NCRI
National
Cancer
Research
Institute

NCRI Upper Gastro-intestinal Cancer Clinical Studies Group

Annual Report 2015-16

Partners in cancer research

NCRI Upper Gastro-intestinal Cancer CSG Annual Report 2015-16

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

The Upper GI CSG is a highly successful group which to date retains a large portfolio of ongoing trials and has a track record in delivering successfully completed studies. This year has seen the presentation of three flagship trials in oesophagogastric cancer: OE05 at ASCO, ST03 at ESMO and Neo-SCOPE at ASCO GI. In pancreatic cancer, ESPAC 4 and PET-PANC will report this year and in liver TACE 2 will also present this year. The main challenge is to retain a suitable portfolio in a different funding environment. Although there have been some successes, such as ROMIO (laparocopic versus open oesophagectomy) funded by NIHR HTA, SCOPE 2 funded by CTAAC and ACCELERATE an industry funded study in advanced pancreatic cancer put up for adoption, all other Group application to CTAAC and now CRC has been declined. Although the direction of travel appears to be to fund only biomarker driven studies, Upper GI Cancer does not at present lend itself to such studies as suitable biomarkers are not mature. Strategically therefore the Group will focus on other funding sources such as NIHR and industry. In an attempt to aid biomarker development, the Group applied to GeL to have an Upper GI CIP and this was successful. The limitation is that oesophagus (covered by OCCAMS) and CUP (a separate CIP not associated with the NCRI Group) are excluded.

The Group continues to enjoy high quality applications from senior clinicians for membership and similarly the quality of the applications for the trainee positions (two in number) have been quite exceptional. 2015/16 was unusual in that there was no annual trials meeting in December and a specific problem is that the work involved in raising industry funding to cover the meeting costs was becoming extremely difficult in the Upper GI area. For the 2016 meeting in September, a less expensive conference venue will be used and a small registration charge will be made for delegates.

2. Structure of the Group

The Group structure with four Subgroups (Oesophagogastric (OG), Pancreatic, Hepatobiliary (HB) and Neuroendocrine (NET)) remains unchanged. Professor David Cunningham (OG) and Professor John Bridgewater (HB) have rotated off the Group after very long tenures and demitted as Subgroup Chairs. Dr Tom Crosby has agreed to Chair the OG Subgroup and Mr Hassan Malik

the HB Subgroup. Dr Stephen Falk continues to chair the Pancreatic Subgroup and Professor Juan Valle the Neuroendocrine Subgroup.

3. CSG & Subgroup strategies

Main CSG

- Seek funding from bodies other than CRUK, such as NIHR and industry. Several studies declined by CTAAC/CRC are currently being reformatted as HTA applications. Negotiation is underway to allow PRECISION PANC to be funded by Celgene. PLATFORM (OG cancer) is mainly industry funded.
- Incorporate whole genome sequencing into the trial portfolio including all new trials and where possible existing trials that are presently just open to recruitment, e.g. ACTICCA-1.
- Develop adaptive trials wherever possible with seamless transition from phase II to phase III comparisons.
- Develop meaningful but high recruiting trials.
- Work with the Colorectal CSG to produce a surgical/chemotherapy trial in colorectal liver metastases.

Neuroendocrine Subgroup (Chair, Professor Juan Valle)

To ensure that the NET portfolio has a multi-disciplinary broad base of studies (clinical and translational) covering all aspects of NETs. This includes:

- Establishing the UK (through the NCRI) as a competitive place for industry to run clinical trials.
- Broadening the scope of the clinical trials portfolio in patients with NETs including:
    - Increasing the number of studies where gastroenterologists are best placed (e.g. gastric or rectal carcinoids).
    - Ensuring the portfolio includes studies focusing on symptoms and quality of life.
    - Increasing the number of studies incorporating radiotherapy-based questions.
    - Providing the opportunity for translational questions to be addressed within the scope.
    - Developing studies addressing surgical questions and the use of adjuvant therapy.
- Development of clinical studies in NETs other than GEP (e.g. lung NETs, phaeochromocytomas and paragaglionomas) with a similar multi-disciplinary approach.
- To develop innovative therapeutic strategies.

Oesophagogastric Subgroup (Chair, Professor David Cunningham)

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.

Hepatobiliary Subgroup (Chair, Dr John Bridgewater)

The HB 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.

Pancreatic Subgroup (Chair, Dr Stephen Falk)

- 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.

4. Task groups/Working parties

A short-lived Task Group has been set up with the Colorectal CSG to develop trials in colorectal liver metastases. The first meeting has been held and proposals are being developed for submission. The highest priority is a RCT of radical cytoreduction/debulking in advanced colorectal cancer in patients in whom the disease is at worst stable on chemotherapy and in whom over 80% of residual tumour can be removed safely. The CTAAC submission of this trial (ORCHESTRA) was declined previously, partly due to concerns about feasibility, but it is recruiting well in the Netherlands. The next task group meeting is planned at ESMO in October.

5. Patient recruitment summary for last 5 years

In the Upper Gastro-intestinal Cancer CSG portfolio, 15 no. of trials closed to recruitment and 23 opened. The trend in recruitment is downward reflecting the lack of funded trials in major areas such as advanced pancreatic cancer. The number of trials is in fact up, which is consistent with the position across cancer in general, reflecting predominance of smaller trials. The Add Aspirin studies may increase recruitment in OG cancer.

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

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	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
2015/2016	1303	1504	969	1236	3.98	5.07

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

As detailed above, there is a Task Group in place with the Colorectal CSG to develop trials in colorectal liver metastases. The International Biliary Cancer Trials Collaboration, led by John Bridgewater, meets at ASCO and ESMO and is growing in strength with more attendees year on year and collaborative trials are already running (e.g. ACTICCA 1).

7. Funding applications in last year

Previously the Group had high levels of success with CTAAC but in recent years and in common with the Colorectal CSG almost no applications are funded. This may relate to funding pressures at CRUK or a change in strategy that is not easily compatible with trials in GI cancer. This is unfortunate as trials previously funded continue to result in high profile presentations (ASCO) and publications. This informs the Group strategy to focus on NIHR funding (e.g. ROMIO) and Industry (e.g. ACCELARATE) as these have proved more successful.

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
O-C Synergy in Upper GI cancers: A Randomised, open label, Phase II study comparing the efficacy of olaparib (AZD2281) alone to olaparib (AZD2281) in combination with cediranib	Outline application	Dr Harpreet Wasan	Full application not invited

(AZD2171) in platinum sensitive pancreatic cancer, cancer of unknown primary and advanced biliary cancer			
Periampullary ESPAC-4: EUROPEAN STUDY GROUP FOR PANCREATIC CANCER (ESPAC) - Trial 4. Combination versus single agent adjuvant chemotherapy in resectable ampullary cancer	Full application *Extension*	Professor John Neoptolemos	Funded (but only ductal part. Further clarification & resubmission required for periampullary)
European Study Group for Pancreatic Cancer Trial 4 prospective sample collection: periampullary-ESPAC-4Tamp	Sample collection *Extension*	Professor Paula Ghaneh	Not funded
December 2015			
Development of a new high throughput test for oesophageal cancer based on a red blood cell mutant phenotype	Feasibility application	Professor Gareth Jenkins	Not funded
An open-label phase Ib/randomised phase II study of temozolomide alone or in combination with olaparib in patients with advanced well-differentiated pancreatic neuroendocrine tumours (pNETs)	Full application	Professor Juan Valle	Not funded
T-SCOPE2: Sample collection for the 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)	Sample collection application	Dr Richard Adams	Scored as Preliminary - invited to resubmit
DIPLOMA: Distal pancreatectomy, laproscopic or open for malignancy	Outline application	Mr Mohammed Abu Hilal	Full application not invited
A Randomised Controlled Trial of Aspirin to prevent Hepatocellular Carcinoma in patients with Liver Cirrhosis	Outline application	Dr Aileen Marshall	Full application not invited
May 2016			
T-SCOPE2: Sample collection for the 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)	Sample collection application	Dr Richard Adams & Dr Thomas Crosby	Not funded
Earlier diagnosis and prevention of oesophageal adenocarcinoma - the role of image cytometry in detecting relevant DNA abnormalities in Barrett's oesophagus patients	Full application	Professor Anthony Watson	Not funded
Stratification of chemotherapeutic response in pancreatic cancer patients to allow personalised choice of treatment based on levels of cellular defence enzymes	Full application	Dr Eithne Costello	Not funded

Validation of a Prognostic Index containing both Clinical and Molecular features to predict outcome in Oesophageal Adenocarcinoma	Full application	Mr Christopher Peters	Not funded
CHARISMA: Neo-adjuvant chemotherapy followed by surgery versus surgery alone in high-risk patients with resectable colorectal liver metastases	Outline application	Professor Daniel Palmer & Mr Hassan Malik	Full application not invited
PRECISION-Panc UK: Personalising treatment for pancreatic cancer	Outline application	Professor Andrew Biankin	Full application invited

8. Collaborative partnership studies with industry

In line with national policy, there has been a large increase in industry trials on the Group's portfolio and these are demonstrated in the portfolio maps. Most trials in the Neuroendocrine Subgroup portfolio are industry funded and international. These have generally recruited very well. In the Pancreatic Subgroup portfolio, Celgene and Nucana have supported major trials. Other partnerships have been more problematic. Considerable effort from Group members has gone into developing protocols through the various Alliances which have gone through CTAAC and unfortunately the company has subsequently either decided to undertake the study themselves or withdrawn support for the compound.

9. Impact of CSG activities

- The Upper GI CSG trials portfolio has had a major impact on routine clinical practice in the UK and worldwide in the last five years. The ABC studies have changed practice in biliary cancer and are now the published standard of care in both Europe and the USA. New EPOC and SCOPE gave evidence of the potential harmful effects of EGFR blockade in certain circumstances. Neo Scope and SCALLOP gave evidence for the use of chemoradiotherapy in OG and locally advanced pancreatic cancer. Although OEO-5 and STO-3 were negative, they added knowledge on chemotherapy in oesophageal adenocarcinoma and stomach cancer respectively. As part of international trials, the NET Subgroup has played a key role in advances in treatment in these tumours.
- Members of the committee regularly serve as experts on NICE technology appraisals, although most applications, e.g. Abraxane, have been declined on the basis of the ICER. The Group Chair chairs the Pancreas Cancer Guidelines Committee and another CSG member also contributes to this.
- The Group regularly inputs into the Horizon Scanning exercise.
- As discussed above, CTAAC/CRC has not in recent years been inclined to fund the type of trial design which has previously proved successful. The cost of phase III clinical trials managed in the traditional way is also proving unaffordable. It should be perfectly possible to radically reduce the cost of pragmatic trials in the NHS using national data sets to evaluate outcome rather than traditional CTU monitoring. Achieving this appears elusive with multiple blocks and barriers.

10. Consumer involvement

Mr David Chuter has demitted from the Group and an interview for a replacement is imminent. Mrs Yvonne Carse joined the CSG at the beginning of the last reporting year. She is been active on the Pancreatic Subgroup as consumer member and involved in the development of the key trials including “Precision Panc”. She participated in the scoping meeting for the NICE Guidelines Committee on Pancreatic Cancer.

11. Open meetings/annual trials days/strategy days

Unusually there was no Annual Trials meeting in 2015. The difficulty in funding these meetings via industry and the Office time involved has proved difficult for upper GI cancer, unlike other disease areas. There is also discomfort in the Group regarding dependence on industry. The next annual trials meeting will be in September 2016 and a small registration fee will be charged to delegates. It remains to be seen what effect this will have on attendance.

12. Priorities and challenges for the forthcoming year

The priorities for the Group are:

1. To obtain grant funding for large scale trials in pancreatic cancer and colorectal liver metastases.
2. To integrate the clinical trails programme as much as possible with GeL.
3. To run a successful Trials meeting in September funded by registration charges for participants.

The three challenges are identical to the priorities.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

- A – Main CSG Strategy
- B – Neuroendocrine Subgroup Strategy
- C – Oesophagogastric Subgroup Strategy
- D – Hepatobiliary Subgroup Strategy
- E – Pancreatic Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Professor John Primrose (Upper Gastro-intestinal Cancer CSG Chair)

Appendix 1

Membership of the Upper Gastro-intestinal Cancer CSG

Name	Specialism	Location
Dr Yuk Ting Ma	Clinical Lecturer	Birmingham
Dr Tom Crosby	Clinical Oncologist	Cardiff
Dr Stephen Falk	Clinical Oncologist	Bristol
Dr Maria Hawkins	Clinical Oncologist	Oxford
Dr Somnath Mukherjee	Clinical Oncologist	Oxford
Mr Tim Underwood	Clinical Scientist	Southampton
Mrs Yvonne Carse	Consumer	Launceston
Mr David Chuter	Consumer	Bognor Regis
Professor Ruth Langley	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
Dr Richard Turkington	Medical Oncologist	Belfast
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
Mr Robert Jones*	Surgeon	Liverpool

*denotes trainee member

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
Mr 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	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
Prof John Primrose	Surgeon	Southampton
Mr Hassan Malik (Chair)	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
Dr Wasat Mansoor**	Medical Oncologist	Manchester
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 (Chair)	Clinical Oncologist	Cardiff
Mr David Chuter**	Consumer	Bognor Regis
Professor Heike Grabsch**	Histopathologist	Leeds
Professor David Cunningham	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
Dr Naureen Starling	Medical Oncologist	London
Professor Anne Thomas	Medical Oncologist	Leicester
Dr Somnath Mukherjee	Clinical Oncologist	Oxford
Professor Jane Blazeby	Surgeon	Bristol
Mr William Allum	Surgeon	London
Professor Robert Mason	Surgeon	London
Mr Shaun Preston**	Surgeon	Surrey
Mr Tim Underwood	Surgeon	Southampton

**denotes non-core member

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 and remains until the next Upper GI CSG strategy day:

1. The subgroup structure was re-examined. It was widely agreed that with the advent of CTRad that radiotherapy should be embedded in the other subgroups and a relationship established with CTRad.
2. It was agreed that the Screening and Prevention Subgroup, which dealt only with Barrett's Oesophagus, was not appropriate and the suggestion was a group be formed which included prevention, screening, early diagnosis and imaging. Subsequently, however, the NCRI review of CSGs and Subgroups set an absolute maximum of four Subgroups and it was subsequently agreed that these areas would be embedded in the four remaining subgroups and a relationship established with the cross cutting Prevention, Screening and Early Diagnosis Advisory Group which has been set up across all CSGs.
3. The four Subgroups (oesophagogastric, pancreatic, hepatobiliary and neuroendocrine tumours) should remain in their present form but the membership and chair arrangements should conform to the new NCRI review proposals with a strict tenure of membership.
4. The membership of the subgroups would be reviewed and it was agreed that a statistician should sit on each subgroup.
5. CUP should be included within the Hepatobiliary Subgroup.
6. The Group felt that GIST, which sat with the Sarcoma CSG, should move to the Upper GI CSG on the basis that 1) GIST was not a sarcoma and 2) in terms of the clinical management it involved principally the Upper GI MDT. The Chair agreed to take this to the NCRI Directors.
7. New trial methodologies were discussed. It was accepted that very large phase III trials using a single chemotherapy schedule in unselected patients was probably in the past and that the future would be dominated by adaptive and biomarker driven trial designs.
8. Surgical trials were discussed. Accepting the problems with recruitment, it was agreed that it was appropriate to try to develop more high quality trials in surgical methodologies.
9. Arrangements for the development of radiotherapy trials were discussed and it was agreed that the Group should work closely with CTRad to develop high quality radiotherapy proposals.
10. A major national strategy was to encourage and develop industry studies and the advantages of an AZ collaboration was discussed. It was agreed the Group would work to increase collaboration with industry trials.
11. The Group also considered various novel trial ideas which would be developed through the subgroups subsequently.

B – Neuroendocrine Subgroup Strategy

Aim:

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

Strategy:

To ensure that the NET portfolio has a multi-disciplinary broad base of studies (clinical and translational) covering all aspects of NETs. This includes:

1. Establishing the UK (through the NCRI) as a competitive place for industry to run clinical trials.
2. Broadening the scope of the clinical trials portfolio in patients with NETs; these include:
    - Increasing the number of studies where gastroenterologists are best placed (e.g. gastric or rectal carcinoids).
    - Ensuring the portfolio includes studies focusing on symptoms and quality of life.
    - Increasing the number of studies incorporating radiotherapy-based questions.
    - Providing the opportunity for translational questions to be addressed within the scope.
    - Developing studies addressing surgical questions and the use of adjuvant therapy.
3. Development of clinical studies in NETs other than GEP (e.g. lung NETs, phaeochromocytomas and paragaglionomas) with a similar multi-disciplinary approach.
4. To develop innovative therapeutic strategies.

C – 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:

1. Continue to support and encourage translational research to increase understanding of the factors that cause and drive OG cancer.
2. Continue to develop strategies to prevent OG cancer and new diagnostic techniques to facilitate an early diagnosis.
3. 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:

1. 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.

2. Encourage industry partnerships, seeking to facilitate the rapid development of trials investigating new therapeutic agents
3. 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.

D – Hepatobiliary Subgroup Strategy

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

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

E – Pancreatic Subgroup Strategy

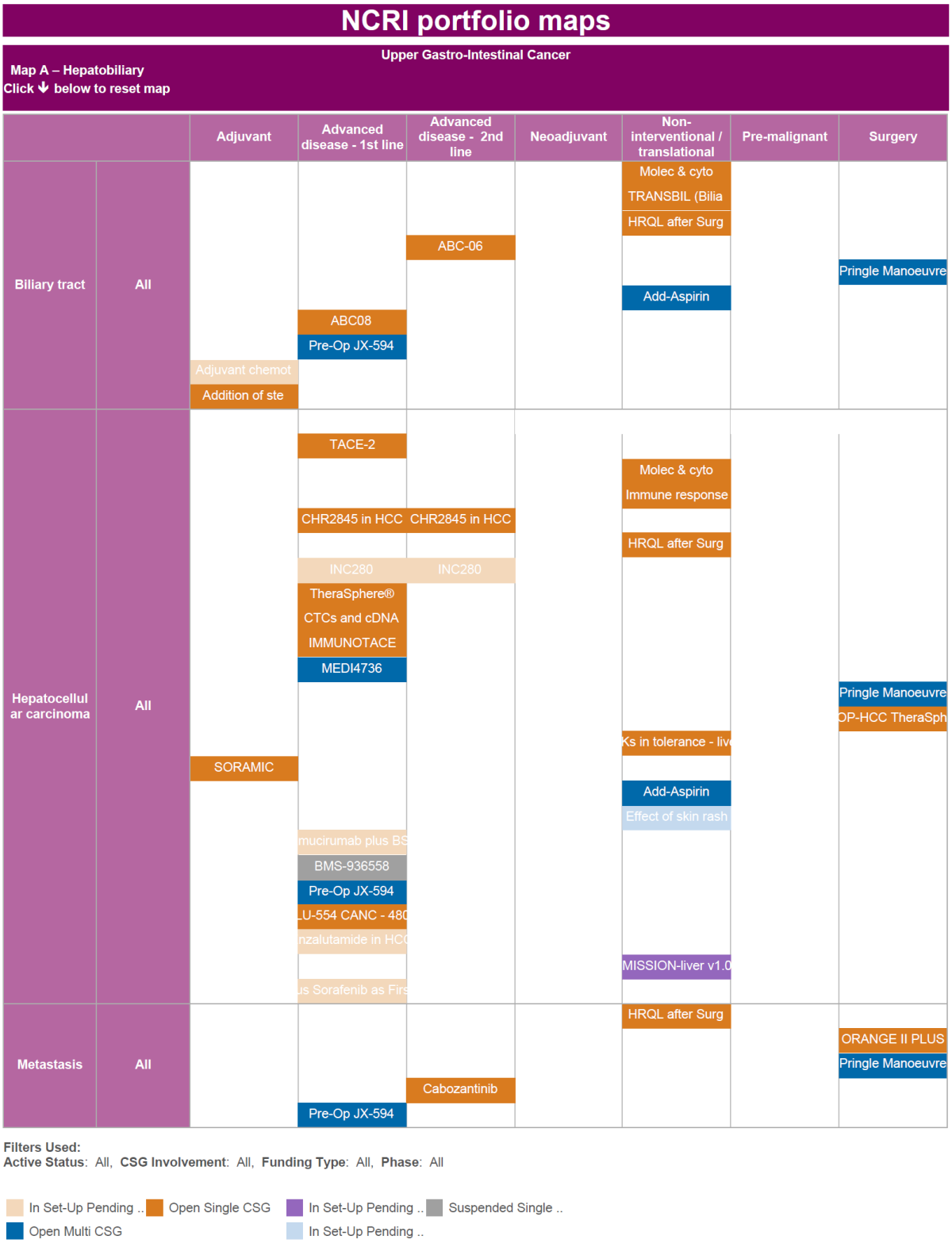
The Pancreatic Subgroup is aware that the findings of ESPAC 4 in adjuvant therapy are likely to make a significant positive impact on the post-operative management of operated pancreas cancer patients in 2016. The outcome is likely to receive significant prominence at ASCO 2016.

The 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. New studies in locally advanced disease, in particular in surgical approaches, techniques and radiation, are newly opened to national recruitment and the commercial portfolio is expanding in advanced disease. All studies are supported by strong translational work. The challenge remains the poor health of many patients with pancreatic 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 2015/16.

A proposed over-arching platform strategy proved too ambitious and is currently being resubmitted but the subgroup believes should provide the necessary spring board for ongoing 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.

Appendix 3

Portfolio maps



NCRI portfolio maps

Upper Gastro-Intestinal Cancer

Map B – Neuroendocrine
Click ↓ below to reset map

		Adjuvant	Advanced disease - 1st line	Neoadjuvant	Surgery	Symptom control / non-interventional / translational
Intestines	High grade (g3)					HRQL after Surg LX1606
	Low grade (g1/g2)					HRQL after Surg
Lung & other	High grade (g3)					HRQL after Surg
	Low grade (g1/g2)	ADIUVO				HRQL after Surg [18F]-FET-ßAG-TOCA
Pancreas	High grade (g3)					HRQL after Surg
	Low grade (g1/g2)		SEQTOR REMINET			HRQL after Surg [18F]-FET-ßAG-TOCA

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

In Set-Up Pending ..
Open Single CSG

NCRI portfolio maps

Upper Gastro-Intestinal Cancer

Map C – Oesophageal, junctional tumours (type I/II)
Click ↓ below to reset map

		Adjuvant	Advanced disease - 1st line	Advanced disease - 2nd line	Neoadjuvant	Non-interventional / translational	Pre-malignant	Surgery
Adenocarcinoma	All	ST03 Chopin STAT-ROC Neo-AEGIS	ST03 Chopin DEBIOC ROCOCO IRON ROCS GO2 CheckMate032 MEDI4736	ST03 Chopin nasitinib vs sunitinib MLN0264 Adeno Capecitabine + Cis..	ST03 Chopin BioStent Neo-AEGIS	Chopin OCCAMS: Multice RTL Peri-operat RTL Advanced St ATTACK-OG PHOENIX HRQL after Surg FAZA-PET -hypoxia The Useful Study Add-Aspirin GI precursor lesion Preoperative Fe	Non-invasive diagn	ST03 Chopin LITE Study BioStent
Barrett's oesophagus	All		Pre-Op JX-594	nasitinib vs sunitinib		Molec & cyto PHOENIX HRQL after Surg MIMOSA GI precursor lesion Preoperative Fe Identifying Pro A feasibility s	RECaD BOOST Chopin Trimodal Imagin BEST2 Non-invasive diagn	LITE Study
Squamous cell carcinoma	All		ROCS GO2		ROMIO BioStent	ATTACK-OG PHOENIX HRQL after Surg FAZA-PET -hypoxia Add-Aspirin PLATFORM Preoperative Fe	Non-invasive diagn	LITE Study BioStent

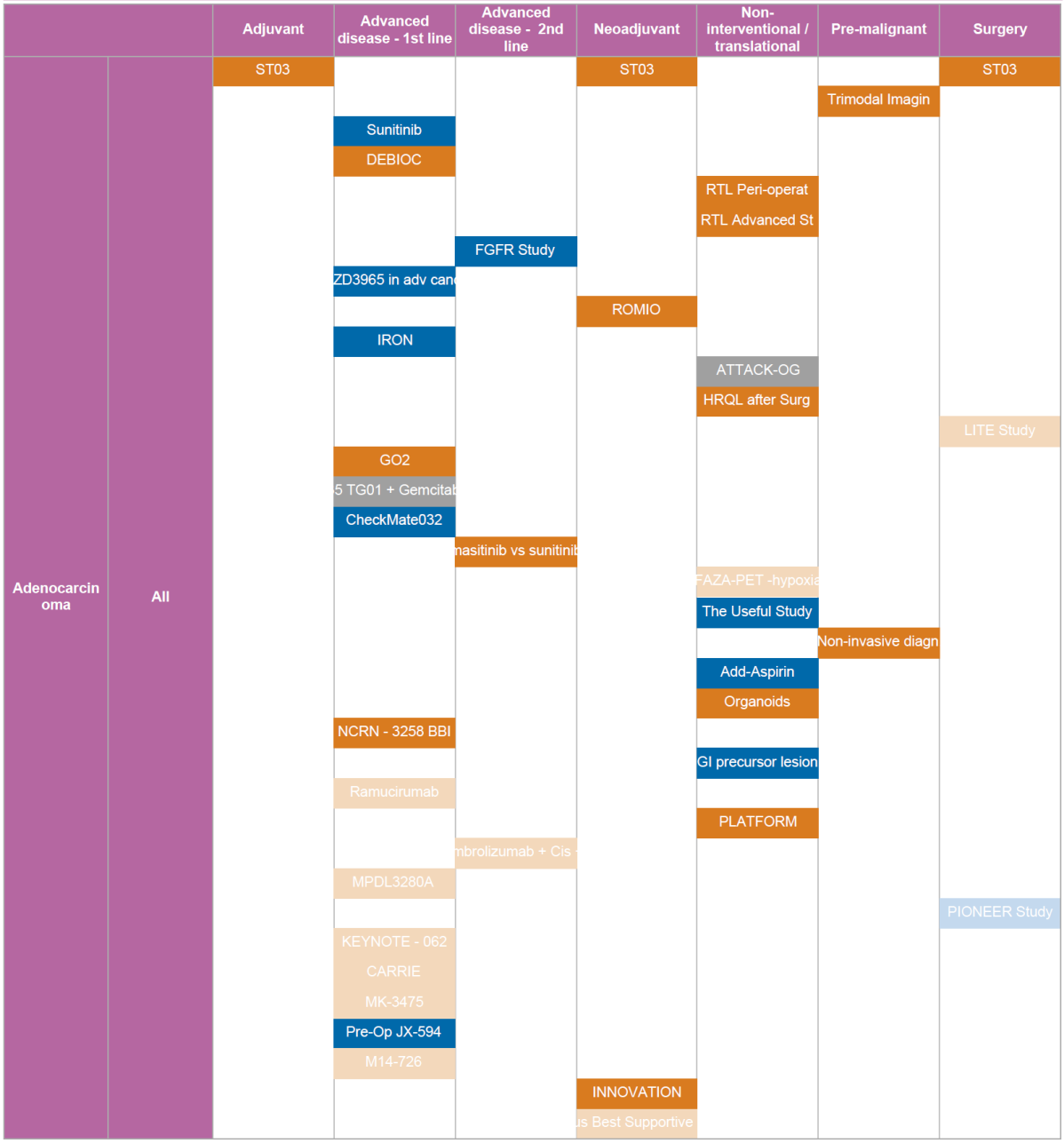
Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

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

NCRI portfolio maps

Upper Gastro-Intestinal Cancer

Map D – Stomach, junctional tumours (type II/III)
Click ↓ below to reset map



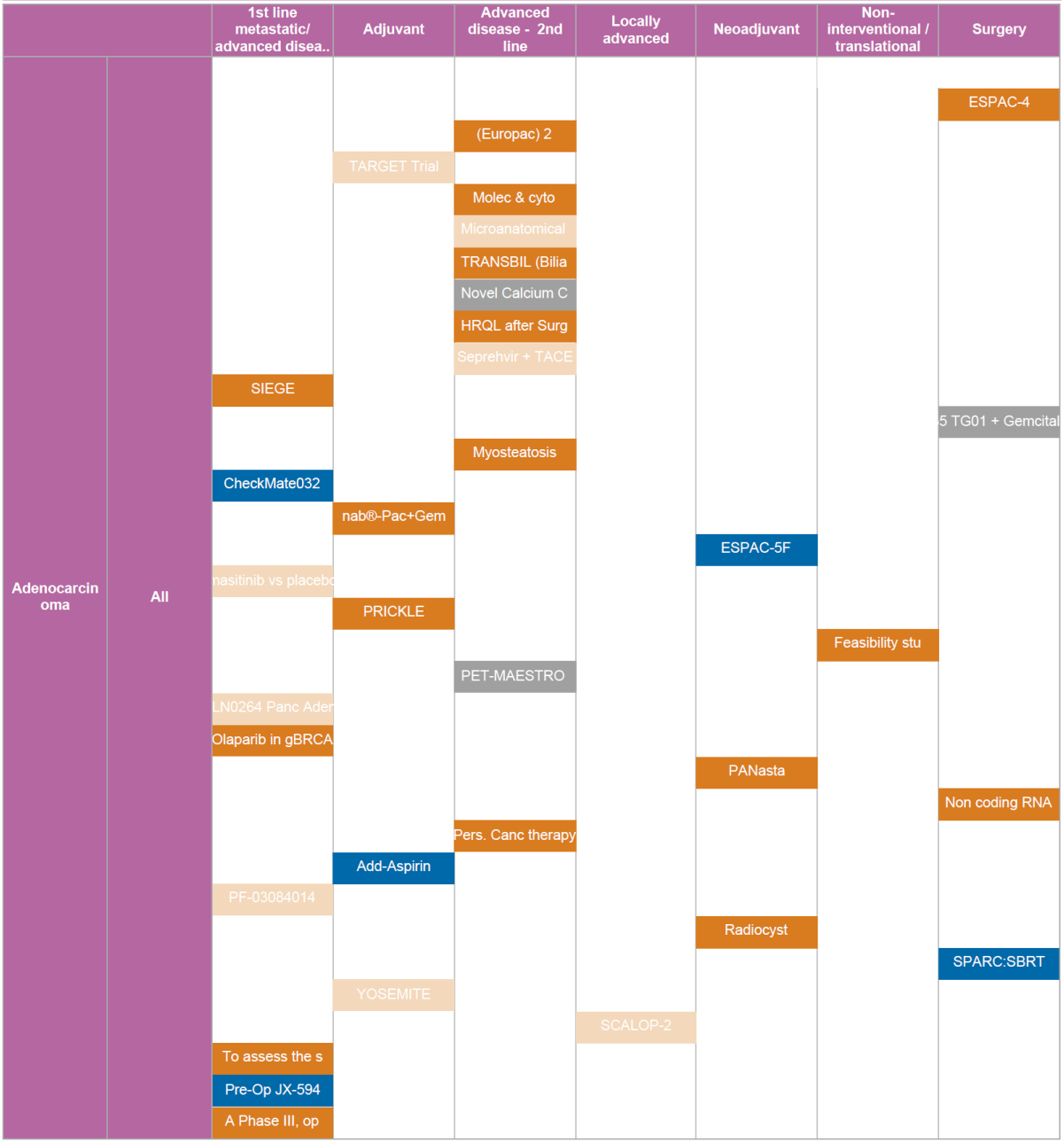
Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

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

NCRI portfolio maps

Upper Gastro-Intestinal Cancer

Map E – Pancreas
Click ↓ below to reset map



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

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

Appendix 4

Publications in the reporting year

SCOPE/NEOSCOPE
Rees J, Hurt CN, Gollins S, Mukherjee S, Maughan TS, Falk S, Staffurth J, Ruby R, Bashir N, Geh I, Cunningham D, Roy R, Bridgewater J, Griffiths G, Nixon L, Blazeby J, Crosby T. Patient reported outcomes during and after definitive chemoradiotherapy for oesophageal cancer. Br J Cancer. 2015 Aug 11;113(4):603-10. doi: 10.1038/bjc.2015.258. Epub 2015 Jul 23

Brusatol provokes a rapid and transient inhibition of Nrf2 signaling and sensitizes mammalian cells to chemical toxicity-implications for therapeutic targeting of Nrf2
Olayanju A, Copple IM, Bryan HK, Edge GT, Sison RL, Wong MW, Lai ZQ, Lin ZX, Dunn K, Sanderson CM, Alghanem AF, Cross MJ, Ellis EC, Ingelman-Sundberg M, Malik HZ, Kitteringham NR, Goldring CE, Park BK. Free Radic Biol Med. 2015 Jan; 78:202-12

Predicting response to neoadjuvant treatment for advanced colorectal cancer – a review of relevant mechanisms and potential biomarkers
P A Sutton, R P Jones, J P Evans, N Kitteringham, C Goldring, DH Palmer, D Vimalachandran, H Z Malik. Colorectal cancer 2015; 4(2): 85-89.

Prognostic molecular markers in resected extrahepatic biliary tract cancers; a systematic review and meta-analysis of immunohistochemically detected biomarkers
Jones RP, Bird NT, Smith RA, Palmer DH, Fenwick SW, Poston GJ, Malik HZ. Biomark Med. 2015 Jul 30:1-13.

Randomized controlled trial of prehabilitation before planned liver resection
Declan FJ Dunne MBChB (Hons), Sandy Jack PhD, Robert P Jones PhD, Louise Jones MSc, Daniel T Lythgoe MSc, Hassan Z Malik MD, Graeme J Poston MS, Daniel H Palmer PhD, Stephen W Fenwick MD. BJS 2016 (in press)

The risk of malignancy in ultrasound detected gallbladder polyps: A systematic review
Mohamed Elmasry, Don Lindo, Declan FJ Dunne, Hassan Malik, Graeme J Poston, Stephen W Fenwick. HPB 2016 (in press)

From mice to men; murine models of colorectal cancer for use in translational research
Evans Jonathan, Sutton Paul , Winiarski Boleslaw, Fenwick Stephen, Malik Hassan, Vimalachandran Dale, Tweedle Elizabeth, Costello Eithne, Palmer Daniel, Park B Kevin and Kitteringham Neil. Crit Rev Oncol Hematol. 2015 Nov 1. pii: S1040-8428(15)30058-5. doi: 10.1016/j.critrevonc.2015.10.009. [Epub ahead of print]

SCOPE 1
Carrington R, Spezi E, Gwynne S, Dutton P, Hurt C, Staffurth J, Crosby T. The influence of dose distribution on treatment outcome in the SCOPE 1 oesophageal cancer trial. Radiat Oncol. 2016 Feb 6;11(1):19. doi: 10.1186/s13014-016-0594-x.PMID:26852238

Carrington R, Staffurth J, Warren S, Partridge M, Hurt C, Spezi E, Gwynne S, Hawkins MA, Crosby The effect of dose escalation on gastric toxicity when treating lower oesophageal tumours: a radiobiological investigation. Radiat Oncol. 2015 Nov 19;10(1):236. doi: 10.1186/s13014-015-0537-y.PMID:26586375

Samantha Warren, Mike Partridge, Alessandra Bolsi, Anthony J Lomax, Chris Hurt, Thomas Crosby, Maria A. Hawkins. An analysis of plan robustness for oesophageal tumours: comparing volumetric modulated arctherapy plans and spot scanning proton planning [associated with SCOPE1 data] Radiat OncolBiol Phys, 2016 May;95(1): 199–207

Patient-reported outcomes during and after definitive chemoradiotherapy for oesophageal cancer

Rees J, Hurt CN, Gollins S, Mukherjee S, Maughan T, Falk SJ, Staffurth J, Ray R, Bashir N, Geh JI, Cunningham D, Roy R, Bridgewater J, Griffiths G, Nixon LS, Blazeby JM and Crosby T. Br J Cancer (2015) 113, 603–610. doi:10.1038/bjc.2015.258 [SCOPE1]

SCALOP

Hurt CN, Mukherjee S, Bridgewater J, Falk S, Crosby T, McDonald A, Joseph G, Staffurth J, Abrans, RA, Blazeby JM, Bridges S, Dutton P, Griffiths G, Maughan T, Johnson C. Health related quality of life in SCALOP, a randomized phase II trial comparing chemoradiotherapy regimens in locally advanced pancreatic cancer (LAPC) Int J Radiat Oncol Biol Phys 24-AUG-2015 DOI information: 10.1016/j.ijrobp.2015.08.026

Fokas E, Clifford C, Spezi E, Joseph G, Branagan J, Hurt C, Nixon L, Abrams R, Staffurth J, Mukherjee S. Comparison of investigator-delineated gross tumor volumes and quality assurance in pancreatic cancer: Analysis of the pretrial benchmark case for the SCALOP trial. Radiother Oncol. 2015 Dec;117(3):432-7.

Hurt CN, Mukherjee S, Bridgewater J, Falk S, Crosby T, McDonald A, Joseph G, Staffurth J, Abrams RA, Blazeby JM, Bridges S, Dutton P, Griffiths G, Maughan T, Johnson C. Health-Related Quality of Life in SCALOP, a Randomized Phase 2 Trial Comparing Chemoradiation Therapy Regimens in Locally Advanced Pancreatic Cancer. Int J Radiat Oncol Biol Phys. 2015 Nov 15;93(4):810-8

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Middleton G, Greenhalf W, Costello E, Shaw V, Cox T, Ghaneh P, Palmer DH, Neoptolemos JP. Immunobiological effects of gemcitabine and capecitabine combination chemotherapy in advanced pancreatic ductal adenocarcinoma. Br J Cancer. 2016 Mar 1;114(5):510-8.

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Nicholson JA, Greenhalf W, Jackson R, Cox TF, Butler JV, Hanna T, Harrison S, Grocock CJ, Halloran CM, Howes NR, Raraty MG, Ghaneh P, Johnstone M, Sarkar S, Smart HL, Evans JC, Aithal GP, Sutton R, Neoptolemos JP, Lombard MG. Incidence of post-ERCP pancreatitis from direct pancreatic juice collection in hereditary pancreatitis and familial pancreatic cancer before and after the introduction of prophylactic pancreatic stents and rectal diclofenac. Pancreas. 2015 Mar;44(2):260-5.

ESPAC 3 & 4

Childs EJ, Mocci E, Campa D, Bracci PM, Gallinger S, Goggins M, Li D, Neale RE, Olson SH, Scelo G, Amundadottir LT, Bamlet WR, Bijlsma MF, Blackford A, Borges M, Brennan P, Brenner H, Bueno-de-Mesquita HB, Canzian F, Capurso G, Cavestro GM, Chaffee KG, Chanock SJ, Cleary SP, Cotterchio M, Foretova L, Fuchs C, Funel N, Gazouli M, Hassan M, Herman JM, Holcatova I, Holly EA, Hoover RN, Hung RJ, Janout V, Key TJ, Kupcinskas J, Kurtz RC, Landi S, Lu L, Malecka-Panas E, Mambrini A, Mohelnikova-Duchonova B, Neoptolemos JP, Oberg AL, Orlow I, Pasquali C, Pezzilli R, Rizzato C, Saldia A, Scarpa A, Stolzenberg-Solomon RZ, Strobel O, Tavano F, Vashist YK,

Vodicka P, Wolpin BM, Yu H, Petersen GM, Risch HA, Klein AP. Common variation at 2p13.3, 3q29, 7p13 and 17q25.1 associated with susceptibility to pancreatic cancer. Nat Genet. 2015 Aug;47(8):911-6.

Takaori K, Bassi C, Biankin A, Brunner TB, Cataldo I, Campbell F, Cunningham D, Falconi M, Frampton AE, Furuse J, Giovannini M, Jackson R, Nakamura A, Nealon W, Neoptolemos JP, Real FX, Scarpa A, Sclafani F, Windsor JA, Yamaguchi K, Wolfgang C, Johnson CD; IAP/EPC study group on the clinical managements of pancreatic cancer. International Association of Pancreatology (IAP)/European Pancreatic Club (EPC) consensus review of guidelines for the treatment of pancreatic cancer. Pancreatology. 2016;16(1):14-27.

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Jenkinson C, Elliott VL, Evans A, Oldfield L, Jenkins RE, O'Brien DP, Apostolidou S, Gentry-Maharaj A, Fourkala EO, Jacobs IJ, Menon U, Cox T, Campbell F, Pereira SP, Tuveson DA, Park BK, Greenhalf W, Sutton R, Timms JF, Neoptolemos JP, Costello E. Decreased Serum Thrombospondin-1 Levels in Pancreatic Cancer Patients Up to 24 Months Prior to Clinical Diagnosis: Association with Diabetes Mellitus. Clin Cancer Res. 2015 Nov 16.

Jenkinson C, Elliott V, Menon U, Apostolidou S, Fourkala OE, Gentry-Maharaj A, Pereira SP, Jacobs I, Cox TF, Greenhalf W, Timms JF, Sutton R, Neoptolemos JP, Costello E. Evaluation in pre-diagnosis samples discounts ICAM-1 and TIMP-1 as biomarkers for earlier diagnosis of pancreatic cancer. J Proteomics. 2015 Jan 15;113:400-2.

W. Abu-Alainin, T. Gana, T. Liloglou, A. Olayanju, L. N. Barrera, R. Ferguson, F. Campbell, T. Andrews, C. Goldring, N. Kitteringham, B. K. Park, T. Nedjadi, M. C. Schmid, J. R. Slupsky, W. Greenhalf, J. P. Neoptolemos, and E. Costello, 'Uhrf1 Regulation of the Keap1-Nrf2 Pathway in Pancreatic Cancer Contributes to Oncogenesis', *J Pathol,* 238 (2016), 423-33.

Ujjwal M. Mahajan, Enno Langhoff, Eithne Costello, William Greenhalf, Christopher Halloran, Theresa Schwaiger, Frank-Ulrich Weiss, John Neoptolemos, Markus W. Buchler, Markus M. Lerch, and Julia Mayerle, '41 Cathepsin D Expression in Pancreatic Ductal Adenocarcinoma (Pdac) Cells Increases Proliferation and Reduces Survival of Pancreatic Cancer Patients', *Gastroenterology,* 148 (2015), S-13.

PANASTA

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ABC-02

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ABC-02 study. Br J Cancer. 2016 Apr 26;114(9):965-71. doi: 10.1038/bjc.2016.64. PMID:27115567

Prognostic factors for progression-free and overall survival in advanced biliary tract cancer
Bridgewater J, Lopes A, Wasan H, Malka D, Jensen L, Okusaka T, Knox J, Wagner D, Cunningham D, Shannon J, Goldstein D, Moehler M, Bekaii-Saab T, McNamara MG, Valle JW. Ann Oncol. 2016 Jan;27(1):134-40. doi: 10.1093/annonc/mdv483. Epub 2015 Oct 19.

Cisplatin and gemcitabine in patients with advanced biliary tract cancer (ABC) and persistent jaundice despite optimal stenting: Effective intervention in patients with luminal disease
Lamarca A, Benafif S, Ross P, Bridgewater J, Valle JW. Eur J Cancer. 2015 Sep;51(13):1694-703. doi: 10.1016/j.ejca.2015.05.018. Epub 2015 Jun 8.

ABC-03
Valle JW, Wasan H, Lopes A, Backen AC, Palmer DH, Morris K, Duggan M, Cunningham D, Anthoney DA, Corrie P, Madhusudan S, Maraveyas A, Ross PJ, Waters JS, Steward WP, Rees C, Beare S, Dive C, Bridgewater JA. Cediranib or placebo in combination with cisplatin and gemcitabine chemotherapy for patients with advanced biliary tract cancer (ABC-03): a randomised phase 2 trial. Lancet Oncol. 2015 Aug;16(8):967-78. doi: 10.1016/S1470-2045(15)00139-4. Epub 2015 Jul 12. Erratum in: Lancet Oncol. 2015 Sep;16(9):e427.

ABC-04
Bridgewater J, Lopes A, Beare S, Duggan M, Lee D, Ricamara M, McEntee D, Sukumaran A, Wasan H, Valle JW. A phase 1b study of Selumetinib in combination with Cisplatin and Gemcitabine in advanced or metastatic biliary tract cancer: the ABC-04 study. BMC Cancer. 2016 Feb 24;16(1):153. doi: 10.1186/s12885-016-2174-8.

ACTICCA-1
Stein A, Arnold D, Bridgewater J, Goldstein D, Jensen LH, Klümpen HJ, Lohse AW, Nashan B, Primrose J, Schrum S, Shannon J, Vettorazzi E, Wege H. Adjuvant chemotherapy with gemcitabine and cisplatin compared to observation after curative intent resection of cholangiocarcinoma and muscle invasive gallbladder carcinoma (ACTICCA-1 trial) - a randomized, multidisciplinary, multinational phase III trial. BMC Cancer. 2015 Jul 31;15:564. doi: 10.1186/s12885-015-1498-0.

Appendix 5

Major international presentations in the reporting year

SCOPE/NEOSCOPE

Mukherjee S, Hurt C, Gwynne G, Bateman A, Gollins S, Radhakrishna G, Canham J, Ray R, Grabsch H, Sharma RA, Maggs R, Hawkins MA, Sebag-Montefiore D, Maughan T, Griffiths G, Crosby TDL. NEOSCOPE: A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine (OXCAP) or carboplatin/paclitaxel (CarPac) based chemoradiation (CRT) as pre-operative regimen for resectable oesophageal adenocarcinoma. J Clin Oncol 34, 2016 (suppl 4S; abstr 3) GI ASCO 2016 (21-23 Jan 2016)

NeoSCOPE

Somnath Mukherjee, Chris Hurt, Sarah Gwynne, Andrew Bateman, Simon Gollins, Ganesh Radhakrishna, Jo Canham, Ruby Ray, Heike I Grabsch, Ricky A. Sharma, Rhydian Maggs, Maria A Hawkins, David Sebag-Montefiore, Tim Maughan, Gareth Griffiths, Tom David Lewis Crosby; A randomised Phase II study of induction chemotherapy followed by either oxaliplatin/capecitabine (OXCAP) or carboplatin/paclitaxel (CarPac) based chemoradiation (CRT) as pre-operative regimen for resectable oesophageal adenocarcinoma. J Clin Oncol 34, 2016 (suppl 4S; abstr 3) GI ASCO 2016

Caitlin Bowden, Adam Selby, Richard Webster, Ganesh Radhakrishna, Gareth Jones, Tom Crosby, Sarah Gwynne Dosimetric analysis of oesophagus plans using 3D-CT vs 4D-CT planning scans within the UK NeoSCOPE trial. Accepted as oral presentation, UKRO 2016

SCOPE1

Samantha Cox, Ceri Powell, Ben Carter, Chris Hurt, Somnath Mukherjee, Tom David Lewis Crosby; Role of nutritional status as predictor of survival in oesophageal cancer treated with definitive chemoradiation (dCRT): outcome from SCOPE1, a phase II/III randomised trial of dCRT +/- cetuximab. J Clin Oncol 34, 2016 (suppl 4S; abstr 103) GI ASCO 2016

Somnath Mukherjee, Chris Hurt, Stephen Falk, Simon Gollins, John Staffurth, Ruby Ray, John A. Bridgewater, David Cunningham, Jane M. Blazeby, Rajarshi Roy, Tim Maughan, Gareth Griffiths, Tom David Lewis Crosby; Long term results and patterns of recurrence from SCOPE 1: A phase II/III randomised trial of definitive chemoradiotherapy (dCRT) plus or minus cetuximab (dCRT+C) in esophageal cancer. J Clin Oncol 34, 2016 (suppl 4S; abstr 118) GI ASCO 2016

Towards real time review of outlining through implementation of standardised multi-centre workflow and software

Sarah Gwynne, T Crosby, J Staffurth, E Spezi. Oral presentation, UKRO 2015

OE05 trial

Cunningham et al. Neoadjuvant Chemotherapy for Resectable Oesophageal and Junctional Adenocarcinoma: Results from the UK MRC OE05 trial. Presented at ASCO 2015, Chicago

ST03 trial

Cunningham et al. Peri-operative chemotherapy ± bevacizumab for resectable gastro-oesophageal adenocarcinoma: Results from the UK Medical Research Council randomised ST03 trial (ISRCTN 46020948). European Cancer Congress 25-29 September 2015 (Vienna, Austria)

ESPAC-4 and ESPAC-5F

John Neoptolemos. Pancreas Cancer - Lessons learned from Significance of neoadjuvant and adjuvant therapy in borderline resectable tumours. World Pancreas Forum. Switzerland, June 2015.

Paula Ghaneh. Neoadjuvant and adjuvant therapy in pancreatic cancer. UEG October 2015, Barcelona.

John Neoptolemos. Pancreatic Cancer. Collaboration in pancreatic research – transatlantic view. EPC Toledo Spain, June 2015.

ESPAC-3

Nils Elander. Cytidine Deaminase (CDA) Transcript Analysis Complements hENT1 Protein Staining in Predicting Gemcitabine Response in the ESPAC-3 Pancreatic Cancer Cohort. APA San Diego 2015.

New EPOC

Pugh SA, Bridgewater JA, Moutasim K et al. Association between c-Met expression, miR-31-3p expression and progression free survival in the New EPOC study. J Clin Oncol 33, 2015 (suppl; abstr 3545) - ASCO 2015

EPOC B

D. Goldstein, J. Fawcett, J. Bridgewater, M. Choti, K. Wilson, V. Gebski, C. Aiken, Z. Eminton, S. Falk, L. Stanton, J. Primrose. Feasibility of trials to assess safety and toxicity of peri-operative and post-operative adjuvant therapy for hepatic metastases from colorectal cancer - ESMO 2015