

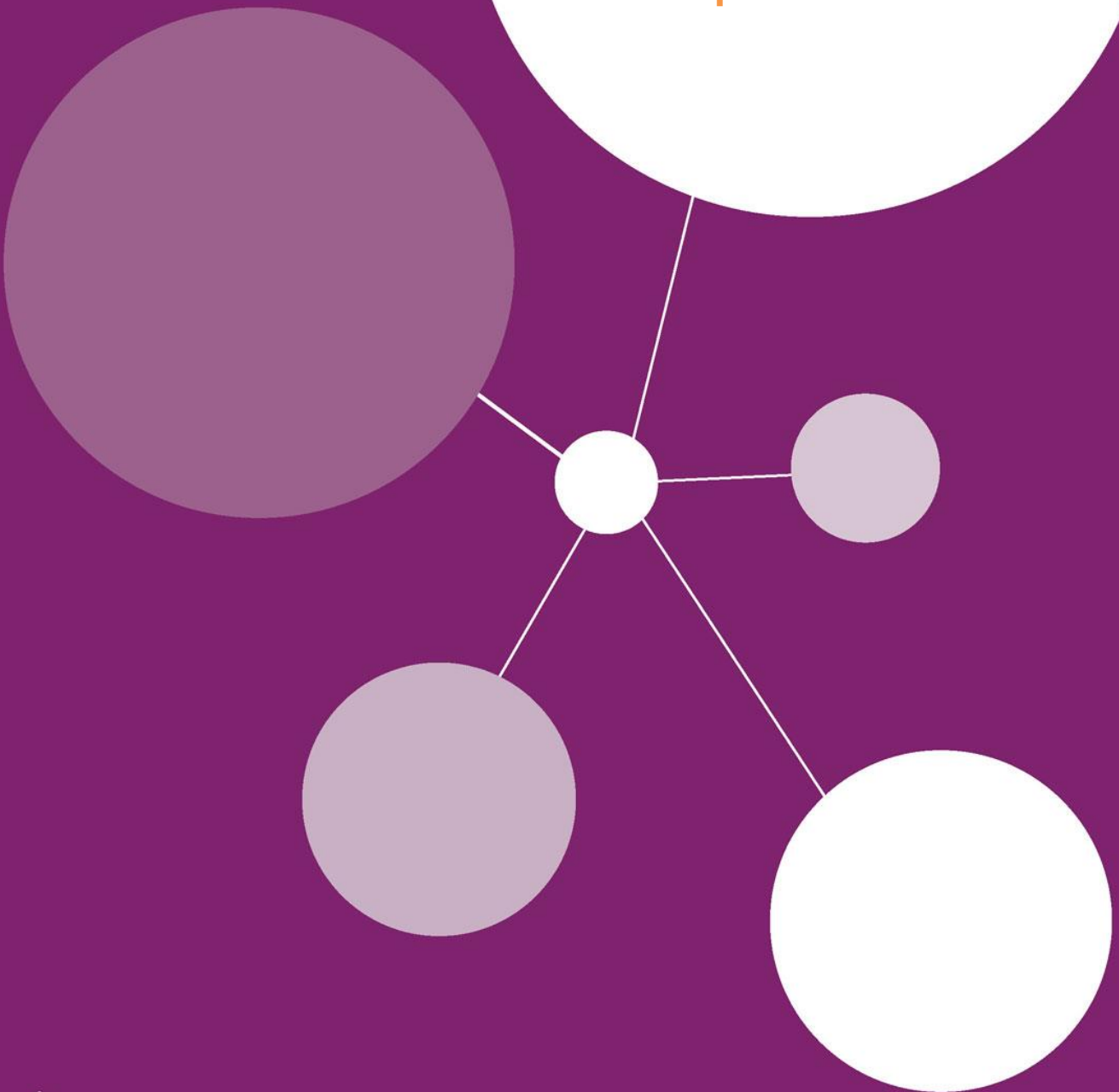


NCRI

National
Cancer
Research
Institute

NCRI Lung Cancer Clinical Studies Group

Annual Report 2017-18



Partners in cancer research



NCRI Lung Cancer CSG Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

The work of the Lung CSG has helped maintain the number of patients accessing the trials portfolio and it is pleasing to see the continued increase in the number of open studies on the portfolio. Members of the Lung CSG continue to lead the development of a number of new study ideas and to contribute to open studies that are at the forefront internationally. These include the Stratified Medicine Programme (SMP) 2, MATRIX and TRACERx, which are recruiting steadily and raising the profile of the UK lung cancer research portfolio. Our consumer representatives continue to excel ensuring the wider engagement and relevance of the Group.

Achievement 2

The CSG has developed its meeting portfolio to increase investigators access to support and advice as they develop their trials ideas. The Lung Cancer CSG Annual Trials Meeting is re-established and our close working relationship with BTOG maintained with the NCRI trials workshops held during their annual meeting in Dublin. We have added a further meeting to our annual schedule, TorchLight, with a faculty able to offer individual support to help investigators develop their trial ideas to the stage where they can go forward to apply for funding. In addition, we have continued to organise workshops addressing specific gaps in our trial portfolio and brought investigators together in early 2018 with the aim of producing study outlines for brain metastases.

Achievement 3

Members have worked to continue to increase the profile of the Lung CSG with agreement to pilot badging investigator lead multicentre studies as UK Lung Study 001, 002 etc. Members maintain strong links with many international groups (e.g. EORTC, ETOP, ELF, IMIG, TACT) and contribute to the development of a number of their trial protocols enhancing the international recognition of the NCRI as a successful trials organisation. CSG members also continue to

regularly volunteer and offer their expert support to NICE evaluations of new drug and applications considered for grant funding.

2. Structure of the Group

Two Subgroup Chairs have rotated off the group (Dr Sanjay Popat and Dr Yvonne Summers) with Professor Fiona Blackhall and Dr Mary O'Brien taking over their roles. New members have maintained a good balance of senior and junior researchers and brought pathology and radiology expertise, strengthening our ability to develop studies and improving ties with the cross-cutting CSGs. The membership within the individual subgroups is being revamped to encourage their development as the drivers of investigator lead trial proposals. Our short-term Lung Cancer Radiotherapy-Drug Combinations Consortium Working Party has made good progress and submitted proposals for funding studies with new drug/radiotherapy combinations.

3. CSG & Subgroup strategies

Main CSG

Portfolio development

The improved recruitment to lung cancer portfolio studies has been maintained, with the increased number in interventional studies particularly pleasing. Lung cancer maintains the third largest number of commercial trials in all the CSGs portfolios, and the sixth largest non-commercial portfolio.

There are 155 trials open to recruitment, of these 68 trials are commercially sponsored with a further 87 non-commercial trials on the portfolio. 41 trials completed recruitment over the past year but there are a further 39 studies in set-up which will maintain the breadth of the portfolio. The portfolio is reviewed at all CSG and Subgroups meetings with a pro-active approach taken to identify and attempt to fill the current (and future gaps) seen in the portfolio.

Maintaining awareness for this number of studies is clearly challenging and CSG members contribute to the regular updating of portfolio maps (Appendix 4b), provided by the NCRI CSG team. However, the worth of the portfolio maps is debated in each CSG meeting and through an ongoing process of improvement we hope they prove of greater use to current and potential investigators, as well as lung cancer specialists and research nurses who may be using them regularly.

Interaction with (inter)national research groups

The CSG has 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 trial; Dr Popat: GEM study; Dr Danson: SPLENDOUR study) active members of our subgroups. The CSG has steering group representation on a number of national and international research group including ETOP, TACT, BTOG and IASLC which enables the Group to host and co-develop studies, notable examples include BELIEF and PROMISE-Meso. The CSG reports back on the functioning of the ITMIG group and is represented by Dr Popat, Regional ITMIG Champion and research group member. Our consumer representative, Ms Janette Rawlinson, is a member of ELF PAG (part of ERS) attending and speaking at international meetings including the EORTC survivorship summit in 2018.

Interaction with Cross Cutting groups

Over the past few years the CSG has built up its links with NCRI cross-cutting Groups. Nationally, Dr Neal Navani is the 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. Four CSG members are currently serving as Lung Sub-Speciality Leads (SSLs) with a joint meeting scheduled for April 2018 to facilitate communication between the CSG and the networks.

These links have facilitated a number of successful applications; among the best examples of these collaborations is with SPED and the Primary Care CSGs for lung cancer screening studies which will be opening to recruitment towards the end of the year. The recent brain metastasis workshop is a further example where a proposal for a cross cutting early detection/imaging will be developed over the coming year.

CSG structure and function

The past year has seen a significant change in membership with 2 Subgroup Chairs, Dr Popat and Dr Summers, stepping down and the appointments of Dr O'Brien as Chair of the LORD Subgroup and Professor Blackhall as Chair of the Advanced Disease Subgroup confirmed. Alongside these changes in leadership we have reviewed too the Subgroup's function and refreshed their membership to enhance their ability to develop studies that help fill the gaps in our current portfolio.

Professor Lucinda Billingham, Dr David Landau and Dr Riyaz Shah also completed their terms of membership of the CSG. Six new members have been appointed (Dr Kevin Franks, Dr Gerry Hanna, Professor James Spicer, Professor Samreen Ahmed, Mr Nicholas Counsell and Professor William Wallace) to maintain the strong statistical and oncological input the group has enjoyed while adding some much-needed pathology expertise.

Our two trainee members, Dr Fiona Taylor and Dr Donna Graham, also completed their term in January. It is very pleasing to see that both are maintaining a continued interest taking on the junior investigator role and inputting into the development of CSG lead non-commercial studies. We look forward to welcoming 2 further trainees to the group in the autumn.

The working party for radiotherapy-drug combination trials has continued to develop two platform studies for patients with stage III and stage IV NSCLC (CONCORDE and SPITFIRE) and with positive feedback from CRUK CRC there are plans to submit for funding over the next 12 months.

Key research priority areas

Surgery/Radiotherapy

The PEARLS adjuvant trial remains the current priority study with strict demand on surgeons to perform appropriate lymph node sampling. Improving fitness for radical treatment remains a priority development area for the CSG with a number of investigators bringing forward early outlines (eg The Northern Early Lung Cancer Study) that we hope can be supported and developed through the Subgroups, TorchLight and Annual Trials meetings.

Early phase

A number of the Group are members of the ECMC network and have funded proposals of new drug trials in lung cancer in set-up or recruiting. These result from successful applications to NAC or CRC, and include Clinical Development Partnerships such as the T-cell engager Tb535 (Professor Spicer) and in the most recent call form expressions of interest for the Combinations Alliance, 3-4 for lung cancer studies. The MATRIX study continues to recruit steadily and has submitted an amendment that further extends the number of new drug study arms molecularly-defined cohorts on the platform. The working party for radiotherapy-drug combination trials is developing a similar platform for radiation new drug combinations (CONCORDE and SPITFIRE).

Advanced disease

The Lung CSG initiated an NCRI workshop in brain metastases in March 2018, when a number of researchers overcame the adverse weather conditions to put forward a number of trial ideas around surveillance for patients with advanced disease and immunotherapy combinations. These investigators will hopefully form the core of a Working Party to develop the ideas further. Efforts to develop a high recruiting immunotherapy study have focused on CONVOLUTE (investigating schedules/duration of PD-1 targeted treatment) but sadly these efforts have yet to gain grant funding.

Translational

Work with members of the Cancer Imaging Centres Network developed the LUCARIO protocol to develop a multi-modality database and translational research platform focused on patients undergoing radical radiotherapy treatment but grant applications over the past year have been unsuccessful.

Smoking cessation research has met with more success with studies funded to examine the role of e-cigarettes in smoking cessation in lung patients and wider examination of smoking cessation strategies within the Yorkshire Lung Screening Trial.

Raising awareness and profile

The Lung Annual Trials Meeting is now re-established with arrangements for our 3rd meeting in June 2018 well advanced. BTOG provided strong support for the initial meetings and feedback from previous meeting has been very positive. There has been continued support from commercial sponsors that has allowed us to develop an independent infrastructure for the planning and running of the meetings going forward. The relationship we have built with BTOG remains strong with NCRI lead workshops as an integral part of their Annual Meeting. In addition, the CSG has continued the annual TorchLight meeting to allow investigators to present to a faculty of experienced lung cancer researchers to help develop their ideas.

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. 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

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. The Lung CSG

members also continue to increase the profile of the group using social media and presentations at national and international meetings.

The flagship studies on our portfolio attract international attention and are starting to publish in high impact journals. We have agreed a system of badging the non-commercial studies on the portfolio with the NCRI secretariat. We feel that naming these studies as NCRI UK Lung (or mesothelioma) studies will enhance the profile of UK lung cancer research and will be contacting Principle Investigators inviting them to register over the coming year.

Advanced Disease Subgroup (Chair, Professor Fiona Blackhall)

Develop academically-led studies in Brain Metastases

The unmet need in studies for patients with brain metastases was discussed at a dedicated study day initiated by the Brain CSG. Several potential studies have been identified and collaboration with colleagues in neuro-oncology initiated. The research themes will be taken forward by the Advanced Disease Subgroup for discussion at the 'Dragon's Den' session of the Lung CSG Annual Trials meeting and for further development at the strategy meeting.

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

The Subgroup has strong representation in the ETOP (Dr Popat, Professor Blackhall) and EORTC (Dr O'Brien) groups. Collaboration with international colleagues is also strong for education and the academic research network. In partnership with EORTC the NIVOTHYM, SOLUTION and REACTION studies are in set up for thymic carcinoma, non-small cell lung cancer and small cell lung cancer patients respectively. The latter address the role of maintenance immune therapy and include a strong translational research component. With ETOP there are several studies currently recruiting and discussions are being held for a study to determine optimal treatment for large cell neuroendocrine cancer according to molecular profiling. There has been no innovation for this histological subtype of lung cancer for decades and a study in this setting would be of high impact.

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

Professor Blackhall, medical oncologist and Professor in thoracic oncology, has been appointed to the chair position and has been a member of the Advanced Disease Subgroup for over 10 years. The Subgroup membership is being renewed with a focus on broadening the expertise of the group (pathology, radiology, statistics, radiobiology and radiotherapy, supportive and palliative care). Professor Blackhall also represents the Lung Cancer CSG on the CM-Path initiative.

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 advanced 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 PARIS 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 is approaching its recruitment target with only 30 more patients needed, but LUNGTECH has closed early in partly due to reported toxicities.

Surgical studies are a current gap but will be addressed by inviting some thoracic surgeons in training to join the Subgroup at the Annual Trials Meeting in June 2018. Surgeons will have to get more involved if the trend back to neoadjuvant studies increases using immunotherapy as induction therapy to explore and optimise timing of local therapy.

Consider earlier involvement with supportive care to develop collaborative research with relevant survivorship questions

This will be readdressed in the 2018/19 strategy with a view to more aggressive documentation of PROs when we are delivering maintenance immunotherapy up to one year.

Incorporate smoking cessation into studies at the development stage

This will reappear in 2018/19 strategy and be incorporated into survivorship issue, smoking cessation, family history and comorbidities as in point above.

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 CSG report.

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 Neal Navani)

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). It is envisaged that both studies will be jointly funded through Cancer Research UK and pharmaceutical companies, with funding applications to be submitted in 2017/18. 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.

Progress to date

CONCORDE

Outline submitted to CRUK CRC, their feedback gave some very strong signals that they liked the concept but needed more information even on the supporting preclinical data and the practicalities. This being addressed with a plan to follow their advice and re-apply at the end of the year.

- 1 AstraZeneca have made available their extensive pre-clinical data with Professor Ryan joining the TMG.
2. Inclusion of RT alone comparator group discussed with EORTC lung Group and supported by a number of independent oncologists.
3. Staffing and costings for the study: follow up meeting with CRUK office planned.
4. Translation Program: Ongoing development.

SPITFIRE

1. Multi-arm phase II design proposed in patients with resistance to initial single agent PD1/L1.
2. Outline being submitted to CRUK and/or MRC Q3 2018.
3. Dr Forster and Professor Harrington are continuing to explore pharma options with optimal drug pipeline at ASCO 2018.
4. ICR PPI event February 2018 – excellent feedback will be incorporated into funding application

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	Application type	CI	Outcome	Level of CSG input
May 2017				
LungMatrix: Multi-drug, genetic marker-directed, non-comparative, multi-centre, multi-arm phase II trial in non-small cell lung cancer	Full application (no-cost amendment)	Professor Gary Middleton	Supported	High, Chief Investigator, members of TMG (including Consumers) past and current members of the Lung CSG.
November 2017				
Prospective longitudinal evaluation of serum RAS related nuclear protein (RAN) as a novel, predictive resistance biomarker for tyrosine kinase inhibitors in non-squamous non-small cell lung cancer (NSCLC)	Biomarker Project Award (Full Application)	Professor Mohamed El-Tanani	Not Supported	Low, CSG review prior to submission for funding
HALT: Targeted therapy beyond progression with or without dose-intensified radiotherapy in oligo-progressive disease in oncogene Addicted Lung Tumours	Late Phase Study Amendment (Full Application)	Dr Fiona McDonald	Supported	High, Chief Investigator, members of TMG (including Consumers) past and current members of the Lung CSG.
CONCORDE NSCLC: A platform study of novel agents in COmbination with COventional RaDiotherapy in locally advanced non-small cell lung cancer	Late Phase Study (Outline)	Dr Gerard Hanna / Dr Alastair Greystoke	Not Invited to Full, but re-submission recommended in 2019.	Very high, study protocol developed through our Short term working party.
Other committees				
Study	Committee & application type	CI	Outcome	Level of CSG input
Identifying missed actionable events in the natural history of lung cancer prior to diagnosis in primary	CRUK EDAG	Mick Peake and Neal Navani (UCL)	Supported	High, Chief Investigator, members of TMG (including

care and implementing them in a learning health system in NE London				Consumers) past and current members of the Lung CSG.
Trends in geographic inequalities in early cancer diagnosis at the time of the implementation of the Health & Social Care Act 2012	CRUK Project grant	Laura Woods (LSHTM)		Low, CSG review prior to submission for funding
Impact of <i>radiographer immediate reporting of chest X-rays from general practice on the lung cancer pathway (radioX): study protocol for a randomised control trial</i>	Cancer Research UK Early Diagnosis Advisory Group grant (C61561/A24046)	Nick Woznita	Supported	Moderate, Collaborative development between SPED, Primary Care CSG and the Early Diagnosis Subgroup of the Lung CSG.

6. Consumer involvement

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

They attended meetings, conferences, trials day, Consumer Forum giving PPI feedback. 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.

PPI highlights included

- Speaker at EORTC Survivorship summit, Cancer PPI at Birmingham University/CRUK, PPI at NCRI annual trials day, Festival of Genomics, Genomics for Birmingham Medical School, SMP session for CRUK's Philanthropy & Partnerships teams (JR)
- European Lung Foundation PAG member, attended ERS Berlin lung cancer meeting (37 countries) NICE Lung Clinical Guidelines Review Panel (TH)
- Consumer member on NCRI's CM-Pathology and CT Rad (TH)
- CRUK Research and Strategy Sounding Board (TH)
- Various cancer research advisory boards, committees and groups. (both)
- Advisory and joint applicant roles on several studies including Core (TH), ADSCaN, (TH) PEPs2, (JR) Lung Matrix, (TH), Macmillan Horizons Study User Reference Group (JR)

Wider involvement includes

- NIHR HSDR and CCG board membership (JR).
- NHSE CEG/lung screening advisory group (JR) and West Midlands Cancer Alliance LC CEG (JR)
- ELF/ERS LC PAG (JR)
- ICPV Trustee (TH)
- International LC PAG (Boehringer) and advisor to pharma on lung drug development (TH)
- Regular contributions locally, nationally and internationally to research bids, articles and groups. (both)

Their involvement provides opportunities to connect work and contacts ensuring a consumer perspective is regularly considered.

7. Priorities and challenges for the forthcoming year

Priority 1

Strengthen subgroup membership and structure to better support ongoing trial development

Priority 2

Maintain the Annual Trials Meeting and develop other collaborative workshops and meetings to extend the trials portfolio.

Priority 3

To work with specific charities (Roy Castle, Meso UK) to continue to improve access to information contained in portfolio maps.

Challenge 1

Ensuring research remains core to NHS service and is recognised in all job plans.

Challenge 2

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.

Challenge 3

The running of academic studies with increasing pressures from commercial studies for limited trial infrastructure.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG 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 Cancer CSG Chair)

Appendix 1

Membership of the Lung Cancer CSG

Name	Specialism	Location
Prof Matthew Hatton (Chair)	Clinical Oncologist	Sheffield
Dr David Landau	Clinical Oncologist	London
Dr Fiona McDonald	Clinical Oncologist	London
Mr Tom Haswell	Consumer	Glasgow
Mrs Janette Rawlinson	Consumer	Sandwell
Dr Martin Forster	Medical Oncologist	London
Dr Donna Graham*	Medical Oncologist	Belfast
Dr Alastair Greystoke	Medical Oncologist	Newcastle
Dr Thomas Newsom-Davis	Medical Oncologist	London
Dr Mary O'Brien	Medical Oncologist	Sutton
Dr Sanjay Popat	Medical Oncologist	London
Dr Riyaz Shah	Medical Oncologist	Kent
Prof Fiona Blackhall	Medical Oncologist	Manchester
Dr Peter Szlosarek	Medical Oncologist	London
Dr Fiona Taylor*	Medical Oncologist	Sheffield
Dr Andrew Wilcock	Palliative Medicine/Medical Oncology	Nottingham
Dr James O'Connor	Radiologist	Manchester
Dr Philip Crosbie	Respiratory Physician	Manchester
Dr Neal Navani	Respiratory Physician	London
Dr Lynn Calman	Senior Research Fellow	Southampton
Professor Lucinda Billingham	Statistician	Birmingham
Mr Babu Naidu	Thoracic Surgeon	Birmingham

* denotes trainee member

Membership of the Subgroups

Advanced Disease Subgroup		
Name	Specialism	Location
Dr Jason Lester	Clinical Oncologist	Cardiff
Dr Hannah Lord	Clinical Oncologist	Dundee
Professor Samreen Ahmed**	Consultant Oncologist	Leicester
Prof Fiona Blackhall (Chair)	Medical Oncologist	Manchester
Prof Charles Swanton	Medical Oncologist	London
Dr Sarah Danson	Medical Oncologist	Sheffield
Dr Carles Escriu**	Medical Oncologist	Liverpool
Dr Sanjay Popat	Medical Oncologist	London
Dr Riyaz Shaw	Medical Oncologist	London
Dr James Spicer	Medical Oncologist	London
Dr Andrew Wilcock	Palliative Medicine/Medical Oncology	Nottingham

LOCoRegionalDisease (LORD) Subgroup		
Name	Specialism	Location
Dr Corinne Faivre-Finn	Clinical Oncologist	Manchester
Dr Susan Harden**	Clinical Oncologist	Cambridge
Professor Matthew Hatton	Clinical Oncologist	Sheffield
Dr David Landau	Clinical Oncologist	London
Dr Fiona McDonald**	Clinical Oncologist	London
Mr Matthew Baker	Consumer	Manchester
Dr Thida Win**	General Medicine	Stevenage
Dr Thomas Newsom-Davis	Medical Oncologist	London
Dr Yvonne Summers (Chair)	Medical Oncologist	Manchester
Dr Denis Talbot	Medical Oncologist	Oxford
Mrs Lavinia Magee	Nurse	Ulster
Dr Anand Devaraj**	Radiologist	London
Dr David Baldwin	Respiratory Physician	Nottingham
Dr Richard Booton**	Respiratory Physician	Manchester
Ms Karen Harrison-Phipps**	Surgeon	London
Mr Babu Naidu	Surgeon	Birmingham
Mr David Waller	Surgeon	Leicester

Mesothelioma Subgroup		
Name	Specialism	Location
Dr Peter Jenkins	Clinical Oncologist	Gloucester
Professor Mike Lind	Clinical Oncologist	Hull
Dr Michael Snee	Clinical Oncologist	Leeds
Dr Alfredo Addeo	Medical Oncologist	Bristol
Professor Dean Fennell	Medical Oncologist	Leicester
Dr Jeremy Steele	Medical Oncologist	London
Dr Peter Szlosarek (Chair)	Medical Oncologist	London
Mr John Edwards	Surgeon	Sheffield
Professor Andrew Ritchie	Surgeon	Gloucester
Mr David Waller	Surgeon	Leicester

Screening & Early Diagnosis Subgroup		
Name	Specialism	Location
Professor Paul Aveyard	Behavioural Medicine	London
Dr Sam Jones	General Medicine	Nottingham
Professor Richard Neal	General Practitioner	Oxford
Professor David Weller	General Practitioner	Edinburgh
Dr Anand Devaraj**	Radiologist	London
Professor Fergus Gleeson	Radiologist	Oxford
Professor David Baldwin	Respiratory Medicine	London
Dr Neal Navani (Chair)	Respiratory Medicine	Cambridge
Dr Mick Peake	Respiratory Physician	Leeds
Dr Robert Rintoul	Respiratory Physician	Cambridge
Dr Lynn Calman	Senior Research Fellow	Southampton

* denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

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

B – Advanced Disease Subgroup Strategy

Aims

- To develop academically-led studies in Brain Metastases – a Workshop planned autumn 2017.
- 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 rotation of membership through the Subgroup including succession planning for the Chair.

C – LocoRegionalDisease (LORD) Subgroup Strategy

- Continue to nurture new investigator-led research in early stage lung cancer, particularly related to new radiotherapy combinations (immunotherapy and targeted agents) and support protocol development and funding applications.
- In all future studies, consider earlier involvement with supportive care to develop collaborative research with relevant survivorship questions (working with Lynn Calman from the Lung CSG and other CSG members).
- As previous funding applications for stand-alone smoking cessation studies have been unsuccessful, plan to incorporate smoking cessation into other studies at the development stage.
- Continue to refresh the Subgroup as members complete their terms and encourage new researchers.
- Continue to work with international groups (ETOP, EORTC) collaboratively on key academic research questions and develop new research protocols with developing organisations (TACT).
- Encourage and support translational research with all projects – TRACERx is the exemplar project where translational research will generate many clinical research questions.

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

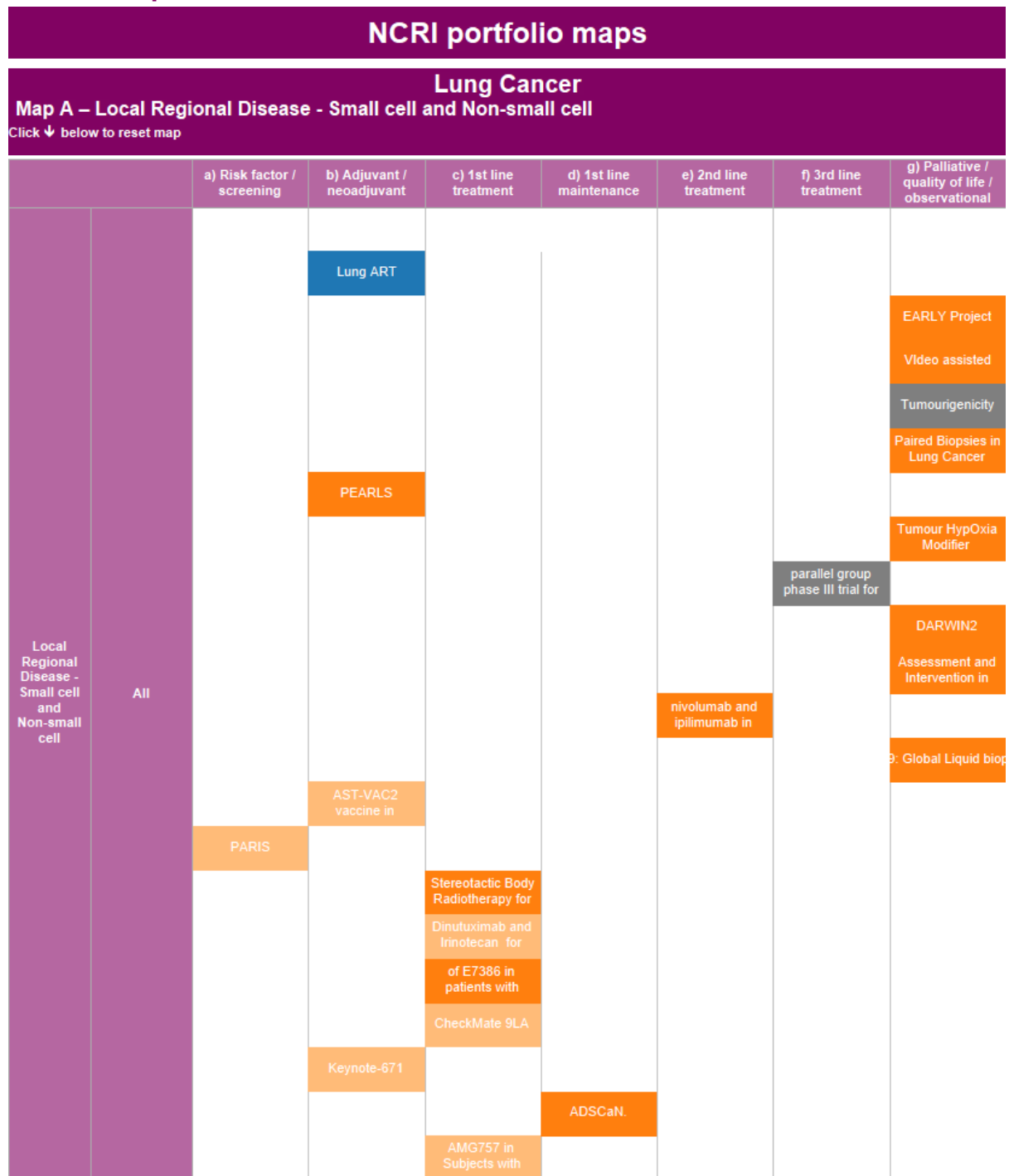
The research landscape will be shaped by the results of the influential NELSON randomised trial of CT screening for lung cancer expected in 2017. Research strategy will then be shaped by a decision on lung cancer screening by the national screening committee.

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



Filters Used:

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

■ Open / multi resea..
 ■ Suspended / singl..
■ In Setup / single re..
 ■ Open / single rese..



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NCRI portfolio maps

Lung Cancer

Map C – Advanced Disease -Non-small cell: Non-biomarker selected

Click ↓ below to reset map

		a) 1st line treatment	b) 1st line maintenance	c) 2nd line treatment	d) 3rd line treatment	e) Supportive care / observational	
Non-biomarker selected	All types			TORCMEK	TORCMEK	REPLICA SPLENDOUR	
		SARON (0010718C) versus platinum				Imaging biomark TARGET Trial OPTIMUM Trial	
				atezolizumab in NSCLC PS2 patients in combination with pembrolizumab	atezolizumab in NSCLC PS2 patients in combination with pembrolizumab		Immunosensitising agents in NSCLC
		IMPROVING - NSCLC-0078/1327				PANORAMA	
				Phase II Safety and Tolerability Study of A10c796T for Advanced NSCLC	Phase II Safety and Tolerability Study of A10c796T for Advanced NSCLC		
		PS2		Anti PD-1 LUC1001	Anti PD-1 LUC1001		
						Support Needs of Curative Lung Cancer Patients	
		Neuroendocrine	SPINET		SPINET		
		Non-squamous	Phase III Study of Atezolizumab in Stage IV Non-Squamous NSCLC		Phase III Study of Atezolizumab in Stage IV Non-Squamous NSCLC		
			B9991025		N3	N3	
		PROCLAIM-CX-2009 with Durvalumab vs Nivolumab					
	Squamous						

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

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



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NCRI portfolio maps

Lung Cancer

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

Click ↓ 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	in Patients with					
		CANC 5371 Pfizer B7461006 NSCLC					
	EGFR	IIIb/IV biomarker positive,			National Lung Matrix	National Lung Matrix	MAGENTA
		or Placebo in					
		DARWIN1			T790M/NSCLC after		
					m/k inhibitor of MET, AXL, FGFR	m/k inhibitor of MET, AXL, FGFR	
	KRas				National Lung Matrix	National Lung Matrix	
		VS-6063 and RO5126766					
	Other				National Lung Matrix	National Lung Matrix	
					/adenocarcinoma tissue/		CANC 5244
ATOMIC-Meso Phase 2/3 Study						NEOlung	
B7661001- additional arm Pembrolizumab + Pembrolizumab Based Pembrolizumab ñ							
ADCT-502 in patients 56/0145-Regeneron-V1-12- SCLC-0456/0146-Regenero						PD-RAD	

Filters Used:

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

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



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NCRI portfolio maps

Lung Cancer

Map E – Screening and Early diagnosis /Other

Click ↓ 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	
		Methodology to Select Tumor/Specific Neo/Antigen	
Data collection/observational	All	INVEST	
		Characterising the Lung cancer Inflammatory response	
		LungCAST	
		TargetLung	
		PEACE	
		Respiratory Distress Symptom Intervention (RDSI)	
		Exploring RATS for lung cancer V1	
		EARL	
Diagnosis / imaging	All	Treatment patterns of SCLC patients in Europe	
		Development of patient derived xenografts (PDXs) for lung cancer.	
		CR UK Stratifie	CR UK Stratifie Study1a
			EARLY Project
			LuCID: Lung Cancer Indicator Detection
		CURVE	
		VOCs in Lung ca	
		CORE Trial	
Quality of life / Supportive..	All	SPECTALung (EORTC 1335)	
			LUSH (Lung Symptom awareness and Health)
		MRI in Lung Cancer Patients	
			The Community Lung Health Study
		Peripheral detection of EGFR status in lung cancer patients	
		Rehabilitation	
		Exercise Regime	
		SIMPLE	
The MENAC Trial			
AC: Effect on Patient Reported Outcomes of Surgery and SABR (V1)			
Phase IV EORTC study to validate new LC29 module			
FACT: Factors Associated with lung Cancer Trial			
OPTBreathe: Preference & cost-effective support for breathlessness			
Integrated rehabilitation for thoracic cancer			

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

Click ↓ 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			<div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">NCRN - 2560 Carfilzomib, Carboplatin + Etoposide in SCLC</div> <div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">ATLANTIS Trial</div> <div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">A multicentre, randomised trial comparing combination</div> <div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">Phase 1/2a to asses PEN-221 in receptor 2 expressing advanced cancers</div> <div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">MK-3475-604 (Phase 3 trial of</div>	<div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">MERU</div> <div style="background-color: #f4a460; padding: 5px; margin-bottom: 2px;">TAHOE</div>				

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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Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
<p>1. TRACERx: Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Abbosh C et.al.. Nature. 2017;545(7655):446-451</p>	<p>Elegant demonstration of tumour heterogeneity that will have profound implication for the management of all patients with lung cancer.</p>	<p>CSG members involved in the development, management and recruitment in the study.</p>
<p>2. BTOG 2: Carboplatin versus two doses of cisplatin in combination with gemcitabine in the treatment of advanced non-small-cell lung cancer: Results from a British Thoracic Oncology Group randomised phase III trial. Ferry D et.al. European Journal Cancer (2017) 83:302-312.</p>	<p>Addressed the uncertainty around standard platinum based chemotherapy for advanced NSCLC helping establish standard practice</p>	<p>CSG members led the development of the study protocol and were instrumental in the running of the study and its subsequent publication.</p>
<p>3. CONVERT: Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. Faivre-Finn C. et.al. Lancet Oncol. 2017 Aug;18(8):1116-1125.</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>4. ERCC1 Trial (ET): Randomized Prospective Biomarker Trial of ERCC1 for Comparing Platinum and Non-platinum Therapy in Advanced Non-Small-Cell Lung Cancer. Lee SM et.al). J Clin Oncol. 2017 35:402-411.</p>	<p>Amongst the first prospective trials of treatment tailored to biomarkers.</p>	<p>CSG members led the development of the study protocol and were instrumental in the running of the study and its subsequent publication.</p>
<p>5. ATOMIC-MESO: Arginine deprivation with pegylated arginine deiminase in patients with argininosuccinate synthetase 1-deficient malignant pleural mesothelioma: a randomized clinical trial. Szlosarek P et.al JAMA Oncology (2017) 3:58-66</p>	<p>Successful Mesothelioma Subgroup study of a novel treatment approach that developed the experimental arm in the ATOMIC-MESO study for first line systemic treatment of mesothelioma.</p>	<p>CSG members led the development of the study protocol and were instrumental in the running of the study and its subsequent publication.</p>

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Lung Cancer CSG portfolio, 40 trials closed to recruitment and 50 opened.

Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	3036	992	2665	942	6.3	2.2
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