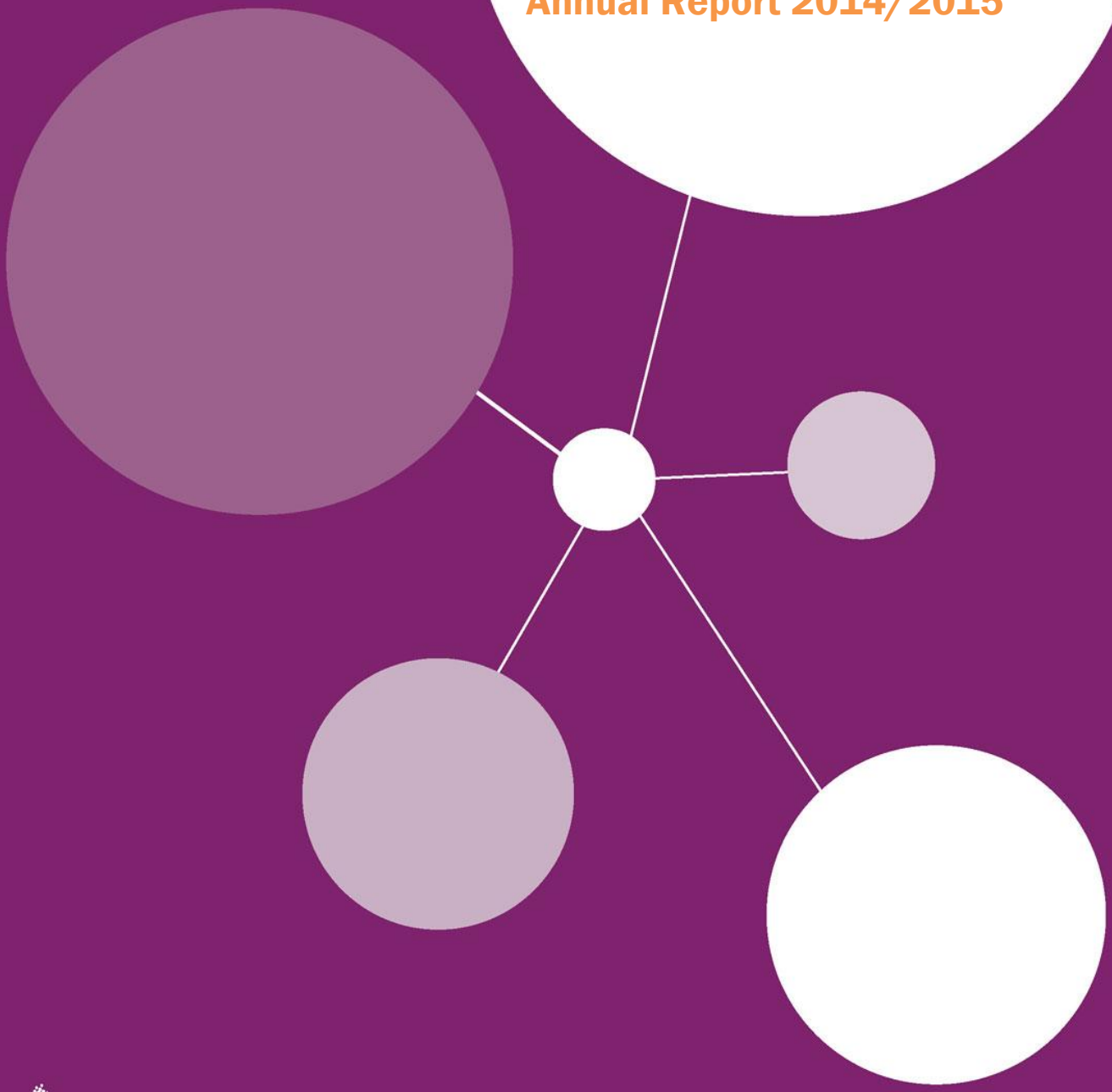
NCRI
National
Cancer
Research
Institute

NCRI Upper Gastro-intestinal Cancer Clinical Studies Group

Annual Report 2014/2015



Partners in cancer research

NCRI Upper Gastro-intestinal Cancer CSG Annual Report 2014/15

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

The Upper GI CSG is a highly successful group which has retained a large portfolio of ongoing trials and has a track record in delivering successfully completed studies. This year has seen the presentation of 2 flagship trials in Biliary Tract Cancer, ABC03 and ABC 04 at ASCO 2014. In addition BILCAP, by far the largest adjuvant bile duct cancer ever undertaken completed recruitment in 2014 and should report in 2016. This confirms the position of the UK as the world leader in research in clinical trials in this disease area. Tran-COG was presented at the same meeting demonstrating the benefit of EGF-R blockade in some patients with oesophageal cancer. 2015 will see the presentation of the results of OE05 at ASCO 2015 and ST03 at ECC, major achievements in oesophagogastric cancer. The Group has engaged in new initiatives such as engagement with the NIHR CRN leads, one successful meeting having been held. This may help to begin to deal with one identified problem, which is large difference in LCRN engagement with trials in Upper GI cancer. We have also appointed 2 trainee members to the group after a national advert attracting an exceptional quality of applicants. A strategy of avoiding serial renewal of membership and rotation of subgroup chairs has produced a vibrant and cohesive group. The level of success in obtaining funding for studies from CTAAC and HTA has been less than ideal in the last year and reflects a relatively constrained funding environment. Adaptive trials are a particular challenge in this respect. The 2014 translational meeting was a success and the Group are assembling a comprehensive list of biological materials in various sites which are related to clinical trials and also documenting the ongoing studies. The aim of this is to enhance the outputs from the material collected. In 2015 a Trial Think Tank will be organised in association with the autumn meeting to help develop new trial ideas. The 2014 Annual Trials Meeting was again successful with a high attendance and excellent feedback.

2. Structure of the Group

The Group structure with 4 subgroups (Oesophagogastric (OG), Pancreas, Hepatobiliary (HPB) and Neuroendocrine) is unchanged as is the composition and chairs (Professor David Cunningham (OG), Dr Stephen Falk (Pancreas), Dr John Bridgewater (HPB) and Professor Juan Valle (Neuroendocrine)). There have been a number of changes in the subgroup membership.

3. CSG & Subgroup strategies

Main CSG

The Group strategy as outlined in October 2011 and supported by the Group's progress review in 2013 was:

- Move to adaptive trials, with seamless transition from phase 2 to phase 3 comparisons. All the subgroups except Neuroendocrine have currently adaptive trials in preparation. The funding result outcome has been mixed. PLATFORM (OG cancer) is funded and PRECISION-PANC (pancreatic cancer) and OCTOPUS (colorectal liver metastases) are in the funding application process.
- Trials of radiotherapy and surgery. Scallop has established a new international standard for chemoradiotherapy in locally advanced pancreas cancer. Scallop 2 and SCOPE-2 have been funded as has the ICOR study of chemotherapy v chemoradiotherapy in oesophageal adenocarcinoma. This latter study has become more attractive since the result of OEO-5. ORANGE 2 (laparoscopic liver surgery) is recruiting well in the UK. ROMIO (laparoscopic v open oesophageal surgery) has successfully completed a feasibility phase and is no open as a Phase 3 trial.
- Develop Translational research. All studies have embedded blood and tissue and register of biological materials from clinical trials and a list of translational studies are being complied. Sample collection from the various OG cancer studies form one of the world's largest such resources. The Barrett's study ASPECT has a large tissue collection now housed in Warwick and the OCCAMS collaborative based in Cambridge has good quality frozen cancer tissue for whole genome sequencing.

Pancreatic Subgroup (Chair, Dr Stephen Falk)

Achievements

The Subgroup has a long track record in delivering large clinical trials including ESPAC trials and SACALLOP. Telovac successfully recruited but was disappointing as negative. A proposed platform strategy founded on a large MRC/CRUK basic science grant (PRECISION-PANC, A Biankin/J Valle) should provide a spring board for fruitful collaboration. This platform approach should provide a large body of samples to properly characterise the disease and lead to novel directed therapeutic approaches within a programme of associated clinical trials

Aim

The Pancreatic Subgroup has developed trial proposals in pre diagnosis, surgery and advanced disease to achieve its aim and strategy of a balanced portfolio with planned or opening studies.

Challenges

The challenge remains the poor health of many patients with pancreas cancer at presentation that limits therapeutic approaches and provides a difficult group to introduce meaningful studies.

Further funding of proposed studies has been problematic in 2014/15 but the proposed CRUK strategy which is consistent with the parliamentary inquiry into pancreas cancer is expected to provide enhanced opportunities to support the groups work.

Neuroendocrine Subgroup (Chair, Professor Juan Valle)

Achievements

- Results of the COOPERATE-2 study (industry-adopted) were presented at the European Neuroendocrine Tumour Society (ENETS) meeting. Although the study did not meet its primary end-point, it has raised the profile of the NCRI as a good recruiter.
- The RADIANT-4 study (industry-adopted) is due to report at European Cancer Congress 2015; the study (likely to result in a high-impact publication) met its primary endpoint.
- A proposal to the ECMC Combinations Alliance of the temozolomide and olaparib combination in patients with well-differentiated pNETs was invited for submission to CTAAC (in development).
- Following a proposal to the International Rare Cancers Initiative (IRCI) to develop a clinical trial for patients with goblet cell carcinoid (GCC) tumours of the appendix, the decision has been made by IRCI to combine three groups (GCC; peritoneal mesothelioma and high-grade pseudomyxoma peritoneii) into a Non-Gynaecological Peritoneal Malignancy CSG Working Group.
- The TRANSNET (translational research in NETs) initiative has successfully rolled out a multi-centre clinical trial (CALM-NET) evaluating circulating biomarkers in patients with well-differentiated NETs with carcinoid syndrome embarking on a somatostatin analogue therapy. In addition, TRANSNET (in conjunction with the NET Patient Foundation), made starter grants available for translational research – these projects will lead to publications over the coming 12-24 months.
- The clinical trials portfolio continues to grow, evidenced by the increasing options on the NCRI NET portfolio map.

Aim

- To improve outcomes for patients with NETs through clinical and translational research, built on a coordinated infrastructure for these rare tumours.

Challenges

- NETs are uncommon by incidence
- Centralisation of treatment of patients with NETs is variable across the country in the absence of Improving Outcomes Guidance (available for most other cancers)
- Successful studies (recruiting promptly) are likely to require international collaboration (increasing the costs and demands on Clinical Trial Units)
- NET studies are likely to recruit small patient numbers within any institution with the risk of de-prioritisation in favour of larger-volume studies in commoner cancers.
- Novel therapies arising as a result of clinical trials are not funded by NICE or the Cancer Drugs Fund, limiting the ability to participate in studies where these are considered standard-of-care.
- Studies are migrating to high-volume centres (specifically ENETS Centres of Excellence); while this is likely to achieve good recruitment, involvement of smaller-volume centres remains a challenge.

Hepatobiliary Subgroup (Chair, Dr John Bridgewater)

Achievements

The Hepatobiliary Subgroup meets biannually and comprises hepatocellullar carcinoma, biliary tract carcinomas, colorectal liver metastasis and carcinoma of unknown primary. The subgroup has a strong record of collaborative working, study generation and high impact publication. There is strong user group involvement with representation from the Carcinoma of Unknown Primary Foundation and the AMMF. There is an international extension of the biliary tract group which has met 1-2 times a year since January 2010.

Delivered publications from ABC-02, New EPOC, Photostent 2, ABC-03, and ABC-04. A large number of academic and industry trial are about to report or in progress, most notably BILCAP with 420 patients in 2016. A further biliary adjuvant trial is funded (ACTICCA-01). TACE-2 is pivotal and continuing to recruit although slowly. Translational studies from ABC trials and New EPOC are in progress and BILCAP will follow. Funding for the assembly translational material from the biliary tract portfolio has been granted.

Aims

The Hepatobiliary Subgroup has been the international leader in the clinical treatment of HB cancers.

Challenges

- Patients with liver cancer frequently have mortality from liver disease not dissimilar from the effects of cancer making interpretation of trial results difficult.
- Biomarkers to inform on the use of targeted therapies are not mature in biliary tract cancer
- Tumours are less common than other Group cancers, less easy to diagnose through histology and assessment of response difficult. International collaboration is needed.
- The set up times for new trials can be problematic. ACTICCA-01 is still not open more than 2 years after grant award due to issues in the CRUK Birmingham Clinical Trials Unit

Oesophagogastric Subgroup (Chair, Professor David Cunningham)

Achievements

- OCCAMS and CHOPIN had high impact publications in Nature Genetics and Gastroenterology on the genomics of OG cancer and Barrett's oesophagus.
- BEST2 demonstrated that the cytosponge-TFF3 may be a simple and inexpensive new diagnostic test for Barrett's oesophagus.
- NeoSCOPE introduced advanced radiotherapy techniques through a comprehensive quality assurance program, raising standards throughout the NHS and delivering improved patient outcomes.
- COUGAR-02 and COG were published in Lancet Oncology. COUGAR-02 led to second-line chemotherapy becoming a standard of care for OG cancer. Trans-COG identified a subgroup of patients who benefit from gefitinib (ASCO 2014).
- Trial recruitment has been excellent. Initial results of OE05 (n=897) were presented at ASCO 2014 and the main ST03 (n=1063) and OE05 results will be presented in 2015. ROMIO will

soon be one of the world's largest trials investigating minimally invasive versus open oesophago-gastrectomy for cancer (n=122). Samples collected for these studies form one of the world's largest OG cancer biobanks.
- Development of important new trials. E.g. the global Add-Aspirin trial will open soon and the national PLATFORM trial opened earlier this year.

Aim
- To improve outcomes for patients with OG cancer through progressive clinical trials and cutting edge translational research.

Challenges
- Patients with OG cancer frequently have disease-related morbidity, leading to a smaller pool of patients to recruit to clinical trials.
- Identifying patients who benefit from targeted therapies has been difficult due to the lack of validated biomarkers in OG cancer, resulting in a number of negative studies.
- Integration of novel immunotherapy drugs into the treatment of OG cancer patients is essential moving forward, especially given the demonstrated benefits in other cancer types.
- The significant set-up time for large multi-centre studies makes preventing gaps in the trial portfolio challenging.

4. Task groups/Working parties

The CSG has had no task groups in the last year.

5. Patient recruitment summary for last 5 years

In the Upper GI CSG portfolio, 15 trials closed to recruitment and 20 opened. The figures for 2012/13 are distorted by some large recruiting studies which have closed. The trend is to have fewer large phase 3 trials on unelected patients so the recruitment testifies to the health of the group's portfolio.

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
2010/2011	3362	3636	3280	3636	14.1	15.6
2011/2012	4686	2616	4405	2616	18.9	11.2

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	1006	3237	964	2777	4.0	11.4
2013/2014	904	1866	882	1652	3.6	6.8
2014/2015	1178	1863	1092	1543	4.5	6.3

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

The Hepatobiliary Subgroup works closely with the Advanced & Adjuvant Disease Subgroup (Colorectal CSG) on operable colorectal liver metastases and also on small bowel cancer. Two CSG representatives sit on the NCRI Screening, Prevention & Early Diagnosis (SPED) Advisory Group. The CSG has good international links, specifically the International Biliary Tract Cancer Collaborative in respect of the HB subgroup and ENETS in respect of the Neuroendocrine Subgroup.

7. Funding applications in last year

The funding environment at CTAAC has been challenging in recent years. In 2014/15 success has been generally high with some anomalies. SCORPION achieved a fundable score but no funding was available. ABC05 was supported when it was an AZ alliance study but when AZ withdrew support the same trial achieved only very low scores suggesting the level of support for the science is very dependent on the means of funding. Outside CTAAC, 2 major group trials have been funded by HTA.

Table 3 Funding submissions in the reporting year

Clinical Trials Advisory and Awards Committee (CTAAC)			
Study	**Application type**	**CI**	**Outcome**
July 2014			
SCOPE 2: A randomised phase II/III trial to study radiotherapy dose escalation in patients with oesophageal cancer treated with definitive chemo-radiation with an embedded phase II trial for patients with a poor early response using positron emission tomography (PET)	Full application	Drs Thomas Crosby, Maria Hawkins, Gareth Griffiths and Somnath Mukherjee	Funded
SPARC: A Phase I trial of pre-operative, margin intensive, stereotactic body radiation therapy for previously untreated borderline resectable pancreatic cancer	Feasibility application	Dr Maria Hawkins	Funded
PRIMUS: Pancreatic cancer investigational multi-agent umbrella study - part of IMPaCT - UK (individualised molecular pancreatic cancer therapy)	Outline application	Professor T R Jeffry Evans	Full application invited
ABC07: Addition of stereotactic radiotherapy to systemic chemotherapy in locally advanced biliary	Feasibility applications	Dr Maria Hawkins	Funded

tract cancers			
ASPECT: Aspirin Esomeprazole Chemoprevention Trial ASPECT Extension	Full application *Extension*	Professor Janusz Jankowski	Funded
T-SCALOP 2: Prospective sample collection in the SCALOP2 trial	Sample collection application	Dr Somnath Mukherjee	Decision deferred (fundable but insufficient funds at this meeting)
CAPSICUM: Randomised two-arm, two-stage trial of S-1 in metastatic pancreatic ductal adenocarcinoma patients whose performance status contraindicates combination chemotherapy and in whom monotherapy is indicated	Full application *Appeal against March 2014 decision*	Dr Pippa Corrie	Original decision upheld – not funded
November 2014			
SCORPION Trial: Prospective randomised trial of adjuvant chemotherapy with Streptozocin and Capecitabine versus Observation following Resection of well differentiated Pancreatic Neuroendocrine tumour	Full Application	Dr Richard Hubner/ Professor Juan Valle	Achieved fundable score – endorsement offered
Establishment of a Database and Biobank Resource for Long-Term Study of Hepatocellular Carcinoma in the UK	Sample Collection Application	Professor William Irving	Not funded
CUP-ONE Translational Tissue collection (CUPONE-T) The collection of biopsies with paired blood, with detailed clinical datasets in cancer of unknown Primary	Sample Collection Application	Dr Harpreet Wasan	Not funded
ABC-05 - A randomised phase II/III study of Selumitinib (AZD6244) or placebo in combination with cisplatin/gemcitabine chemotherapy for patients with advanced biliary tract cancers	Full Application	Dr John Bridgewater	Not funded
CAPSICUM II: Randomised phase II trial of S-1 with a dose escalation run-in stage in metastatic pancreatic ductal adenocarcinoma patients whose performance status contraindicates combination therapy and monotherapy is indicated	Feasibility Application	Dr Pippa Corrie	Not funded
March 2015			
NET-02: A multi-centre, randomised, open-label, phase II trial of IrMdG or temozolomide/capecitabine combination as second-line therapy in patients with progressive poorly differentiated gastrointestinal neuroendocrine carcinoma	Outline application	Dr Mairead McNamara	Full application not invited
ESPAC-6: A randomised phase III trial of gemcitabine vs. S-1 vs. gemcitabine + S-1 as adjuvant chemotherapy in patients with resected pancreatic ductal adenocarcinoma	Outline application	Professor Daniel Palmer	Revised outline requested
ACELARATE: A Phase III, open label, multicentre randomized clinical trial comparing Acelarin with Gemcitabine in patients with metastatic pancreatic	Full application *Endorsement*	Professor Daniel Palmer	Endorsed

adenocarcinoma			
OPERa: A randomised, double-blind, placebo controlled, multi-centre phase II study to assess the efficacy and safety of 2nd line olaparib in combination with paclitaxel, in Western patients with advanced gastric and gastro-oesophageal junction (GOJ) cancer	Feasibility application	Dr Naureen Starling	Endorsed
Biliary Tract Cancer Studies translational material bank	Sample collection application	Dr John Bridgewater	Funded
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
Thermal ablation versus surgery for patients with colorectal liver metastases	HTA	Professor Brian Davidson	Funded
The ROMIO trial. Randomised Oesophagectomy: Minimally Invasive or Open	HTA	Professor Jane Blazeby	Funded

8. Collaborative partnership studies with industry

In line with national policy there has been a large increase in industry trials on the Groups portfolio and these are demonstrated in the portfolio maps. Generally these are smaller studies which do not have a major impact on the recruitment to academic trials. Other partnerships have been more problematic. Considerable effort from Group members has gone into developing protocols which have gone through CTAAC and unfortunately subsequently the company has withdrawn support for the compound.

9. Impact of CSG activities

The Group's completed studies in the last 5 years have had a major impact on clinical practice in the UK and worldwide. They are too numerous to annotate completely but examples would be COUGAR/COUGAR-02, SCOPE and NeoScope in OG cancer, ABC-02 in biliary tract cancer, SCALLOP in locally advanced pancreas cancer and a variety of international studies in NETs. BEST2, ASPECT and BOSS will similarly change practice in pre-malignant conditions of the oesophagus and the result of BILCAP in 2016 is likely to change the adjuvant management of resected bile duct cancer. We are less certain on the impact on NICE appraisals. We are frequently asked to provide members for technology appraisals and where the compound or treatment is of interest this is straightforward. However many appraisals are conducted on compound that have no obvious merit and it is increasingly difficult to get busy members to participate in a process which is of no real value. We also are uncertain mechanisms exist for NICE to change decisions or issue caution on that basis of finding from a Group study. For instance New EPOC demonstrated very significant harm from the use of cetuximab in operable colorectal liver metastases but NICE guidance still advocates its use in a very similar setting. Reform of the workings of NICE may be indicated. In respect of Horizon scanning the Group makes suggestions but we have no means to assess impact. Advice is commonly given to CTAAC over grant proposals but we are never consulted with respect to NIHR/HTA grants. This is regrettable as it may help prevent inappropriately designed trials being funded. With respect to

CTAAC most advice related to Group proposals, is commonly positive and hence it unclear that it is of value in this setting.

10. Consumer involvement

Mrs Yvonne Carse joined the CSG at the beginning of the reporting year. She has been active on the Pancreatic Subgroup. She has reviewed the ABC-07 trail for the UCL CTU. She has reviewed A Patient Guide to Your PET/CTscan and for the charity Pancreatic Cancer Action and also looked at a booklet advising on diet and nutrition in patients having had pancreatic surgery. Outside NCRI she has been participated in Cancer Peer Review and had involvement in a Macmillan survey of exercise during and after cancer. Mentorship is being provided by Professor Ghaneh by electronic means.

11. Open meetings/annual trials days/strategy days

The Annual Trials meeting was successful with several hundred attendees at a meeting that focused on trial results. The feedback was highly favourable. However, the viability of such meetings which are free for attendees is questionable. The funding for the meeting is derived from industry that have increasingly tight budgets and are less inclined to support such meetings. An alternative long term strategy needs discussion within NCRI. An initial meeting with the Chair and one subgroup chair has been held with the NIHR LCRN cancer representatives. This was combined with the Colorectal CSG. This meeting has the potential to increase engagement although representatives from the worst performing networks were not present. At the next CSG there will be discussion on the best formal for future meetings.

12. Progress towards achieving the CSG's 3 year strategy

The Group strategy as outlined in October 2011 and supported by the Group's progress review in 2013 was:

- Move to adaptive trials, with seamless transition from phase 2 to phase 3 comparisons. All the subgroups except Neuroendocrine have currently adaptive trials in preparation. The funding result outcome has been mixed. PLATFORM (OG cancer) is funded and PRECISION-PANC (pancreatic cancer) and OCTOPUS (colorectal liver metastases) are in the funding application process.
- Trials of radiotherapy and surgery. Scallop has established a new international standard for chemoradiotherapy in locally advanced pancreas cancer. Scallop 2 and SCOPE-2 have been funded as has the ICOR study of chemotherapy v chemoradiotherapy in oesophageal adenocarcinoma. This latter study has become more attractive since the result of OEO-5. ORANGE 2 (laparoscopic liver surgery) is recruiting well in the UK. ROMIO (laparoscopic v open oesophageal surgery) has successfully completed a feasibility phase and is no open as a Phase 3 trial.
- Develop Translational research. All studies have embedded blood and tissue and register of biological materials from clinical trials and a list of translational studies are being complied. Sample collection from the various OG cancer studies form one of the world's largest such resources. The Barrett's study ASPECT has a large tissue collection now housed in Warwick and the OCCAMS collaborative based in Cambridge has good quality frozen cancer tissue for whole genome sequencing.

13. Priorities and challenges for the forthcoming year

Priorities of the Upper GI CSG in the coming year are outlined below:

- It is important that the size of the Upper GI portfolio is maintained. We therefore need to develop new trials that add significant numbers of recruits. Although focusing on numbers *per se* is not academically attractive, without numbers cancer stands to lose significant funding in the new system.
- We need to be successful in getting new, stratified adaptive trials through the funding bodies which to date have been resistant partly as a result of costs and also perhaps lack of expertise on the funding committee.
- We should endeavour to increase the number of good quality industry trials that complete to time and target in line with the NIHR CRN High Level Objectives.

Challenges of the Upper GI CSG in the coming year are outlined below:

- Obtaining funding for stratified and adaptive trials may be difficult as these are often costly and may be poorly understood by committee reviewers. The success of the Prostate CSG trial STAMPEDE may make funding bodies more inclined to realise the benefit of these trial designs. Whatever, the increasing cost of late phase trials and the reduced levels of funding available is making undertaking such trials increasingly difficult. The solution must be in moving to "real world" trials where after recruitment all data is captured from IT systems. Although such systems are said to exist at NCIN, internal issues within Public Health England at present seem to prevent trials using these systems being realised.
- The importance of recruitment numbers for networks makes adaptive stratified trials unattractive. This is because as configured at present there may be a great deal of work and cost identifying a cohort of patients suitable to recruit yet no recruitment is associated with this activity. In some cases only a small proportion of patients may be suitable for a study thus creating a perverse disincentive. We need to work towards trials separating the assessment phase (a band 2 study) and the phase 3 (band 3 study) components
- Network data shows marked variation in recruitment to Upper GI cancer studies between Networks even though they may be adjacent. For instance Wessex performs well whereas Thames Valley and South Midlands (including Oxford) performs very badly. There is no facility or disease incidence explanation for these differences so it comes down to the interests and culture of local clinicians. Rectifying these differences is a major challenge for the Group.

14. Concluding remarks

The Upper GI Group has been highly successful throughout its existence and under its only two Chairs. There is every expectation that that this will continue as the Subgroups are successful, vibrant, inclusive and are developing and supporting new study designs. However succession planning is urgent as in the next year the Chair and two key subgroup chairs are due to rotate without the possibility to remain in these roles. To maintain the success of the Group care will be needed in the selection of the replacements.

15. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
- A – Main CSG Strategy
- B – Pancreatic Subgroup Strategy
- C – Neuroendocrine Subgroup Strategy
- D – Hepatobiliary Subgroup Strategy
- E – Oesophagogastric Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Professor John Primrose (Upper GI CSG Chair)

Appendix 1

Membership of the Upper GI CSG

Name	Specialism	Location
Dr Stephen Falk	Clinical Oncologist	Bristol
Dr Maria Hawkins	Clinical Oncologist	Oxford
Dr Somnath Mukherjee	Clinical Oncologist	Oxford
Mrs Yvonne Carse	Consumer	Launceston
Mr David Chuter	Consumer	Bognor Regis
Professor Rebecca Fitzgerald	Gastroenterologist	Cambridge
Dr John Bridgewater	Medical Oncologist	London
Professor David Cunningham	Medical Oncologist	London
Dr Wasat Mansoor	Medical Oncologist	Manchester
Professor Daniel Palmer	Medical Oncologist	Liverpool
Professor Russell Petty	Medical Oncologist	Aberdeen
Dr Paul Ross	Medical Oncologist	London
Professor Juan Valle	Medical Oncologist	Manchester
Dr Fieke Froeling*	Medical Oncologist	London
Dr Gordon Hutchins	Pathologist	Leeds
Mr Trevor Cox	Statistician	Liverpool
Mr Chris Hurt	Statistician	Cardiff
Professor Hugh Barr	Surgeon	Gloucester
Professor Andrew Biankin	Surgeon	Glasgow
Professor Paula Ghaneh	Surgeon	Liverpool
Mr Hassan Malik	Surgeon	Liverpool
Professor John Primrose (Chair)	Surgeon	Southampton
Ms Olga Tucker	Surgeon	Birmingham
Mr Robert Jones*	Surgeon	Liverpool

* denotes trainee

Membership of the Subgroups

Pancreatic Subgroup		
Name	**Specialism**	**Location**
Dr Stephen Falk (Chair)	Clinical Oncologist	Bristol
Dr Somnath Mukherjee	Clinical Oncologist	Oxford
Mrs Yvonne Carse	Consumer	Launceston
Professor John Bridgewater	Medical Oncologist	London
Dr Pippa Corrie	Medical Oncologist	Cambridge
Professor Jeff Evans	Medical Oncologist	Glasgow
Professor Daniel Palmer	Medical Oncologist	Liverpool
Professor Will Steward	Medical Oncologist	Leicester
Professor Juan Valle	Medical Oncologist	Manchester
Dr Karin Oien	Pathologist	Glasgow
Trevor Cox	Statistician	Liverpool
Professor Paula Ghaneh	Surgeon	Liverpool
Professor John Primrose	Surgeon	Southampton
Professor Andrew Biankin	Surgeon	Glasgow

Hepatobiliary Subgroup		
Name	**Specialism**	**Location**
Mrs Helen Morement	AMMF Chair of Trustees	London
Dr Maria Hawkins	Clinical Oncologist	Oxford
Mr John Symons	Consumer	Newbury
Dr John Bridgewater (Chair)	Medical Oncologist	London
Dr Tim Meyer	Medical Oncologist	London
Professor Daniel Palmer	Medical Oncologist	Liverpool
Mr Paul Ross	Medical Oncologist	London
Professor Juan Valle	Medical Oncologist	Manchester
Dr Harpreet Wasan	Medical Oncologist	London
Ms Pam O'Donoghue	Nurse	London
Dr Andre Lopes	Statistician	London
Dr John Primrose	Surgeon	Southampton
Mr Hassan Malik	Surgeon	Liverpool

Neuroendocrine Subgroup		
Name	**Specialism**	**Location**
Dr Nick Reed	Clinical Oncologist	Glasgow
Dr Jonathan Wadsley	Clinical Oncologist	Sheffield
Ms Carole Beckett	Consumer	Manchester
Professor Mark Pritchard	Gastroenterologist	Liverpool
Dr John Ramage	Gastroenterologist	Hampshire
Dr Alan Anthoney	Medical Oncologist	Leeds
Professor Juan Valle (Chair)	Medical Oncologist	Manchester
Professor Ashley Grossman	Neuroendocrinologist	London
Dr Prakash Manoharan	Radiologist	Manchester
Mrs Louise Stanton	Statistician	Southampton
Mr Neil Pearce	Surgeon	Southampton

Oesophagogastric Subgroup		
Name	**Specialism**	**Location**
Dr Tom Crosby	Clinical Oncologist	Cardiff
Professor Heike Grabsch	Histopathologist	Leeds
Professor David Cunningham (Chair)	Medical Oncologist	London
Professor Jeff Evans	Medical Oncologist	Glasgow
Dr Hugo Ford	Medical Oncologist	Cambridge
Professor Janusz Jankowski	Medical Oncologist	Warwick
Dr Ruth Langley	Medical Oncologist	London
Professor Anne Thomas	Medical Oncologist	Leicester
Dr Kate Sumpter	Medical Oncologist	Newcastle
Professor Jane Blazeby	Surgeon	Bristol
Professor Derek Alderson	Surgeon	Bristol
Mr William Allum	Surgeon	London
Professor Robert Mason	Surgeon	London
Mr Tim Underwood	Surgeon	Southampton

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

The Group strategy as outlined in October 2011 and supported by the Group's progress review in 2013 was:

- Move to adaptive trials, with seamless transition from phase 2 to phase 3 comparisons. All the subgroups except Neuroendocrine have currently adaptive trials in preparation. The funding result outcome has been mixed. PLATFORM (OG cancer) is funded and PRECISION-PANC (pancreatic cancer) and OCTOPUS (colorectal liver metastases) are in the funding application process.
- Trials of radiotherapy and surgery. Scallop has established a new international standard for chemoradiotherapy in locally advanced pancreas cancer. Scallop 2 and SCOPE-2 have been funded as has the ICOR study of chemotherapy v chemoradiotherapy in oesophageal adenocarcinoma. This latter study has become more attractive since the result of OEO-5. ORANGE 2 (laparoscopic liver surgery) is recruiting well in the UK. ROMIO (laparoscopic v open oesophageal surgery) has successfully completed a feasibility phase and is no open as a Phase 3 trial.
- Develop Translational research. All studies have embedded blood and tissue and register of biological materials from clinical trials and a list of translational studies are being complied. Sample collection from the various OG cancer studies form one of the world's largest such resources. The Barrett's study ASPECT has a large tissue collection now housed in Warwick and the OCCAMS collaborative based in Cambridge has good quality frozen cancer tissue for whole genome sequencing.

B – Pancreatic Subgroup Strategy

The strategy of the Pancreatic Subgroup is to:

- Have a portfolio actively recruiting and in development within early diagnosis, staging, therapy and supportive care
- Continue to support and encourage translational research to increase understanding of the factors that cause and drive pancreas cancer
- Continue to develop innovative new therapeutic strategies. This includes:
    - Investigating novel targeted therapies, immunotherapy, new surgical techniques and advanced radiotherapy techniques such as intensity-modulated radiotherapy (IMRT).
    - Developing and refining therapeutic strategies for all stages of disease, including neoadjuvant therapy, surgery/local therapies and adjuvant therapy for localised disease and multiple lines of treatment for advanced disease.
    - Developing trials that focus on common challenges in the management of pancreas cancer, including symptoms such as cachexia.
    - Developing an evidence base for the molecular biology of pancreas cancer to inform decision-making and health policy

C – Neuroendocrine Subgroup Strategy

The strategy of the NET subgroup is to ensure that the NET portfolio has a multi-disciplinary broad base of studies (clinical and translational) covering all aspects of NETs. This includes the use of novel agents and multi-modality treatments including surgery and other interventional treatments.

D – Hepatobiliary Subgroup Strategy

The Hepatobiliary Subgroup has been the international leader in the clinical treatment of HB cancers. The challenge is now to:

- Expand this activity internationally, exploiting novel trial design to deliver meaningful data more rapidly.
- To develop translational aspects in order to best exploit the novel molecularly targeted agents.
- To continue to deliver meaningful clinical studies to the oncological community.

E – Oesophagogastric Subgroup Strategy

The strategy of the OG Subgroup is to ensure that the OG trial portfolio provides comprehensive coverage of all aspects of OG cancer and achieves a balance between translational and clinical research. In particular, we will:

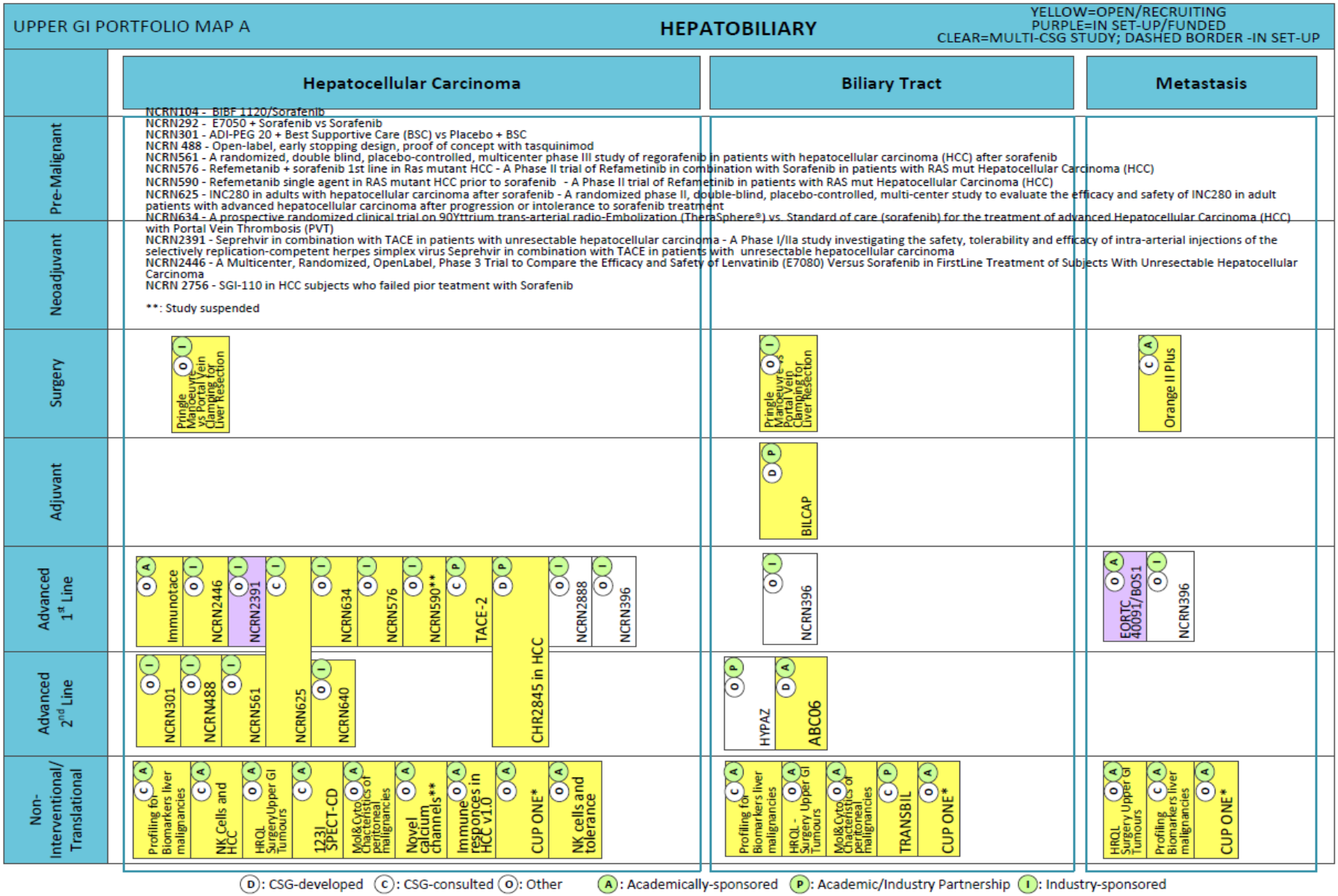
- Continue to support and encourage translational research to increase understanding of the factors that cause and drive OG cancer
- Continue to develop strategies to prevent OG cancer and new diagnostic techniques to facilitate an early diagnosis
- Continue to develop innovative new therapeutic strategies. This includes:
    - Investigating novel targeted therapies, immunotherapy, new surgical techniques and advanced radiotherapy techniques such as intensity-modulated radiotherapy (IMRT).
    - Developing and refining therapeutic strategies for all stages of disease, including neoadjuvant therapy, surgery/local therapies and adjuvant therapy for localised disease and multiple lines of treatment for advanced disease.
    - Developing trials that focus on common challenges in the management of OG cancer, including elderly patients, with an emphasis on research that can be translated into meaningful outcomes for patients
    - Developing an evidence base for OG cancer to inform decision-making and health policy

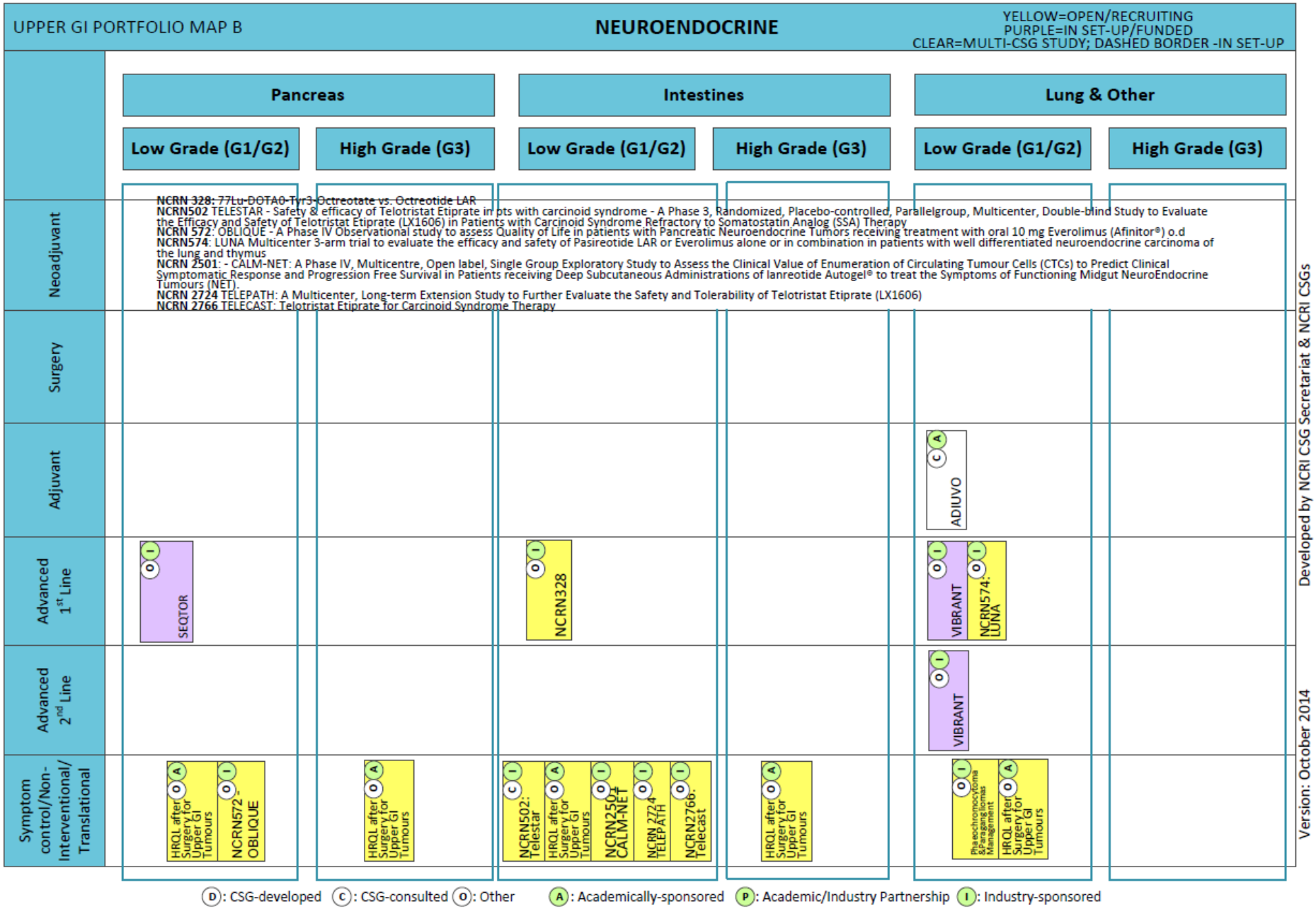
To deliver these priorities we will:

- Encourage collaborative approaches, seeking to increase both national and international partnerships to facilitate rapid study recruitment and cutting edge translational research. This includes supporting the establishment of national and international multi-centre trials, including trials with adaptive designs.
- Encourage industry partnerships, seeking to facilitate the rapid development of trials investigating new therapeutic agents
- Continue to support and develop the best researchers, at all stages of their careers, by encouraging researchers to submit trial proposals for discussion and feedback from the OG subgroup

Appendix 3

Portfolio maps




UPPER GI PORTFOLIO MAP B
NEUROENDOCRINE
YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
CLEAR=MULTI-CSG STUDY; DASHED BORDER -IN SET-UP
Pancreas
Intestines
Lung & Other
Low Grade (G1/G2)
High Grade (G3)
Low Grade (G1/G2)
High Grade (G3)
Low Grade (G1/G2)
High Grade (G3)
Neoadjuvant
Surgery
Adjuvant
Advanced 1st Line
Advanced 2nd Line
Symptom control/Non-Interventional/ Translational
NCRN 328: 77Lu-DOTA0-Tyr3-Octreotate vs. Octreotide LAR
NCRN502 TELESTAR - Safety & efficacy of Telotristat Etiprate in pts with carcinoid syndrome - A Phase 3, Randomized, Placebo-controlled, Parallelgroup, Multicenter, Double-blind Study to Evaluate the Efficacy and Safety of Telotristat Etiprate (LX1606) in Patients with Carcinoid Syndrome Refractory to Somatostatin Analog (SSA) Therapy
NCRN 572: OBLIQUE - A Phase IV Observational study to assess Quality of Life in patients with Pancreatic Neuroendocrine Tumors receiving treatment with oral 10 mg Everolimus (Afinitor®) o.d
NCRN574: LUNA Multicenter 3-arm trial to evaluate the efficacy and safety of Pasireotide LAR or Everolimus alone or in combination in patients with well differentiated neuroendocrine carcinoma of the lung and thymus
NCRN 2501: - CALM-NET: A Phase IV, Multicentre, Open label, Single Group Exploratory Study to Assess the Clinical Value of Enumeration of Circulating Tumour Cells (CTCs) to Predict Clinical Symptomatic Response and Progression Free Survival in Patients receiving Deep Subcutaneous Administrations of lanreotide Autogel® to treat the Symptoms of Functioning Midgut NeuroEndocrine Tumours (NET).
NCRN 2724 TELEPATH: A Multicenter, Long-term Extension Study to Further Evaluate the Safety and Tolerability of Telotristat Etiprate (LX1606)
NCRN 2766 TELECAST: Telotristat Etiprate for Carcinoid Syndrome Therapy
SEQTOR
NCRN328
ADIUVO
VIBRANT
NCRN574. LUNA
VIBRANT
HRQL after Surgery for Upper GI Tumours
NCRN572 OBLIQUE
HRQL after Surgery for Upper GI Tumours
NCRN502: Telestar
HRQL after Surgery for Upper GI Tumours
NCRN2501 CALM-NET
NCRN 2724 TELEPATH
NCRN2766: Telecast
HRQL after Surgery for Upper GI Tumours
Phaeochromocytoma & Paraganglioma Management
HRQL after Surgery for Upper GI Tumours
Developed by NCRI CSG Secretariat & NCRI CSGs
Version: October 2014
(D): CSG-developed (C): CSG-consulted (O): Other (A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored

UPPER GI PORTFOLIO MAP C
OESOPHAGEAL & TYPE I/II JUNCTIONAL TUMOURS
YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
CLEAR=MULTI-CSG STUDY; DASHED BORDER -IN SET-UP
Barrett's Oesophagus
Adenocarcinoma
Squamous Cell Carcinoma
Pre-Malignant
Neoadjuvant
Surgery
Adjuvant
Advanced 1st Line
Advanced 2nd Line
Non-Interventional/ Translational
* - Translational element included **: Study suspended until further notice
NCRN 366: Rilotumumab (AMG 102) + Epirubicin, Cisplatin, and Capecitabine (ECX)
NCRN512 masitinib vs sunitinib in gastrointestinal stromal tumour after imatinib progression
NCRN635 - LJM716 with BYL719 compared to taxane or irinotecan in esophageal cancer
NCRN 2265 MET Amplified Gastric/Gastroesophageal Junction/Esophageal Adenocarcinoma
ChOPIN
BOOST
RECaD
Trimoda imaging
BEST 2
LITE Study
NCRN396
LITE Study
Biostent
Vit D Replacement
ROMIO Feasibility Study
STAT-ROC Feasibility
NCRN2888
NCRN2808
GO2
DEBIOC
ROCOCO
IRON
FACING
ROCS
NCRN366
NeoSCOPE
ST03*
NCRN2265
HYPAZ
FGR Study
ChOPIN
PhOeNIx study
HRQLSurg Upper GI Tumours
Mimosa
The Useful Study
ATTACK-OG
PhOeNIx study
CUP ONE*
HRQL- Surg Upper GI Tumours
Mol&Cyto Chacteristics peritoneal malignancies
OCCAMS
RTL Adv Study
ST03- Trans
LITE Study
Biostent
NCRN635
HYPAZ
GO-2
ROCS
NEOSCOPE
NCRN396
ATTACK-OG
PhOeNIx study
CUP ONE*
HRQL - Surg for Upper Gi Tumours
Mol&Cyto Chacteristics peritoneal malignancies
Version: October 2014
Developed by NCRI CSG Secretariat & NCRI CSGs
(D): CSG-developed (C): CSG-consulted (O): Other
(A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored

UPPER GI PORTFOLIO MAP D

STOMACH & TYPE II/III JUNCTIONAL TUMOURS

YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
CLEAR=MULTI-CSG STUDY; DASHED BORDER -IN SET-UP

Adenocarcinoma

Pre-Malignant	Trimodal imaging (O, A)
Neoadjuvant	ST03- * (D, A)
Surgery	LITE Study (O, A); ROMIO Feasibility Study (C, A)
Adjuvant	ST03- * (D, A)
Advanced 1st Line	NCRN227 (O, I); NCRN2635 (C, I); NCRN2265 (O, I); NCRN366 (O, I); IRON (C, P); DEBIOC (D, P); FACING (C, A); GO-2 (O, P); CRUK AZD3965 (O, I); NCRN2808 (O, I); NCRN396 (O, I)
Advanced 2nd Line	HYPAZ (O, P); NCRN369-GATSBY (O, I); FGFR Study (C, P); NCRN488 (O, I)
Non-Interventional/ Translational	ATTACK-OG (O, P); ASCIT** (O, A); HRQL after Surgery for Upper GI Tumours (O, A); Mol&Cyto Chacteristics peritoneal malignancies (O, A); RTL Perioperative Study (C, A); RTL Adv' Study (C, A); ST03- Trans (D, A); CUP ONE* (O, A); Detection of Hypox (O, A); The Useful Study (C, A)

NCRN 416: Efficacy & safety of onartuzumab (MetMab) + 5-fluorouracil, leucovorin & oxaliplatin (mFOLFOX6)
NCRN 366: Rilotumumab (AMG 102) + Epirubicin, Cisplatin, and Capecitabine (ECX)
NCRN 369: Efficacy & safety of trastuzumb emtansine (T-DM1) vs. taxane (docetaxel or paclitaxel)
NCRN 488: A multicentre, open-label, early stopping design, proof of concept study with tasquinimod
NCRN 502: A Phase 3, Randomized, Placebo-controlled, Parallelgroup, Multicenter, Double-blind Study to Evaluate the Efficacy and Safety of Telotristat Etiprate (LX1606) in Patients with Carcinoid Syndrome Refractory to Somatostatin Analog (SSA) Therapy
NCRN512 masitinib vs sunitinib in gastrointestinal stromal tumour after imatinib progression
NCRN 2265 MET Amplified Gastric/Gastroesophageal Junction/Esophageal Adenocarcinoma
NCRN 2724 TELEPATH: A Multicenter, Long-term Extension Study to Further Evaluate the Safety and Tolerability of Telotristat Etiprate (LX1606)
NCRN 2766 TELECAST: Telotristat Etiprate for Carcinoid Syndrome Therapy

**-Suspended * - Translational element included

(D): CSG-developed (C): CSG-consulted (O): Other (A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored

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UPPER GI PORTFOLIO MAP E

PANCREAS

YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
CLEAR=MULTI-CSG STUDY; DASHED BORDER -IN SET-UP

Adenocarcinoma

Neoadjuvant	SCALLOP2 (C, A); ESPAC-5 (D, A); The TARGET Trial (O, A)
Surgery	LITE Study (O, A)
Adjuvant	NCRN 2902 (O, I); ESPAC-4* (D, A); NCRN2635 (O, I)
Advanced 1st Line	PRICKLE (C, A); SIEGE (D, P); NCRN503 (C, I); CRUK MK 0752 (C, A); NCRN2808 (O, I); NCRN396 (O, I)
Advanced 2nd Line	HYPAZ (C, P)
Non-Interventional/ Translational	Myosteatosis muscle wasting in pancreatic cancer (C, A); HRQL after Surgery Upper GI Tumours (C, A); FLT-PET (C, A); EUROPAC (A, I); TRANSBIL (C, A); Mol&Cyto characteristics of peritoneal malignancies (C, A); Study of proliferation (C, A); Mol & Gen (C, A); The Symptom Study (C, A); CUP ONE* (C, A); CTC & cDNA in cancer patients (C, A); CTC in Pancreatic Cancer (C, A); CANC -3514 (C, A)

NCRN 503 - Efficacy and Safety of Gemcitabine + TH-302 vs. Gemcitabine + Placebo
SIEGE: Scheduling nabpaclitaxel with GEmcitabine (SIEGE): Randomised phase II trial to investigate two different schedules of nabpaclitaxel (Abraxane) combined with gemcitabine as first line treatment for metastatic pancreatic ductal adenocarcinoma
NCRN 2635: TG01 + Gemcitabine in resected pancreatic adenocarcinoma
NCRN - 2902: nab®-Paclitaxel+Gemcitabine vs. Gemcitabine as Adj.therapy in pancreatic adenocarcinoma

* - Translational element included
**– Study suspended

Version: October 2014

Developed by NCRI CSG Secretariat & NCRI CSGs

(D): CSG-developed (C): CSG-consulted (O): Other (A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored

Appendix 4

Publications in the reporting year

New EPOC

Primrose J, Falk S, Finch-Jones M, Valle J, O'Reilly D, Siriwardena A, Hornbuckle J, Peterson M, Rees M, Iveson T, Hickish T, Butler R, Stanton L, Dixon E, Little L, Bowers M, Pugh S, Garden OJ, Cunningham D, Maughan T, Bridgewater J. Systemic chemotherapy with or without cetuximab in patients with resectable colorectal liver metastasis: the New EPOC randomised controlled trial. *Lancet Oncol* 2014 May;15(6):601-11

COG

Dutton SJ, Ferry DR, Blazeby JM, Abbas H, Dahle-Smith A, Mansoor W, Thompson J, Harrison M, Chatterjee A, Falk S, Garcia-Alonso A, Fyfe DW, Hubner RA, Gamble T, Peachey L, Davoudianfar M, Pearson SR, Julier P, Jankowski J, Kerr R, Petty RD. Gefitinib for oesophageal cancer progressing after chemotherapy (COG): a phase 3, multicentre, double-blind, placebo-controlled randomised trial. *Lancet Oncol*. 2014 Jul;15(8):894-904. doi: 10.1016/S1470-2045(14)70024-5. Epub 2014 Jun 17. PMID: 24950987

OCCAMS

Weaver JM, Ross-Innes CS, Shannon N, Lynch AG, Forshew T, Barbera M4, Murtaza M, Ong CA, Lao-Sirieix P, Dunning MJ, Smith L, Smith ML, Anderson CL, Carvalho B, O'Donovan M, Underwood TJ, May AP, Grehan N, Hardwick R, Davies J, Oloumi A, Aparicio S, Caldas C, Eldridge MD, Edwards PA, Rosenfeld N, Tavaré S, Fitzgerald RC, OCCAMS Consortium. Ordering of mutations in pre-invasive disease stages of esophageal carcinogenesis: *Nat Genet*.2014 Aug: 46(8):837-43.

TIME

di Pietro M, Boerwinkel DF, Shariff MK, Liu X, Telakis E, Lao-Sirieix P, Walker E, Couch G, Mills L, Nuckcheddy-Grant T, Slininger S, O'Donovan M, Visser M, Meijer SL, Kaye PV, Wernisch L, Ragunath K, Bergman JJ, Fitzgerald RC (2015) The combination of autofluorescence endoscopy and molecular biomarkers is a novel diagnostic tool for dysplasia in Barrett's oesophagus. *Gut* 64 (1):49-56. doi:10.1136/gutjnl-2013-305975

BEST2 Study

Ross-Innes CS, Debiram-Beecham I, O'Donovan M, Walker E, Varghese S, Lao-Sirieix P, Lovat L, Griffin M, Ragunath K, Haidry R, Sami SS, Kaye P, Novelli M, Disep B, Ostler R, Aigret B, North BV, Bhandari P, Haycock A, Morris D, Attwood S, Dhar A, Rees C, Rutter MD, Sasieni PD, Fitzgerald RC, Group BS (2015) Evaluation of a minimally invasive cell sampling device coupled with assessment of trefoil factor 3 expression for diagnosing Barrett's esophagus: a multi-center case-control study. *PLoS medicine* 12 (1):e1001780. doi:10.1371/journal.pmed.1001780

ABC 02

Grenader T, Plotkin Y, Valle JW, et al: Does the derived neutrophil lymphocyte ratio predict benefit from cisplatin and gemcitabine compared with gemcitabine alone in advanced biliary cancer? an exploratory study of the ABC-02 trial. *Annals of Oncology* 25:iv212, 2014

Lamarca A, Benafif S, Ross P, et al: Cisplatin and gemcitabine in patients with advanced biliary tract cancer (ABC) and persistent jaundice despite optimal stenting: Effective intervention in patients with luminal disease. *European Journal of Cancer*, 2015: S0959-8049(15)00449-9. doi: 10.1016/j.ejca.2015.05.018. [Epub ahead of print]

NCRN366: Rilotumumab + ECX in 1st line c-Met Gastric or Gastroesophageal Junction Adenocarcinoma

Iveson T, Donehower RC, Davidenko I, Tjulandin S, Deptala A, Harrison M, Nirni S, Lakshmaiah K, Thomas A, Jiang Y et al. 2014 Rilotumumab in combination with Epirubicin, cisplatin and capecitabine as first-line treatment for gastric or oesophagogastric junction adenocarcinoma: an open label. dose de-escalation phase 1b study and a double-blind, randomised phase 2 study. *Lancet Oncol* Published Online June 23, 2014 http://dx.doi.org/10.1016/S1470-2045(14)70023-3

Doshi S, Olsson Gisleskog P, Zhang Y, Zhu M, Oliner K, Loh E, Perez-Ruixo JJ (2015) Rilotumumab Exposure-Response Relationship in Patients With Advanced or Metastatic Gastric Cancer. *Clin Cancer Res*. doi:10.1158/1078-0432.CCR-14-1661

The ROCs trial

Adamson D, Blazeby J, Nelson A, Hurt C, Nixon L, Fitzgibbon J, Crosby T, Staffurth J, Evans M, Kelly NH, Cohen D, Griffiths G, Byrne A. Palliative radiotherapy in addition to self-expanding metal stent for improving dysphagia and survival in advanced oesophageal cancer (ROCS: Radiotherapy after Oesophageal Cancer Stenting): study protocol for a randomized controlled trial. *Trials*. 2014 Oct 22;15:402. doi: 10.1186/1745-6215-15-402. PMID:25336193

Feasibility trial of chemoradiation versus chemo and surgery for oesophageal cancer

Blazeby JM, Strong S, Donovan JL, Wilson C, Hollingworth W, Crosby T, Nicklin J, Falk SJ, Barham CP, Hollowood AD, Streets CG, Titcomb D, Krysztopik R, Griffin SM, Brookes ST. Feasibility RCT of definitive chemoradiotherapy or chemotherapy and surgery for oesophageal squamous cell cancer. *Br J Cancer*. 2014 Jul 15;111(2):234-40. doi: 10.1038/bjc.2014.313. Epub 2014 Jun 12. PMID: 24921919

Jacobs M, Henselmans I, Macefield RC, Blencowe NS, Smets EM, de Haes JC, Sprangers MA, Blazeby JM, van Berge Henegouwen MI. Delphi survey to identify topics to be addressed at the initial follow-up consultation after oesophageal cancer surgery. *Br J Surg*. 2014 Dec;101(13):1692-701. doi: 10.1002/bjs.9647. Epub 2014 Oct 15. PMID: 25319127

NEOSCOPE

Mukherjee S, Hurt CN, Gwynne S, Bateman A, Gollins S, Radhakrishna G, Hawkins M, Canham J, Lewis W, Grabsch HI, Sharma RA, Wade W, Maggs R, Tranter B, Roberts A, Sebag-Montefiore D, Maughan T, Griffiths G, Crosby T (2015) NEOSCOPE: a randomised Phase II study of induction

chemotherapy followed by either oxaliplatin/capecitabine or paclitaxel/carboplatin based chemoradiation as pre-operative regimen for resectable oesophageal adenocarcinoma. *BMC cancer* 15:48. doi:10.1186/s12885-015-1062-y

TELOVAC

Middleton G, Silcocks P, Cox T, Valle J, Wadsley J, Propper D, Coxon F, Ross P, Madhusudan S, Roques T, Cunningham D, Falk S, Wadd N, Harrison M, Corrie P, Iveson T, Robinson A, McAdam K, Eatock M, Evans J, Archer C, Hickish T, Garcia-Alonso A, Nicolson M, Steward W, Anthoney A, Greenhalf W, Shaw V, Costello E, Naisbitt D, Rawcliffe C, Nanson G, Neoptolemos J. Gemcitabine and capecitabine with or without telomerase peptide vaccine GV1001 in patients with locally advanced or metastatic pancreatic cancer (TeloVac): an open-label, randomised, phase 3 trial. *Lancet Oncol.* 2014 Jul;15(8):829-40. doi: 10.1016/S1470-2045(14)70236-0. Epub 2014 Jun 19.

ESPAC 3

Valle JW, Palmer D, Jackson R, Cox T, Neoptolemos JP, Ghaneh P, Rawcliffe CL, Bassi C, Stocken DD, Cunningham D, O'Reilly D, Goldstein D, Robinson BA, Karapetis C, Scarfe A, Lacaine F, Sand J, Izbicki JR, Mayerle J, Dervenis C, Oláh A, Butturini G, Lind PA, Middleton MR, Anthoney A, Sumpter K, Carter R, Büchler MW. Optimal duration and timing of adjuvant chemotherapy after definitive surgery for ductal adenocarcinoma of the pancreas: ongoing lessons from the ESPAC-3 study. *J Clin Oncol*. 2014 Feb 20;32(6):504-12. doi: 10.1200/JCO.2013.50.7657. Epub 2014 Jan 13.

Greenhalf, W., Ghaneh, P., Neoptolemos, J.P. et al, (2014). Pancreatic Cancer hENT1 Expression and Survival From Gemcitabine in Patients From the ESPAC-3 Trial. *J Natl Cancer Inst*, 106, djt347.

NET 01

Meyer, T., Qian, W., Caplin, M.E., Armstrong, G., Lao-Sirieix, S.H., Hardy, R., Valle, J.W., Talbot, D.C., Cunningham, D., Reed, N., Shaw, A., Navalkissoor, S., Luong, T.V. & Corrie, P.G. (2014). Capecitabine and streptozocin+/-cisplatin in advanced gastroenteropancreatic neuroendocrine tumours. *Eur J Cancer* 2014; 50(5): 902-11.

Middleton G, Silcocks P, Cox T, Valle J, et al. Gemcitabine and capecitabine with or without telomerase peptide vaccine GV1001 in patients with locally advanced or metastatic pancreatic cancer (TeloVac): an open-label, randomised, phase 3 trial. *Lancet Oncol* 2014; 15(8): 829-40

ABC

Valle, J.W., Furuse, J., Jitlal, M., Beare, S., Mizuno, N., Wasan, H., Bridgewater, J. & Okusaka, T. (2014). Cisplatin and gemcitabine for advanced biliary tract cancer: a meta-analysis of two randomised trials. *Ann Oncol*, 25, 391-8.

COUGAR-02

Ford HE, Marshall A, Bridgewater JA, Janowitz T, Coxon FY, Wadsley J, Mansoor W, Fyfe D, Madhusudan S, Middleton GW, Swinson D, Falk S, Chau I, Cunningham D, Kareclas P, Cook N, Blazeby JM, Dunn JA, Investigators C- (2014) Docetaxel versus active symptom control for

refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet oncology* 15 (1):78-86. doi:10.1016/S1470-2045(13)70549-7

Home Jejunostomy Feeding after Oesophagectomy/Gastrectomy

Bowrey D, Baker M, Halliday V, Thomas A, Pulikottil-Jacob R and Smith K. 2014 Six weeks of home enteral nutrition versus standard care after esophagectomy or total gastrectomy for cancer: study protocol for a randomized controlled trial. *Trials* 15:187

Appendix 5

Major international presentations in the reporting year

TIME

Autofluorescence–targeted optical biopsy accurately diagnoses dysplasia in Barrett's esophagus and can detect the field of molecular change. UEGW (Vienna) 2014.

Trans-COG

Petty RD, Dahle-Smith A, Miedzybrodzka Z, Dutton SJ, Murray GI, Stevenson D, Massie D, Osbourne A, Clark C, Mansoor W, Thompson J, Harrison M, Chatterjee A, Falk S, Elyan S, Garcia-Alonso A, Fyfe DW, Chau I, Collinson D, Ferry D. Epidermal growth factor receptor copy number gain (EGFR CNG) and response to gefitinib in esophageal cancer (EC): Results of a biomarker analysis of a phase III trial of gefitinib versus placebo (TRANS-COG). Abstract Number: 4016, J Clin Oncol 32:5s, 2014 (suppl; abstr 4016). ASCO 2014 and NCRI 2014

Phoenix Study

Noorani A, Wedge DC, Lao-Sirieix P, Weaver J, Crawte J, Eldridge M, Bower L, Grehan N, Debiram I, Hindmarsh A, Goddard M, Hardwick R, Fitzgerald RC. Novel insights into metastatic spread of oesophageal adenocarcinoma from whole genome sequencing data. Cold Spring Harbor Asia Conferences (China) 2015 conference.

OCCAMS

A Lynch, Telomere Lengths, Presentation, December 10th 2014, ICGC Pan-cancer Analysis Working Group 6

Turkington RC, Hill LA, McManus D, McQuaid S, Arthur K, James J, Salto-Tellez M, Davison TS, Harrison C, Purcell C, Wilson RH, McGregor TP, Sharma R, Fitzgerald RC, Johnston PG, Harkin P, Eatock M, Kennedy RD. Association of a DNA Damage Response Deficiency (DDRD) assay and prognosis in early stage Oesophageal Adenocarcinoma. The 15th International Conference on Human Genome Variation and Complex Genome Analysis, Belfast, 17th-19th September 2014.

Underwood T, Garcia E, Howbrook, A, Cowie A, Derouet M, Fitzgerald R, on behalf of the OCCAMS Consortium; University Hospital Southampton NHS Foundation Trust; University of Southampton UK; University Health Network, Toronto/Canada, University of Cambridge, UK, International Cancer Genome Consortium, International Cancer Genome Consortium, UK. Presentation, September 2014, International Society for Diseases of the Esophagus, Vancouver, Canada.