NCRI Lung Group

Annual Report 2020 - 2021

NCRI Partners

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

List of Appendices

NCRI Lung Group

Annual Report 2020-21

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

Achievement 1 Our adaption to the COVID-19 pandemic enabling us to continue business as 'normal'. Moving the Group and Subgroup meetings to a virtual space, maintaining our ability to review study proposals and to continue developing studies that fill the gaps in our trial portfolio.
Achievement 2 The CONFIRM study led by members of our Mesothelioma Subgroup reported in the Presidential session of the World Conference on Lung Cancer with results that have been practice changing with the rapid introduction of immunotherapy as a standard of care treatment in this disease.
Achievement 3 Completion of our Quinquennial review with encouraging feedback from the panel - 'clear evidence of significant progress over the last five years and that the Group has raised the bar of excellence for themselves'.

2. Structure of the Group

In keeping with other Groups, our response to the COVID-19 pandemic was to move from face to face to virtual meetings. We were able to continue to run the Subgroup meetings in conjunction with the main Group meeting. While this approach allows for good multi-disciplinary input which continues to garner positive feedback, the most recent Group meeting showed strong support for the evolution into the new NCRI operating model of the core Executive and Working groups over the coming year. We feel this approach will help with the development of studies that address our key priority areas and hopefully give younger investigators in the wider community extra opportunities to participate in our meetings and new / on-going studies.

The limits on membership rotation imposed by the pandemic mean that the only member to rotate off the Group was William Wallace. We owe him a debt of gratitude for his hard work and the pathology insights he was able to contribute to our discussions. This means our current group membership is - 6 Medical Oncologists, 4 Clinical Oncologists, 2 Respiratory Physicians, 1 Consumer representative, 1 Radiologist, 1 Thoracic Surgeon, 1 Statistician, 1 Support Care Senior Research Fellow, 1 GP and 1 Transitional Scientist.

We are aware that we need to maintain our multi-disciplinary expertise - we have one Consumer and one expert vacancy on the Group as it is currently constituted. Therefore, we are planning for targeted adverts when it is clear what the requirements of a new operating structure are to ensure we have the expertise required in both the core Executive and the trial delivery groups.

3. Lung Group & Subgroup strategies

Lung Group

Our strategy development meeting was held in December 2018.

Understandably, our recruitment numbers were well below those of 2018-19 though we note our screening studies recruited very strongly with in excess of 20,000 people have been recruited to lung cancer screening portfolio adopted studies (SUMMIT (London), Manchester Lung Health Study and the Yorkshire Lung Screening Trial (Leeds)). The number of studies on our portfolio remains healthy and data from the NIHR Clinical Research Network (NIHR CRN) indicate that as the COVID-19 situation has eased, the majority of studies on our portfolio have reopened. Therefore, we expect recruitment to pick up to the 2018-9 levels as the year progresses and cancer research infrastructure is restored across UK centres.

In addition to our strong portfolio of screening / early diagnosis studies, CONCORDE, developed through our radiotherapy / new drug working party has opened to recruitment - a welcome addition to the flagship studies on our portfolio. Through virtual meetings our Subgroups were able to continue their work on further screening studies and we have added (neo)-adjuvant treatment and lung cancer in non-smokers to our list of key research priorities, organising workshops to develop research strategies in these areas.

We had some success with those key priorities listed in our 2018 strategy. Efforts to develop a high recruiting immunotherapy study have led to NIHR funding for the REFINE-LUNG (CONVOLUTE) study and an invitation for a full submission of the TOURIST palliative radiotherapy trial platform. Sadly, the EDAM proposal for cerebral metastasis did not receive a similar invitation but it triggered a multicentre audit of the incidence of asymptomatic brain metastases at diagnosis during COVID-19 (Cui W, Milner-Watts C, Saith S, J. Bhosle[1], A.R. Minchom[1], M. Davidson[1], S. Page[1], I. Locke[1], N. Yousaf[1], S. Popat[2], M.E.R. O'Brien. Incidence of brain metastases (BM) in newly diagnosed stage 4 NSCLC during COVID-19. Journal of Thoracic Oncology (2021) 16 (suppl_4): S748-S802) which, when presented, was picked up by the European Oncology Conference news shots. Plans for small cell lung cancer (SCLC) trial platform advance towards a funding submission later this year.

The COVID-19 epidemic delayed our progress with funding applications and the subsequent drop in cancer research funding is a clear threat that challenges our ability to continue building our portfolio. It is also clear that lung cancer was one of the tumour sites most impacted by COVID-19 with Group/Subgroup members documenting a drop in incidence alongside an increase in the numbers of patients presenting with advanced disease, while studies looking at the impact of the pandemic on treatment is on-going.

We maintain our strong links with national and international research groups albeit virtually. We are well represented in European Organisation for Research and Treatment of Cancer (EORTC) Lung Group with a number of chief investigators of EORTC studies active members of our group. Our members have steering group representation on many others including, British Thoracic Oncology Group (BTOG), International Association for the Study of Lung Cancer (IASLC), European Thoracic Oncology Platform (ETOP), enabling the Group to co-develop studies.

The Group and Subgroup members enjoy close links with the Screening Prevention and Early Diagnosis (SPED) Advisory Group and the Living With and Beyond Cancer (LWBC) whose Chairs (Professors David Baldwin and Sam Ahmedzai) share our lung cancer research interest. In addition one of our SG members, Lynn Calman, Co-Chairs the Advanced Disease & End of Life Care Workstream for the LWBC Group. Members of our Group are active in CTRad (Dr McDonald, Professor Hatton).

We have strong links with the National Lung Cancer Audit and our active lobbying, alongside other interested groups, was able to secure funding to maintain this valuable tool for lung cancer researchers.

Mesothelioma Subgroup (Chair, Professor Peter Szlosarek)

Strategic Priorities

To develop phase 2/3 academically directed studies based on the new knowledge of mesothelioma as an immunologically tractable disease (Checkmate-743)

- Ipilimumab and nivolumab has been adopted as a new standard of care by the FDA and EMA based on the Checkmate-743 data and a decision is pending by NICE.
- A new trial is under review by the EORTC called ATOMIC-meso 2 (CI, Szlosarek) which seeks to redefine chemotherapy with the addition of arginine depletion in patients relapsing on front-line ipilimumab and nivolumab immunotherapy.
- The Phase 3 CONFIRM Study led by members of the Mesothelioma Subgroup was recently presented at World Lung 2021 and a manuscript has been submitted revealing a practice changing 2.7 month survival advantage of nivolumab immunotherapy versus placebo for relapsed mesothelioma (Fennell et al, 2021).

To define novel biological targets for relapsed mesothelioma exemplified by the MIST programme (CI, Fennell)

- Several studies including PARP and CDK4/6 inhibition have matured and are being reviewed for randomised phase 2 studies with commercial support, e.g. NERO: Niraparib Efficacy in unResected MesOthelioma testing the role of maintenance PARP blockade in a randomised phase 2/3 study following standard chemotherapy (Rucaparib in patients with BAP1-deficient or BRCA1-deficient mesothelioma (MiST1): an open-label, single-arm, phase 2a clinical trial. Fennell DA, King A, Mohammed S, Branson A, Brookes C, Darlison L, Dawson AG, Gaba A, Hutka M, Morgan B, Nicholson A, Richards C, Wells-Jordan P, Murphy GJ, Thomas A; MiST1 study group.Lancet Respir Med. 2021 Jan 27:S2213-2600(20)30390-8. doi: 10.1016/S2213-2600(20)30390-8. Online ahead of print.)

- Ongoing front-line phase 3 studies supported by the Mesotheloma Subgroup may lead to further options for patients with mesothelioma: BEAT-meso (PemCarboBev vs PemCarboBevAtezo; CI, Popat) and ATOMIC-meso PemPtPlacebo vs PemPtADI; CI, Szlosarek)

To perform a feasibility neoadjuvant study of biological therapy - ADI-PEG20 plus pembrolizumab with radiation followed by pleurectomy decortication (i.e. MARS3 study) as a follow on to MARS2.

- If the results of MARS3 are positive this would potentially lead to a phase 2/3 study involving neoadjuvant systemic therapy and randomisation to surgery/no surgery (Co-CIs Szlosarek, Waller)

To encourage young investigators to contribute novel study proposals for further development by the Mesothelioma Subgroup.

To engage new Consumer membership to provide insights into trial design and uptake

- Ms Virginia Sherborne has been appointed recently to the Group as a Consumer member.

LOcoRegional Disease (LORD) Subgroup (Chair, Dr Mary O'Brien)

The LORD Subgroup is divided into operable disease using surgery (stage I and II mostly) and inoperable (stage III) which can be treated with curative intent using chemotherapy and radiotherapy. To this is now added immunotherapy.

The rapidly accrued, successful, UK Violet study continues to accrue data from the comparison a VATS resection versus a resection via lobectomy. The use of adjuvant immunotherapy after surgery is being compared in the international PEARLS trial which should read out in 2021. Neoadjuvant chemotherapy and immunotherapy trials are also running. The results of the ADAURA study were presented in 2020 and showed the benefit for adjuvant Osimertinib. The adjuvant and neoadjuvant areas are potential areas for new trials within the UK lung cancer trials portfolio.

A large data base of stage III patients was reported and presented by Matthew Evison -

Predicting the risk of disease recurrence and death following curative intent radiotherapy for NSCLC: the development & validation of two risk prediction models from a large multicentre UK cohort. Evison M, Barrett E, Cheng A, Mulla A, Walls G, Burke D, McAleese J, Moore K, Hicks J, Blyth K, Denholm M, Magee L, Gilligan D, Silverman S, Hiley C, Qureshi M, Clinch H, **Hatton M,** Philips L, Brown S, **Macdonald F,** Faivre-Finn C. Clinical Oncology 2021:33;145- 54 DOI: 10.1016/j.clon.2020.09.001

This gives us prognostic indexes for further studies, the first of which (PIONEER) is now open and actively recruiting. The therapy area is still dominated by variations of the standard of care using durvalumab, in randomised large pharmaceutical sponsored trials.

The Never Smoker Lung Cancer workshop feeds into the data on patients with epidermal growth factor receptor (EGFR) mutated tumours which have become a subgroup of special interest and different prognosis from smoking induced lung cancer.

Advanced Disease Subgroup (Chair, Professor Fiona Blackhall)

Aims and progress:

- To continue to develop academically led studies in brain metastases. A funding application for a CRUK Biomarker Award was not successful and this remains a significant and increasing unmet need. An opportunity has arisen to collaborate on a study with ETOP and an EORTC study of brain surveillance is now in development and further opportunities will be scoped over the coming year.

- Continue to work with international groups (ETOP, EORTC) collaboratively on key academic research questions to address other gaps in the portfolio. A major development is the emergence of KRAS inhibitors for this significant oncogenic driven, smoking related non-small cell lung cancer (NSCLC) subtype. We are working with ETOP on an academic study with early career grade PIs for this indication; a study for anaplastic lymphoma kinase (ALK) + NSCLC with progression after initial tyrosine kinase inhibitors (TKI) treatment is also being developed, led by S Popat, in collaboration with ETOP and Pfizer.

- 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. The TOURIST trial platform for radiotherapy in advanced NSCLC has been submitted for funding with a senior (M Hatton) / junior investigator (D Woolf) model. Similarly, REFINE-lung was developed with a senior/ junior investigator team.

- To develop biomarker directed academically led studies in SCLC. A SCLC Working Party is currently being set-up. The remit of the Party 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.

- The promotion of Living With and Beyond Cancer nested studies to new treatment trials or the development of stand-alone studies remains an area of active focus. An application for a study of exercise intervention was unsuccessful, we will continue to revise this strategy and identify funding routes.

- To focus on promoting and progressing key '*flagship studies*' in terms of recruitment and protocol development respectively. Key flagship studies are highlighted in Table 1. Despite COVID it was possible to maintain recruitment to TRACERX and PEACE although at a slower pace.

- MAGE: A CRUK Phase I/IIA trial of chimpanzee adenovirus Oxford 1 (CHADOX1) and modified vaccina ankara (MVA) vaccines against MAGE-A3 and NY-ESO-1 with standard of care treatment (chemotherapy and immune checkpoint inhibitor). A first in human vaccine trial funded by the CRUK Centre for Drug Development, has received all regulatory approvals and close to UK site activation.

Table 1

STUDY THEME	STUDY NAME	CURRENT STATUS
Translational Research	TRACERx	Actively Recruiting
	PEACE	Actively Recruiting
NSCLC Advanced Disease	SMP2 & National Lung Matrix Trial	Actively Recruiting Publication
	SARON	Actively Recruiting
	HALT	Actively Recruiting
	PePS2	Published
	CONVOLUTE / NOW REFINE	Funded
	EDAM	Not funded
	ARROW	Protocol under development
	TOURIST	In application; stage 2
SCLC Extensive Disease	Study 15	Completed/ closed to recruitment

	DISCOVER SCLC	Protocol under development

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

The NELSON RCT, which was published in 2020, demonstrated a 24% reduction in lung cancer specific mortality with low dose CT screening (de Koning HJ, et al. N Engl J Med. 2020 382(6):503-513). Taken alongside results from the National Lung Screening Trial this provides robust evidence that screening saves lives. A key strategic focus for early detection research is how best to implement screening.

The key strategic aims in the coming years remain:

- **Develop cohesive working and applications with the LWBC Group (previously with the Primary Care CSG) and SPED Advisory Group.**
  - The Chair of the Screening and Early Diagnosis Subgroup now attends the SPED Advisory Group.

- **Encourage trials of interventions to reduce tobacco harm.**
  - The Yorkshire Enhanced Stop Smoking study (YESS) has completed recruitment (>1,000 participants). Its main objectives are to explore the optimal approach to delivering smoking cessation within a screening programme as well as assessing a novel intervention for smoking cessation.

- **Work with primary care researchers to develop risk prediction models.**
  - Prospective evaluation of the performance of risk prediction models ($PLCO_{M2012}$ and LLP_{v2}) compared to NLST eligibility criteria are being assessed in large scale prospective studies including SUMMIT (>12,000 recruited) and the Yorkshire Lung Screening Trial (YLST, >6,000 recruited).

- **Facilitate research into optimising lung cancer screening, e.g. recruitment, scanning interval and nodule management.**
  - The Manchester Lung Health Check pilot provided important evidence relating to a community-based model of screening implementation. This approach was included in the NHS Long Term plan leading to a national Targeted Lung Health Check programme.
  - The NHS England funded Targeted Lung Health Check programme is assessing screening implementation at scale (there are currently ≈23 sites involved). Research is not funded by the national pilot but individual sites are exploring ways of aligning research alongside local services.

- **Develop closer links with qualitative researchers**
  - Qualitative research is fully integrated in the SUMMIT and YLST studies.

4. Cross-cutting research

Working Parties

1. **Radiotherapy – Drug Combination Working Party 2018 - 20**

This working party developed the CRUK funded CONCORDE study protocol which has now opened with its first patient recruited in May 2021.

2. **Small Cell Lung Cancer Working Party**

The team meetings have highlighted the heterogeneity in SCLC treatment modalities across the UK and aims to nationally standardise the SCLC patient treatment pathway. An initial focus is harnessing non-invasive translational methods – such as ctDNA – to identify biomarkers of response, progression / deterioration prior to imaging results to tailor treatment. Data and networks with the larger SCLC populations will inform the development of an adaptive platform trial designed to increase accessibility, and inclusivity of clinical trials for SCLC patients, with an emphasis on under-represented groups such as poor PS, frail and co-morbid patients.

3. **Never Smoker Lung Cancer**

Our Consumer representatives highlighted this gap in our research portfolio. We have arranged and now run a virtual meeting 'Developing a research strategy for never smoker lung cancer patients'. This workshop attracted > 250 registrants and with strong Consumer input identified some key research questions. We will be forming a delivery group to develop and progress studies in this area.

CRUK Lung Centre of Excellence – UCL / Manchester

This strong partnership continues. The Flagship studies, TRACERX and PEACE have been able to recruit through the COVID pandemic and are generating impact factor publications in translational research, immune landscape and mechanisms of treatment resistance.

Living with and Beyond Cancer

These research priorities remain a focus as highlighted in our strategy document. Dr Calman sitting on both the Lung Research Group and the LWBC Group has ensured good communication between the lung and facilitating our access to specific expertise. Our portfolio contains studies addressing many of the LWBC top 10 research priorities with at least 4 of these priorities identified as specific research questions in the study outlines / protocols that are being developed.

5. Funding applications in last year

Table 1 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Cancer Research UK*					
Dec 2020					
PRIMALUNG: Prophylactic cerebral irradiation or magnetic resonance imaging surveillance in small cell lung cancer patients	Endorsement (May 2020)	Professor Corinne Faivre-Finn	Supported - Endorsement	Developed in collaboration with EORTC. Co-CI Faivre-Finn subgroup member.	
Atezolizumab For Treatment Naïve Patients with Malignant Mesothelioma Not Suitable for Platinum Doublet Chemotherapy (AiM)	Clinical Trial Award - Outline (May 2020)	Dr Dionysis Papadatos-Pastos	Full application not invited	Advisory subgroup review	
A randomised phase II trial with non-randomised run-in of karonudib, an oral MTH inhibitor, as maintenance treatment post 1st line chemotherapy for small cell lung cancer	Clinical Trial Award - Outline (May 2020)	Professor Sarah Danson	Full application not invited - Resubmission welcome	Advisory subgroup review	
Other committees**					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of Group input**	**Funding amount**
REFINE-Lung (formerly known as CONVOLUTE): A randomised open-label phase III trial of REduced Frequency pembrolizumab ImmuNothErapy for first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) utilising a novel multi-arm frequency-response optimisation design.	NIHR	Prof Seckl	Funded	Developed with the Group; Group members co-applicants Blackhall, O'Brien	TBC Application £3,112,025.85 Excluding NHS costs

A randomised phase II study of baseline MRI brain scanning versus no MRI braining scaning in patients with stage IV non-small cell lung cancer without neurological symptoms. Early Detection of Asymptomatic Metastases – the EDAM-BRAIN, trial.	NIHR RfPB	Dr Page / Prof O Brien	Not Funded	Developed with the Brain Research Group; Group members co-applicants Blackhall, O'Brien, Hatton, McDonald, Calman	N/A

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

6. Consumer involvement

Apologies that this section has not been completed.

We have sadly lost two of our Consumer champions over the past couple of months – Tom Haswell and Paul Cosford. Their contribution to our Group was immense and both already greatly missed by us and the wider community as demonstrated by the posthumous British Thoracic Oncology Group (BTOG) Lifetime Achievement Award given to Tom Haswell at their Annual Meeting. We would also note Paul's work was key in initiating our drive to develop a research strategy for never smoking lung cancer patients which will remain an important focus for the Group over the coming years.

The other Consumer member on the Group, Lynne Wright has unfortunately failed our 'three strikes and out' rule, not attending 3 successive Group meetings. However, we would note that one of our previous Group Consumer members, Janette Rawlinson, has remained very active, contributing to our Advanced Disease Subgroup and presenting at the recent Never Smoker Lung Cancer Workshop.

We were out to advert for new Consumer members earlier in the year and are pleased to report that we had a number of high-quality applications. The result is that we have been able to appoint new Consumer member Glenn Edge to the Research Group and now have a Consumer representative in all the Subgroups. However, as they are all new in post, we have not imposed upon them to complete this section of the report.

7. 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 our MATRIX, CONCORDE and MIST flagship studies.

The Group continues to actively seek opportunities with Pharma. A study in ALK rearranged NSCLC in collaboration with the European Thoracic Oncology Platform and Pfizer is being scoped by S Popat. Several companies are working with lung group colleagues on trials of KRAS inhibitors with translational studies being developed in collaboration in Manchester and UCL.

The NHSE National Genomics Test Directory now provides panel gene testing for NSCLC and pharma collaborations are in discussion for circulating tumour DNA platforms to be applied in NHS service with a line of sight to collating data on clinical utility for advanced NSCLC (Greystoke, Popat, Blackhall with Guardant, Roche (Foundation Medicine).

8. Priorities and challenges for the forthcoming year

We do not feel that our key priorities and challenges have changed from those we listed in the last annual report, namely:

Priority 1

To continue to support investigators as they develop research protocols and funding submissions with a focus on studies to address the gaps that we have identified in our research portfolio.

Priority 2 To prepare a strategy document for 2022 – 25 and act upon the advice and recommendations made by the Quinquennial Review panel.
Challenge 1 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 Clinical Research Network (CRN) level to deliver complex biomarker-directed studies.
Challenge 2 Increasing costs, funding competition and limited infrastructure within the NCRN leading to significant delays in trial set up and opening of centres.

Professor Matthew Hatton (Lung Cancer Group Chair)

Appendix 1

Membership of the Lung Group

Name	Specialism	Location
Dr Kevin Franks	Clinical Oncologist	Leeds
Prof Matthew Hatton (Chair)	Clinical Oncologist	Sheffield
Dr Fiona McDonald	Clinical Oncologist	London
Dr Iain Phillips	Clinical Oncologist	London
Mr Glenn Edge	Consumer	Newmarket
Professor Frank Sullivan	General Practitioner	St Andrews
Professor Samreen Ahmed	Medical Oncologist	Leicester
Dr Alastair Greystoke	Medical Oncologist	Newcastle
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 Igor Vivanco	Molecular Oncologist	London
Professor Gary Cook	Radiologist	London
Dr Philip Crosbie	Respiratory Physician	Manchester
Dr Frank McCaughan	Respiratory Scientist	Cambridge
Dr Lynn Calman	Senior Research Fellow	Southampton
Mr Nicholas Counsell	Statistician	London
Mr John Edwards	Surgeon	Sheffield

Consumer Representation

Name	Location
Mr Glenn Edge	Newmarket

Membership of the Subgroups

Mesothelioma Subgroup		
Name	**Specialism**	**Location**
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
Ms Virginia Sherborne	Consumer	Sheffield
Professor Dean Fennell	Medical Oncologist	Leicester
Dr Jeremy Steele**	Medical Oncologist	London
Professor Peter Szlosarek (Chair)	Medical Oncologist	London
Dr Robert Rintoul	Respiratory Physician	Cambridge
Mr John Edwards	Surgeon	Sheffield
Mr David Waller**	Surgeon	Leicester

LOcoRegional Disease (LORD) Subgroup		
Name	**Specialism**	**Location**
Dr Corinne Faivre-Finn**	Clinical Oncologist	Manchester
Dr Susan Harden**	Clinical Oncologist	Cambridge
Prof Matthew Hatton	Clinical Oncologist	Sheffield
Dr Iain Phillips	Clinical Oncologist	London
Dr Fiona McDonald**	Clinical Oncologist	London
Dr David Landau**	Clinical Oncologist	London
Ms Sally Hayton	Consumer	Manchester
Dr Fiona Taylor**	Medical Oncologist	Sheffield
Professor Samreen Ahmed	Medical Oncologist	Leicester
Dr Thida Win**	General Medicine	Stevenage
Dr Sherin Payyappilly	Histopathologist	Birmingham
Dr Donna Graham**	Medical Oncologist	Belfast
Professor Mary O'Brien (Chair)	Medical Oncologist	London
Ms Lavinia Davey**	Nurse	Kent
Professor Fergus Gleeson	Radiologist	Oxford
Dr Richard Booton**	Respiratory Physician	Manchester
Professor David Baldwin	Respiratory Physician	Nottingham
Ms Karen Harrison-Phipps**	Surgeon	London
Mr Babu Naidu	Surgeon	Birmingham
Mr David Waller	Surgeon	Leicester

Advanced Disease Subgroup		
Name	**Specialism**	**Location**
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 Igor Vivanco	Molecular Oncologist	London
Ms Pippa Labuc	Occupational Therapist	London
Dr Andrew Wilcock	Palliative Medicine/Medical Oncology	Nottingham
Professor Lucinda Billingham	Statistician	Birmingham

Screening & Early Diagnosis Subgroup

Name	Specialism	Location
Professor Paul Aveyard	Behavioural Medicine	London
Mr Graham Nicoll	Consumer	West Sussex
Professor Richard Neal	General Practitioner	Leeds
Professor John Field	Molecular Oncologist	Liverpool
Dr Anand Devaraj**	Radiologist	London
Dr Arjun Nair	Radiologist	London
Professor David Baldwin	Respiratory Medicine	London
Dr Philip Crosbie (Chair)	Respiratory Medicine	Manchester
Dr Frank McCaughan	Respiratory Medicine	Cambridge
Dr Michael Peake	Respiratory Physician	Leicester
Dr Robert Rintoul	Respiratory Physician	Cambridge

* denotes trainee member
**denotes non-core member

Appendix 2

Lung Group & Subgroup Strategies

A – Lung Group Strategy

Objective	Key actions	Leads	Timeline
Group membership / structure	Refresh Group and Subgroups to maintain balanced membership representative of disciplines involved in lung cancer research. Consider geographical spread, Basic Science, Surgical, AHP, and Public Health representation. Promote face to face subgroup meetings to coincide with meeting of the main Group.	MH, RH MH / Subgroup leads	Ongoing Ongoing
Portfolio	Continue to develop and deliver investigator led studies to complement the current portfolio and industry sponsored studies Key research priority areas include - Brian mets Palliative radiotherapy SCLC Living with and beyond Added in 2020 – Never Smoker Lung Cancer	Group MOB MH FB LC	Ongoing Submission '20 Submission '21
UK researcher engagement new trial development	Promote opportunities for investigators to present study outline through Annual Trials Meeting, BTOG and Subgroup meetings Define a new trial development process across the Group and subgroups with scoring systems for new trial ideas Ensure supportive environment for honest feedback to those proposing studies Advise on future-proofing trials in light of the fast moving changes in of standard of care treatments for lung cancer		Ongoing Investigator presentations to subgroup meeting, and organised virtual workshops
Biobanking/Translational research	Maximise the opportunities of for translational research when developing study outlines		

Early phase trials	Increase engagement with CRUKs ECMC Network to facilitate early phase trial to late phase trial transition. Build on the work of the Novel Drug Radiotherapy Short Term Working Party promoting innovative phase I trials	JS AG, FM	
LWBC	Consider the 10 LWBC research priorities and their application to the lung cancer research portfolio Engage with Specialised Clinical Frailty Network and consider case for a fitness for treatment workshop / working group	LC JE	
Routinely collected data	Maintaining clear links with NCIN to exploit routinely collected datasets For assessing feasibility of studies For long-term follow-up Support analysis of National Lung Cancer Audit Data Develop a strategy to encourage AI research applications in lung cancer		Renewed funding of NLCA
Subgroup specific objectives (Subgroup Chairs to populate with anything not captured in the themes above)	Ensure that each Subgroup has a cohesive strategy of clinical trials development that refreshes the portfolio and seeks to fill any gaps that are present. **Screening & Early Diagnosis** Rotation of Subgroup chair Review and update membership Screening Engage with the UK National Screening Committee (UKNSC) Identify research opportunities around implementation of a national screening program e.g. database integration, smoking cessation, biological samples. Screening for other high risk groups e.g. lymphoma radiation exposure Identification of a biomarker for early detection **Loco-Regional Disease** Review and update membership Work with screening subgroup to consider management studies for the cohort of patients identified through a national screening program.	 PC MOB	

	Work with Roche on their virtual MDT platform to document treatment decisions in stage III disease. Explore research opportunities for the next adjuvant international trial. Consider the LWBC research priorities and their applications to improve fitness for radical treatment. Management of patients with driver mutations presenting with loco-regional disease given the new generation of active TKIs. **Advanced Disease** Review and update membership Nurture the development of studies /platforms for SCLC, palliative radiotherapy and brain metastasis. **Mesothelioma** Review and update membership. Work to maintain and update the current trials portfolio Develop a platform for early phase studies in mesothelioma	FB PS	
Industry engagement	Continue engagement with Phama/biotech companies and explore opportunities to extend this to the subgroup level. Monitor impact of mesothelioma compensation claims to fund access drugs being tested in portfolio studies.		CONFIRM results have made immunotherapy available in NHS
next generation of researchers	Appoint and Mentor Trainee Group members to subgroups	MA, MR	Junior / senior CI model used for EDAM and TOURIST applications

	Engage younger scientists and physicians through BTOG and other national meetings Work with Royal Colleges and other training bodies		
Consumer involvement	Continue to involve consumers across the work of the Group to encourage their input at an early stage in all new trial proposals Ensure Subgroup has consumer involvement	MH/RH	2021
International	Maintain strong links with international research groups Identify Group leads to link to BTOG, EORTC, ETOP, IMIG, ITMIG Review membership of TACT		
Engagement with other NCRI activities	Identify leads within the Group to increase engagement with cross cutting Groups and advisory groups: • Primary Care Group • SPED Advisory Group • CTRad • Supportive and Palliative Care Group • CM-Path	FS FM LC WW	
Trial delivery	Group and subgroup members to commit to delivering studies developed by the Group Integrate trials/research into every day work and continue work to ensure research remains core NHS business that is fully recognised in job plans Work with CTUs running Lung Cancer trials, NCRN, SSLs to reduce bureaucratic issues around trial set-up to facilitate swift trial opening. Review the value of the portfolio maps and explore app development with Roy Castle Lung Cancer Foundation/Mesothelioma UK	ALL MH, FB	
Brand/comms/Researcher engagement	Regular dissemination of study recruitment activity and outcomes through newsletters, annual meetings Annual Report. Promotion of NCRI Lung Cancer Trial Badging		

	Continue the presence at BTOG Annual Meeting and expand this presence to other meetings/conferences e.g. UK Oncology Forum Engagement with CRN subspecialty leads through The main Group and/ or Subgroup meetings. Use Lung Cancer Awareness month to highlight lung cancer research.		

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 Table 1 (Section 3, page 8).

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 – Keynote 671, Pacific 4.

- 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 and virtual platform.
- To develop MR LINAC / proton therapy protocols.
- To develop protocols for 3rd gen TKIs with radical RT.

D – Mesothelioma Subgroup Strategy

The last year has been an active period with a range of mesothelioma studies recruiting 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.
With these studies starting to report the Subgroup will work to engage the mesothelioma community with studies that continue to assess the role of immuno- and other novel therapies in this disease. It is important that we maintain the interest of our surgical and Clinical Oncology colleagues in developing the follow-on studies for MARS2 and SYSTEMS2.
Aims

- To maintain an emphasis on high quality biomarker drive studies and a balanced trial portfolio focused on all subtypes of 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

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Middleton, G., Fletcher, P., Popat, S. *et al.* The National Lung Matrix Trial of personalized therapy in lung cancer. *Nature* **583,** 807–812 (2020). https://doi.org/10.1038/s41586-020-2481-8	Publication contain the first interim results from the SMP2 / MATRIX program confirm the feasibility of the umbrella trial design / approach.	Concept developed through the Group with the CI and other members of the Steering Committee members of our Group.
2. Ghorani, E., Reading, J.L., Henry, J.Y. *et al.* The T cell differentiation landscape is shaped by tumour mutations in lung cancer. *Nat Cancer* **1,** 546–561 (2020). https://doi.org/10.1038/s43018-020-0066-y	TRACERx study paper characterize the effect of tumour mutational burden on the differentiation of CD4 and CD8 T cell subpopulations in non-small cell lung cancer identifying prognostic gene signatures.	Concept supported by the Group with a number of the Steering Committee members of our Group.
3. Middleton G, Brock K, Savage J, Mant R, Summers Y, Connibear J, et.al. Pembrolizumab in patients with non-small-cell lung cancer of performance status 2 (PePS2): a single arm, phase 2 trial. Lancet Respir Med. 2020 Sep;8(9):895-904. doi: 10.1016/S2213-2600(20)30033-3. Epub 2020 Mar 19. PMID: 32199466.	Safety / efficiency study of immunotherapy in poorer performance status patients indicating similar outcomes to those with good PS.	Concept developed through the Group with the CI and other members of the Steering Committee members of our Group.
4. D. Fennell, C. Ottensmeier, R. Califano, C. Poile, J. Lester, G. GriffithsO et.al. Nivolumab Versus Placebo in Relapsed Malignant Mesothelioma: The CONFIRM Phase 3 Trial. DOI:https://doi.org/10.1016/j.jtho.2021.01.323	Provided the evidence of immunotherapy in the second line treatment setting, used by NICE to make the drug available through CDF for treatment within the NHS.	CI and other members of the steering Committee members of our Mesothelioma Subgroup.
5. Crosbie PA, Gabe R, Simmonds I, et al. Yorkshire Lung Screening Trial (YLST): protocol for a randomised controlled trial to evaluate invitation	Lung Cancer screening trial aimed at the hard to reach population	Concept development aided by the Group with a number of the Steering

	to community-based low-dose CT screening for lung cancer versus usual care in a targeted population at risk. *BMJOpen* 2020;10:e037075. doi: 10.1136/bmjopen-2020-037075	containing a nested smoking cessation study.	Committee members of our Early Diagnosis Subgroup. .

Appendix 4

Recruitment to the NIHR portfolio

Summary of patient recruitment by Interventional/Non-interventional and number of studies opened/closed.

Year	All participants		Cancer patients only*		Number of studies	
	Non-interventional	Interventional	Non-interventional	Interventional	Opened	Closed
2016/17	5143	2833	5143	2833	54	35
2017/18	6458	2096	6458	2096	45	40
2018/19	4414	3000	4414	3000	42	33
2019/20	21424	5406	9786	5406	37	39
2020/21	5245	3185	4276	3185	23	18

*This data is based on a proxy from CPMS (the NIHR database used to collect patient recruitment data) and includes diagnostics, screening and prevention patients.

Appendix 5

Annual report feedback 2019-20

Dear Matthew

Re: NCRI Lung Group Annual Report 2019-20

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

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

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

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

Generic feedback for all the Groups

Strategic objectives and the impact of COVID 19

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

Multidisciplinary approach to research and membership

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

Linking with the wider research community

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

Funding opportunities

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

Consumers involvement:

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

Specific feedback for the Lung Group

Areas of strength:

- The Panel was impressed by the breadth of the Group's remit and impressive portfolio, especially the screening studies, as this patient population will be of significant impact for informing future trials. The Group should take advantage of the high-risk screening populations that are coming forward into these national screening programmes.
- Effective engagement with other NCRI Groups and initiatives including CTRad, SPED and LWBC. The Panel thought the combination of radiotherapy with other techniques and the incorporation of them into national management guidance documents, expedited due to COVID 19 outbreak, was particularly impactful.
- The Panel supported the placement of a LWBC representative on the Group as an effective strategy to cement the LWBC agenda within studies and treatment trials; the creation of stand-alone studies was commended.
- The Panel commended the Group on their work with the National Lung Cancer Audit, and hope that this strong collaboration and lobbying for funding would continue. The Panel hoped that the Group will use these outputs to direct future strategic areas to build on this connection.
- The Group's funding success was congratulated, in particular for CONCORDE.
- The Panel were impressed by the number of NICE evaluations the Group had contributed to, showing a huge amount of effort and was reflective of the direction of the lung cancer community over the past years.
- The Panel highlighted the Group's Consumers on the shaping of the Group's agenda and championing of the needs for studies addressing every stage of Lung cancer to ensure that each patient has a trial option. The Panel encouraged the Group to continue this level of involvement.

Areas which the Group need to consider:

- The Panel suggested that the Group focus their efforts on collaborating with fewer key, transformative interactions with other lung groups in the coming year as opposed to numerous less impactful ones.
- The Panel noted that the Group had a broad portfolio although suggested they consider more opportunities relating to the biology of lung cancer, e.g. biological response and biomarker directed treatment; they recognized that precision medicine is already a huge area of activity - and opportunity - for the Group.
- The Panel would have liked to see more on the topic of prevention in their strategic aims especially moving forwards into a post-COVID world.

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

- The Panel asked the Group to harness opportunities for the imaging data that is being generated through the screening studies and consider exploring the advances in technology in terms of AI and radiomics. The Panel were sure that there was activity in these areas, but this may not have been detailed in the report.

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

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

Best wishes,

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

Dr Gillian Rosenberg
Head of Research Groups,
NCRI

Appendix 6

Quinquennial review feedback - 2020

Comments and recommendations

The Panel thanked the Lung Cancer Research Group for the well written and clear documentation provided and the openness with which they had engaged in discussions.
The Panel identified several strengths of the Research Group and a number of areas for future consideration.

Areas of strength;

- The Panel thought that the report was comprehensive and commended the group on breadth and size of their portfolio as well as their funding success rate.
- There was clear evidence of significant progress over the last five years and that the Group has raised the bar of excellence for themselves. Based on this the panel did challenge the Group to now match and exceed this in years to come.
- The Group were commended on the identification of their four strategic areas of interest helping to drive research into these important areas of unmet need.

Areas for the Group to consider;

- The Panel encouraged the group to use their position in the community to address underfunded and under researched areas more including more biological driven studies, *in vivo* and in vitro studies, immunotherapy and Brain Mets but to also not be afraid to avoid competing studies especially in the currently constrained funding environment. The Panel would encourage the Group to think prudently about the studies they have planned and manage the prioritisation of these studies
- With respect to biology driven studies, the Group is asked to specifically consider AI, genomic studies and imaging within their portfolio.
- The Group should continue to build active PPI engagement at their consultations, studies, and meetings.

- The Group were advised to take advantage of all the resources and expertise across the nation, specifically including members of the multidisciplinary teams and consider diversifying the Group's membership. The panel suggested the recruitment of AHPs and Basic and Translational Scientists to the Group to support the development of high impact research and researchers to develop and run future studies.
- The Group should continue to collaborate with NCRI Cross-cutting Groups (SPED, LWBC, CTRad), and create more meaningful collaborations with them to support the development of research in these multidisciplinary strategic areas.
- The Panel suggested the Group think strategically about the value of the studies that are endorsed by the Group on the portfolio and be bold in articulating shifts that they want to see in the portfolio. The Group should continue to have a wide oversight and develop breadth in the portfolio, however the Group should not be afraid to not-endorse studies that they feel do not fit in the portfolio, are not strategically relevant or in an area of unmet need which could prevent large impact studies from recruiting quickly and providing results. The Panel asked that the Group incorporate proposed outputs, metrics and endpoints into their strategy. Whilst the four important priority areas of the Group are clear, in the strategy document submitted there was a lack of a plan for how to tackle these or clarity regarding additional key questions.
- The Panel felt that the Group should have more of a role in working with study teams from large trials in their portfolio such as MATRIX to ensure that they develop these studies in a strategic way to answer important questions of the community. The Panel also felt that there are several data resources available that the Group could work with, including the SMP2 data set and the new dataset that will come from RadNet.

Issues for the NCRI to consider.

- The NCRI will investigate potential changes to the report structure and content to allow the Groups to better showcase their invaluable work.
- The NCRI will identify ways to better support and facilitate meaningful cross-cutting Group interactions to support the development of research in strategic areas. This is especially important for the Lung Research Group to link with the LWBC Group.
- The NCRI will provide more clarity to the Groups to support creating a strategic vision with deliverable and actionable aims.
- The NCRI will review their Group membership recruitment process to ensure that the Group membership reflects the diverse range of people involved in research and the Groups strategic needs.

In concluding the Review, Professor Jenney thanked the Panel and Group members for their participation. ***The Group will be reviewed in five years' time.***

Advancing Cancer Research Together

National Cancer Research Institute
2 Redman Place,
London, E20 1JQ

T: +44 (0)20 3469 8460
F: +44 (0)20 3014 7658

info@ncri.org.uk
www.ncri.org.uk