

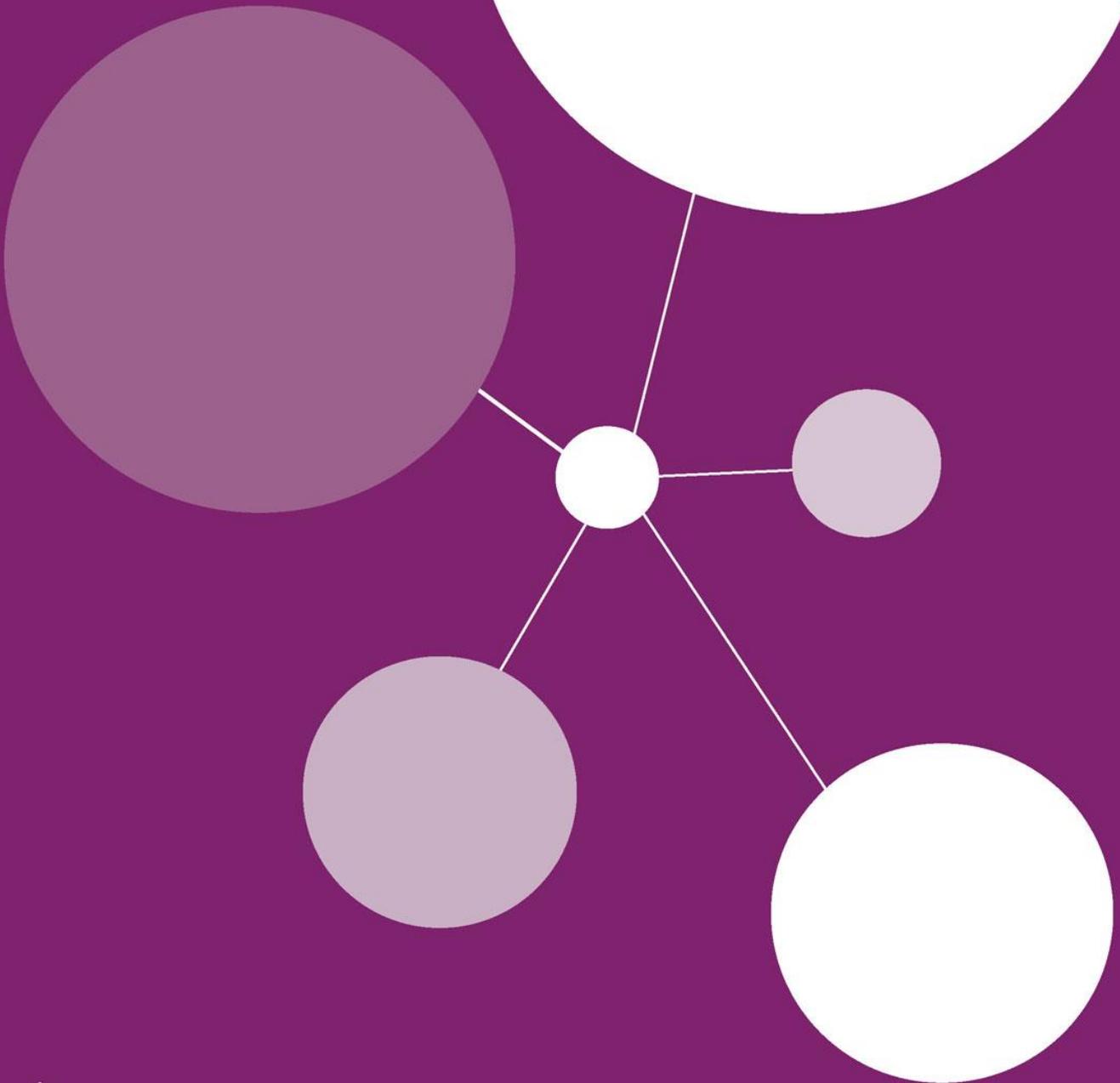


**NCRI**

National  
Cancer  
Research  
Institute

# **NCRI Lung Group**

**Annual Report 2018-19**



Partners in cancer research





## NCRI Lung Group 2018-19

### 1. Top 3 achievements in the reporting year

#### **Achievement 1**

The work of the Lung CSG has helped maintain the number of open studies on our portfolio allowing lung cancer patients across the UK access to trials. A number of high profile studies successfully completed their recruitment (LungART, SPLENDOUR, VIOLET) while open studies on our portfolio continue to be at the forefront internationally and are recruiting well. There are gaps in our trial portfolio and members of the Lung CSG continue to lead the development of new study ideas with the aim of offering all patients the opportunity to participate in research studies. We have initiated our badging of UK lung cancer studies which will raise the profile of the individual studies and UK lung cancer research in general. Our profile is enhanced by the activity of our consumer representatives at home and abroad.

#### **Achievement 2**

The development of cohesive working and applications with the Primary Care CSG and SPED Advisory Group has led to a number of grant successes in this area - Professor Una Macleod's (YCR) grant is looking at earlier presentation of lung cancer in primary care and Professor Mick Peake (CRUK) early diagnosis advisory group is to link primary care data to the cancer registry. These successes build on the research ongoing in lung cancer screening including the Yorkshire Lung Screening Trial and the SUMMIT trial in London which aims to recruit 75,000 participants.

#### **Achievement 3**

The CSG held a strategy meeting and set out our short, medium and longer term goals. An immediate focus is to continue our work refreshing subgroup membership, initiating face to face meetings running alongside the CSG meetings adding to the Annual Trials Meeting and BTOG workshops as opportunities for investigators to present their ideas. During the year we have had workshops that addressed difficult clinical problems – cerebral metastasis, Small Cell Lung Cancer and palliative radiotherapy, which brought together teams of investigators who are now tasked to develop studies to be taken forward with funding applications over the coming year.

## **2. Structure of the Group**

Our focus over the past year has been to reinvigorate the subgroups, refreshing their membership and initiating twice a year face to face meeting that run alongside the CSG meetings.

Dr Navani completed his term on the CSG and has passed the chairmanship for the Early Diagnosis subgroup to Dr Crosbie, Respiratory Physician. We have also thanked the others CSG member who are rotating off the group – Janette Rawlinson, Dr Newsom-Davis, Dr Foster, Mr Naidu and Dr Hanna. This rotation of CSG membership has allowed us to broaden expertise and maintain our geographical spread with the appointment of a respiratory physician (Dr McCaughan), radiologist (Prof Cook), academic GP (Prof Sullivan) and transitional scientist (Dr Vivanco). The trainee rotation has brought us a clinical oncologist (Dr Ashton) and respiratory physician (Dr Ruparel) whose enthusiasm for research will be mentored by Dr Crosbie and Dr Franks.

### 3. Group & Subgroup strategies

#### Lung Group

##### **Group membership & structure**

This year's advert for members focused on broadening multi-disciplinary expertise of the group which now comprises of 6 Medical Oncologists, 3 Clinical Oncologists (+ 1 trainee), 2 Respiratory Physicians (+ 1 trainee), 2 Consumer representatives, 2 Radiologists, 1 Thoracic Surgeon, 1 Pathologist, 1 Palliative Care Physician, 1 Statistician, 1 Support Care Senior Research Fellow, 1 GP and 1 Transitional Scientist. We believe this balance will enable to address the gaps in our portfolio and the Living with and Beyond Cancer research priorities.

A similar refreshment process has been undertaken within the subgroups. We have also increased the number of face to face subgroup meetings. At the time of the December strategy / CSG meeting we invited all subgroups to hold their face to face as part of the program. This gave investigators further opportunities to interact with the CSG and we plan to continue to incorporate the subgroup meeting into CSG meeting program going forward.

Of key importance to the CSG will be our ongoing commitment to engage younger scientists and physicians through our trial meeting, BTOG and working with Royal Colleges and other training bodies.

##### **Strategy Update**

The strategy meeting was held in December 2018 and has recommitted the CSG to:

- Support researchers in developing their study ideas
- Developing studies to cover gaps in the portfolio
- Maintain our strong links with national / international lung cancer research groups
- Nurture the next generation of lung cancer researchers
- Enhance the recognition of the NCRI as a successful trials organisation

A draft strategy document has been prepared and will be reviewed / signed off at the next CSG meeting in May.

##### **Portfolio development**

There are 49 trials open to recruitment and 39 trials completed recruitment over the past year with further studies in set-up which will maintain the breadth of the portfolio.

The improvement in recruitment to interventional lung cancer portfolio studies remains pleasing but our overall study recruitment has mirrored that seen across the NCRI with a drop-in numbers over the past few months. The portfolio is reviewed at all CSG and Subgroups meetings with a pro-active approach taken to identify and attempt to fill gaps seen in the portfolio. The current initiatives are focusing on studies for patients with SCLC, have brain metastasis or require

palliative radiotherapy with groups developing trial outline that we hope to progress through short term working parties to funding applications.

#### **Interaction with (inter)national research groups**

The CSG has good representation in the EORTC Lung Group with the immediate past president (Dr O'Brien) a member of our CSG, with a number of chief investigators of EORTC studies (O'Brien, PEARLS Study, Dr MacDonald: HALT study), active members of our CSG / Subgroups.

The CSG has steering group representation on a number of national and international research group including, BTOG (Prof Hatton, Prof Ahmed, Dr McDonald, Prof Spicer), IASLC (Prof Hatton), ETOP (Prof Blackhall), and TACT which enables the Group to host and co-develop studies, notable examples include BELIEF and PROMISE-Meso.

Our consumer representative, Ms Janette Rawlinson, is a member of ELF PAG (part of ERS) and CSG member representation now extends to European Palliative Care Research Centre (Dr Wilcock), British Psychosocial Oncology Society (Dr Calman) and the CRUK's New Agents Committee & Exploratory Research Panel (Prof Blackhall).

#### **Interaction with cross-cutting groups**

CSG and subgroup member continue to increase the links with NCRI cross-cutting Groups. Dr Navani is a clinical lead for the National Lung Cancer Audit and there are close links with the SPED Advisory Group (chaired by Professor David Baldwin, previous Lung CSG member), Supportive & Palliative Care CSG (Chair, Professor Sam Ahmedzai), Primary Care CSG (Chair, Professor Richard Neal), CTRad (Dr Fiona McDonald) and the Psychosocial Oncology & Survivorship CSG (Dr Lynn Calman), CM-Path (Professor Blackhall) with complimentary attendance at the CSG meetings. 4 our CSG members are currently serving as Lung Sub-Speciality Leads (SSLs). A number of other lung SSLs attended and contributed to our strategy meeting.

These links have facilitated a number of successful applications; among the best examples of these collaborations are the lung cancer screening studies which are now open to recruitment.

#### **Key research priority areas**

##### **Living with and Beyond Cancer**

These research priorities were a focus of the recent strategy meeting and we would plan to run a workshop over the coming year to focus on their implications for lung cancer patients.

##### **Surgery/Radiotherapy**

The PEARLS adjuvant trial will close to recruitment in November 2019, and the LORD subgroup will be exploring research opportunities for investigator led studies around neo-adjuvant treatment. Improving fitness for radical treatment remains a priority development area for the CSG with the opportunity to tie in LWBC workshop giving a number of investigators bringing forward early outlines (eg The Northern Early Lung Cancer Study).

##### **Early phase**

A number of the Group are members of the ECMC network with funded proposals of new drug trials in lung cancer now recruiting. The most recent call form expressions of interest for the Combinations Alliance included 3-4 for lung cancer studies. The MATRIX study continues to recruit steadily and amendments have extended the number of new drug study arms molecularly-defined cohorts on the platform. The working party for radiotherapy-drug combination trials is developing a platform for radiation new drug combinations (CONCORDE / SPITFIRE).

### **Advanced disease**

The Lung CSG has held workshops for brain metastases (EDAM), palliative radiotherapy (TOURIST) and SCLC research. Study outlines will be developed under the wing of the Advanced Disease subgroup to take studies through to funding applications. Efforts to develop a high recruiting immunotherapy study are ongoing and focus on CONVOLUTE (investigating schedules/duration of PD-1 targeted treatment).

### **Raising awareness and profile**

The Lung Annual Trials Meeting is now an established part of the lung cancer calendar with the program for 2019 meeting in May finalised with sponsorship support. The close working relationship we enjoy with BTOG continues to give a strong presence at the Dublin meeting and the opportunity to present our portfolio and trial outlines in development.

We successfully launched our NCRI Lung Cancer Trial Badging scheme with 7 investigator lead studies now register as UK NCRI Lung Cancer Studies. The worth of the portfolio maps is debated in each CSG meeting. With Lung CSG members becoming increasingly adept at using social media we have engaged with Roy Castle Lung Cancer Foundation / Mesothelioma UK to explore the development of the maps into apps etc that could improve access for both public and professionals.

The significant workload engendered by NICE evaluations continued over the past year and the CSG Chair is extremely grateful that members continued to willingly offer their expert, voluntary support for that process.

### **Patient and Public Involvement and Impact**

Our PPI representatives have continued to be incredibly active, accepting the opportunity to become involved in a number of the studies being developed through the CSG and advising investigators presenting their ideas at our trials meetings. We particularly acknowledge the contribution of Janette Rawlinson who has just stepped down from the group.

Their involvement has continued to shape our agenda championing the need for studies considering every stage of the patient journey including living with and beyond cancer as we are seeing more non-smokers with disease and long-term survivors.

Our PPI reps are also conscious that they are advocating on behalf of the whole lung cancer patient community and have been very supportive of studies such as the Yorkshire Lung Screening Trial targeting the difficult to reach population.

### **Strengthen UK wide and international working**

BTOG has a key role in promoting and supporting lung cancer research and the nurturing of the relationship remains a key strategy goal in engaging the wider lung cancer community in planning and delivering our research portfolio.

The flagship studies on our portfolio attract international attention publishing in high impact journals. The work with other research groups has led to CSG members leading a number of international collaborations with studies that are appearing on our trials portfolio, for example, NIVOTHYM, HALT, SOLUTION and REACTION studies are open / in set up for thymic carcinoma, non-small cell lung cancer and small cell lung cancer patients respectively.

In the December strategy meeting the changing nature of research was discussed with increasing importance on AI development in medium and long term giving opportunities for big data research. The CSG is clear that we need to maintain clear links with NCRAS to exploit routinely collected datasets and build on our current use in assessing feasibility of studies and support analysis of the Lung Cancer Audit data.

## Advanced Disease Subgroup (Chair, Professor Fiona Blackhall)

### **Cerebral metastasis**

Following on from last year's discussions around progressing the development of studies for patients with brain metastases as an area of unmet clinical need, the 'Early Detection of Asymptomatic Metastases by brain imaging in advanced lung cancer patients' (EDAM) study has been proposed. The expertise required for the progression of this study spans both the NCRI LORD and Advanced Disease Subgroups. This study is currently being developed by a junior investigator under senior investigator supervision in order to encourage the education and engagement of the next generation of researchers.

The EDAM study concept and design was presented at the NCRI satellite symposium session at the British Thoracic Oncology Group (BTOG) Annual Meeting in January 2019. Audience feedback to guide further protocol evolution was obtained as part of an interactive session. Overall 75% of the audience felt that the results of this trial could be practice changing and 81% indicated that they would be happy to open and recruit to the study at their site. The specific audience feedback is currently being incorporated into the study protocol with expert guidance from both the Advanced Disease and LORD subgroup members.

### **Continue work with international groups (ETOP, EORTC) collaboratively on key academic research questions to address other gaps in the portfolio**

The Advanced Disease Subgroup has strong representation across international groups. Dr Popat is an active member of the EORTC and serves on the Foundation Council of the ETOP group. Professor Blackhall is an active member of the ETOP lung group. While Dr O'Brien chairs the LORD subgroup and is no longer a member of the Advanced Disease subgroup, relationships remain strong. The two groups are working collaboratively on the EDAM brain metastases study, with Dr O'Brien acting as CI. Dr O'Brien is a member and past chair of the EORTC lung cancer group and this linkage will be key to advancing the EDAM project (in addition to other flagship studies) on the international stage.

In partnership with the EORTC the NIVOTHYM, SOLUTION and REACTION studies have now been set-up for thymic carcinoma, non-small cell lung cancer and small cell lung cancer patients respectively. These studies address the role of maintenance immunotherapy and include a strong translational research component. Work with the EORTC will now focus on ensuring optimal recruitment to these studies. With ETOP, discussions are currently being held to design studies with a molecular profiling component for large cell neuroendocrine cancer as this cancer subtype is recognised as an area of unmet need.

### **Continue rotation of membership through the Subgroup including succession planning for the Chair**

This year the membership of the subgroup has been renewed with a focus on broadening the expertise and geographical reach of the group. Dr Lynn Calman has been welcomed to the group and is an expert in the field of Patient Centred Research in Southampton. Dr Robin Young has been welcomed from Sheffield. The devolved nations are also represented with Dr Hannah Lord and Dr Jason Lester being active members from Dundee and Cardiff respectively. The focus of the group is now on succession planning for the future by engaging with and educating the next generation of researchers. The EDAM and TOURIST trials are moving forwards

with junior researchers leading on the projects under the supervision of senior investigators. This model of working will be actively encouraged by the Advanced Disease subgroup over the next year.

## **LOcoRegionalDisease (LORD) Subgroup (Chair, Dr Mary O'Brien)**

### **Continue to nurture new investigator-led research in early stage lung cancer**

Locally advanced lung cancer has benefitted from a major advance published in 2017 which will increase the impetus to recruit to ongoing studies. The PACIFIC study (a commercial study) showed a positive benefit from immunotherapy given after concurrent chemo-radiation. Our portfolio studies like PACIFIC 4, 6 and PEARLS are now more important to recruit to quickly to answer these important questions on the role of immunotherapy in different situations in patients with local disease.

Translational research is part of most studies but TRACERx, leads on this with the detailed identification and description of (among other things) truncal antigen patterns as lung cancer evolves.

More technical radiotherapy studies opened to recruitment (ADSCaN) and planned platform study (CONCORDE) for novel drugs-radiation combinations continues development. LUNGART has completed its recruitment target, but LUNGTECH has closed early due to reported toxicities.

Surgical studies are ongoing with completion of recruitment to the VIOLET study ahead of schedule. Discussion at BTOG 2019 January was brisk with surgeons getting behind the idea of neoadjuvant studies using immunotherapy as induction therapy to improve cure rates.

### **Continue to refresh the Subgroup as members complete their terms and encourage new researchers**

As new specialities develop more commitment to oncology e.g. acute oncology, acute medicine, geriatrics etc we need to be broad in our membership – this is a general strategy and the LORD Subgroup membership is being updated to help it drive new trial development.

### **Continue to work with international groups (ETOP, EORTC) collaboratively on key academic research questions and develop new research protocols with developing organisations (TACT)**

As detailed in the main Group strategy.

### **Specific areas of LORD interest and development**

Data from the NLCA suggests that only 30% of stage III patients are receiving radical multi-modality therapy. This area is now the subject of a planned audit to dig into the quality of service delivered in the UK.

MR LINAC and Protons will become part of radiotherapy practice in the coming years and the LORD Subgroup plans to help develop the evidence base for these treatments. The changing profile of lung cancer with the development of screening will produce more small cancers. The Stile study is in this zone looking at immunotherapy after SBRT.

## Mesothelioma Subgroup (Chair, Dr Peter Szlosarek)

### **Maintain an emphasis on high quality biomarker drive studies to keep the balances trial portfolio and focus in MPM**

There is a healthy balance of trials in first, second, and third-line plus settings. Greater personalisation with biomarkers/histology-driven trials should be encouraged going forwards.

### **Encourage greater involvement by all sectors of the mesothelioma community and develop closer links with qualitative researcher**

Alongside the Subgroup the Mesothelioma Subgroup membership has been reviewed and refreshed with several vacancies in the Mesothelioma Subgroup expected to be filled in 2018/2019 to ensure the Subgroup is better equipped to develop study ideas.

### **Nurture new talent in mesothelioma research**

We aim to encourage greater involvement by younger investigators interested in a career in mesothelioma translational research via the Mesothelioma Research Network which has support from the BLF.

## Screening & Early Diagnosis Subgroup (Chair, Dr Philip Crosbie)

### **Develop cohesive working and applications with the Primary Care CSG and SPED Advisory Group**

A highlight of the year was the BTOG screening and early diagnosis workshop in January 2018 in Dublin. Professor Richard Neal, Chair of the Primary Care CSG, gave the major presentation on primary research in the early detection of lung cancer. The meeting was attended by Professor David Baldwin, Chair of the SPED Advisory Group.

There have been a number of grant successes in this area – Professor Una Macleod has received funding from Yorkshire Cancer Research (YCR) to fund an ambitious project looking at earlier presentation of lung cancer in primary care. With Professor Mick Peake and primary care colleagues in London, we have received funding from the CRUK early diagnosis advisory group to link primary care data to the cancer registry. This is with the aim of identifying primary care factors and co-morbidities that can affect the diagnostic pathway in primary care.

### **Encourage trials of interventions to reduce tobacco harm**

This remains a key strategic aim for this Subgroup and the Lung CSG as a whole. Some strides forward have been made: Professor Linda Bauld holds a grant from the Roy Castle Lung Cancer Foundation to examine the role of e-cigarettes in aiding smoking cessation in patients undergoing treatment for lung cancer. Dr Matt Callister and colleagues and have received further funding from YCR to examine smoking cessation strategies within a screening trial. The Subgroup would benefit for further expertise on the group in academic tobacco harm reduction research.

**Work with primary care researchers to develop risk prediction models and targeted population lung health checks**

Lung health checks have become a national agenda item and were discussed in Parliament in April 2018. This has led to government funding of targeted lung health checks in selected areas. Academically, the identification of individuals from the population at high risk of lung cancer remains a priority and proposals are being developed for new risk prediction models in collaboration with primary care and international key researchers, led by Professor Baldwin.

**Facilitate research into optimising lung cancer screening, e.g. recruitment, scanning interval and nodule management**

This remains an important priority for this subgroup and important progress is being made with this being a particular strength in the portfolio. The lung screen uptake trial aims to optimise recruitment strategies by comparing invitation strategies and has developed a prizewinning film for participants.

The UK has world leading research ongoing in lung cancer screening including the Yorkshire Lung Screening Trial and the SUMMIT trial in London which aims to recruit 75,000 participants. The SUMMIT trial will examine the role of circulating tumour DNA in early detection of cancers and also have a randomisation to clarify CT screening interval. Sub-studies will look at radiological aspects of screening including nodule management and co-morbidities, particularly coronary artery calcification.

**Develop closer links with qualitative researchers**

Many trials within the portfolio have developed important qualitative aspects. For example, the Lung screen uptake trial seeks to investigate the psychological burden and barriers to screening working with qualitative experts. Dr Calman has been an important addition to the Subgroup bringing her qualitative expertise to the group and to each application.

#### **4. Task groups/Working parties**

**Remit of Lung Cancer Radiotherapy-Drug Combinations Consortium Working Party**

The Lung CSG worked with CTRad to set up a Working Party which has been established to develop a UK research program for radiotherapy new drug combinations in NSCLC (non-small cell lung cancer) in 2016.

The Working Party has developed an outline from two platform studies: in stage III NSCLC, we will focus on the addition of new drugs to radical radiotherapy fractionations in stage III disease (Concorde) and in stage IV disease to explore immunotherapy/stereotactic radiation combinations (Spitfire). Trial Management Groups with membership from clinical and medical oncology have been established and draft protocols presented and discussed at a number of National and International meetings. Funding applications were submitted in 2017/18.

### **Progress to date**

#### **CONCORDE**

Updated outline submitted to CRUK CRC in September 2018 and invited to full application January 2019. Positive peer-review feedback received with CRUK panel interview on 9<sup>th</sup> April and decision on funding expected on 16<sup>th</sup> May 2019

1. AstraZeneca and Merck have given top-line agreements to fund 5 arms including inhibitors of PARP, ATR, WEE-1, DNA-PK and ATM.
2. Expansion of the TMG to include a pre-clinical expert as joint lead-applicant Professor Ryan (Oxford), an additional trainee Dr Walls (Belfast) and two early career researchers as study arm leads Dr Hudson (Manchester) and Dr Hiley (University College London).
3. Replacement of Dr Hanna as Clinical Oncology Chief Investigator by Professor Faivre-Finn due to emigration of Dr Hanna to Australia
4. Agreement with EORTC lung Group to be a preferred partner of CONCORDE in planning registration studies as agents emerge from the platform
5. Translation Program agreed with planned submissions for funding during 2019

#### **SPITFIRE**

Multi-arm phase II design proposed in patients with resistance to initial single agent PD1/L1.

Outline submitted to CRUK CRC in September 2018, not invited to full application because of concerns of concerns about the immaturity of treatment data in this setting.

## 5. Funding applications in last year

**Table 2 Funding submissions in the reporting year**

<b>Cancer Research UK Clinical Research Committee (CRUK CRC)</b>					
<b>Study</b>	<b>Application type</b>	<b>CI</b>	<b>Outcome</b>	<b>Level of CSG input</b>	<b>Funding amount</b>
<b>May 2018</b>					
LungMatrix: Multi-drug, genetic marker-directed, non-comparative, multi-centre, multi-arm phase II trial in non-small cell lung cancer	Late Phase Study	Professor Gary Middleton	Supported	Members of CSG on TMG	
<b>November 2018</b>					
A phase II trial of CYC065 in patients with MYC-amplified small cell lung cancer	Clinical Trial Award	Prof Sarah Danson	Not supported	Review / Advice during study development	NA
A phase II/III randomised trial of pembrolizumab in patients with advanced malignant pleural mesothelioma	Clinical Trial Award	Professor Gareth Griffiths	Conditionally Supported	Review / Advice during study development	
Phase I study combining the tumour hypoxia modifier atovaquone with radical chemoradiotherapy in locally advanced NSCLC	Clinical Trial Award	Dr Geoff Higgins	Conditionally supported	Review / Advice during study development	
CONCORDE - NSCLC: Platform study of novel agents in COmbinatioN with COnventional RaDiothErapy in locally advanced disease	Clinical Trial Award Outline	Dr Alastair Greystoke	Invited to full	Lung CSG Working Party	TBC
<b>Other committees</b>					
<b>Study</b>	<b>Committee &amp; application type</b>	<b>CI</b>	<b>Outcome</b>	<b>Level of CSG input</b>	<b>Funding amount</b>

Lung MRI for risk stratification to select non-small cell lung cancer patients for radical treatment.	YCR 2018 Funding Round "Saving 2000 lives a year in Yorkshire by 2025"	M Hatton / J Wild	Supported	CI member of Lung CSG, Review / Advice during study development	£390K
PREHABS: Prehabilitation Radiotherapy Exercise smoking Habit cessation and Balanced diet Study	YCR 2018 Funding Round "Saving 2000 lives a year in Yorkshire by 2025"	K Franks & C Burnett	Supported	CSG developed	
AZTEC - Does Azithromycin improve the response to platinum-based chemotherapy in advanced non-small cell lung cancer? A randomised controlled phase I/II trial	Anticancer Fund.	Dr Wilcock / Prof Billingham	Not Supported	Developed by members of Lung CSG	NA
The management of oligo metastatic disease	Macmillan Research Grants	Calman et.al	Not Supported	CI member of Lung CSG,	£146k
Understanding the needs of lung cancer patients on immunotherapy			Not Supported		£250K
Understanding the needs of cancer patients living in areas of deprivation			Not Supported		£120k
Supporting physical activity in lung cancer patients through development of an app	NIHR RFPB	Calman et.al	Not Supported	CI member of Lung CSG,	£241k

## 6. Consumer involvement

Core consumer members, Tom Haswell and Janette Rawlinson actively contributed to the CSG's and wider lung cancer research community's work, aided by Mat Baker on the LORD Subgroup. Tom and Janette became BTOG steering committee members and hold roles on CRUK's Stratified Medicine Programme board and Lung Matrix Trial Management Group.

They attended Group meetings, conferences, Consumer Forum meetings giving PPI feedback and the Annual Lung Trials meeting. Strategic aspects included awareness raising, screening, early diagnosis, quality of life, treatment modes/combinations, patient participation, collaboration with other CSGs and general trial feedback.

Conference attendance included NCRI, BTOG, Britain Against Cancer, ECMC, ESMO, EORTC survivorship summit, Precision Medicine Congress, Royal Marsden, CRUK LC Centre of Excellence and PHE/NCRAS Cancer Outcomes, Early Diagnosis Conference.

Janette completed her tenure on the CSG and is now a member of the Advanced Disease Subgroup and will no doubt continue her involvements in lung cancer both nationally and internationally. Mat has been working with Kings College linking National Cancer Patients Experience Survey with the Cancer Registry. Tom was a member of NICE Lung Cancer Guidelines Review Committee and is also a member of the NICE Lung Cancer Quality Standards Expert Committee.

The consumer members are actively involved in clinical trials sitting on TMG's and TSC's as well as being co applicants, co investigators, collaborators and advisors on trials such as Matrix, ADSCAN, CORE, CONCORDE. They are also very much involved with numerous other organisations, groups and committees where they spread the word about NCRI and its use of consumers as well as promoting consumer involvement and PPI within these groups.

There are also international involvements including Cochrane Reader, EORTC Study Reviewer, member of Boehringer Ingelheim International Lung Cancer Patient Advisory Group.

Measuring impact can be difficult however the consumers input is continually requested, and their comments and suggestions are frequently added to study proposals.

Advice, support, information is always made available on request from the CSG membership for which the consumers are much appreciative.

## 7. Priorities and challenges for the forthcoming year

<b><u>Priority 1</u></b> To develop the outlines from the three workshops (SCLC, Brain metastasis, Palliative radiotherapy) into funding submissions
<b><u>Priority 2</u></b> Strengthen Subgroup membership and structure to better support ongoing trial development
<b><u>Priority 3</u></b> To promote the Living With and Beyond Cancer research priorities across the lung cancer trials portfolio.
<b><u>Challenge 1</u></b> Increasing costs, funding competition and limited infrastructure within the NCRI CRN leading to significant delays in trial set up and opening of centres.
<b><u>Challenge 2</u></b> The running of academic studies with increasing pressures from commercial studies for limited trial infrastructure
<b><u>Challenge 3</u></b> The changing treatment landscape (advent of immunotherapy) and increasing molecular subtyping makes treatment studies more focused on small populations of patients and having adequate delivery resource at CRN level to deliver complex biomarker-directed studies.

## 8. Collaborative partnership studies with industry

The Lung Cancer trials portfolio contains a significant number of industrial studies which challenges the development of investigator lead studies in some areas of our portfolio e.g. immunotherapy.

However, there is strong support from industry for some of our flagship studies and there has been a strong relationship and support for our Novel Drug Radiation Working Party developing both the CONCORDE and SPITFIRE studies. There has also been support for concepts put forward through the Cancer Alliance (Danson et al) though the application was not supported and is now seeking funding through other channels.

## 9. Appendices

Appendix 1 - Membership of Lung Group and Subgroups

Appendix 2 – Lung Group and Subgroup strategies

A – Lung Group Strategy

B – Advanced Disease Subgroup Strategy

C – LocoRegionalDisease (LORD) Subgroup Strategy

D – Mesothelioma Subgroup Strategy

E – Screening & Early Diagnosis Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

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

**Professor Matthew Hatton (Lung Group Chair)**

## Appendix 1

### Membership of the Lung Cancer Group

<b>Name</b>	<b>Specialism</b>	<b>Location</b>
Dr Miranda Ashton*	Clinical Oncologist	Glasgow
Dr Kevin Franks	Clinical Oncologist	Leeds
Prof Matthew Hatton (Chair)	Clinical Oncologist	Sheffield
Dr Fiona McDonald	Clinical Oncologist	London
Mr Tom Haswell	Consumer	Glasgow
Professor Samreen Ahmed	Medical Oncologist	Leicester
Dr Alastair Greystoke	Medical Oncologist	Newcastle
Dr Thomas Newsom-Davis	Medical Oncologist	London
Prof Mary O'Brien	Medical Oncologist	Sutton
Prof Fiona Blackhall	Medical Oncologist	Manchester
Professor James Spicer	Medical Oncologist	London
Prof Peter Szlosarek	Medical Oncologist	London
Dr Andrew Wilcock	Palliative Medicine/Medical Oncology	Nottingham
Professor William Wallace	Pathologist	Glasgow
Dr James O'Connor	Radiologist	Manchester
Dr Philip Crosbie	Respiratory Physician	Manchester
Dr Neal Navani	Respiratory Physician	London
Dr Mamta Ruparel*	Respiratory Physician	London
Dr Lynn Calman	Senior Research Fellow	Southampton
Mr Nicholas Counsell	Statistician	London
Mr Babu Naidu	Thoracic Surgeon	Birmingham

\* denotes trainee member

## Membership of the Subgroups

<b>Advanced Disease Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
Dr Kevin Franks	Clinical Oncologist	Leeds
Dr Jason Lester	Clinical Oncologist	Cardiff
Dr Hannah Lord	Clinical Oncologist	Dundee
Professor Samreen Ahmed**	Consultant Oncologist	Leicester
Mrs Janette Rawlinson	Consumer	Birmingham
Dr Lynn Calman	Health Service Researcher	Southampton
Prof Fiona Blackhall (Chair)	Medical Oncologist	Manchester
Dr Carles Escriu**	Medical Oncologist	Liverpool
Professor Gary Middleton	Medical Oncologist	Birmingham
Dr Sanjay Popat	Medical Oncologist	London
Professor James Spicer	Medical Oncologist	London
Dr Robin Young	Medical Oncologist	Sheffield
Dr Riyaz Shah	Medical Oncologist	Kent
Dr Andrew Wilcock	Palliative Medicine/Medical Oncology	Nottingham
Professor Lucinda Billingham	Statistician	Birmingham

<b>LOCoRegionalDisease (LORD) Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
Dr Corinne Faivre-Finn	Clinical Oncologist	Manchester
Dr Susan Harden**	Clinical Oncologist	Cambridge
Dr Fiona McDonald**	Clinical Oncologist	London
Dr Fiona Taylor**	Medical Oncologist	Sheffield
Professor Samreen Ahmed	Medical Oncologist	Leicester
Mr Matthew Baker	Consumer	Manchester
Dr Thida Win**	General Medicine	Stevenage
Dr Sherin Payyappilly	Histopathologist	Birmingham
Dr Donna Graham**	Medical Oncologist	Belfast
Dr Thomas Newsom-Davis	Medical Oncologist	London
Professor Mary O'Brien (Chair)	Medical Oncologist	London
Ms Lavinia Davey	Nurse	
Dr Richard Booton**	Respiratory Physician	Manchester
Ms Karen Harrison-Phipps**	Surgeon	London
Mr Babu Naidu	Surgeon	Birmingham
Mr David Waller	Surgeon	Leicester

<b>Mesothelioma Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
Dr Peter Jenkins	Clinical Oncologist	Gloucester
Professor Mike Lind	Clinical Oncologist	Hull
Dr John Conibear	Clinical Oncologist	London
Dr Patricia Fisher	Clinical Oncologist	Sheffield
Dr Michael Snee	Clinical Oncologist	Leeds
Dr Alfredo Addeo	Medical Oncologist	Bristol
Professor Dean Fennell	Medical Oncologist	Leicester
Dr Jeremy Steele**	Medical Oncologist	London
Prof Peter Szlosarek (Chair)	Medical Oncologist	London
Dr Robert Rintoul	Respiratory Physician	Cambridge
Mr John Edwards	Surgeon	Sheffield
Mr David Waller**	Surgeon	Leicester

<b>Screening &amp; Early Diagnosis Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
Professor Paul Aveyard	Behavioural Medicine	London
Professor Richard Neal	General Practitioner	Oxford
Professor John Field	Molecular Oncologist	Liverpool
Dr Anand Devaraj**	Radiologist	London
Professor David Baldwin	Respiratory Medicine	London
Dr Philip Crosbie (Chair)	Respiratory Medicine	Manchester
Dr Frank McCaughan	Respiratory Medicine	Cambridge
Dr Neal Navani	Respiratory Medicine	Cambridge
Dr Mick Peake	Respiratory Physician	Leeds
Dr Robert Rintoul	Respiratory Physician	Cambridge

\* denotes trainee member

\*\*denotes non-core member

## Appendix 2

### Lung Group & Subgroup Strategies

#### A – Lung Group Strategy (2015 – 18)

Strategic objective	Action	CSG Lead	Date	Outcomes
1e. Portfolio development – Meso subgroup	Ensure cohesive strategy for meso thelioma clinical trials, taking into account: <ul style="list-style-type: none"> <li>- Opportunities within the international agenda,</li> <li>- Balance between late and early phase studies</li> <li>- Multicentre studies with good regional coverage</li> <li>- All disease stages</li> <li>- Transitional subgroups</li> <li>- Supportive care studies</li> <li>- Interaction with CRN subspecialty leads</li> </ul>	PS  MN, GM, TY, JR  JM, LB, DR	Identified at Strategy Day 27 Nov 15  Progress review 6 monthly at CSG meetings	Annual meeting / workshops to identify new studies / leads to fill gaps in portfolio.  Radical third line treatment
1f. Interaction with (inter)national research groups	Identify leads within the CSG to link with the following research groups:  IMIG EORTC ETOP BTOG ITMIG TACT	DF  SP  MN	Mar 2016	To keep under review at 6 monthly CSG meeting
1g. Interaction with Cross Cutting groups	Identify leads within the CSG to link with the following cross cutting CSGs and advisory groups:  •Primary Care CSG •Screening, Prevention and Early Diagnosis (SPED) Advisory Group •CTRAD •Supportive and Palliative Care CSG	DB MF	Mar 2016	To keep under review at 6 monthly CSG meeting
1h. National Cancer Intelligence Network (NCIN)	Establish clear link with Lung Cancer Clinical Reference Group  Maintain clear links with NCIN the use of data to inform study design and take over long term follow-up	NN / ALL	Report 6 monthly at CSG meeting	Invite NCIN Lung Cancer CRG Chair to attend next CSG meeting

## B – Advanced Disease Subgroup Strategy

### Aims

- To continue to develop academically-led studies in Brain Metastases
- Continue to work with international groups (ETOP, EORTC) collaboratively on key academic research questions to address other gaps in the portfolio, e.g. SCLC, the PS2 population.
- To continue succession planning for the future. New studies will be encouraged to be developed by junior investigators under the supervision of senior investigators in order to engage and educate the next generation of researchers.
- To develop biomarker directed academically-led studies in SCLC. A SCLC working group is currently being set-up. The remit of the group is to establish a translational UK-wide network directing SCLC patient samples towards leading experts in biomarker and genomic sciences to identify novel targets for therapeutic intervention. This ‘network’ will be developed in the form of a platform style clinical trial. It is hoped that when the SCLC network infrastructure is established, there will be opportunity to collaborate with Pharmaceutical companies to direct new agents currently under development towards newly identified subpopulations of SCLC patients within the network. As such the SCLC Working Party would also be established as a forum to include representatives from SCLC hotspots within the UK which could be approached by Pharma and non-commercial entities developing new agents for clinical trial, and advise on where trials would be best placed based upon the local patient populations.
- To promote the addition of Living With and Beyond Cancer nested studies to new treatment trials or the development of stand-alone studies within this research area.
- To focus on promoting and progressing key ‘*flagship studies*’ in terms of recruitment and protocol development respectively. Key flagship studies are highlighted in the below table:

STUDY THEME	STUDY NAME	CURRENT STATUS
Translational Research	TRACERx	Actively Recruiting
	PEACE	Actively Recruiting
NSCLC Advanced Disease	SMP2 & National Lung Matrix Trial	Actively Recruiting
	SARON	Actively Recruiting
	HALT	Actively Recruiting
	PePS2	Recruitment Complete – manuscript under preparation
	CONVOLUTE	Protocol under development
	EDAM	Protocol under development

	ARROW	Protocol under development
	TOURIST	Protocol under development
<b>SCLC Extensive Disease</b>	Study 15	Actively Recruiting
	DISCOVER SCLC	Protocol under development

### **C – Loco-Regional Disease (LORD) Subgroup Strategy**

- Continue to expand research in early stage lung cancer, particularly related to new radiotherapy combinations (immunotherapy and targeted agents) and support protocol development and funding applications.
- Continue to work with international groups (ETOP, EORTC) collaboratively on key academic research questions and develop new research protocols with developing organisations (TACT) in adjuvant and neoadjuvant therapy.
- To audit treatment in stage III disease and collect data for PACIFIC 4.
- To develop MR LINAC / proton therapy protocols.

## **D – Mesothelioma Subgroup Strategy**

The next year promises to be an active period with the following opening across the UK as follows: (1) CHECKMATE 743 study of IPINIVO versus PEMPLATINUM in first-line disease, (2) CONFIRM (CRUK) study of nivolumab versus placebo in patients with third-line mesothelioma and beyond, (3) PROMISE-ETOP, a study of the immunotherapy agent pembrolizumab versus gemcitabine/vinorelbine in second-line disease (academic Anglo-Swiss Study) and (4) ATOMIC-meso assessing the role of ADIPEMCIS versus PEMCISplacebo in non-epithelioid mesothelioma. An emphasis on hypothesis-driven studies will fuel our overall strategy going forwards.

With a number of new studies opening, the Subgroup will work to continue deliver on trial recruitment with further engagement with the regional lung cancer leads.

### **Aims**

- To maintain an emphasis on high quality biomarker drive studies to keep the balanced trial portfolio and focus in MPM.
- To encourage greater involvement by all sectors of the mesothelioma community and develop closer links with qualitative researchers.

## **E – Screening & Early Diagnosis Subgroup Strategy**

The research landscape will be shaped by the results of the influential NELSON randomised trial of CT screening for lung cancer expected in 2017. Research strategy will then be shaped by a decision on lung cancer screening by the national screening committee.

The key strategic aims in the coming years remain:

- Develop cohesive working and applications with the Primary Care CSG and SPED Advisory Group.
- Encourage trials of interventions to reduce tobacco harm.
- Work with primary care researchers to develop risk prediction models.
- Facilitate research into optimising lung cancer screening, e.g. recruitment, scanning interval and nodule management.
- Develop closer links with qualitative researchers.

## Appendix 3

### Portfolio maps

NCRI Portfolio Maps									
Lung Cancer									
Map A – Local Regional Disease - Small cell and Non-small cell									
ê below to reset map									
		a) Risk factor / screening	b) Adjuvant / neoadjuvant	c) 1st line treatment	d) 1st line maintenance	e) 2nd line treatment	f) 3rd line treatment	g) Palliative / quality of life / observational	
Local Regional Disease - Small cell and Non-small cell	All							EARLY Project	
								Video assisted	
			PEARLS						DARWIN2
				AST-VAC2 vaccine in		nivolumab and ipilimumab in			
				Keynote-671			of E7386 in patients with		
			ADSCaN.						STILE V1
				KEYNOTE-799			AMG757 in Subjects with		
				PACIFIC 4					in Lung Cancer Patients
					Phase 3 study in stag				Non-Invasive Ventilation for
								CA209-73L in LA NSCLC	

**Filters Used:**

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

- Open / single rese..
- In Setup / single re..



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# NCRI Portfolio Maps

## Lung Cancer

### Map B – Mesothelioma

↻ below to reset map

		a) Risk factor / screening	b) Diagnosis	c) 1st line treatment	d) 1st line maintenance	e) 1st line relapsed	f) 2nd line treatment	g) 3rd line treatment	h) Palliative / quality of life / observational	
Mesothelioma	All			MARS2					EIM	
									MesoTRAP feasibility study	
							CONFIRM			
				ATOMIC-Meso Phase 2/3 Study						SYSTEMS/2
										ASSESS-meso
		TILT								
							(EORTC 08112-LCG)			
				TR301MPM						novel immunotherapy
								Mesothelioma Stratified Therapy (MiST)		
										PRISM
										patients' experiences of
						MESO-PRIME				Meso-ORIGINS
							DENDritic cell Immunotherapy			

**Filters Used:**

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

- Open / single rese..
- In Setup / single re..



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# NCRI Portfolio Maps

## Lung Cancer

### Map D – Advanced Disease - Non-small cell: Biomarker selected

⌵ below to reset map

		a) 1st line treatment	b) 1st line maintenance	c) 2nd line treatment	d) 3rd line treatment	e) Supportive care / observational	
Biomarker	Alk	Pfizer B7461006 NSCLC					
	EGFR	IIIb/IV biomarker positive,			National Lung Matrix	National Lung Matrix	
		DARWIN1					
					T790M/NSCLC after		
					with EGFR wild-type in		
		MK3475-789					Ab,JNJ-61186372, in Non-Small Cell Lung
	KRas				National Lung Matrix	National Lung Matrix	
		VS-6063 and RO5126766					
	Other				National Lung Matrix	National Lung Matrix	
		ATOMIC-Meso Phase 2/3 Study					PEACE
		B7661001- additional arm					NEOlung
		Pembrolizumab Based					
		Pembrolizumab n					
		SCLC-0456/0146-Regeneron					PD-RAD
		Adjuvant Platinum-Based					
				ADC for tissue factor, Tisotumab Vedotin			
			LU177SSTR2 - somatostatin receptor				
					Non-Invasive Ventilation		

**Filters Used:**

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

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- In Setup / multi res..
- Open / multi resea..
- Suspended / singl..



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# NCRI Portfolio Maps

## Lung Cancer

### Map E – Screening and Early diagnosis /Other

↻ below to reset map

		Post-diagnosis	Pre-diagnosis
Biomarkers	All	LLP	LLP
		CLUB	
		Tumour Angiogen	
		Pleural effusion biomarker study	
		TRACERx	
		Quant of neutrophil	Quant of neutrophil
		Predicting drug	
		INVEST	
Data collection/observational	All	Characterising the Lung cancer Inflammatory response	YLIST: Biomarker sub-study
		LungCAST	
		TargetLung	
		BMS-986016 +/- BMS-936558 in Adv. Solid Tumour	
		Respiratory Distress Symptom Intervention (RDSI)	
		Exploring RATS for lung cancer V1	
		EARL	
		Development of patient derived xenografts (PDXs) for lung cancer. Clyz CanCertain Assay V1.3	
Diagnosis / imaging	Null	ICI Genetics	TARGET
	All	CR UK Stratifie	PLUS 1: Pharmacy referral for lung cancer symptoms
			CR UK Stratifie
			EARLY Project
			LuCID: Lung Cancer Indicator Detection
		VOCs in Lung Cancer	
		SPECTALung (EORTC 1335)	
		Peripheral detection of EGFR status in lung cancer patients	LUSH (Lung Symptom awareness and Health)
			The Yorkshire Lung Screening Trial
			SUMMIT Study
	IDEAL	IDEAL - prospective	
Quality of life / Supportive..	All	ImageILD (EORTC 1658-IG)	PEOPLE-HULL Study: Improving help-seeking for lung symptoms in H
		Rehabilitation	TIPS
		Exercise Regime	
		SIMPLE	
		The MENAC Trial	
		FACT: Factors Associated with lung Cancer Trial	
		The EXHALE 1B Study	
Treatment /Pharmacology	All	YESS	
		Tactical	
		UVEA-Brig	
		NAVABLATE	

**Filters Used:**

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

- In Setup / multi res..
- Open / multi resea..
- In Setup / single re..
- Open / single rese..



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# NCRI Portfolio Maps

## Lung Cancer

### Map F – Advanced Disease - Small cell

⌵ below to reset map

		a) Risk factor / screening	b) Adjuvant / neoadjuvant	c) 1st line treatment	d) 1st line maintenance	e) 2nd line treatment	f) 3rd line treatment	g) Palliative / quality of life / observational	
Advanced Disease - Small cell	All							PEACE	
				A multicentre, randomised trial comparing combination		MERU			
				Phase 1/2a to assess PEN-221 in receptor 2 expressing				HALT - Stereotactic Body Radiotherapy for the treatment of	
				Combination therapy with Isatuximab in solid tumour A Phase I/IIa trial of BT 1718 in patients with advanced solid					
				BP40234: RO6874281 in combination with atezolizumab in Rucaparib Hepatic Impairment Study in Patients with a					
				BGB-290-103 A Phase 1b Study of BGB-290				C2321001	
				REACTION (EORTC 1417-LCG)					
									MATTERHORN
									Rapid Shallow Non-Invasive Ventilation for Radiotherapy
								LY3295668 erbumine in extensive-stage small-cell lung	

**Filters Used:**

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

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- Open / single rese..
- In Setup / multi res..
- Open / multi resea..



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## Appendix 4

### Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Rosenthal R et.al on behalf of The TRACERx Consortium. <a href="#">Neoantigen directed immune escape in lung cancer evolution Nature 2019 ;567:79-485</a>	Increasing understanding of role of the immune system in development of NSCLC.	CSG members involved in the development, management and recruitment in the study.
2. Lindsay CR et.al <a href="#">Somatic cancer genetics in the UK: real-world data from phase I of the Cancer Research UK Stratified Medicine Programme. ESMO Open. 2018 Sep 5;3(6):e000408. doi: 10.1136/esmoopen-2018-000408. eCollection 2018.</a>	This study provided the basis for our flagship studies SMP2 and MATRIX and we expect presentation / publication of first results from these studies later this year.	CSG members involved in the development, management and recruitment in the study.
3. Bayman N et al. <a href="#">Prophylactic irradiation of tracts (PIT) in patients with pleural mesothelioma: results of a multicentre phase III trial. JCO Published on line. Mar 2019 DOI: 10.1200/JCO.18.01678</a>	Practice changing study confirming that prophylactic irradiation of biopsy tracts in pleural mesothelioma has no benefits.	CSG members involved in the development, management and recruitment in the study.

<p>4. Salem A, et.al. <a href="#">Association of Chemoradiotherapy With Outcomes Among Patients With Stage I to II vs Stage III Small Cell Lung Cancer: Secondary Analysis of a Randomized Clinical Trial</a>. JAMA Oncol. 2018 Dec 6:e185335. doi: <a href="#">10.1001/jamaoncol.2018.5335</a>.</p>	<p>Practice changing setting international standard care for radiotherapy fractionation in concurrent chemo-radiotherapy for SCLC.</p>	<p>UK Led international study with CSG members involved in the development, management and recruitment.</p>
<p>5. Putora PM et.al. <a href="#">Prophylactic cranial irradiation in stage IV small cell lung cancer: Selection of patients amongst European IASLC and ESTRO and experts</a>.</p>	<p>One of a series of European Expert Consensus papers giving important background for studies being developed through the CSG and its subgroups.</p>	<p>4 CSG members involved in these consensus papers.</p>

## Appendix 5

### Recruitment to the NIHR portfolio in the reporting year

In the Lung Group portfolio, 39 no. of trials closed to recruitment and 49 opened.

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

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2014/2015	3396	1236	3074	1236	7.3	2.9
2015/2016	3541	1724	3270	1724	7.76	4.09
2016/2017	5593	2384	5123	2337	12.15	5.54
2017/2018	6501	1958	5145	1886	12.2	4.47
2018/2019	3838	2829	3684	2788	7.94	6.01