NCRI Upper Gastrointestinal Group

Annual Report 2020 - 2021

NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of the NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.

List of Appendices

NCRI Upper Gastrointestinal Group

Annual Report 2020-21

1. Top achievements in the reporting year (up to three)

Achievement 1 SAFIR-ABC10: molecular screening for precision medicine in advanced biliary cancer. Funded by CRUK 2021. This study has been in development for several years in collaboration with UNICANCER and the Belgian Research Foundation. To be funded in the context of cuts to the CRUK budget is remarkable.
Achievement 2 CytoSponge and TFF3 to detect Barrett's oesophagus was published in the Lancet (*Fitzgerald RC et al. Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. Lancet 2020;396(10247):333-344*.
Achievement 3 ESPAC-5F: presented by Paula Ghaneh at ASCO 2020; feasibility trial in borderline resectable pancreatic cancer evaluating 3 different neoadjuvant strategies with immediate surgery. Despite recruitment challenges, the trial demonstrated significant survival advantage with neoadjuvant therapy compared with immediate surgery and has added to the growing evidence supporting adoption of a neoadjuvant approach in borderline resectable pancreatic cancer.

2. Structure of the Group

The devolved structure of the Group, with a strategic oversight committee and four workstreams, has run for approaching 2 years without major issues. There has been a robust discussion following proposals to move to a model of more short-term goal driven ad hoc groups however this has been resisted *pro tempore* by the membership because:

1. The workstreams felt strongly that the ensemble had great unifying and collegiate value in the context of funding and NHS uncertainties, driven in part by COVID-19.
2. More than ever, the fostering and mentorship of juniors is central to the work of the workstreams. The EORTC practice of a mandated junior investigator for every study is being considered.
3. Our meetings still deliver concrete outcomes, be they virtual or face to face. A hybrid model will be considered as COVID-19 lifts.

An extremely successful PPI recruitment round saw the largest number of new members ever. The challenge will now be for the executive Group and workstreams to best utilise their considerable strengths.

Christopher Peters is our new Oesophagogastric (OS) Workstream Chair.

3. Upper Gastrointestinal Group & Workstream strategies

Upper Gastrointestinal Group

The Upper GI Group has been working on strategic aims, proposed at the last strategy meeting in April 2019 although COVID-19 has significantly impacted on the environment, particularly funding.

Individual strategies are given with each workstream report.

Membership	Translational scientists in every meeting: largely delivered
New trial development/trial design	Significantly impacted by COVID changes to funding
Translational research and correlative science	Central for CRUK applications
Routinely collected data	Difficult to assess as approved studies are few
Genomics	New studies, e.g. ABC10 now embedded in GLH's
Engagement with other NCRI activities	Cross working with Children's and TYA & GCT Groups proposed
Horizon scanning for opportunities	
Industry engagement	Particularly active in context of CRUK downsizing
International presence	
Engaging the next generation of researchers	Proposals being considered
Securing funding	Full range of academic and commercial funding being considered
Brand/comms/researcher engagement	
Consumer involvement	Excellent recruitment round

Hepatobiliary Workstream (Chair, Mr Hassan Malik)

The Hepatobiliary Workstream has achieved its 3 main strategic aims related to the last quinquennial review (QQR):

1. Development of a precision platform biliary study, ABC 10 which has received funding from CRUK in 2021.

2. Development of a non-colorectal metastatic trail. A working party was set up and the OLIGO-1 GI study was developed and submitted to CRUK in 2019, invited for full application. Currently on hold due to COVID-19 pandemic impacting grant funding.

3. Development of a screening/prevention study. An Aspirin cancer prevention study in patients with PSC has been developed by members of the Workstream and discussed at the recent NCRI Screening, Prevention & Early Diagnosis Proposals Guidance meeting.

The main impact from COVID-19 has been restriction in access to funding for new studies. However, the pandemic has facilitated the Group to develop its program via on-line meetings rather than face to face. This will facilitate on-going growth in the group's membership, which is essential to engagement with the wider community.

Neuroendocrine (NET) Workstream (Chair, Dr Alan Anthoney)

The past year has seen development of projects and strategy within, or supported by, the Neuroendocrine Workstream towards its goals and, despite slowed progress due to COVID-19, the recent trajectory has been encouraging with successful funding of a number of new studies.

Increased collaboration with translational research:

Workstream input into the development of the phase II LANTANA study (Sharma: Imperial). A novel demethylating agent, ASTX727, will aim to increase expression of SSTR2 on NET with low levels of receptor as determine by [^{68}Ga]-DOTATOC-Positron Emission Tomography. Upregulation will result in treatment with Lu^{177}-Dotatate. Commercial funding (£750,000) and provision of study therapeutics approved. Study opened 2020.

Although the effect of immune checkpoint inhibitors in NET has been disappointing to date, potential synergy between lenvatinib and pembrolizumab has led, with support from the Workstream, to development of the PELICAN study (Pinato:Imperial). This phase II study of carboplatin/etoposide + pembrolizumab followed by maintenance pembrolizumab +/- lenvatinib has been funded (unrestricted grant from MSD) to open in 10 sites within UK. A funding application to CRUK to support a translational sub-study is in development for submission this year.

The phase 1b TEMIRA study (Barriuso/Valle: Christie) exploits the differential sensitivity of tumour cells, including pancreatic NET, to temozolamide and PARPi depending on MGMT biomarker expression. The study has tolerability, response and exploratory pharmacodynamic endpoints.

Increase in trials in areas of unmet need:

ASA NELM (Frilling: Imperial): Adjuvant Somatostatin Analogues (Lanreotide) versus Placebo after Resection of Neuroendocrine Liver Metastases. This unique adjuvant study in resected neuroendocrine tumour liver metastases is finalising funding and is supported by the EORTC. Translational endpoints of study include determination of utility of liquid biopsy transcriptomic panel for neuroendocrine tumours in determining relapse post treatment.

Although COVID-19 caused a hiatus in trial recruitment during the first half of 2020 the portfolio of studies has now re-opened with NET-02 (McNamara: Christie) being open in all sites and approaching 50% recruitment. NETTER-2 (Srirajaskanthan: Kings) and ARTISAN (Sharma: Imperial) are also recruiting well.

Studies in development:

The survival benefit of resecting the primary tumour and associated mesenteric lymph nodes, in the presence of unresectable metastatic disease in well differentiated small intestinal NET, is the focus of a multi-centre, Phase III, randomized trial (Ford: Birmingham). Strong local patient involvement has been key to development of this study.

Exploring the effectiveness of peptide receptor radiotherapy (PRRT) to SSTR expressing NET beyond the current clinical indications is being evaluated in a phase II study (Caplin: Royal Free). Significant areas of unmet need including, paraganglioma/phaeochromocytoma and bronchial NET, are represented in this study.

Strategically, over the coming year, the Workstream will focus on development of trials in areas of unmet need, collaborating with national and international partners: adrenal tumours (ENSAT), grade 1 and 2 bronchial NET (Lung Group), carcinoid heart disease (NIHR Cardiovascular CRN) and follow-up of resected neuroendocrine tumours (Lung Group). Short term, theme focused and cross-cutting, working groups will be used to generate proposals for the Workstream to prioritise.

Oesophagogastric Workstream (Chair, Dr Christopher Peters)

2020-2021 was a year of transition for the OG workstream as the chair passed from Tom Crosby (Oncologist) to Christopher Peters (Surgeon). The goal was to build on our past successes delivering large scale, practice changing trials, but widen our focus to include the aims set out in the Quinquennial Review (QQR). Therefore, our key strategic aims for this year were to:

1) Consider carefully current gaps in the portfolio to create new trials that will become the next practice changers.
2) Increase research activity in radiotherapy field.
3) Continue the focus on translational research and embed biobanking and precision medicine approaches wherever possible.
4) Consider how existing tissue and data collections can be leveraged to develop new research ideas.
5) Broaden the portfolio to include trials encompassing early detection, surgical and radiological studies, and quality of life projects.

Partner professional & patient /charitable organisation supporting the Priority setting exercise	
Partner professional organisation	**Partner patient/charitable organisation**
Association of Cancer Physicians (ACP)	Action Against Heartburn
Association of Upper Gastrointestinal Surgeons (AUGIS)	Barrett's Oesophagus Campaign (pending)
British Dietician Association	Barrett's Wessex (pending)
British Society of Gastroentrology (BSG)	Cancer Research UK
British Society of Gastrointestinal & Abdominal Radiology (BSGAR)	Guts UK
Cancer Research UK	GUTSY Group
National Cancer Research Institute (NCRI)	Heartburn Cancer UK
The Primary Care Society for Gastroenterology (PCSG)	Oesophageal Patients Association
Royal College of General Practitioners (RCGP - pending)	Ochre Charity
Royal College of Pathologists (RCPath)	OG Cancer NI
Royal College of Radiologists (RCR)	Oxfordshire Oesophageal & Stomach Association

In addition, we have begun a large consensus project to determine the key research questions we should be asking for OG cancer moving forward and have successfully obtained accreditation for this piece of work from the following groups.

Despite COVID-19 we have carried on meeting four times per year, shifting to the Teams platform. We have continued the process started in previous years to widen the attendees to include those that have not previously participated in the Workstream. We are currently in the middle of a review of the core committee members list to make sure it accurately reflects the people attending and contributing.

Key outputs of the Workstream this year include the presentation of the preliminary NEO-AEGIS results at ASCO and the ongoing output of high impact papers from OCCAMS including (1) *Knight WRC et al. Endoscopic tumour morphology impacts survival in adenocarcinoma of the oesophagus. Eur J Surg Oncol 2020;46(12):2257-2261*, (2) *Rogerson C et al. Repurposing of KLF5 activates a cell cycle signature during the progression from a precursor state to oesophageal*

adenocarcinoma. Elife 2020;9:e57189, (3) *Ococks E et al. Longitudinal tracking of 97 esophageal adenocarcinomas using liquid biopsy sampling. Ann Oncol 2021;32(4):522-532,* (4) *Jammula SG et al. Identification of Subtypes of Barrett's Esophagus and Esophageal Adenocarcinoma Based on DNA Methylation Profiles and Integration of Transcriptome and Genome Data. Gastroenterology 2020;158(6):1682-1697,* (5) *Rahman SA et al. Machine learning to predict early recurrence after oesophageal cancer surgery. Br J Surg 2020;107(8):1042-1052.*

In terms of realising the aim to develop studies in early detection, the BEST3 study involving the primary care use of the CytoSponge and TFF3 to detect Barrett's oesophagus was published in the Lancet (*Fitzgerald RC et al. Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. Lancet 2020;396(10247):333-344.*

Consistent with the diversification of the portfolio, studies under development include SARONG to randomise to differing surveillance strategies following OG resection, NEEDS study (in combination with Sweden) comparing radical chemo radiation versus neoadjuvant chemoradiotherapy and surgery for SCC, LINARCE to consider the lynx anti reflux device to manage Barrett's, TUDAR to assess different techniques to manage the pylorus following oesophagectomy, CYTOFLOC2 to explore the use of cytosponge to monitor patients post radical chemoradiotherapy, DECIPHER to use ctDNA to predict and manage recurrence following OG resection, and OLIGO-1 which was initially a multiple GI cancer oligo metastatic disease study but is now focusing on OG cancer.

Other trials currently being considered for funding include the PROTEUS trial of proton beam therapy which is under consideration by CRUK and CITADEL, a randomised Phase 2 precision medicine trial to tackle trastuzumab resistance in oesophageal adenocarcinoma. CITADEL formed part of the unsuccessful OElixir bid but was invited for submission for a CRUK clinical trial award.

Existing studies struggled with recruitment or had to be paused during the COVID-19 pandemic but centres are now in a recovery phase and generally beginning to recruit again (Add ASPIRIN, CHARIOT, CytoSponge Project Delta, ELEVATE, EMERGE, ICONIC, PLATOFRM, SCOPE 2 and SOLAR).

We also continue to work closely with patient-facing groups and have facilitated the publication of another trials-related article in the Oesophageal Patients Association magazine. This was authored by the Add-Aspirin study team and follows an earlier article that provided an overview of the Workstream's activities.

Pancreatic Workstream (Chair, Dr Pippa Corrie)

The key strategic aims of the Pancreatic Workstream this year were to:

1) Work with the Precision Panc team to facilitate its ongoing delivery
2) Extend the repertoire of associated Primus trials, with a focus on generating biomarker-selected protocols
3) Extend the research portfolio in early pancreatic cancer
4) Extend the research portfolio with a focus on supportive care for patients

Despite the challenges of COVID-19, the Workstream continued to hold six monthly virtual meetings, with large numbers of attendees extending the wider membership to over 40 colleagues from multiple disciplines and across the devolved nations. Meetings have included focussing on both NCRI and PrecisionPanc activities, as well as a dedicated meeting held in October 2021 to focus specifically on transitioning molecular profiling from research to service, preparing for the PrecisionPanc grant to end and need to move towards NHSE GLHs.

As of April 2021, there are now 8 PRIMUS studies: 1 is closed, 2 are open and actively recruiting, 5 are in set up. The NCRI group has been responsible for securing a first biomarker-selected study funded by NIHR-EME (Pembrolizumab+olaparib in high TMB PDAC, CI PCorrie) and is currently working on securing a novel proton beam substudy to be embedded in PRIMUS 002 (G Radhakrishnan).

Progress regarding studies being developed this year with key relevant PDAC targets/biomarkers are as follows:

- DDR proficient segment: BRD4+olaparib = PRIMUS004 (D Chang/A Biankin) in set up
- Role of combining metformin+ascorbate with standard chemotherapy – (S Mukherjee/E O'Neil) not funded by MRC
- Dendritic cell attraction – Gem+Pem+IMM101 (J Evans/D Chang) – CRUK CRC endorsement confirmed
- WNT pathway: RNF43 mutations – Industry sponsored study, REDx = PRIMUS007(CI J Valle), in set up
- KRAS WT – (B Basu) In concept

In recognition of the challenges associated with early PDAC, a new working party was established, now entitled the Early PDAC Framework (co-Chairs, J Valle & D Palmer). The working party is making progress towards standardising reporting (of pre-surgical images) and patient pathways (surveillance post-surgery), which need to be established in order to conduct meaningful research with standard benchmarks (see below).

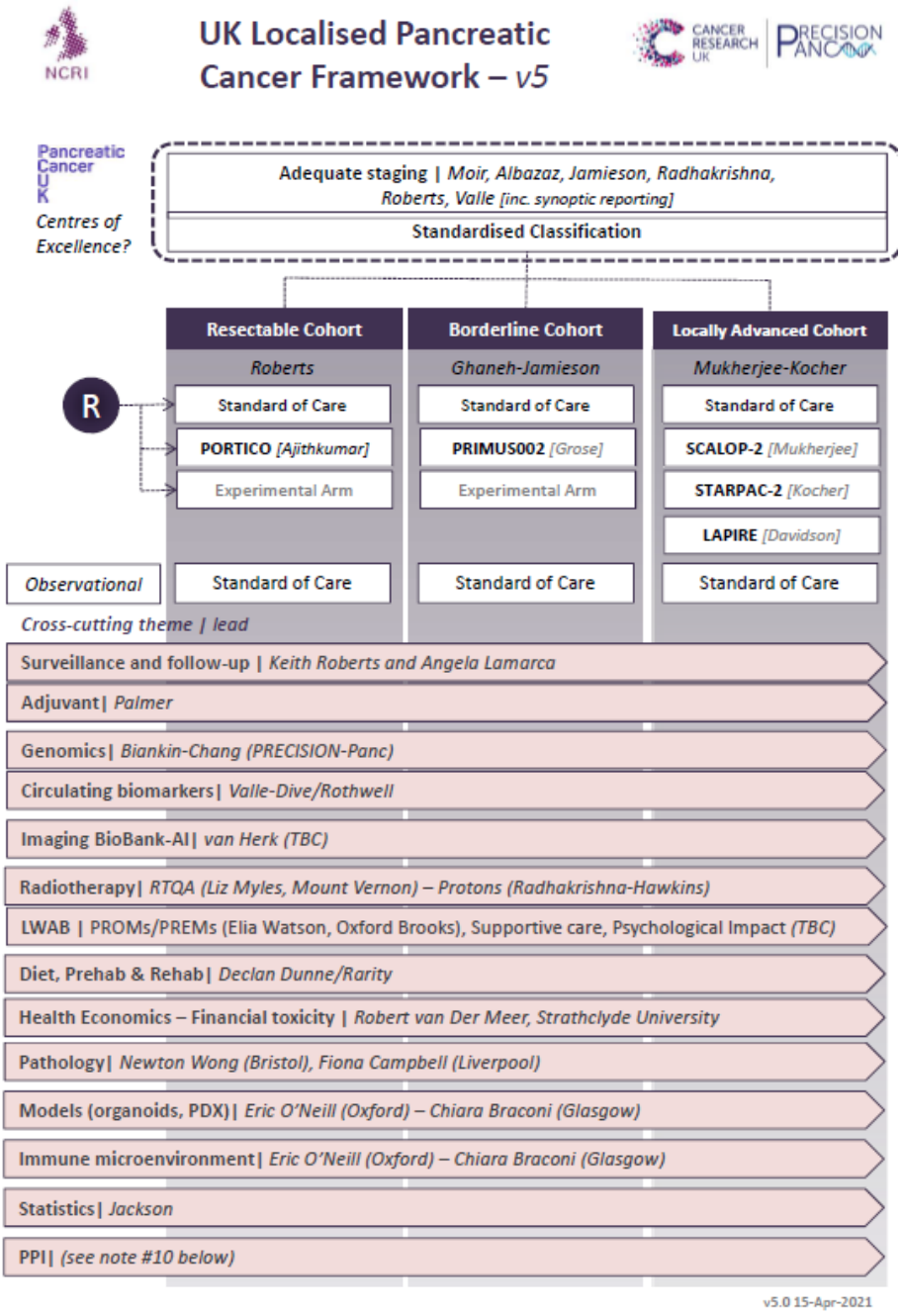
Our intention to develop patient-focussed supportive care studies has been hampered by COVID-19, although the groundwork has been done, collating information from a recent German James Lind Alliance project as well as a Delphi prioritisation study undertaken by UK pancreatic cancer surgeons.

During the COVID-19 pandemic of 2020, NCRI members were highly active in raising awareness of the challenges associated with delivering treatment to patients with PDAC. A position statement regarding treatment recommendations was published (Jones et al, BJC 2020); multiple webinars were undertaken hosted by Pancreatic Cancer UK, often with NCRI members either chairing or presenting. Many specialist teams established large scale databases to collate anonymised patient data to learn from the pandemic experience. The NCRI pancreatic cancer community has fed into several of these, including Covid-Surg and CONTACT. 'Big Data' are now recognised as being unique resources for informing clinical practice and will hopefully attract greater recognition in the future as credible initiatives which are invaluable to the research community.

4. Cross-cutting research

NCRI Early Pancreatic Cancer Framework

The NCRI Early Pancreatic Cancer Framework was set up as a time-limited working group and met for the first time on 05/12/2019. The group was set up as a national, multi-disciplinary collaboration, linked to patients and their advocates, to deliver improved outcomes (treatment and research) of early pancreatic cancer. The group aims to clearly-define patient subgroups with resectable, borderline-resectable and locally advanced pancreatic cancer based on standardised radiological assessment and subsequent definition of disease status/resectability. Downstream, a number of cross-cutting groups would be tasked with specific themes which would build on these clearly-defined groups – see Figure.



Several initiatives have been developed as part of this Framework:

i. **Synoptic radiology report** for the assessment of patients with pancreatic cancer – this multidisciplinary group was set up in March 2020; it is geographically inclusive and has been badged by a number of professional societies, including the Royal College of Radiologists, British Society of Gastrointestinal and Abdominal Radiology, Royal College of Surgeons, pancreatic Cancer UK, the Association of Upper GI Surgeons as well as the NCRI.

The project had progressed very well with an initial review of currently - available tools; synthesis of a new tool based on the "best features"; a pilot (surgical survey); a refinement process leading to roll-out (phase 1) + survey feedback. The project is currently at the roll-out (phase 2) step aiming to have the synoptic report adopted across most of the major HPB MDTs in the UK. Next steps include a publication as well an integration of the synoptic report into the clinical trial protocols.

ii. **Surveillance and follow-up** – this project aims to optimise and standardise the follow-up of patients following resection of pancreatic cancer, in order to incorporate this into clinical trial protocols. Two aspects have been developed:

a. A systematic review and meta-analysis has been completed of surveillance following resection of pancreatic cancer in the published literature. This has been submitted to the Eur J Surg Oncol for consideration of publication (*Clinical Benefit of Surveillance after Resection of Pancreatic Ductal Adenocarcinoma: A Systematic Review and Meta-Analysis; James M Halle-Smith et al.*).

b. A UK Consensus Statement is now being developed. This has started with a survey of UK current practice (https://www.surveymonkey.co.uk/r/WFQNTRH) circulated on 13.04.2021. In parallel, a literature review is being performed of protocolised follow-up within the published adjuvant clinical trials.

Once these two elements are complete, a manuscript will be developed with a view to integrating this standardised follow-up into clinical trial protocols.

iii. A platform is under construction (see figure below) to optimise involvement of patients across the UK in addressing questions relating to therapy for resectable pancreatic cancer. Having established standardisation of assessment and staging pre-op as well as follow-up post-op, this schema enables a number of clinical questions to be addressed including neo-adjuvant therapy, adjuvant therapy, resection margin status, etc. This platform will require complex statistics which are under development by Richard Jackson, statistician at Liverpool Clinical Trials Unit.

The Early Pancreatic Cancer Framework group acknowledged the help from Pancreatic Cancer UK in the coordination of the meetings.

Professor Juan W Valle (Chair) and Professor Daniel Palmer (Co-Chair)

5. Funding applications in last year

Table 1 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Cancer Research UK*					
December 2020					
Adjuvant chemotherapy with gemcitabine and cisplatin compared to standard of care after curative intent resection of cholangiocarcinoma and muscle invasive gallbladder carcinoma (ACTICCA-01)	Clinical Trial Award - Amendment (May 2020)	Professor John Bridgewater	Not supported		
PRIMUS-006: Phase II signal seeking trial of gemcitabine and pembrolizumab and IMM-101 as first line treatment of metastatic pancreatic cancer in patients with lower performance status	Endorsement New	Dr David K Chang	Supported - Endorsement		
Aspirin Esomeprazole Chemoprevention Trial - EXension Long-term (AspECT EXceL); for the definitive risks vs. benefits	Clinical Trial Award - Extension (May 2020)	Professor Janusz Jankowski	Supported		
March 2021					
SAFIR-ABC10: molecular screening for precision medicine in advanced biliary cancer	Clinical Trial award	Professor John Bridgewater	Conditionally Supported	Hepatobiliary Group developed	
CITADEL – An open label randomised phase II study of Capivasertib in combination with Trastuzumab or Paclitaxel in HER2+ oesophago-gastric adenocarcinoma progressing after chemotherapy	Clinical Trial Award	Professor Russel Petty and Professor Gareth Griffiths	Not Supported		

ProtOeus - Proton Beam Therapy for cancer of the Oesophagus	Clinical Trial Award-Outline	Professor Maria Hawkins, Dr Ganesh Radhakrishna and Dr Elizabeth Smyth	Full Application Invited		
A randomized phase II trial of transarterial chemoembolization (TACE) versus lenvatinib + pembrolizumab in patients with intermediate stage hepatocellular carcinoma using novel statistical methodology		Professor Daniel Palmer and Dr Richard Jackson	Pending	Hepatobiliary Group developed	
Other committees**					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of Group input**	**Funding amount**
CT-DNA study following curative intent liver resection for m-CRC	Industry	Mr Robert Jones	Funded	Hepatobiliary Group developed	-
PemOla - A phase II study combining pembrolizumab with Olaparib in metastatic pancreatic adenocarcinoma patients with high tumour mutation burden	NIHR EME	P Corrie	Funded	Leading	£580,000

**CRUK CRC applications for table 1 completed by NCRI Executive.*
***Other applications in the table to be completed by the Group Chair*

6. Consumer involvement

Lesley Goodburn

Lesley Goodburn has been involved in activities across the workstreams and has been an active Consumer representative on the Pancreatic Workstream.

The more intensive work across the Pancreatic Workstream has seen Lesley apply for research funding as co-applicant and the Premola trial where the feedback on the application noted the strong patient and career input into the application. Lesley has completed the Consumer training this year and has also presented the work of the Pancreatic Workstream at the Consumer representatives meeting. She has also undertaken research to understand the outputs of the work completed in Germany on the by the James Lind Alliance on a research prioritisation process led by researchers but based on the views of patients and their carers as well as previous carers. There is a hope to complete a similar piece of work here in the UK in relation to pancreatic cancer. Scientific mentoring has been provided by Dr Pippa Corrie.

A second consumer, Janice Whitby was recently appointed to the Upper GI Group.

7. Collaborative partnership studies with industry

The ELEVATE study will analyse temozolomide + nivolumab in MGMT deficient gastroesophageal cancers and has been funded by BMS.

8. Priorities and challenges for the forthcoming year

Priority To develop a strategic approach to UK Oesophagogastric cancer research which attempts to meet the needs of key stakeholders and has a coherent approach. In particular it is important we have a joined-up strategy which links translational science to clinical trials including biobanking where appropriate.
Challenge To develop more non drug / radiotherapy trials in the UK including those in diagnosis, surgery, and survivorship. Funding of surgical trials in particular has been a major problem in the UK where they often fall in between the gaps when it comes to funding schemes.
Priority or challenge Developing right relationship with NHSE GLHs to ensure we can access molecular profiling to maintain current research and facilitate new biomarker-specific studies in the future.

Professor John Bridgewater (Upper Gastrointestinal Group Chair)

Appendix 1

Membership of the Upper Gastrointestinal Group

Name	Specialism	Location
Prof John Bridgewater (Chair)	Medical Oncologist	London
Dr Pippa Corrie	Medical Oncologist	Cambridge
Dr Alan Anthoney	Medical Oncologist	Leeds
Mr Hassan Malik	Surgeon	Liverpool
Mr. Christopher Peters	Surgeon	London

Consumer Representation

Name	Location
Mrs Lesley Goodburn	Staffordshire
Dr Jane Whitby	Surrey

Membership of the Workstreams

Hepatobiliary Workstream		
Name	**Specialism**	**Location**
Mrs Helen Morement	AMMF Chair of Trustees	London
Dr Saoirse Dolly	Clinical Fellow	London
Dr Yuk Ting Ma	Clinical Lecturer	Birmingham
Mr Samir Pathak*	Clinical Lecturer	Bristol
Dr Maria Hawkins	Clinical Oncologist	Oxford
Ms Yolanda Green	Consumer	
Mr John Symons	Consumer	Newbury
Professor Helen Reeves	Gastroenterologist	Newcastle
Dr Tom Bird	Hepatologist	Glasgow
Dr Matthew Hoare	Hepatologist	Cambridge
Dr Ian Rowe	Hepatologist	Leeds
Dr Bristi Basu**	Medical Oncologist	Cambridge
Dr John Bridgewater	Medical Oncologist	London
Dr Mairead Mcnamara**	Medical Oncologist	Manchester
Professor Tim Meyer	Medical Oncologist	London
Professor Daniel Palmer	Medical Oncologist	Liverpool
Dr Paul Ross	Medical Oncologist	London
Dr Rohini Sharma	Medical Oncologist	London
Professor Juan Valle	Medical Oncologist	Manchester
Dr Harpreet Wasan	Medical Oncologist	London
Ms Pam O'Donoghue	Nurse	London
Dr Tim Kendall	Pathologist	Edinburgh
Dr Andre Lopes	Statistician	London
Professor John Primrose	Surgeon	Southampton
Mr Hassan Malik (Chair)	Surgeon	Liverpool

Neuroendocrine (NET) Workstream		
Name	**Specialism**	**Location**
Ms Cathy Bouvier**	Consumer	Coventry
Ms Lindsey Devlin**	Consumer	Coventry
Maia Sissons	Consumer	Leamington Spa
Professor Martyn Caplin**	Gastroenterologist	London
Professor Jonathan Wadsley	Clinical Oncologist	Sheffield
Professor Ashley Grossman	Endocrinologist	London
Dr Alia Munir	Endocrinologist	Sheffield
Dr Daniel Cuthbertson	Endocrinologist	Liverpool
Dr John Ramage	Gastroenterologist	Hampshire
Dr Mohin Khan	Gastroenterologist	Cardiff
Dr Wasat Mansoor	Medical Oncologist	Manchester
Dr Mairead Mcnamara	Medical Oncologist	Manchester
Dr Alan Anthoney (Chair)	Medical Oncologist	London
Dr Debashis Sarker**	Medical Oncologist	London
Dr Christina Thirlwell**	Medical Oncologist	London
Professor Denis Talbot	Medical Oncologist	Oxford
Professor Andrea Frilling**	Surgeon	London
Mr Neil Pearce	Surgeon	Southampton

Oesophagogastric Workstream		
Name	**Specialism**	**Location**
Dr Somnath Mukherjee	Clinical Oncologist	Oxford
Mr Christopher Jones*	Clinical Research Fellow	Leeds
Dr Elizabeth Smyth**	Clinical Research Fellow	London
Dr Leena Mukherjee	Clinical Lecturer	Glasgow
Mr John Bradwell	Consumer	Lincolnshire
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
Professor Ruth Langley	Medical Oncologist	London
Dr Naureen Starling	Medical Oncologist	London
Professor Anne Thomas	Medical Oncologist	Leicester
Professor Rebecca Fitzgerald	MRC Programme Lead	London
Mr William Allum	Surgeon	London
Mr Christopher Peters (Chair)	Surgeon	London
Mr Shaun Preston**	Surgeon	Surrey
Professor Tim Underwood	Surgeon	Southampton

Pancreatic Workstream		
Name	**Specialism**	**Location**
Dr Shivan Sivakumar*	Clinical Research Fellow	Oxford
Dr Thankamma Ajithkumar	Clinical Oncologist	Cambridge
Dr Somnath Mukherjee	Clinical Oncologist	Oxford
Dr Eric O'Neill	Clinical Oncologist	Oxford
Dr Ganesh Radhakrishna	Clinical Oncologist	Manchester
Mrs Lesley Goodburn	Consumer	Staffordshire
Mrs Karen Stead	Consumer	Wakefield/ West Yorkshire
Professor Stephen Pereira	Gastroenterologist	London
Mr Chris MacDonald**	Pancreatic Cancer UK	London
Dr Bristi Basu	Medical Oncologist	London
Professor John Bridgewater	Medical Oncologist	London
Dr Pippa Corrie (Chair)	Medical Oncologist	Cambridge
Professor Jeff Evans	Medical Oncologist	Glasgow
Professor Daniel Palmer	Medical Oncologist	Liverpool
Dr David Propper	Medical Oncologist	London
Professor Juan Valle	Medical Oncologist	Manchester
Dr Newton Wong	Pathologist	Bristol
Dr Richard Jackson	Statistician	Liverpool
Dr David Chang	Surgeon	Glasgow
Professor Paula Ghaneh	Surgeon	Liverpool
Dr Nigel Jamieson	Surgeon	Glasgow
Professor Hemant Kochar	Surgeon	London
Professor Andrew Biankin	Surgeon	Glasgow
Mr Keith Roberts	Surgeon	Birmingham

* denotes trainee member
**denotes non-core member

Appendix 2

Group & Workstream Strategies

A – Upper Gastrointestinal Group Strategy March 2018

Objective	Key actions	Leads	Timeline
1. Membership	• Ensure CSG and Subgroup membership is appropriate and multidisciplinary (including engagement with the spectrum of basic through to clinical researchers)		
2. New trial development/trial design	• CSG/SG Chairs to take a more active approach to trial development – drive an agenda rather than a passive approach, i.e. identify a gap in the portfolio and fill it • Improve the early phase trial to late phase trial transition – need a better line of sight for phase I trials (science should lead and clinical trials should follow) • Consider innovative trials designs, e.g. MAMS trials, to involve multiple diseases in a single trial • Future-proof trial design to allow outcomes of NICE appraisals to be accommodated • Ensure existence of trials suitable for opening in DGHs • Engage with CRUKs ECMC Network • Appoint a clinical and a basic science lead for every trial being developed • Develop a checklist for 'have you engaged with….' when developing a new trial • Important to recognise that we have leaders in the field and when designing a grant application it is necessary to pull these people together		
3. Translational research and correlative science	• Translational research to be at the heart of every study developed by the CSG and integrated into the trial design • Co-ordinate translational research across the CSG		

	• For correlative science, define the question and then obtain the required material, rather than the other way round • Biobanking, consent for future studies and LTFU to be built into every protocol		
4. Routinely collected data	• Keep a watching brief on progress with the completeness of the datasets available • Use routinely collected data for: o Scoping work (e.g. demographics, prevalence) o High-level outcome data to inform trial design and sample size calculations o Long-term follow up of patients on trials		
5. Genomics	• Integration of genomic capability and data in the NHS into clinical trial designs • Pursue any opportunities to collaborate with Genomics England		
6. Engagement with other NCRI activities	• Improve links with other CSGs as appropriate, both site-specific and cross-cutting. • Consider what the CSG can do to address the JLA PSP LWBC priorities • Engage re lack of investigator time within the NHS • Engage re the struggles of trial set-up times		
7. Horizon scanning for opportunities	• All CSG members to look for opportunities for the CSG	All Group members	
8. Industry engagement	• Continue to engage with Pharma/biotech companies • Work with industry regarding site selection to ensure a more equitable access for patients to clinical trials • Involve junior researchers when approaching Pharma (see section 9) • Use CRUKs endorsement process (time consuming) as leverage with Pharma		
9. International presence	• Develop international links as appropriate, especially for rare patient populations • Maintain international leadership		

10. Engaging the next generation of researchers	• Increase the number of trainees involved with the CSG ○ Recruit one trainee to each Subgroup • Embed a junior co-PI system across the CSG and Subgroups • Involve junior researchers when approaching Pharma • Encourage investigators to include a trainee on their TMGs		
11. Securing funding	• Adopt a strategy across the CSG to ensure that Subgroups are not competing with each other for study funding (i.e. do not apply for funding from the same meeting round) • Engage with funders at an early stage in trial development • Consider approaching a broad range of funders when looking to secure support for new studies, including research council funding		
12. Brand/comms/researcher engagement	• Improve CSG web presence • NCRI to be name checked on every publication/presentation in order to help to build a stronger brand • Engagement with the scientific community • Encourage researchers to bring their proposals to the CSG and its SGs at an early stage		
13. Consumer involvement	• Continue to involve consumers in the work of the CSG • Increase consumer involvement in study design to ensure the research developed is of relevance and interest to patients		

B – Hepatobiliary Workstream Strategy

Aim: Hepatobiliary malignancy is associated with poor outcomes. The aim of the Workstream is to improve patient outcomes through the combination of translational research and clinical trials that facilitate change in practice as well as service development.

Strategy: Build upon the strong track record of the group as well as engaging with the broader multi-disciplinary community that treats these patients. The Workstream has remit over a number of areas:

- Metastatic disease
  Following feedback from the QQR report, the Workstream set up a time limited working party with other CSG stakeholders to investigate the possibility of developing an umbrella study in the area of Oligiometastatic disease. This working party has developed a clinical trial proposal, OLIGO-1, which has been submitted to CRUK in Q3 2019. This proposal was invited for a full application to be submitted which was done so in Q1 2020. Unfortunately, due to COVID-19 pandemic and change to CRUK funding, this study proposal has been on hold. The study team are looking at gaining industry support prior to full application being re-submitted to CRUK. The team are also in discussion with the trials unit as to the feasibility of a NIHR application. Final decision will be made Q3 2021 as how to proceed. Parallel to this, we have worked with our trainee representative to support the development of a prospective observational study of oligometastic disease that will be led by the Upper GI surgical trainee collaborative, the Roux group. This parallel project has been delayed due to the COVID-19 pandemic but will be due to re-start in Q4 2021.

  Members of the Workstream collaborate with the Advanced Colorectal Studies Group to develop a CT-DNA study in liver limited, resectable, metastatic colorectal cancer. This study has recently received funding from an industry partner to proceed in a limited number of UK sites.

- Hepatocellular carcinoma
  Following feedback from the QQR, we have contacted the UK HCC consortium to look at developing closer links with hepatologists and the CSG. Several members of the Hepatobiliary CSG sit on the board of HCC UK. This will enable us to support further epidemiological, surveillance and preventative studies in high-risk population for HCC.

  We continue to develop innovative therapeutic strategies. PRIMER-1, a neo-adjuvant Devolumab study has been funded, as has CUBIC: A Phase I/II study of the CXCR2 inhibitor, AZD5069, in combination with Durvalumab, inpatients with advanced Hepatocellular Carcinoma.

- Cholangiocarcinoma
  Following on from the success of ABC studies, the Workstream was keen to build a platform through which a biomarker driven approach to advanced disease could be investigated. ABC10 which is a biomarker driven maintenance study in advance disease has been submitted to CRUK in 2020 and was successfully funded in the latest round. The ACTICCA adjuvant biliary study will be due to complete within the next 18 months. The sub-group is keen to develop the next adjuvant biliary study. We arranged a biliary away day in Jan 2021 to discuss options for the next round of biliary trials. Further discussion will be undertaken at the next Workstream meeting in May.

Hepatology members of the Workstream have developed an Aspirin cancer preventative study in patients with primary sclerosing cholangitis (Asp-PSC). This proposal was reviewed at the recent NCRI Screening, Prevention & Early Diagnosis Proposals Guidance meeting; feedback will be discussed at the Workstream meeting in May. Aim is to submit application to the NIHR in Q4 2021.

Hassan Malik will be stepping down as Subgroup Chair in May 2021 and Prof Maria Hawkins from UCL will be taking his place.

C – Neuroendocrine (NET) Workstream Strategy

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

Strategy

Increase proportion of academically sponsored trials
The UK has been successful in attracting and leading impactful commercial trials in neuroendocrine tumours; CLARINET, RADIANT-4, LUNA and NETTER-1. However, the development of high-quality, academically sponsored trials is a major priority for the NET Workstream and several proposals are currently in evolution. Building on NET01, NET02 (CI Mairéad McNamara) will evaluated nanoliposomal irinotecan (nal-IRI)/5-fluorouracil (5-FU) or docetaxel as second-line therapy in patients with progressive poorly differentiated extra-pulmonary NET/NEC in a multi-centre, randomised, open-label, phase II trial. The trial will open in 2018. A trial of checkpoint inhibition and chemotherapy has been developed through the Combinations Alliance with AstraZeneca, and a revised proposal has been invited (CI Debashis Sarker). There is pressing need for a trial of adjuvant therapy following liver resection and this is being developed by Andrea Frilling.

Strengthen links with translational research
Dr Chrissie Thirlwell, chair if UKINETS research committee now sits on the NET Workstream forming a key strategic link. She leads the NET GCIP which is anticipated to inform strategies for stratified approaches in NET. Despite limited success in attracting translational research funding in the UK, several investigators have been awarded significant funding from the US-based Neuroendocrine Tumor Research Foundation; Tim Meyer (IMMUNET), Chrissie Thirlwell (Causes of small intestinal NET), Raj Srirajaskanthan (Development of ex-vivo models). These proposals will build international links and strengthen the biological knowledge base on which to develop further studies.

Develop clinical studies in other NET tumours where there is an unmet need
The main focus of clinical trials to date, has been pancreatic and midgut NETs. There is a significant unmet need for bronchial NETs, hind-gut NETs and well differentiated G3 NETs. The development of clinical trials in these areas will be encouraged. To facilitate developments in bronchial NETs, Denis Talbot from the Lung Group has also been appointed to the NET Workstream. Quality of life studies will remain important John Ramage will build on a well-established track record in this area. Given the rarity of these tumours, international links will remain key and strong links with the European Neuroendocrine Tumour Society maintained and developed.

D – Oesophagogastric Workstream Strategy

Aim
The Oesophagogastric (OG) Workstream aims to improve outcomes for patients with OG cancer through progressive clinical trials and cutting-edge translational research.

Strategy
The strategy of the Workstream 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:

- Carry out a broad consensus process to identify the UK priorities for Oeosphago-Gastric cancer research over the next 5 years (to be complete by the end 2021).

- 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 the role of immunotherapy in OG cancer and how it may be integrated into the paradigm for early and advanced disease, including possible combinations with radiotherapy, chemotherapy or targeted agents and biomarker selection. *The goal is to have 2 studies in this field funded and recruiting by the end 2021*
    - Investigating novel therapies, new surgical techniques and advanced radiotherapy techniques such as intensity-modulated radiotherapy (IMRT). *We have a proton beam study already under consideration and aim to have 2 surgical studies successfully funded by mid-2022*.
    - Developing and refining therapeutic strategies for all stages of disease, including diagnosis, 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 and survivorship 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 submission of trial proposals for discussion and feedback from the OG Workstream.
- Assist with grant funding applications by providing a forum for peer-review and discussion of trial proposals, and letters outlining support for important new studies.

Discuss areas of unmet need in cancer research, to enable trials to be developed to addressed.

D – Pancreatic Workstream Strategy

Objective	How?	Leads	Progress made by end March 2021
1. Embed Precision Panc as the national platform for molecular profiling of PDAC	Establish close working relationship between NCRI and PPanc Leadership Team • Work with the Precision Panc Leadership Team to integrate exploratory and larger scale studies, where feasible • Learn from Precision Panc outputs to identify novel targets and develop novel biomarker-selected interventions for PDAC	PC/JV/AB/DC	Joint face-face meetings held April and October 2020; April 2021 Supported PPanc team through Covid-19 pandemic PemOla (PRIMUS 008)* – Pembrolizumab in metastatic high TMB PDAC funded by NIHR EME Jan 2021 Discussions at advanced stage to add Proton beam substudy to PRIMUS 002*
2. Establish a CSG-led multicentre study in each of the key disease stages:	Neoadjuvant	AB/DC/DG Ganesh/Ajith	ESPAC 5F oral presentation at ASCO 2020 Incorporate next studies into Early PDAC Framework Proton beam substudy* progressing as above
	Adjuvant	DP/PG	Incorporate in Early PDAC Framework ESPAC 6** protocol in development
	LAPC	SM *HK*	SCALOP2* recruitment completed STARPAC2/PRIMUS 005** in set up
	First line metastatic	AB/DC/JG SM/EO'N	PRIMUS 001** ongoing – recruitment picking up in 2021 MAP* study not funded by MRC Gem-Pem-IMM101** secured for less fit pts
	Subsequent line metastatic	AB/DC	Negotiations ongoing to secure agents for first appendix study
3. Address opportunities for surgical studies		PG/NJ/KR	Contributed to Covid-Surg** and CONTACT** 'big data' national audits

			Ricochet audit completed – first analysis findings presented to the group April 2021. Three key areas of particular interest for future research: 1. Use of PERT – wide variation nationally and regionally 2. Diagnostic pathway – resectable pathway longer than unresectable 3. Biliary drainage – high 30 day mortality
4. Address opportunities for immunotherapy studies	Develop immune checkpoint inhibitor study for high TMB patients	PC/DC/AB	Funding for PemOla* secured – see above
5. Explore novel approaches through early phase studies	Consider Alliance Opportunities	JE/BB	Opportunities being explored for new biomarker-directed studies eg. for KRAS WT*
6. Embrace the need for psychosocial, nutritional and supportive care studies, pertinent to the PDAC patient population		ALL	Communications with Barry Laird, Be Alpha study CI
7. Identify approaches to address frailty associated with PDAC			PC to contact Paul Ross re CGA study proposal
8. Consider opportunities for screening, prevention and early detection		SP	CRUK-PCUK-EPSRC Early detection Sandpit**: 5 pilot projects funded , to report back within 1 year time frame
9. Involve patients and the public in prioritising research topics	Work with PPI, PCUK and other UK PDAC charities	PC/LG/CM	James Lind Alliance recently undertaken in Germany – multiple areas of unmet need as expected. New PPI member appointed March 2021 Plan to explore supportive care research opportunities in coming year.
10. Involve trainees in developing new research protocols		PC/SS	SS now in consultant post Consider Associate CIs – link a trainee with each new study in development
Early Pancreatic Cancer Framework*	1. Synoptic Reporting 2. Surveillance imaging 3. Clinical trial opportunities	JV/DP	1. Good progress – data being collated and publication being drafted 2. National survey underway 3. For consideration

*Pancreatic Workstream leading
**Pancreatic Workstream supporting

Appendix 3

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Corrie PG, Qian W, Basu B, Valle JW, Falk S, Lwuji C, Wasan H, Palmer D, Scott-Brown M, Wadsley J, Arif S, **Bridgewater J**, Propper D, Gillmore R, Gopinathan A, Skells R, Bundi P, Brais R, Dalchau K, Bax L, Chhabra A, Machin A, Dayim A, McAdam K, Cummins S, Wall L, Ellis R, Anthoney A, Evans J, Ma YT, Isherwood C, Neesse A, Tuveson D, Jodrell DI. Scheduling nab-paclitaxel combined with gemcitabine as first-line treatment for metastatic pancreatic adenocarcinoma. Br J Cancer. 2020 Jun;122(12):1760-1768. doi: 10.1038/s41416-020-0846-2.	Established importance of scheduling for Gem-Abraxane	Fully developed
2. McNamara MG, Lopes A, Wasan H, Malka D, Goldstein D, Shannon J, Okusaka T, Knox JJ, Wagner AD, André T, Cunningham D, Moehler M, Jensen LH, Koeberle D, Bekaii-Saab T, **Bridgewater J**, Valle JW. Landmark survival analysis and impact of anatomic site of origin in prospective clinical trials of biliary tract cancer. J Hepatol. 2020 Nov;73(5):1109-1117. doi: 10.1016/j.jhep.2020.05.014.	Actuarial survival of BTC	Fully developed
3. Patterns of Recurrence After Resection of Pancreatic Ductal Adenocarcinoma: A Secondary Analysis of the ESPAC-4 Randomized Adjuvant Chemotherapy Trial. Jones RP, Psarelli EE, Jackson R, Ghaneh P, Halloran CM, Palmer DH, Campbell F, Valle JW, Faluyi O, O'Reilly DA, Cunningham D, Wadsley J, Darby S, Meyer		Fully developed

T, Gillmore R, Anthoney A, Lind P, Glimelius B, Falk S, Izbicki JR, Middleton GW, Cummins S, Ross PJ, Wasan H, McDonald A, Crosby T, Ting Y, Patel K, Sherriff D, Soomal R, Borg D, Sothi S, Hammel P, Lerch MM, Mayerle J, Tjaden C, Strobel O, Hackert T, Büchler MW, Neoptolemos JP; European Study Group for Pancreatic Cancer.JAMA Surg. 2019 Nov 1;154(11):1038-1048. doi: 10.1001/jamasurg.2019.3337		
4. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomised, controlled trial. Lamarca A, Palmer DH, Wasan HS, Ross PJ, Ma YT, Arora A, Falk S, Gillmore R, Wadsley J, Patel K, Anthoney A, Maraveyas A, Iveson T, Waters JS, Hobbs C, Barber S, Ryder WD, Ramage J, Davies LM, **Bridgewater JA**, Valle JW; Advanced Biliary Cancer Working Group.Lancet Oncol. 2021 May;22(5):690-701. doi: 10.1016/S1470-2045(21)00027-9. Epub 2021 Mar 30	2nd line therapy in BTC	Fully developed
5. A Phase Ib Study of NUC-1031 in Combination with Cisplatin for the First-Line Treatment of Patients with Advanced Biliary Tract Cancer (ABC-08). McNamara MG, **Bridgewater J**, Palmer DH, Faluyi O, Wasan H, Patel A, Ryder WD, Barber S, Gnanaranjan C, Ghazaly E, Evans TRJ, Valle JW.	Phase 1B leading to phase 3 study	Fully developed

Appendix 4

Recruitment to the NIHR portfolio

Summary of patient recruitment by interventional/non-interventional and number of studies opened/closed over the past 5 years.

Year	All participants		Cancer patients only*		Number of studies	
	Non-interventional	Interventional	Non-interventional	Interventional	Opened	Closed
2016/17	1385	1852	1385	1852	31	19
2017/18	2079	1753	2079	1750	31	38
2018/19	2538	1798	2538	1798	58	29
2019/20	2703	1475	2611	1475	37	41
2020/21	945	927	852	927	36	11

*This data is based on a proxy and includes diagnostics, screening and prevention patients.

Appendix 5

Annual report feedback 2019-20

Dear John

Re: NCRI Upper GI Group Annual Report 2019-20

Thank you for submitting an annual report for the Upper GI Group for 2019/20, especially given the challenges with the ongoing COVID-19 pandemic which will have impacted on both the Group and the report itself.

All the Group's annual reports were reviewed at a two-day meeting on the 12th and 13th October 2020 by a panel consisting of some former NCRI Group Chairs, NCRI CMPath Chair, former NCRI CTRad and the current NCRI Strategic Advisory Group (SAG) Chair, NCRI Head of Research Groups and representatives from the NIHR Cancer Coordinator Centre, NHS Cancer Alliances, epidemiology, CTU/basic science, allied health profession, NCRI Consumer Forum and the Canadian Cancer Clinical Trials Network.

We are writing to you now with a summary of the feedback which is based on the information provided in the report. It was noted that there is likely to be more activity taking place within the Group than is documented.

Please share the contents of this letter with your members for discussion at the next Group meeting.

Generic feedback for all the Groups

Strategic objectives and the impact of COVID 19

- Due to the research funding challenges and restrictions on NHS resources resulting from COVID 19, the Panel recommended the Groups evaluate their strategic objectives and focus on the most important priorities or questions that need to be answered as it would not be feasible for the Groups to be doing everything they planned or continue to "plug in the gaps." Additionally, the Panel suggested looking for more cost-efficient methods of working where they can.
- The Panel felt that the strategic objectives for most Groups were too broad especially in the current climate. The Groups were asked to provide specific, measurable aims for their strategic objective and attach timelines/metrics to them.

Multidisciplinary approach to research and membership

- The Panel noted the importance of collaborative and multidisciplinary working, especially in the current climate, and would encourage all Groups to continue to reach out to other relevant NCRI Groups and consider the NCRI strategic priorities where appropriate.

Linking with the wider research community

- The Groups were asked to link with the wider research community and engage with relevant networks, in particular, with researchers who are developing or are running large national platform studies when there is one available in the disease site e.g. PrecisionPanc (Upper GI Group) and TRACERx (Lung Group). The NCRI recognised that there is a role for them to play in promoting collaboration and will be working with the partners to encourage greater interaction between the Groups and the networks in future.

Funding opportunities

- Given the potential decrease in funding opportunities, the Groups are encouraged to explore alternative funding sources and collaborations e.g. with industry, government funders, NHS Cancer Alliances etc.

Consumers involvement:

- The Panel encouraged Groups to integrate public and patient involvement (PPI) in all aspects of the Group's activities e.g. study design, proposal development, prioritisation of strategic areas etc.
- The Panel wanted to ensure that the consumer activity was captured throughout the report and not just in the consumer section, especially where the consumer reports are missing.

Specific feedback for the Upper GI Group

Areas of strength:

- The Panel commended the Group on their impactful work and studies i.e. ASPECT-5, EPOC and the work on Barrett's Oesophagus. The Group have had several high impact publications, two of which are practice changing.
- The Panel noted that the introduction of capecitabine has altered the standard of care.
- The Panel notes that the diversity in Upper GI malignancies was a challenge, but that the Group had good champions to address these key areas, and the Groups strategic aims focusing on early detection is of great importance for the patient community.
- The Panel commended the Group on their engagement with the Neuroendocrine Tumour Group. This collaboration with a niche tumour community was commended.
- The Panel noted the very strong involvement with Pancreatic Cancer UK which has been beneficial to ensure integration between the Pancreatic Workstream and PrecisionPanc initiative. This was seen as a good example of how other Groups might be encouraged to work within other niche tumour sites.
- The Panel were impressed by the Groups statement about their commitment to early career researchers.

Areas which the Group need to consider:

- The Panel thought it would have been good for the Group to recognise the link between their strategy and the national rollout of rapid diagnostic clinics, which are helping to increase early detection of Upper GI cancers. Harnessing this patient population in terms of their strategy to deliver on translational and treatment research is likely to be relevant.

- Early diagnosis was briefly raised in the report, however CTRad involvement was not mentioned. The Panel thought that making meaningful connections with both CTRad and SPED would be highly beneficial to the Group's progress. The Panel thought that expertise from primary care and imaging would also be valuable additions to the Group.

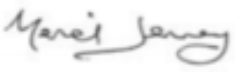
Areas requiring further clarity due to limited information provided in the report as a result of COVID 19:

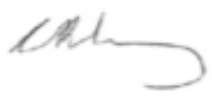
- The Panel noted that the failure to secure funding for ELEXIR was disappointing for the Group, as a substantial amount of work went into the development of this large platform study in oesophageal cancer. The Panel hoped that the Group had taken the time to discuss any feedback from this application to digest the points and work towards new trials.
- The Panel was interested to understand whether the NET Workstream was linking with the Business Development team within NIHR which may be able to further support research within the UK Cancer Community.
- The Panel noted the surgical work was absent from the report and would recommend the Group focuses on how this can be added to the Group's strategy/priorities as this is an important part of the patient management.

Congratulations to you and your members for all your hard work and achievements in 2019/20.

If you have any comments on this year's process, please send them to Nanita Dalal (Nanita.Dalal@ncri.org.uk) for collation.

Best wishes,





Professor Meriel Jenney
Annual Reports Review Committee Chair, NCRI
Consultant Paediatric Oncologist,
University Hospital of Wales

Dr Gillian Rosenberg
Head of Research Groups,
NCRI

Appendix 6

Quinquennial review feedback - 2017

3. Comments and recommendations

The Panel thanked the Upper GI CSG for the documentation provided and the openness with which they had engaged in discussions. The Panel considered at some length options for a radical restructuring of the CSG (e.g. splitting into two, for oesophagogastric and other cancers), but concluded that at this point the basic structure of the Group should remain the same.

The Panel identified a number of strengths of the Group and issues which the CSG need to consider:

Strengths

- The Panel felt that the CSG was more successful than the report indicated, had good examples of impact and should be proud of the achievements over the past five years.
- The CSG's portfolio of studies has had clear international impact and changed practice.
- The Panel congratulated the Group on the PRECISION Panc award, and felt that the oesophagogastic precision medicine bid to MRC, if successful, could be an important development.
- The Panel were pleased that, after being under-represented in the Group's past, radiotherapy research is now being recognised as an important topic.
- NETs and biliary tract were considered important areas with good work emerging from the Subgroups.

Issues for the CSG to consider

- The main CSG and Subgroups are lacking a clear Strategy, and this should be addressed with some urgency. A Strategy Day will be an important step, and should include the Group's strategic response to challenges identified through this review process.
- Screening and early diagnosis requires more focus, especially in the non-OG cancers. The Group should interact with the SPED Advisory Group and other CSGs including, but not limited to, the Primary Care CSG. The CSG should also work to collaborate with researchers in other relevant diseases, e.g. diabetology and hepatology.
- The incoming Chair will need to look at the balance of expertise on the CSG and Subgroups, and consider using the rotation/appointment system to bring in new expertise including immunotherapy, radiotherapy, radiology and gastroenterology.
- It was felt that there should be a greater link with the emerging basic research when developing trials and that this should be addressed in the new strategy and reflected in the makeup of the CSG and Subgroups.
- The Panel recommended the establishment of a vice-Chair role for the CSG which could provide additional translational research input.
- The Panel recommended learning from the successful funding of PRECISION Panc and using this model to develop work in other areas.
- The Panel agreed with the CSG that pragmatic "A-versus-B" studies addressing relevant clinical questions are still important. However, they must also capture scientific opportunities and respond to the funding environment and the current clinical research landscape, e.g. through strong translational components which might also help understand why trials are unsuccessful and inform future research and hypothesis driven sample collections built into their design.
- Consumers were considered vital to the Group and more must be done to recruit and engage consumers, and support them to be effective and fully integrated members of the Group and Subgroups.

Issues for the NCRI/NIHR CRN to consider

- The optimum arrangements for Cancer of Unknown Primary (CUP) and Acute Oncology research to be considered at a planned NCRI Workshop.
- The NCRI CRG team will assist the Upper GI Chair and Subgroup Chairs in carrying out the recommendations of the QQR, including helping set up interactions with other groups as detailed above.
- NIHR CRN CC to work with the UGI CSG to strengthen the interactions with the Upper GI Cancer Subspecialty Leads and Divisional Research Managers at regional level (LCRNs).

In concluding the Review, Professor Seymour thanked everybody for participating and the NCRI CSG Team for preparing the paperwork and organising the Review.

The business of the meeting took four hours. ***The Group will be reviewed in five years' time.***

Set of objectives – 10 point plan

1. Hold a Strategy Day to develop a clear way forward for the CSG and Subgroups.
2. Explore opportunities for using routinely collected data.
3. Build on the existing emphasis on screening, prevention and early detection.
4. Steer the community to maximise the opportunity they have through the PRECISION Panc award.
5. Learn from the successful funding of PRECISION Panc as a model for the development of studies in other areas. Include basic sample collection with pre-planned idea for usage.
6. Embed a greater emphasis on translational research with stronger links to the emerging basic science.
7. Review the skills balance of the CSG and Subgroups to deliver on the new strategy and recommendations of this review. This includes appointments in immunotherapy, radiotherapy, radiology and gastroenterology and more effective use of consumer members (this to be supported by the NCRI Executive).
8. Consider the creation of a vice Chair role who has expertise in translational research to support this area.
9. Improve communication with the research funders to better understand their funding priorities and criteria for a successful application.
10. Use of rigorous internal peer review system within the CSG for new funding applications arising from the Subgroups.
11. Consider greater joint working with other CSGs in areas of shared interest, e.g. metastatic disease.

NCRI Advancing Cancer Research Together