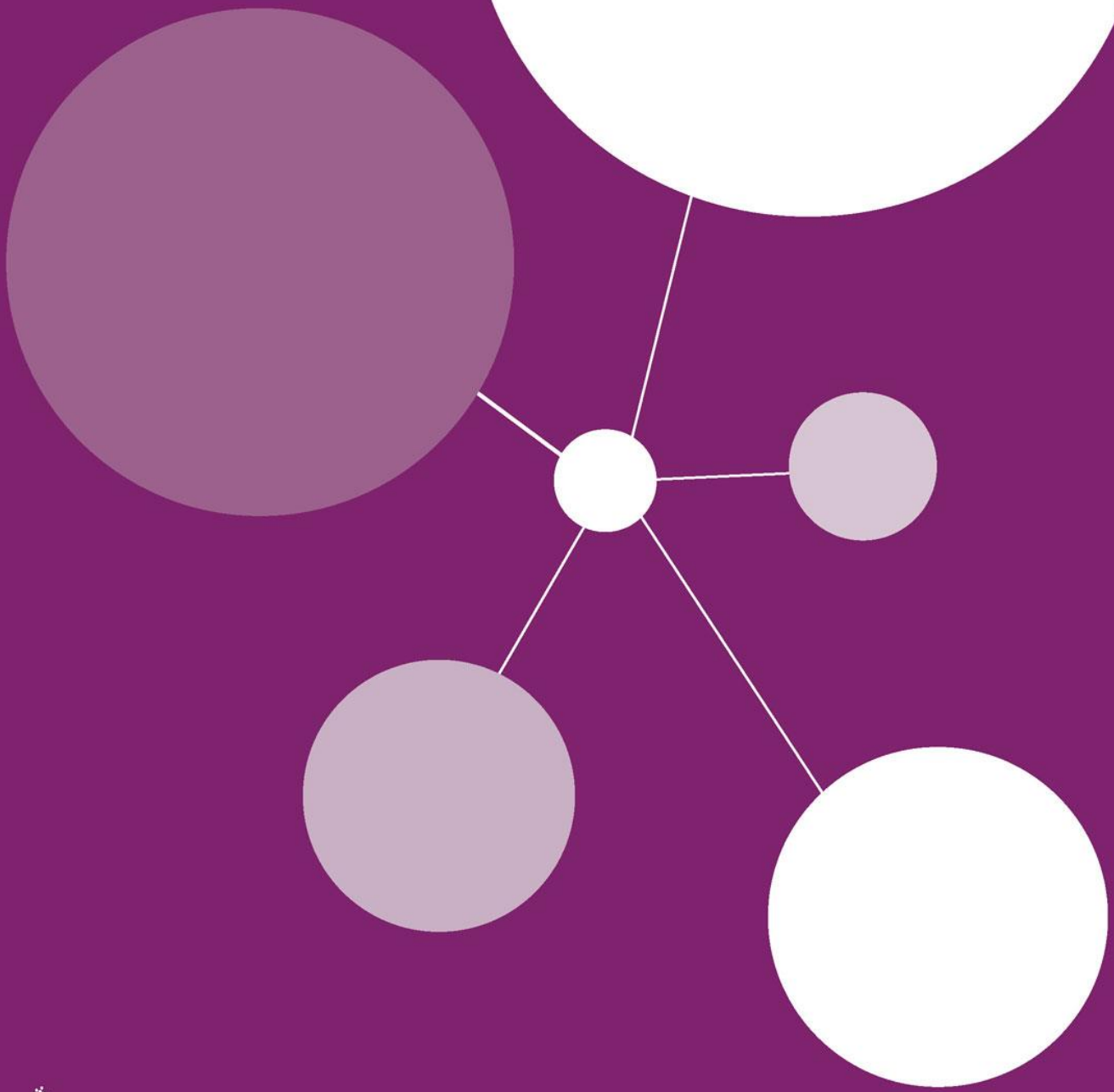
# NCRI Colorectal Cancer Clinical Studies Group

## Annual Report 2017-18



Partners in cancer research

# NCRI Colorectal Cancer CSG
# Annual Report 2017-18

## 1. Top 3 achievements in the reporting year

**Achievement 1**

**Funding/opening of new trials**

- The opening of the phase II/III PLATO umbrella trial personalising radiotherapy in anal cancer with the development of a national IMRT radiotherapy protocol with robust quality assurance, funded translational research project and integrated PROM assessment. Aligned with a novel early phase trial of immunotherapy in combination with chemo-radiotherapy in locally advanced anal cancer.
- Funding success for POLEM, examining the benefit of Avelumab immunotherapy in dMMR/MSI resected stage III colon cancer.
- Funding success for other trials listed in Section 5.

**Achievement 2**

**Completion of recruitment to significant trials**

- Accrual to FOxTROT was completed in December 2016, examining the benefit of neoadjuvant chemotherapy in colon cancer, with 1053 total patients being recruited. Key, potentially practice-changing results, are expected in 2018.
- The seAFOod chemoprevention trial completed recruitment of 904 patients in 60 centres in June 2017. In high risk patients in the Bowel Cancer Screening Programme, this multi-centre randomised trial examined the efficacy of aspirin and EPA-free fatty acid in polyp prevention. This was the first large chemoprevention trial delivered in the BCSP and results are currently being analysed.
- BADENOMA was a multi-centre trial delivered in flexible sigmoidoscopy screening, examining adenoma detection rate. This trial was undertaken in 16 centres across the UK and reached its recruitment target of 3222 patients in just 9 months, 9 months ahead of target (November 2017). The results are currently being analysed.

- Completion of the International Rare Cancers Initiative (IRCI) metastatic anal cancer trial INTERAACT, demonstrating feasibility of international recruitment and timely delivery of a phase II trial in a rare disease entity
- The phase III ARISTOTLE trial combining chemoradiotherapy +/- irinotecan in patients with locally advanced rectal cancer, will complete accrual in June 2018.
- The phase III CReST trial is the largest stenting trial worldwide, in the context of obstructing bowel cancer, with publication expected in 2018.
- TREC is a phase II study in early rectal cancer, examining the feasibility of randomisation to an organ preservation approach, of pelvic radiotherapy followed by trans-anal endoscopic microsurgery (TEM). Publication is expected in 2018.

**Achievement 3**

**Publication of important trial results:**

- Publication of the phase III SCOT trial (Lancet Oncology 2018; 19:562-578). This practice-changing trial in 6088 UK patients established that overall, 3 months of oxaliplatin-containing adjuvant chemotherapy was non-inferior to 6 months of the same therapy for patients with high-risk stage II and stage III colorectal cancer and was associated with reduced toxicity and improved quality of life. The UK results were combined with data from 5 other trials internationally within the IDEA collaboration in 12,834 patients total, showing that for patients treated with oxaliplatin/capecitabine, 3 months of therapy was as effective as 6 months (New Eng J Med 2018; 378:1177-1188).
- The first results from one of the arms of the FOCUS4 trial were published (Lancet Gastroenterol and Hepatol 2018; 3:162-171). There was a lack of benefit from Her-1, 2, 3 inhibition in 'all wild type' CRC. However, the MAMS trial design for FOCUS4 demonstrated efficiency and effectiveness in trial outcome delivery, informing the decision to proceed or stop clinical evaluation of a targeted treatment within a molecularly defined cohort of patients. The infrastructure around the UK has been established to deliver large, complex platform studies.
- ADENOMA was a multi-centre trial of Endocuff vision to improve detection at colonoscopy. This trial recruited 1772 patients and demonstrated that in FOB positive bowel cancer screening patients, the adenoma detection rate (ADR) was increased by 10.8% (Gut 2018: doi:10.1136/gutjnl-2017-3148889). This is one of the largest increases in ADR of any intervention and based upon this trial the NHS has chosen Endocuff vision as one of 4 innovations to be fast tracked and funded into clinical practice. In March 2018 the ADENOMA and BADENOMA trials (above) won a Medilink Healthcare Award for the collaboration between NHS, Academia and industry.

## 2. Structure of the Group

The Colorectal Cancer CSG continues with the same structure as for recent years. There have been significant changes in leadership of the CSG and three out of the four Subgroups. Leadership of the CSG was assumed by Dr Simon Gollins in August 2017 (from Professor Richard Wilson), the Screening & Prevention Subgroup by Professor Colin Rees in 2017 (from Professor Mark Hull) the Adjuvant & Advanced Disease Subgroup by Dr Janet Graham in March 2018 (from Professor Anne Thomas), and the Surgical Subgroup will be led by Miss Nicola Fearnhead from April 2018 (from Mr Simon Bach). We extend deep gratitude to all the individuals who have rotated off as Chairs for all their many years of dedication and excellent work. The Anorectal Subgroup continues to be chaired by Dr Richard Adams.

There are currently 25 members on the Colorectal CSG (see Appendix 1). Of these, 22 are clinical/scientific members, two are consumer representatives and one a trainee member. Our membership represents a broad balance of specialties with three clinical oncologists, six medical onocologists, five surgeons (one of whom is also a translational scientist), one gastroenterologist, two consumer representatives, two pathologists, two radiologists, one research nurse, one statistician, one translational scientist and one trainee. We have representation from all four UK devolved nations.

There have been changes in membership over the last year and we said farewell and thank you to Professor David Sebag-Montefiore, Professor Manuel Salto-Tellez, Mr James Hernon, Professor Ricky Sharma and Professor Gina Brown for many years of dedicated and productive work. We welcome five new members Dr Tony Dhillon, Dr Philip Dunne, Dr Manuel Rodriuez-Justo, Mr Andrew Beggs and Professor Vicky Goh. Two trainees, Dr Alex Gilbert and Dr Chris Coyle, have now rotated off the Group.

## 3. CSG & Subgroup strategies

### Main CSG

**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 Gastrointestinal CSG on studies in colorectal cancer (CRC) liver metastases, peritoneal malignancies and small bowel cancer**

Collaboration and interaction with the ECMCs and ECMC Network has developed through the FOCUS4 trial and the ECMC Combinations Alliance. There have been grant application success via the ECMC Combinations Alliance (e.g. PRIME RT). Interaction with the Supportive & Palliative Care CSG and the Psychosocial Oncology & Survivorship CSG have occurred via presentations and attendance at main CSG and subgroup meetings and relevant trial development input. Involvement of CTRad has occurred through formal presentation of radiotherapy trials to the regular CTRad Proposals Guidance Meeting for review and feedback, interaction on specific trials and on methodology development. Interaction on the Upper GI CSG on studies in colorectal cancer liver metastases and small bowel cancer continues.

**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**

We continue to develop international collaboration via several avenues including participation in the IRCI rare cancers, the European PETACC group (adjuvant trial development) and an Australian/Canadian/UK lower gastrointestinal clinical research collaboration. The international randomised phase II INTERAACT trial in metastatic anal cancer completed accrual, with a planned follow-on phase III trial. The small bowel adjuvant BALLAD trial continues recruitment on the UK and France. The CHALLENGE study is taking place in UK/Australia/Canada/US. The ambitious COLO-SPEED current grant application aims to collaborate internationally with colleagues within screening and prevention. STAR-TREC is an international study evaluating organ saving treatment versus standard surgery for early rectal cancer in three European countries with bowel screening. It is led from UK and funded by CRUK. Parallel funding was obtained by the Dutch and Danish Cancer Societies and the study is now open and recruiting in all three countries. This international platform will support a potentially practice changing study in organ preservation and also provide unique translational opportunities due to the high proportion of early tumours that respond completely to radiation therapy.

**Increase our engagement and networking with relevant stakeholders, including consumers, early career researchers and clinical trainees, gastroenterologists and CIs of UKCRN Cancer portfolio trials who do not currently liaise with the Colorectal CSG**

Involvement of consumers is integral to all aspects of the work of the CSG and Subgroups. The Surgical Subgroup contributed to a very successful national public prioritisation event involving 300 members of the public (Delphi exercise).
We have increased our involvement with early career researchers and clinical trainees through rotating CSG and Subgroup membership. The surgical trainee trial networks have been very successful and it is proposed to extend this model to the other Subgroups.
An ambitious final proposal for a CRUK Catalyst award (COLO-SPEED) is due to be submitted by the Screening & Prevention Subgroup in the near future, aiming to produce a paradigm shift in prevention and early diagnosis research, by building a ground-breaking national and international multidisciplinary academic, clinical, patient, public, stakeholder and industry collaboration.
Engaging CIs who do not currently liaise with the CSG is challenging. Encouraging application to Subgroup membership and involvement in working parties and collaborative networks are initiatives being developed. All investigators are urged to formally present their proposed studies to the CSG for review prior to funding submission, meetings for which now occur 3-monthly.
We will encourage interaction by reinstating the Colorectal Annual Trials Meeting.

**Ensuring our studies are patient-centred and we are answering the questions most relevant to them**

We will continue our efforts to include and refer to consumers at all stages of trial development, management and eventual publication and dissemination of results. We will continue the drive to use patient-reported outcome measures as an important part of our trial methodology. We will increasingly harness the power of 'Big Data' from sources such as Public Health England and the National Cancer Registration and Analysis Service (NCRAS), to inform about treatment and outcomes occurring in the 'real world', to help in designing patient-relevant trials. We will expand the successful Delphi/CREATE cycle to other disciplines to involve consumers as far as possible.

**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**

There is representation from all these disciplines on the CSG and Subgroups, who are involved in national QA initiatives, and actively involved in clinical trial development and management. This aspect has been strengthened by recent appointments to the CSG.

**Get treatment right first time: 'Mistreatment is as bad as misdiagnosis' (recent PPI quotation at S:CORT Think Tank).**

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. 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.

The availability of new technologies, a better knowledge of the molecular biology and the identification of novel therapeutic targets hold the potential to implement effective primary/secondary prevention measures and personalised treatment approaches in the near future. The S:CORT stratified research programme on colorectal cancer biology is investigating the current and historical portfolio clinical trials and translational studies to improve our understanding of the molecular subtypes within CRC, to discover and develop biomarker stratifications that predict outcomes from current and novel therapies and enable personalised treatments that improve outcomes in early and late stage CRC. It is hoped that stratifiers discovered in the S:CORT programme will be assessed in new trials designed for validation. Other UK groups' initiatives are also occurring using samples stored from completed trials, to define predictive molecular biomarkers. There have been recent funding successes for biomarker-driven immunotherapy studies in the advanced (ANICCA-Class I. HIGH POLE) and adjuvant (POLEM) contexts. Sample collection is included in the majority of recent studies. The emerging discipline of digital pathology, with which various trial programmes are involved, offers promise in defining treatment stratifiers, in conjunction with molecular signatures. Recent appointments to the CSG have strengthened the translational science representation.

**Systematically collect germline and tumour tissue throughout the disease pathway including investigation of post mortem studies**

The collection and biobanking of good quality tissue biopsies and blood in standard clinical practice, in addition to good quality clinical data and outcomes, has potential use in systematic evaluation and validation of new prognostic and predictive markers, technologies and interventions for colorectal cancer (as intended in the Dutch ColoRectal Cancer Cohort). Multiomics is likely to drive treatment decisions in the future, demanding good quality specimens. However, there is currently a lack of UK standardised tissue collection protocols. Efforts are underway to develop standardised protocols for prospective, pre-treatment tissue collection in terms of both endoscopic sampling method and immediate tissue processing, transfer and storage, with initial grant success. The COLO-SPEED ambition is to create a network of endoscopy units throughout the UK, capable of collecting and processing tissue systematically to the highest standards. The challenging area of post mortem sample collection, especially in order to examine heterogeneity and differences between primary tumour and metastases, has been sensitively and successfully initiated with the ground-breaking GIFT study in Leeds. There are opportunities to collaborate with the 100,000 Genomes Project and interact with GCIP and GEL to maximise the use of stored clinical and genomic data.

**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 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**

Large clinical and pathological datasets are crucially important in the identification of molecular predictors and stratifiers for future use, therefore larger well-designed pragmatic trials are important for the future, in addition to a balance of smaller niche studies. Future trials in discussion will attempt to achieve this. Many CSG and Subgroup members have worked with the charity Bowel Cancer UK on a project to identify research gaps in the colorectal portfolio, which has recently been published. This information will help inform discussion on future research directions for the CSG and Subgroups, although certain aspects will be challenging. Our aim is to provide a balance between complex 'niche' studies and larger pragmatic studies. The pragmatic ADD ASPIRIN trial has recruited well, with almost half of the target 2600 patients accrued. The pragmatic CHALLENGE exercise trial is now recruiting. However, this aspect needs further development.

**Expand the range and number of funding bodies to which our funding submissions are made and improve their likelihood of funding success**

There have been recent funding successes, as illustrated in Section 5. We are increasing our discussion with alternative funders, including their presence at the CSG and Strategy meetings. We are developing studies which probably fit with HTA funding e.g. DPD Deficiency and CT DNA (Advanced and Adjuvant Subgroup).

## Advanced & Adjuvant Disease Subgroup (Chair, Dr Janet Graham incoming chair)

**Develop early phase studies to feed through to future RCTs**

Accelerator award submitted to CRUK by Sansom et al which would aim to link preclinical work with early phase colorectal trials in a more coordinated manner.

**Extend links with the ECMC network**

The Subgroup aim to hold a brainstorming event with key pharma partners and basic scientists in October 2018.

**Collaboration with Psychosocial Oncology and Survivorship, Supportive & Palliative Care and Primary Care CSGs**

A significant amount of effort went into setting up a trial for elderly/frail patients but there was limited input from non-colorectal members. Dr Paul Ross has now presented at the Supportive & Palliative Care CSG and we aim to set up a Working Party to set up a trial jointly between both groups (with first meeting probably Q3 2018).

**Ensure close working relationships with the Upper GI CSG with respect to CRC liver metastases, peritoneal malignancies and small bowel cancer studies**

A significant amount of work was put into a CRLM study and debulking study but funding not successful. This had been supported by the Southampton CTU. CRLM will be re investigated by a Working Party which we will apply for funding for and aim to have first meeting in Q3 2018.

**Set up a post mortem tumour heterogeneity study**

Ongoing and recruiting.

**Explore the development of studies for different subgroups of patients and at different stages of the patient journey**

We currently have an adjuvant study and first line maintenance study. We are keen to have a study for every patient – and in every part of the UK. We are very keen to increase links with cancer charities to deliver on the previously identified "key research gaps".

**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**

Dr Vicky Coyle, Professor Richard Wilson. Professor Anne Thomas and Dr Janet Graham are developing a CT DNA study in the adjuvant setting.

## Anorectal Subgroup (Chair, Professor Richard Adams)

**Develop seamless portfolio of trials**

A series of phase I/II trials are in development to replace the phase III ARISTOTLE trial as this closes to accrual in mid-2018. These studies will help inform the direction of travel for future phase III approaches. The results of the IRCI anal cancer study, InterAACT, will be presented in late 2018 and significant work has been done internationally to develop the follow-on phase III study.

**Use complex design in the delivery of future trials**

The PLATO Umbrella trial has been funded and is open recruiting patients with localised anal cancer with differing prognosis.

**Collaboration with other CSGs and international groups to develop studies**

Close working with the surgical subgroup to support development of the TREC and STAR TREC studies. Regular meeting with AGITG and Canadian groups to establish future rectal cancer trials. Working through the IRCI anal cancer initiative to deliver an international trial, develop the follow-on trial and work more strategically in the field of anal cancers.

**Develop trials for organ preservation in rectal cancer**

TREC and STAR TREC and more recently Aphrodite have been funded with national discussions on a future platform study ARTEMIS.

**Develop trials which test the effectiveness of systemic treatments replacing resection in resectable rectal cancer**

Proposal submitted for funding for phase III study in collaboration with Australian AGITG but not funded. EOI approved for a phase II trial exploring the role of immunotherapy in combination with chemotherapy and radiotherapy.

**Explore the options for a trial in synchronous resectable metastatic disease from rectal cancer**

Discussions on going, with significant engagement with international colleagues.

**Develop a study which focuses on improving toxicity and PROM assessment**

The PLATO anal cancer study will both explore the use of PROMs and dose de-escalation to improve functional outcomes for patients.

**Continue to develop combination trials of radiotherapy and novel agents**

CEDAR has been funded and EOI for PRIME RT has been approved.

**Link with other CSGs on understanding the biology of and advancing trial development in HPV-driven cancers**

The CSG worked with other CSGs including Cervix, H&N and penile to develop a translational research proposal which has been funded within the PLATO trial.

## Screening & Prevention Subgroup (Chair, Professor Colin Rees)

**Development of COLO-SPEED collaboration across UK and Netherlands**

Several grant submissions to CRUK catalyst programme of the COLO-SPEED study.

**Endocuff Vision: Device attached to distal end of colonoscope to improve detection of polyps at colonoscopy**

- Publication of ADENOMA trial in GUT. 1800 patient RCT. Demonstrated 10.8% improvement in Adenoma Detection Rate in FOB positive bowel cancer screening patients. Based on this trial the NHS has chosen this device as one of 4 innovations nationally to be fast-tracked and funded for delivery into NHS bowel cancer screening programme.
- Delivery of B-ADENOMA trial of Endocuff Vision in Bowelscope screening. 3222 patients recruited across 16 sites in 9 months. 6 months ahead of target. This is one of the world's

largest ever endoscopy trials and one of the fastest recruiting. Results currently being analysed.

- The successful ability of Endocuff Vision work led to the award of medilink NHS / Business acute sector award in March 2018.

**Delivery of Seafood trial: Aspirin and EPA for high risk patients in bowel cancer screening programme**

Multi centre larger polyp prevention trial completed in June 2017. Results are currently being analysed.

### Surgical Subgroup (Chair, Mr Simon Bach, outgoing chair)

**Enhance the portfolio of surgical trials including the development of two new surgical trials by the end of 2015**

In 2017 the Surgical Subgroup completed a 3-yearly cycle of research prioritization, stakeholder engagement and research workshops to facilitate new surgical studies. This 'Delphi project' came to a climax at the ACPGBI Bournemouth meeting as research was centre stage for the whole conference. We highlighted the breadth and depth of colorectal surgical research in the UK. This initiative has led to 3 major NIHR studies: PREPARE ABC (prehabillitaton), ALLEGRO (gastrointestinal recovery following bowel surgery) and CIPER (avoidance of parastomal herniation). NIHR have also funded the CREST 2 study (covered stents for palliation of colorectal cancer) and the ambitious GLOBAL surgery project (£7M) which will develop a cancer project in its second year. In colorectal cancer surgery BDRF have funded the HiP and SAILOR studies. BDRF have also funded an initiative (with ECMC's) to develop a standardized pre-treatment biopsy template that will support translational research in colorectal cancer.

**Develop a study for patient optimisation prior to surgery**

NIHR have funded the PREPARE ABC study which is evaluating whether introduction of a structured exercise programme before bowel cancer surgery improves patient outcomes (both short term morbidity and 12-month QoL). This study has already recruited 200 patients from 17 UK sites and satisfactorily passed its internal pilot feasibility stage.

**Develop a new study in organ preservation**

The Surgical and Anorectal Subgroups previously collaborated to develop the CRUK STAR TREC phase 2b study to evaluate the feasibility of recruiting to a randomized study comparing organ saving treatment with conventional radical surgery for patients with small rectal cancers. We have now developed the APHRODITE study (Yorkshire Cancer Research) which will evaluate different methods of achieving organ preservation in a frail population where radical surgery is considered high risk and therefore not the standard of care.

## 4. Task groups/Working parties

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

## 5. Funding applications in last year

### Table 2 Funding submissions in the reporting year

| Cancer Research UK Clinical Research Committee (CRUK CRC) | | | | |
|---|---|---|---|---|
| **Study** | **Application type** | **CI** | **Outcome** | **Level of CSG input** |
| **May 2017** | | | | |
| CaPP3 - a double blind randomised controlled dose inferiority trial of aspirin prevention in people with Lynch syndrome: high risk of cancer due to mutations in the mismatch repair genes (supported by Stand Up To Cancer) | Full application (Amendment) | Professor Sir John Burn | Supported | Developed by the Screening & Prevention Subgroup |
| PLATO - Personalising Radiotherapy in Anal Cancer - integrated sample collection and biomarker validation application | Full application | Dr Duncan Gilbert | Supported | Developed by the Anorectal Subgroup & CSG |
| Validation of Raman spectroscopy blood based biomarker for colorectal cancer | Full application | Professor Dean Harris | Not supported | No CSG input |
| CEDAR: Chemoradiation with Enadenotucirev as a radiosensitiser in locally advanced colorectal cancer | Full application | Professor Maria Hawkins | Supported | Developed by the Anorectal Subgroup |
| Validating genetic biomarkers of survival for colorectal cancer | Full application | Professor Jeremy Cheadle | Not supported | No CSG input |
| AMPhItheATre: A Multicentre Open Label Parallel Phase Ib Trial and Feasibility Study Using Induction carboplatin/paclitaxel plus the anti-PD-L1 | Full application | Dr Marcia Hall | Not supported | No CSG input |

| | | | | |
|---|---|---|---|---|
| Monoclonal Antibody - Avelumab before Radical Treatment in Locally Advanced or Locally Recurrent Anal Cancer | | | | |
| CoRInTH: Phase 1b/II trial of Checkpoint InhibitoR (Pembrolizumab an anti PD-1 antibody) plus standard IMRT in HPV induced stage III/IV carcinoma of anus | Full application (Endorsement) | Dr Marcia Hall | Endorsement not supported | No CSG input |
| CaPP3 - a double blind randomised controlled dose inferiority trial of aspirin prevention in people with Lynch syndrome: high risk of cancer due to mutations in the mismatch repair genes (supported by Stand Up To Cancer) | Full application (no-cost amendment) | Professor Sir John Burn | Supported | No CSG input |
| **November 2017** | | | | |
| Personalised colorectal cancer management using next generation sequencing based low cost microsatellite instability testing | Biomarker Project Award<br><br>(Full Application) | Professor Sir John Burn | Not Supported | No CSG input |
| ARISTOTLE: a phase II/III trial comparing standard versus novel CRT as pre-operative treatment for MRI defined locally advanced rectal cancer | Late Phase Study Extension<br><br>(Full Application) | Professor David Sebag-Montefiore | Supported | Developed by the Anorectal Subgroup & CSG |
| Other committees | | | | |
| Study | Committee & application type | CI | Outcome | Level of CSG input |
| Long term Survivors in colorectal cancer | Queen Mary University | Professor John Bridgewater | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |

| | | | | |
|---|---|---|---|---|
| APHRODITE | Yorkshire Cancer Research | Joint CIs: Dr Simon Gollins and Dr Ane Appelt | Funded | Developed by the Anorectal Subgroup |
| ANICCA-Class II | BMS Pharmaceuticals | Professor Gary MIddleton | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| CRUK Clinical Training Studentship | CRUK | Professor Gary MIddleton | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| Understanding the molecular basis and consequences of chemoradiosensitivity in rectal cancer in order to improve therapy (MOL-RSRC) | CRUK | Professor Gary MIddleton | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| HIGH POLE | BMS Pharmaceuticals | Dr Tony Dhillon | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| POLEM | Merck/Pfizer | Dr Tony Dhillon | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| Pilot Project: Developing a Standardised Colorectal Biopsy Template | Bowel Disease Research Foundation | Mr Dale Vimalachandran | Funded | Developed by the Surgical Subgroup |
| What Biomarkers Affect Response to CRT? | BDRF | Mr Dale Vimalachandran | Funded | Developed by the Surgical Subgroup |
| Role of Acid Ceramidase in rectal cancer | BDRF | Mr Dale Vimalachandran | Funded | Developed by the Surgical Subgroup |
| HiP Study | BDRF | Mr Dale Vimalachandran | Funded | Developed by the Surgical Subgroup |
| Brief Intervention with Cyclophosphamide in patients with Colorectal Cancer (CRC) who have completed treatment (BICCC) | Anticancer Fund | Professor Andrew Godkin | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| Workup of trial examining resection of primary in metastatic CRC | BDRF | Dr Jenny Seligmann | Funded | Developed by the Advanced & Adjuvant Disease Subgroup |
| Volatile Organic compounds for the DEtection of Colorectal cAncer: VODECA.. CRUK Early Diagnosis | CRUK Early Diagnosis | Dr Chris Probert | Funded | Developed by the Screening & Prevention Subgroup |

| | | | | |
|---|---|---|---|---|
| WASH study for mucosal visualisation at flexible sigmoidoscopy | RfpB | Dr Matt Rutter | Funded | Developed by the Screening & Prevention Subgroup |
| National Endoscopy database interrogation grant | Healthcare Foundation | Dr Matt Rutter | Funded | Developed by the Screening & Prevention Subgroup |
| Enhancing uptake of flexible sigmoidoscopy screening | Yorkshire Cancer Research | Dr Christian Von Wagner | Funded | Developed by the Screening & Prevention Subgroup |
| ALLEGRO | NIHR HTA | Mr Hugh Paterson | Funded | Developed by the Surgical Subgroup |
| CIPER | NIHR HTA | Mr Neil Smart | Funded | Developed by the Surgical Subgroup |
| CReST 2 | NIHR HTA | Professor Jim Hill | Funded | Developed by the Surgical Subgroup |
| COLO-SPEED | CRUK | Professor Colin Rees | Pending | Supported by the CSG |

## 6. Consumer involvement

Our consumer representatives continue to be very active and have provided excellent and effective support and input into all aspects of the workings of the Colorectal Cancer CSG, both at the main CSG and Subgroup meetings. They provide written comments on a large volume of documents circulated for discussion, are heavily involved in commenting on trial proposals and are part of the TMG of several trials. Mentorship for our consumer members continues as a fundamental aspect of their work where necessary.

### Sandra Irvine

Sandra Irvine is a member of the Northern Ireland Cancer Consumer Forum and its Bowel Cancer Interest Subgroup. She is PPI representative for the S-CORT Belfast centre and sits on the DMEC for the VitD and colorectal study. She is also a member of the All Ireland Hospice and Palliative Care group and the NCRI Adjuvant & Advanced Disease Subgroup.
She attended the attended NCRI Consumer Forum & Public Health England Summer Summit, the NCRI conference in Liverpool and the European Alliance for Personalised Medicine in Belfast and contributed to posters presented at the latter meetings. She was also a speaker at an Advance Care Planning event hosted by the Health & Social Care Board/Public Health Agency and MacMillan Cancer Support as part of the Palliative Care in Partnership public health agenda. She acted as facilitator for two courses on Building Research Partnerships hosted by the Public Health Agency. She was a member of two of the subgroups involved in the project to identify research gaps in bowel cancer research and named in the final publication in Gut (Gut 2018;67:179-193).

She has reviewed literature produced by Beating Bowel Cancer & Bowel Cancer UK, was co-applicant on a grant submission (unsuccessful) with Dr Bernard Rachet, London School of Hygiene & Tropical Medicine and contributed to a further project with Professor Melanie Morris, London School of Hygiene and Tropical Medicine.

### Monica Jefford

Monica Jefford is an integral member of the Colorectal CSG and makes valuable contributions to the main meeting, the Anorectal Subgroup and the APHRODITE (rectal cancer funded) and the ARTEMIS (rectal cancer proposal in development) trials. These are enhanced by other aspects of her eclectic PPI portfolio and likewise feed into the wider research picture. This is underpinned by an ethos of ‘research for patient benefit’. Her provision of written or verbal comments ensures the CSG documents are user friendly and support research delivery.

She is a member of TRACC TMG. She provides the patient view for NHS England Bowel Screening Programme. Volunteering with Bowel Cancer UK provides the opportunity for her to speak to various community groups about colorectal cancer. She is patient advisor to the London Research Design Service and a REC member.

## 7. Priorities and challenges for the forthcoming year

**Priority 1**

**Patient-centred trials**

Ensure trials are patient centred, available to as many patients as possible and engage consumers. Aim to integrate patient reported outcomes (PROMS) as far as possible. Harness the power of Big Data including NCRAS and PHE, to inform about 'real world' practice and outcomes, to help in the design of future patient-centred studies. Increase engagement with the research community including consumers, for example by extending the Delphi then CREATE model of dedicated research events so well demonstrated in the Surgical Subgroup, to other Subgroups.

**Priority 2**

**Expand the range of funders**

Increase the range of funders for the CSG's trials outside of CRUK. Increase interaction with funders including NIHR, to adapt and tailor our ideas. Align funding ideas to available funding streams. Appraise how to make trials attractive to funders, learn from what we do well; learn from others who are particularly successful at targeting certain funders. Develop third sector collaborations. Work more closely particularly with Beating Bowel Cancer/Bowel Cancer UK to raise the profile of CRC research in the UK. Gain funding in areas that are traditionally underfunded by major funders. Widen the portfolio e.g. demonstrating the importance of prevention and pre-cancer to cancer funders. Determination to take funding to the next level for clinical researchers (e.g. converting RfPB to HTA or EME).

**Priority 3**

**Maintain a balanced portfolio**

Discuss the BCUK recent gap analysis. Reinvigorate early phase work (AADSG) at the same time as developing more pragmatic/conceptual trials e.g. ADD ASPIRIN, CHALLENGE UK. Ensuring follow-on trials are developed in a timely fashion to fill anticipated gaps in the portfolio as others close.

**Challenge 1**

**Facilitating networking**

Bringing strong multi-disciplinary groups together with a common cause to create the best trials (from all angles). For example, around 4-5 large lab groups in UK are focused on colon, including Glasgow, Birmingham, Oxford and others). The aim would be to formalise a group of leaders who are early phase colorectal researchers around the UK, who could brainstorm and share ideas. Greater clarity on the value added of NCRI support for some groups e.g. Screening and Prevention Subgroup.

**Challenge 2**

**Capacity and infrastructure**

Support infrastructure for trials: Many units are very short staffed, particularly in terms of trials nurse support. Many units are over capacity and struggling to take on trials, particularly ones with a long maintenance period. Smaller trials are on the portfolio with a much higher administration burden than historically. With some units less well staffed and funded, trial set up is taking longer. Excess treatment costs are currently picked up by local commissioning groups or trusts but if the current review in progress means that this aspect comes under the remit of CRN's, then it will become essential that all costs are properly included in grant submissions e.g. RECIST reporting or biopsies.

**Challenge 3**

**Supporting and developing research-orientated clinicians**

A more challenging NHS environment, with a reduction in paid PA support for research activity, means that it is more challenging to maintain research-interested clinicians and to develop future leaders.

## 8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
A – Main CSG Strategy
B – Advanced & Adjuvant Disease Subgroup Strategy
C – Anorectal Disease Subgroup Strategy
D – Screening & Prevention Subgroup Strategy
E – Surgical Disease Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

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

**Dr Simon Gollins (Colorectal Cancer CSG Chair)**

# Appendix 1

## Membership of the Colorectal Cancer CSG

| Name | Specialism | Location |
|---|---|---|
| Professor Richard Adams | Clinical Oncologist | Cardiff |
| Dr Alexandra Gilbert* | Clinical Oncologist | Leeds |
| Dr Simon Gollins (Chair) | Clinical Oncologist | Denbighshire |
| Dr Alexandra Irvine | Consumer | Belfast |
| Ms Monica Jefford | Consumer | Surrey |
| Professor Colin Rees | Gastroenterologist | Newcastle |
| **Dr Tony Dhillon | Medical Oncologist | Surrey |
| Dr Michael Braun | Medical Oncologist | Manchester |
| Dr Vicky Coyle | Medical Oncologist | Belfast |
| Dr Janet Graham | Medical Oncologist | Glasgow |
| Dr Sheela Rao | Medical Oncologist | London |
| Professor Anne Thomas | Medical Oncologist | Leicester |
| Dr Manuel Rodriguez-Justo | Pathologist | UCL |
| Dr Nick West | Pathologist | Leeds |
| Professor Vicky Goh | Radiologist | London |
| Dr Rohit Kochhar | Radiologist | Manchester |
| Dr Jane Winter | Research Nurse | Southampton |
| Dr Louise Brown | Statistician | London |
| Mr Simon Bach | Surgeon | Birmingham |
| Mr Stephen Fenwick | Surgeon | Liverpool |
| Dr Andrew Beggs | Surgeon and translational scientist | Birmingham |
| Professor James Hill | Surgeon | Manchester |
| Ms Susan Moug | Surgeon | Glasgow |
| Dr Philip Dunne | Scientist | Belfast |
| *Dr Chris Coyle | | |
| *Dr Alex Gilbert | | |

* denotes trainee member

## Membership of the Subgroups

| Advanced & Adjuvant 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 | Eaton Ford |
| Dr John Bridgewater | Medical Oncologist | London |
| Dr Ian Chau | Medical Oncologist | London |
| Dr Janet Graham (incoming chair) | Medical Oncologist | Glasgow |
| Dr Tim Iveson** | Medical Oncologist | Southampton |
| Professor Gary Middleton** | Medical Oncologist | Birmingham |
| Dr Paul Ross** | Medical Oncologist | London |
| Jenny Seligmann** | Medical Oncologist | Leeds |
| Professor Anne Thomas (outgoing Chair) | Medical Oncologist | Leicester |
| Professor Phil Quirke | Pathologist | Leeds |
| Dr Louise Brown** | Statistician | London |
| Mr Hassan Malik** | Surgeon | Liverpool |
| Professor John Primrose | Surgeon | Southampton |
| Dr Chris Coyle* | | |

| Anorectal Subgroup | | |
|---|---|---|
| **Name** | **Specialism** | **Location** |
| Professor Richard Adams (Chair) | Clinical Oncologist | Cardiff |
| Dr Alexandra Gilbert* | Clinical Oncologist | Leeds |
| Dr Duncan Gilbert | Clinical Oncologist | Brighton |
| Dr Simon Gollins | Clinical Oncologist | Denbighshire |
| Dr Mark Harrison | Clinical Oncologist | Watford |
| Dr Leslie Samuel | Clinical Oncologist | Aberdeen |
| Ms Monica Jefford | Consumer | Surrey |
| Dr Sheela Rao | Medical Oncologist | London |
| Dr Susan Richman | Pathologist | Leeds |
| Dr Gina Brown | Radiologist | London |
| Mr Andrew Renehan | Surgeon | Manchester |

| Screening & Prevention Subgroup | | |
|---|---|---|
| **Name** | **Specialism** | **Location** |
| Professor Ian Tomlinson | Consultant in Genetics and Molecular Pathology | Birmingham |
| Mrs Lindy Berkman | Consumer | London |
| Professor Roger Blanks | Epidemiologist | Oxford |
| Professor John Burn | Epidemiologist | Newcastle |
| Professor Linda Sharp | Epidemiologist | Newcastle |
| Dr Christian von Wagner** | Epidemiologist | London |
| Dr Laura Neilson | Gastroenterologist | Newcastle |
| Professor Colin Rees (Chair) | Gastroenterologist | Newcastle |
| Professor Matt Rutter** | Gastroenterologist | Middlesbrough |
| Professor Diana Eccles** | Geneticist | Southampton |
| Professor John Saxton | Scientist | Northumbria |
| Professor Karen Brown | Scientist | London |
| Mr Simon Bach** | Surgeon | Birmingham |

| Surgical Subgroup | | |
|---|---|---|
| **Name** | **Specialism** | **Location** |
| Mrs Ann Russell | Consumer | Eaton Ford |
| Mr Simon Bach (outgoing chair) | Surgeon | Birmingham |
| Mr Aneel Bhangu** | Surgeon | Birmingham |
| Miss Nicola Fearnhead (incoming chair) | Surgeon | Cambridge |
| Ms Deena Harji* | Surgeon | Leeds |
| Mr James Hernon | Surgeon | Norwich |
| Mr James Hill | Surgeon | Manchester |
| Mr Matt Lee* ** | Surgeon | Sheffield |
| Professor Dion Morton** | Surgeon | Birmingham |
| Ms Susan Moug | Surgeon | Glasgow |
| Mr Tom Pinkney** | Surgeon | Birmingham |
| Mr Doug Speake | Surgeon | Edinburgh |
| Mr Jared Torkington | Surgeon | Cardiff |
| Ms Abigail Vallance | Surgeon | London |
| Mr Dale Vimalchandran | Surgeon | Chester |
| Mr Nicholas West | Surgeon | Leeds |

* denotes trainee member

**denotes non-core member

## Appendix 2

### CSG & Subgroup Strategies

### A – Main CSG Strategy

Our 2014-18 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. A formal Strategy Meeting will take place on 11th May 2018. The most recent Strategy, and our progress against it, is illustrated below.

- 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 – Advanced & Adjuvant Disease Subgroup Strategy

**Advanced and Adjuvant Disease subgroup 3 main achievements (2017-2018)**

1. Publication of the SCOT study.
2. FOCUS 4 and ADD ASPIRIN– set up of infrastructure around the UK to deliver large complex platform studies. Quick turnaround of FOCUS 4D. Recruitment to target of FOCUS 4C. Excellent recruitment in colorectal arm of ADD ASPIRIN.
3. Emerging group of immunotherapy studies; POLE M, HIGH POLE, ANICCA, Celleron, EMERGE, ElevatION and others.

**Advanced and Adjuvant Disease Subgroup priorities:**

1. Align funding ideals to available funding streams: How to make trials attractive to funders, learn from what we do well; learn from others who are particularly successful at targeting certain funders.
2. Develop more Pragmatic/ conceptual trials: The UK have a track record in pragmatic trials e.g. 3 versus 6/12, cont versus intermittent, elderly, more recently exercise (CHALLENGE) and ADD ASPIRIN. Continue to design studies like this that probably fit with HTA funding e.g. DPD Deficiency (PR) and CT DNA (VC).
3. Reinvigorate early phase work: At other end of development spectrum: Around 4-5 large lab groups in UK who are focused on colon (Glasgow, Birmingham, Oxford and others). Aim to formalise a group of leaders, early phase colorectal cancer CRC researchers around the UK who could brainstorm and share ideas. Integrate more with S-CORT.
4. Mentorship: Continue to support and develop trainees and new consultants with an academic interest.
5. Patient involvement and engagement: Ensure trials are patient centred and available to as many patients as possible. Aim to integrate PROMS, new technology etc into studies.
6. Third sector collaborations**:** Work more closely with Beating Bowel Cancer/ Bowel Cancer UK to raise the profile of CRC research in the UK.

**2014-2018 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.

## C – Anorectal Subgroup Strategy

**Anorectal Subgroup top 3 achievements (2017-2018):**

1. Completion of the IRCI metastatic anal cancer trial demonstrating feasibility of international recruitment and timely delivery of a phase II trial in a rare disease entity
2. The opening of the phase II/III PLATO umbrella trial personalising radiotherapy in anal cancer with the development of a national IMRT radiotherapy protocol with robust quality assurance, funded translational research project and integrated PROM assessment. Aligned with a novel early phase trial of immunotherapy in combination with chemo-radiotherapy in locally advanced anal cancer
3. Delivering the final stages of the phase III ARISTOTLE trial combining chemoradiotherapy +/- irinotecan in patients with locally advanced rectal cancer

**Anorectal Subgroup priorities:**

1. Develop the follow-on trials to ARISTOTLE, integrating biological understanding in a more effective manner and working up robust proposals with a broad range of expertise
2. Working to deliver trials to time and with broader reach with international colleagues
3. Delivery of the anal cancer radiotherapy trials and development of a phase III metastatic anal cancer trial
4. Ensuring we are answering the questions most relevant to our patients

**2014-2018 Strategy**

- Develop a seamless portfolio of trials that allow timely follow-on with no significant gaps between.
- Use complex design in the delivery of future trials, e.g. MAMS design, umbrella trials.
- Develop and get funded an international phase III trial for metastatic anal cancer.
- Explore the options for trials in synchronous metastatic disease from rectal cancer.
- Develop studies which focus on improving toxicity and PROM assessment.
- Continue to develop combination trials of radiotherapy and novel agents.
- Link with other CSGs and international groups to develop studies to optimise outcomes for patients with rectal cancer including avoidance of surgery and improving survival.
- Link with pre-clinical and translational scientists to improve our understanding of biology to identify optimised prognostic and predictive markers.

## D – Screening & Prevention Subgroup Strategy

### Screening and Prevention Subgroup priorities (2017-2018)

1. Develop COLO-SPEED further – ideally with CRUK catalyst funding. Collaboration to continue in parallel
2. Develop and gain funding for COLOCOHORT study – this is a 10,000 patient cohort study to be led from NE England exploring risk factors for CRC and Adenomas including familial, genetic, lifestyle, behavioural.
3. Develop and submit POLCA-DOT study for funding – A study of PT1 cancers and their management across UK – is organ preservation possible for these cancers.
4. Develop COLO-PREVENT – in development phase – a study of combination chemopreventative agents for colorectal adenomas.
5. Develop further trials that span disciplines and methodologies

### 2014-2018 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 – Surgical Subgroup Strategy

**Surgical Subgroup top 3 achievements (2017-2018)**

1. In 2018 we will publish a series of landmark papers in colorectal surgical oncology each evaluating an important new approach to patient care: FOxTROT (neoajuvant chemotherapy for colon cancer), CREST (stenting for obstructing bowel cancer) and TREC (a multimodality organ saving approach to treatment of early stage rectal cancer).
2. We have successfully completed 3 yearly Delphi cycle which has dramatically increased participation in surgical research both from patients and clinicians.
3. We have developed a training package that is now being disseminated as part of the site set up process for our surgical studies that provides investigators with a framework for conducting the recruitment interview. This was borne out of the GRANULE training course (Generating student recruiters for randomised trials), an initiative to provide practical training for undergraduates in recruitment training (https://publishing.rcseng.ac.uk/doi/full/10.1308/rcsbull.2017.260).

**Surgical Subgroup priorities for the forthcoming year:**

Members of the surgical subgroup are interested in developing research studies in the following areas:

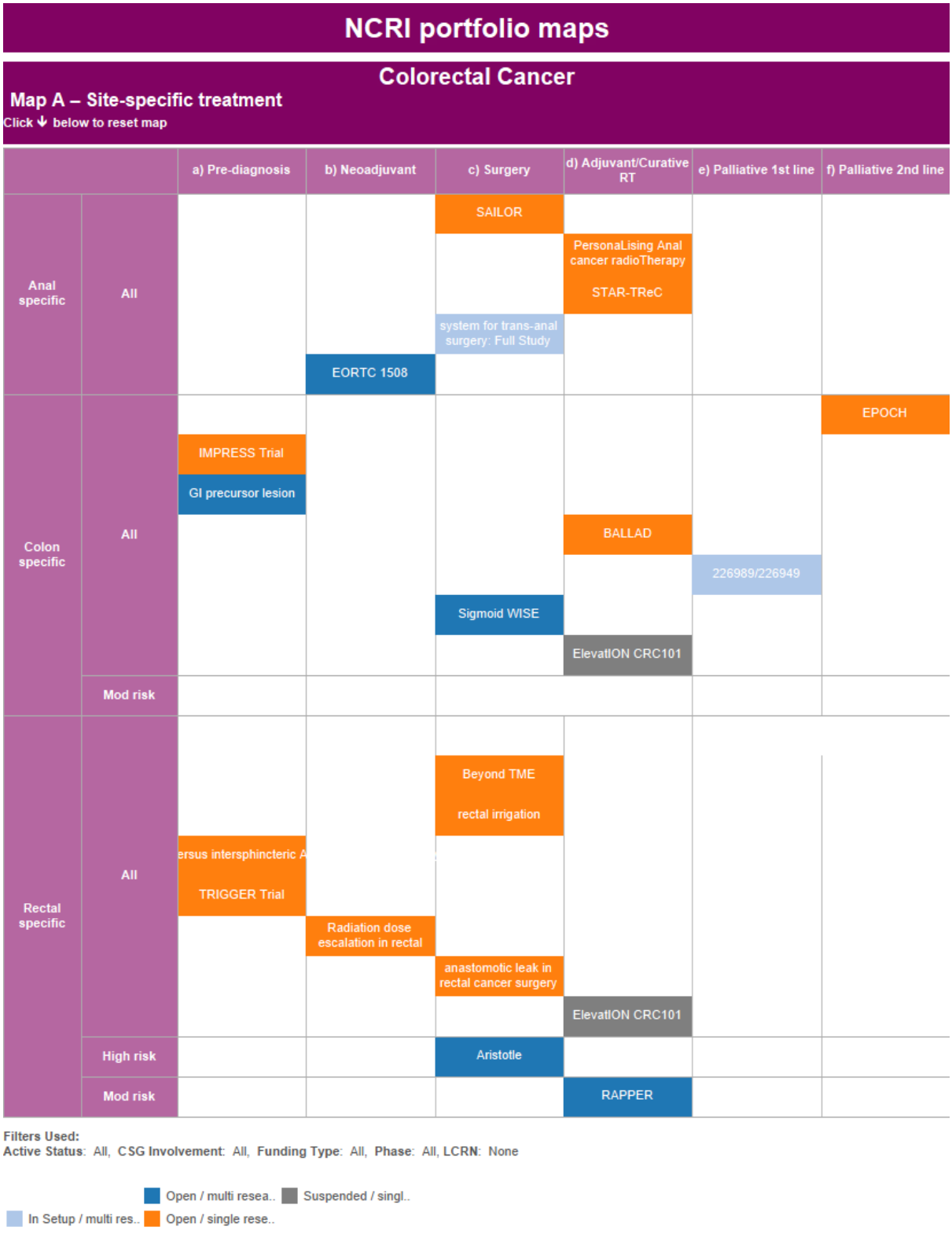
1. Early stage colorectal cancer -we will submit the STAR-TREC phase 3 application to CRK in Jan 2019. We are also developing a separate study to evaluate organ sparing treatment for colon polyp cancers (POLCA DOT).
2. Advanced disease – members of the group have expressed interest in evaluating new methodologies that would introduce goal directed therapy endpoints for the evaluation of surgical intervention for patients with incurable colorectal cancer. To date we have created the IMPACT initiative (Improving Management of Patients with Advanced Colorectal Tumours).
3. Members of the group have been working with RCS, NHS England and NIHR to develop a commissioning brief to evaluate robotic assisted surgery in the NHS.
4. We have set a new research framework to replace the Delphi initiative. This incorporates the Colorectal Research and Trial Engagement (CREATE) roadshows which will travel to different regions providing practical advice on how to set up and recruit to portfolio studies (https://www.acpgbi.org.uk/news/create-roadshow/). Our '2020 vision' project will encourage new collaborations between the six surgical societies affiliated to the Tripartite colorectal organization (ACPGBI, ASCRS, CSSANZ, ESCP, RACS and RSM) prior to the Tripartite colorectal meeting in Auckland 2020.

**2014-2018 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.

# Appendix 3

## Portfolio maps

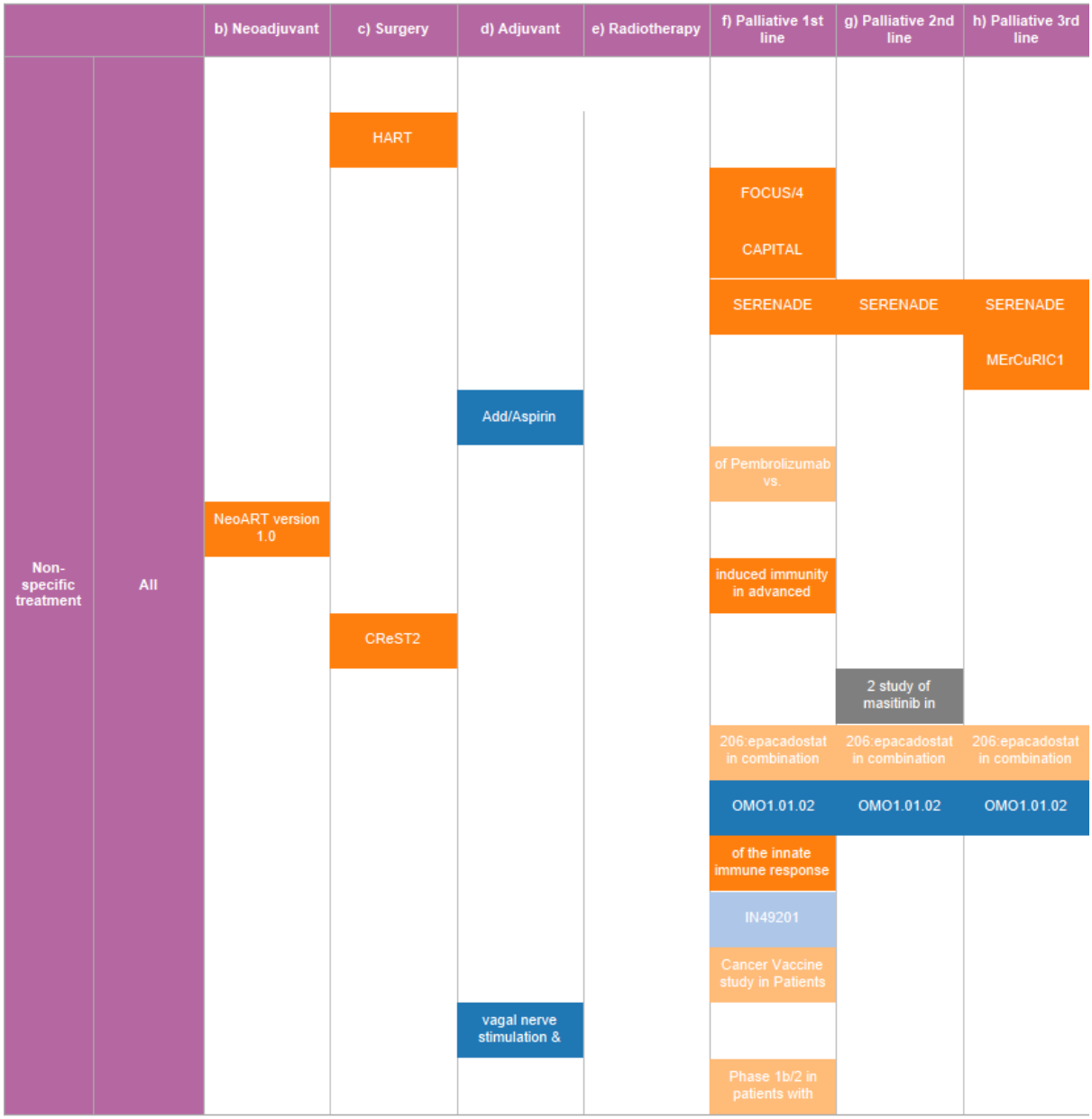


# NCRI portfolio maps

## 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, **LCRN**: None

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

# NCRI portfolio maps

## Colorectal Cancer

### Map C – Non-treatment, translational

Click ↓ below to reset map

| | | a) Pre-diagnosis | b) Diagnosis / screening / prevention | c) Neoadjuvant | d) Surgery | e) Adjuvant | f) Palliative 1st line | g) Therapeutic / translational |
|---|---|---|---|---|---|---|---|---|
| Biomarkers | All | Tumour Angiogen<br>el lymph node biop<br>NICE FIT | Tumour Angiogen<br>ctDNA v6.0<br>TRACCr<br>wel cancer risk: 10 y<br>MECANO study V1 | Tumour Angiogen | Tumour Angiogen | Tumour Angiogen | Tumour Angiogen | Tumour Angiogen |
| Diagnostics / imaging | All | Raman<br>MAGENTA<br>EDICT DISEASE R<br>ctroscopy and colore | Raman<br>orectal disease in sy<br>lonoscopy for polyp<br>for CT colonography<br>ion of Human Colore<br>out colorectal cance<br>al breath analysis (C<br>COMET | Raman | Raman<br>rectal surgery: ranc | Raman | Raman | Raman |
| Genetics / mechanisms | All | CORGI<br>COGS2<br>Pop. DNA collxns<br>SOCCS3<br>Vitamin D and C<br>RAFV600E immuno<br>n in non/invasively<br>DEterminants of Al | CORGI 2<br>rised 13C-Pyruvate | NSCCG<br>Molecular patho | NSCCG<br>Molecular patho<br>tic system for trans/ | NSCCG<br>Molecular patho | NSCCG<br>Molecular patho | NSCCG<br>Molecular patho<br>EpiMET<br>Nrf2 pathway in tumo |

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

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NCRI National Cancer Research Institute

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# NCRI portfolio maps

## Colorectal Cancer

### Map D – Non-treatment, supportive care, primary care

Click ↓ below to reset map

| | | a) Pre-diagnosis | b) Diagnosis / screening / prevention | c) Neoadjuvant | d) Surgery | f) Palliative 1st and 2nd line | g) Other |
|---|---|---|---|---|---|---|---|
| Lifestyle / psychosocial onc.. | All | | eRAPID feasibility pilot study in pelvic radiotherapy | | Prepare/ABC<br>PARiS<br>EPOP 2- Peri -Operative Isometric Exercise Programme | eSMART: Randomi<br>Challenge<br>Perspectives on Peritoneal Metastasis | International validation of the EORTC QLQ-ANL27 |
| Primary care / data collection / Services | All | Risk factors for colorectal precursor lesions | Emergency Presentation Study (Empress) v1.0<br>The SCOTTY Study<br>Uterine Protection in Lynch Syndrome (UP study) | Anal Cancer Survival Analysis | EMT2: EPA for Metastasis Trial 2<br>COALS: Coagulation in Liver Surgery | | Research Bowel Cancer Improvement Program<br>Real World Outcomes of Patients with mCRC |

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

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NCRI National Cancer Research Institute

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

## Appendix 4

### Top 5 publications in the reporting year

| Trial name & publication reference | Impact of the trial | CSG involvement in the trial |
|---|---|---|
| 1. 3 versus 6 months of adjuvant oxaliplatin-fluoropyrimidine combination therapy for colorectal cancer (SCOT): an international, randomised, phase 3, non-inferiority trial. Iveson TJ et al Lancet Oncol. 2018 Apr;19(4):562-578. | Practice-changing trial in adjuvant colorectal cancer, halving treatment for many patients from 6 to 3 months. | Developed by the CSG |
| 2. Bowel Cancer UK Critical Research Gaps in Colorectal Cancer Initiative. Critical research gaps and recommendations to inform research prioritisation for more effective prevention and improved outcomes in colorectal cancer. Lawler M et al; Gut. 2018 Jan;67(1):179-193. | Gap analysis, which should help inform future strategy. | |
| 3. Improving adenoma detection at colonoscopy with Endocuff Vision: the ADENOMA randomized controlled trial. WS Ngu et al. Gut 2018; 66:1–9. | Large trial from the Screening & Prevention Subgroup showing Endocuff Vision improves adenoma detection rates. | Developed by the CSG |
| 4. Investigating the poor outcomes of BRAF-mutant advanced colorectal cancer: Analysis from 2530 patients in randomised clinical trials. | First author is an Advanced & Adjuvant Disease Subgroup member who was a trainee at the time of publication. | Developed by the CSG |

| | | |
|---|---|---|
| Seligmann JF et. Ann Oncol. 2017 Mar 1;28(3):562-568. | | |
| 5. Dexamethasone versus standard treatment for postoperative nausea and vomiting in gastrointestinal surgery: randomised controlled trial (DREAMS Trial). BMJ 2017 Apr 18;357:j1455. | Large successful randomised trial run largely by surgical trainee network | Developed by the CSG |

# Appendix 5

## Recruitment to the NIHR portfolio in the reporting year

In the Colorectal Cancer CSG portfolio, 20 trials closed to recruitment and 21 opened.

**Summary of patient recruitment by Interventional/Non-interventional**

| Year | All participants | | Cancer patients only | | % of cancer patients relative to incidence | |
|---|---|---|---|---|---|---|
| | Non-interventional | Interventional | Non-interventional | Interventional | Non-interventional | Interventional |
| 2013/2014 | 3276 | 4432 | 1908 | 1924 | 4.7 | 4.8 |
| 2014/2015 | 4825 | 1081 | 4728 | 1020 | 11.7 | 2.5 |
| 2015/2016 | 4679 | 1765 | 4651 | 1213 | 11.52 | 3.00 |
| 2016/2017 | 2044 | 1772 | 2031 | 1544 | 5.03 | 3.82 |
| 2017/2018 | 3226 | 5232 | 3144 | 5058 | 7.79 | 12.53 |