

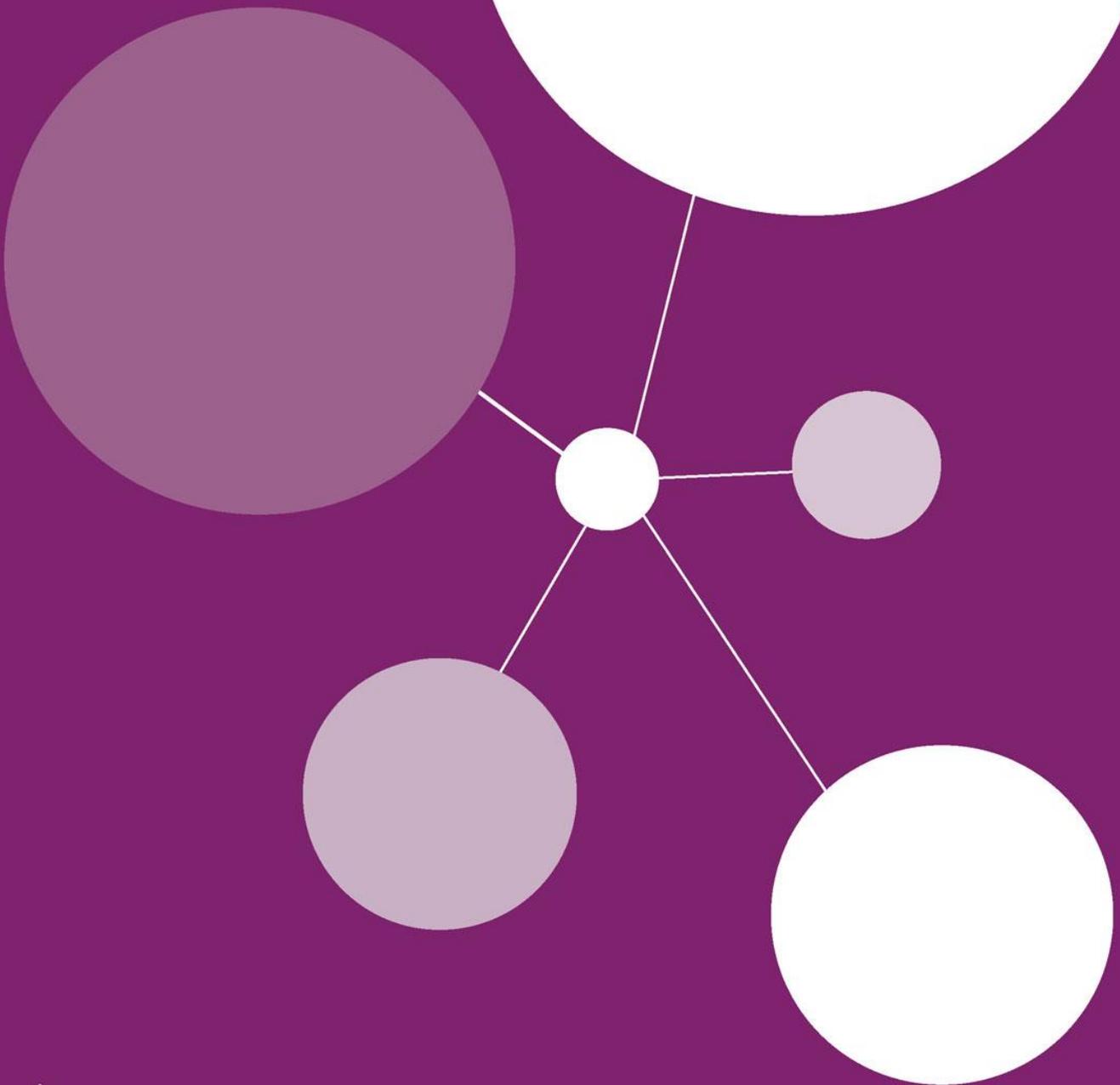


NCRI

National
Cancer
Research
Institute

NCRI Lung Group

Annual Report 2019-20



Partners in cancer research

The NCRI Group Annual Reports 2019/2020 span the time period April 2019 – March 2020.

The reports were submitted during a challenging time for all in the healthcare sector due to the COVID-19 pandemic. This has had an unprecedented impact on the activity of both the Research Group itself and wider research activities, ranging from the time available for research work versus clinical commitments to the funding of new trials and the recruitment of existing trials. Due to this the NCRI significantly extended the deadline for submission of annual reports and allowed the Groups to submit reduced reports, if time permitted, with the following sections at a minimum:

- Achievements (section 1 of the report)
- Funding Submissions over the last 12 months (section 5)
- Priorities and Challenges (section 7)

In addition to this, Consumer representatives of each Group were asked to only complete their sections if they feel able to. Most of our Consumers have submitted reports, however where reports have *not* been submitted this was due to extended periods of ill health, or additional work/home life constraints, as a result of COVID-19.

NCRI Lung Cancer Group Annual Report 2019-20



1. Top 3 achievements in the reporting year

Achievement 1

The flagships trials incorporating radiotherapy with other therapies have led to a strong body of expertise within the group and key opinion leaders internationally. This was called to further use for the COVID-19 pandemic where experts were drawing on the UK experience with accelerated radiotherapy fractionations to draw up management guidance documents.

Achievement 2

The recruitment to lung cancer screening studies this year has been excellent, in excess of 21,000 participants have been recruited e.g. SUMMIT (n=11,639), YLST (n=3,171), YLST-biomarker (n=3,054) and the Manchester Lung Health Study (n=3,143). A significant proportion of those recruited are from areas of high socio-economically deprivation, which is commendable and makes research outputs directly relevant to lung cancer screening implementation.

Achievement 3

We are extremely proud that the efforts of our short term working party have been rewarded with the funding of CONCORDE which can be added to our list of flagship trials and hopefully will be in a position to recruit by the end of this year.

2. Structure of the Group

In keeping with our strategy document we have continued to refresh our Group and the 4 Subgroups have taken advantage of the option of face to face meeting that are run in conjunction with the main Group meeting.

We owe a debt of gratitude for the hard work by the members rotating off the Group – Mr Tom Haswell, Dr Andrew Wilcock and Dr James O'Connor. In particular thanks go to Mr Haswell, who has been an active consumer representative for many years. It is a pleasure welcoming Lynne Wright and Professor Paul Cosford into that role. New members, Mr John Edwards and Dr Iain Philips are adding expertise in Thoracic Surgery/Clinical Oncology to maintain our balanced representation of disciplines. We were unable directly to address the geographical gaps highlighted in feedback and note that our devolved nation colleagues continue their active participation though the subgroups.

Our trainee representatives are proving active, engaging their research interests and contributing to the work of the Group and Subgroups.

3. Lung Cancer Group & Subgroup strategies

Lung Cancer Group

Group membership & structure

This year's advert for Group members focused on maintaining the multi-disciplinary expertise of the group which now comprises of 4 Medical Oncologists, 4 Clinical Oncologists (+ 1 trainee), 2 Respiratory Physicians (+ 1 trainee), 2 Consumer representatives, 1 Radiologists, 1 Thoracic Surgeon, 1 Pathologist, 1 Statistician, 1 Support Care Senior Research Fellow, 1 GP and 1 Transitional Scientist. This balance leaves us with one vacancy, and we plan a targeted advert that addresses the areas of need identified at the next Group meeting.

Running face to face subgroup meetings alongside the main Group has received very positive feedback and is helping in the development of studies that address our key priority areas including Living with and Beyond Cancer research. Investigators are taking advantage of these extra opportunities and we are particularly pleased with the engagement of younger investigators at our Annual and Subgroup meetings with a number allocated to new and on-going studies.

Strategy Update

The strategy document that came out of the meeting held in December 2018 was signed off in the Group meeting in May 2019.

The document is attached and confirms our commitment to:

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

Portfolio development

Data on the number of studies open, in set up and closed for the time period is captured by the portfolio maps and will be updated later in the year when the COVID-19 situation eases. Our general impression is that the number of studies on our portfolio remains healthy and recruitment levels to lung cancer portfolio studies have been stable over the past couple of years.

While we actively explore early stage disease through screening trials, The National Lung Cancer Audit presented and published compelling data on significant variations in radical treatment rates across the UK – and in particular a low radical treatment rate overall. The Group and Subgroups have taken this alongside regional variations seen in NCRI trial

recruitment data across England to make this a priority to develop trials that will fill gaps seen in the portfolio, but also inform and potentially improve outcomes in the delivery of treatment with radical intent (Locoregional Disease (LORD) Subgroup). In the advanced setting, we continue our focus on Small Cell Lung Cancer (SCLC), brain metastasis and palliative radiotherapy where, unfortunately, the COVID-19 epidemic is delaying the progress of funding applications. It is clear that the impact of COVID-19 epidemic across our patient populations is going to be another priority area for us over the coming year alongside research to address the needs of increasing.

Interaction with (inter)national research groups

The Group has good representation in the European Organisation for Research and Treatment of Cancer (EORTC) Lung Group with two of their lung steering group (Professor Mary O'Brien, Mr John Edwards) members of our Group. The result is a number of chief investigators of EORTC studies are based in the UK with Prof O'Brien, (PEARLS Study) and Dr Fiona MacDonald (HALT study), active members of our Group.

The Group has steering group representation on a number of other national and international research group including, British Thoracic Oncology Group (BTOG) (Prof Matthew Hatton, Prof Samreen Ahmed, Dr McDonald, Professor James Spicer), International Association for the Study of Lung Cancer (IASLC) (Professor Hatton), European Thoracic Oncology Platform (ETOP) (Prof Blackhall), Cancer Research UK (CRUK) Lung cancer centre of excellence (Professor Blackhall, Dr Crosbie) and Thoracic Alliance for Cancer Trials (TACT) (Professor O'Brien) which enables the Group to host and co-develop studies, notable examples include BELIEF and PROMISE-Meso.

We have maintained our links with British Psychosocial Oncology Society (Dr Lynn Calman) and the CRUK's New Agents Committee & Exploratory Research Panel (Professor Blackhall).

Interaction with cross-cutting groups

We have strong links with the clinical lead for the National Lung Cancer Audit and have been actively lobbying alongside other interested groups to maintain this valuable tool for lung cancer researchers as it faces closure if a further funding agreement is not reached over the next few months.

The Group and Subgroup members enjoy close links with the Screening Prevention and Early Diagnosis (SPED) Advisory Group, Supportive & Palliative Care subgroup and Primary Care subgroup whose Chairs (Professor David Baldwin, Professor Sam Ahmedzai and Professor Richard Neal respectively) all share our lung cancer research interest. Members of our Group are active in CTRad (Dr McDonald, Professor Hatton), the Psychosocial Oncology & Survivorship Group (Dr Calman) and CM-Path (Professor Wallace). 4 of our Group members are currently serving as Lung Sub-Speciality Leads (SSLs) and we pleased that a number of other lung SSLs attended and contributed to our strategy meeting.

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

Key research priority areas

COVID 19

The current epidemic is having a profound effect on the presentation, diagnosis and management of patients with lung cancer. The majority of members of the Group and Subgroups are involved in research/service evaluation projects assessing the impact on our patient population and the group will offer oversight and co-ordination of these efforts over the coming year.

Living with and Beyond Cancer

These research priorities remain a focus as highlighted in our strategy document. Dr Calman sitting on both the Methodology and Advanced Disease and End of Life Care workstreams has ensured good communication between the lung and Living With and Beyond Cancer (LWBC) group 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 priority identified as specific research questions in the study outlines/protocols that are being developed.

Surgery/Radiotherapy

TRACERx remains a flagship study on our portfolio and we are pleased that Dr Jamal-Hanjani has joined our Advanced Disease Subgroup and is ideally placed to be our key link with their team. Investigators have progressed proposals to explore the role of proton beam radiotherapy in stage III NSCLC and surgery/radical radiotherapy as a local consolidative treatment in stage IV disease (RAMON) with funding submissions prepared. Group/LORD Subgroup member are leading studies (PREHAB, PIONEER), which are now funded, examining quality of life in the context of the treatment of stage III NSCLC and are relevant to the LWBC agenda. They will hopefully open for recruitment later this year.

Early phase

The MATRIX study continues to recruit steadily and has started to present outcome data at the major international meetings. The working party for radiotherapy-drug combination trials has seen the CONCORDE study funded by CRUK and is working towards opening at the end of this year. A number of the Group members are active in the ECOM network with funded proposals of new drug trials in lung cancer now recruiting.

Advanced disease

The Subgroup workshops for brain metastases (EDAM), palliative radiotherapy (TOURIST) and SCLC research have funding submissions prepared or in development awaiting the post COVID-19 resumption of 'normal' business. Efforts to develop a high recruiting immunotherapy study continue to focus on CONVOLUTE (investigating schedules/duration of PD-1 targeted treatment) with a current funding application to NIHR through to the next round. A CRUK Centre for Drug Development (CDD) study of a novel vaccine therapy to augment response to first line chemo-immunotherapy is in development with funding approval pending from the CRUK NAC. Biomarker driven studies on evolutionary biology and therapy target discovery (TRACERX, DARWIN, PEACE) and the precision medicine platform study MATRIX continue to recruit well with high impact presentations and publications generated.

Raising awareness and profile

The Lung Annual Trials Meeting 2019 generated much positive feedback and was an established part of the lung cancer meetings calendar. Advanced preparations for the 2020 meeting were in place prior to cancellation due to COVID-19. Alternative dates are being considered as are virtual meetings with investigators keen for input and advice on their proposals. The close working relationship we enjoy with BTOG continues to give a strong presence at the Dublin meeting and the opportunity to present our portfolio and present the trial outline in development.

We successfully launched our NCRI Lung Cancer Trial Badging scheme with 9 investigator lead studies now registered as UK NCRI Lung Cancer Studies. The significant workload engendered by National Institute of Clinical Excellence (NICE) evaluations continued over the past year and the Group Chair is extremely grateful that members continued to willingly offer their expert, voluntary support for that process.

Patient and Public Involvement and Impact

Our Public and Patient Involvement (PPI) representatives remain incredibly active, accepting the opportunity to become involved in a number of the studies being developed through the Group and advising investigators presenting their ideas at our trials meetings. We particularly acknowledge the contribution of Mr Haswell who has just stepped down from the main Group.

We have been able to increase the PPI representation in our subgroups and their involvement has continued to shape our agenda championing the need for studies considering every stage of the patient journey including a focus on the non-smoking cohort for whom the living with and beyond cancer agenda is particularly pertinent.

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 our screening study portfolio targeting the difficult to reach population.

Strengthen UK wide and international working

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

A number of flagship studies have international collaboration e.g. HALT and potentially SARON and studies in rarer tumours can run efficiently through the lung RG e.g. Nivothym and Promise Meso. The work with other research groups has RG members leading a number of international collaborations with studies that are appearing on our trials portfolio, for example, Teravolt documenting the impact of COVID-19 on lung cancer treatment.

In the strategy meeting the changing nature of research was discussed with increasing importance on Artificial Intelligence (AI) development in medium and long term giving opportunities for big data research. The Group is clear that we need to maintain clear links with National Cancer Intelligence Network (NCIN) to exploit routinely collected datasets and

build on our current use in assessing feasibility of studies and support analysis of the Lung Cancer Audit data.

Advanced Disease Subgroup (Chair, Professor Fiona Blackhall)

Cerebral metastasis

The treatment of brain metastases is a gap in the portfolio and a gap in our clinical knowledge. The EDAM trial is being led by one of our young investigators on the Group who has taken the opportunity to get a good review published on brain metastases. The study has undergone extensive scoping and PPI and has the support of the brain tumour group, funding is required and a grant has been submitted to the NIHR. A grant to CRUK in 2019 was not successful but further feedback has shaped and improved the current submission.

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

The ALKALINE trial is an EORTC led study in ALK gene fusion positive Non-Small Cell Lung Carcinoma (NSCLC) currently in set up in the UK (UK CI Professor Blackhall). The ETOP LUNGSCAPE translational biomarker research platform continues to assess therapeutic biomarkers for implementation in treatment decision making and includes several UK lung cancer sites. International consortia approaches are essential for study of rare molecularly defined patient subtypes. The HALT and SARON studies of radiotherapy in oligometastatic disease have expanded to include international/European centres in close collaboration with ETOP and EORTC investigators. The impact of COVID-19 will be severe on the latter due to suspension of trials and radiotherapy for oligometastatic disease alongside the increased risks of COVID-19 infection for patients with lung cancer.

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

The Subgroup has recruited a scientist Dr Vivanko who has a specialism in preclinical drug development and target discovery and a clinician scientist Dr Jamal-Hanjani who is an early stage career researcher with a clinical translational and evolutionary biology focus.

To develop biomarker directed academically-led studies in SCLC

A SCLC working group has been approved and will convene post COVID-19. 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. A preclinical study is in progress using SCLC patient derived mouse models to identify novel drug combinations to take forward to clinical trial ideally with drug-biomarker target identified for selection of patients.

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

Dr Calman and Professor Ahmed have scoped the potential and need for an exercise intervention study in patients with advanced disease. Feedback from PPI including at BTOG 2020 has been positive to proceed with a pilot study funding application which is in progress.

To focus on promoting and progressing key 'flagship studies' in terms of recruitment and protocol development respectively

Key flagship studies (as per table in appendix) have a 'trials champion' assigned from the subgroup to promote, liaise with the study Principal Investigator (PI) and flag any recruitment barriers or concerns.

TRACERX, PEACE, SMP2/MATRIX have had funding renewals/extensions from CRUK and continue to recruit well with published, high impact factor presentations and outputs in the past year. HALT and SARON have expanded to include European centres.

MATRIX was presented in the plenary session/Presidential symposium as one of the top 5 abstracts at the World Lung Cancer Conference 2019 (Professor Gary Middleton, presenting author)

PEPS2 has been published. (Middleton G et al. Lancet Respiratory Medicine 2020)

CONVOLUTE and EDAM have funding applications to NIHR in progress.

ARROW, TOURIST, DISCOVER SCLC are in development for funding application.

A new collaboration has been fostered with CRUK DDO and NAC for a novel vaccine trial.

L0coRegionalDisease (LORD) Subgroup (Chair, Professor Mary O'Brien)

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

Following a very successful VIOLET study we are awaiting detailed analysis of the data to plan the next intervention lung cancer surgery trial.

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

The move the holding face to face meeting alongside the RG meeting has allowed a number of new research to present ideas and engage with the subgroup.

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

The PEARLS trial has closed and the next adjuvant study will be designed in 2020-21 while waiting on the PEARLS read out.

Specific areas of LORD interest and development

Poor rates of radical treatment on offer in the UK for stage III disease will be the focus of a proposal to develop a virtual Multidisciplinary Team (MDT) to discuss all stage III patients, to collect data and understand better why radical treatments are not offered – using virtual platform with ROCHE.

Mesothelioma Subgroup (Chair, Dr Peter Szlosarek)

Maintain an emphasis on high quality biomarker driven studies and a balanced trial portfolio focusing on all subtypes of Malignant pleural mesothelioma (MPM)

The MIST (Mesothelioma Stratified Therapy) programme co-ordinated from Leicester (Professor Fennell) with early signal-finding trials of novel targeted agents e.g. the PARP inhibitor rucaparib (MIST-1); the CDK4/6 inhibitor ambemaciclib (MIST-2). Further MIST arms are added testing molecularly-driven hypotheses with novel agents as these become available.

The global ATOMIC-meso phase 2 (Professor Szlosarek), focusing on non-epithelioid mesothelioma, has moved to phase 3, and exemplifies how phase 1 to phase 3 activity has been supported within the Subgroup as a novel biomarker developed area of research activity.

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

- Additional studies ongoing with input from the Subgroup include:
- MARS2 (Professor Lim) to determine the role of surgery for respectable mesothelioma.
- BEAT-meso (Professor Popat) to assess the role of chemo-immunotherapy versus chemotherapy for mesothelioma.
- The Checkmate-743 study comparing ipilimumab and nivolumab immunotherapy versus standard platinum-pemetrexed doublet chemotherapy is reportedly positive according to a Sponsor statement issued in April 2020. Consequently, the first-line treatment approach within the NHS and late stage trial development may be affected going forward. Wider engagement with the mesothelioma community will be critical to improve access to novel therapies shown to be of benefit to patients.

Nurture new talent in mesothelioma research

Young investigators are encouraged to contribute novel study proposals either via the MIST.

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

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

A re-organisation of how the sub-group and SPED interact has been developed and enacted.

Encourage trials of interventions to reduce tobacco harm

A number of applications to CRUK related to tobacco harm were reviewed by the sub-group. To deepen our expertise in this area we will invite an additional member to join the group who has a specialist interest in tobacco control research. The YESS Randomised Control Trial (RCT) is successfully recruiting smokers to an intervention study at the time of lung cancer screening.

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

This is being addressed in a number of studies across the UK e.g. Yorkshire Lung Cancer Screening Study.

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

Large scale screening studies are recruiting in the UK to answer these questions. Indeed, the UK is at the forefront of lung cancer screening implementation research internationally.

Develop closer links with qualitative researchers

Qualitative research is integral to early detection studies especially related to screening uptake/experience e.g. Lung Screen Uptake Trial.

4. Task groups/Working parties

Remit of Lung Cancer Radiotherapy-Drug Combinations Consortium Working Party

Progress to date

CONCORDE

A Platform study of novel agents in COmbination with COventional RaDioTherapy in NSCLC.

Funded by the Cancer Research UK Clinical Trials Committee in July 2019 with a start date for the funding of November 2019.

The novelty of the design has been recognised by an invited editorial in Clinical Oncology The protocol has been finalised and submitted for publication at Clinical and Translational Radiation Oncology.

Advanced negotiations are going on with AstraZeneca (one of our pharmaceutical partners) to open the first two arms in November 2020.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Cancer Research UK					
May 2019					
XIP1: Hyperpolarised Xenon Imaging in Chemotherapy Induced Pneumonitis	Biomarker Project Award	Professor Fergus Gleeson	Not Supported	Group/Subgroup consulted	
Characterising the role of STK11/LKB1 co-mutation as a negative predictive marker for immune checkpoint inhibition in KRAS-mutant non-small cell lung cancer	Biomarker Project Award	Dr Colin Lindsay	Not Supported	No input	
CONCORDE - NSCLC: Platform study of novel agents in COmbinatioN with COnventional RaDiothErapy in locally advanced disease	Clinical Trial Award (full)	Dr Alastair Greystoke	Conditionally Supported	The study is being led by members through a Group Short Term Working Party.	
November 2019					

EDAM - Early Detection of Asymptomatic Metastases in the brain - a phase 2 randomised trial comparing regular brain MRI imaging versus no brain imaging in advanced lung cancer patients, to test if the MRI could be a biomarker of symptomatic brain metastases symptomatic incidence (sBrM)	Biomarker Project Award	Dr Mary O'Brien	Not Supported	The study is being led by members of the Group/ Advanced Disease Subgroup.	
Biomarkers to Optimise Lung Screening: A New Partnership between Manchester, Leeds, and IARC.	Project Award	Dr Phil Crosbie and Hilary Robbins	Not Supported		
Optimising GP recognition and referral to increase earlier diagnosis of lung cancer	Project Award	Dr Sara McDonald	Not Supported		
Other committees					
Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount

PIONEER. ImPact on Quality Of life from multi-modality treatment for lung caNcEr: A randomised controlled fEasibility tRial of surgery versus no surgery as part of multi-modality treatment in potentially resectable Stage III-N2 NSCLC.			Supported	Group/Advanced Disease members involved in development of study and appointed to TMG	
CONVOLUTE. A randomised trial of continuous verses non-continuous anti PD-1 monoclonal antibody for patients with relapsed non-small cell lung cancer	NIHR	Dr Mike Seckl	Not supported	Group/Advanced Disease members involved in development of study.	
Avoiding cardiac toxicity in lung cancer patients treated with curative-intent radiotherapy to improve survival.	Yorkshire Cancer Research reference number M401	Professor C Faivre-Finn / Dr K Franks	Supported	The study is being led by members of the Group	£272,141.90
PREHABS: Pre-habilitation Radiotherapy Exercise, smoking Habit cessation and Balanced diet Study.	Yorkshire Cancer Research reference number: L426	Dr K Franks / Dr C Burnett	Supported	The study is being led by members of the Group	£188,744.37

6. Consumer involvement

Consumer: Lynne Wright

No consumer report submitted – please refer to page 2.

Consumer: Paul Cosford

No consumer report submitted – please refer to page 2.

7. Priorities and challenges for the forthcoming year

<u>Priority 1</u> To support and develop research and service evaluation of the impact of COVID 19 on the management and treatment of thoracic cancers across the UK.
<u>Priority 2</u> To continue to support investigators as they develop research protocols and funding submissions that were initiated by our SCLC, brain metastasis, and palliative radiotherapy workshops.
<u>Priority 3</u> To prepare for the 2020 Quinquennial Review and act upon the advice and recommendations made by the panel.
<u>Challenge 1</u> The effects of COVID-19 pandemic on recruitment into the current trial portfolio and its impact on future funding and support for non-COVID-19 related research.
<u>Challenge 2</u> 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.
<u>Challenge 3</u> Increasing costs, funding competition and limited infrastructure within the NCRN leading to significant delays in trial set up and opening of centres.

8. Collaborative partnership studies with industry

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

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

Discussion has opened with Roche on the role of their virtual MDT platform as an adjunct to treatment decision making in the UK in stage III disease.

9. Appendices

Appendix 1 – Lung Group and Subgroup strategies

- A – Lung Group Strategy
- B – Advanced Disease Subgroup Strategy
- C – LocoRegionalDisease (LORD) Subgroup Strategy
- D – Mesothelioma Subgroup Strategy
- E – Screening & Early Diagnosis Subgroup Strategy

Appendix 2 – Top 5 publications in reporting year & Group involvement with NICE appraisals



Professor Matthew Hatton (Lung Cancer Group Chair)

Appendix 1

Lung Cancer Group and 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.	MH, NK	Ongoing
	Promote face to face subgroup meetings to coincide with meeting of the main Group.	MH / Subgroup leads	Ongoing
Portfolio	Continue to develop and deliver investigator led studies to complement the current portfolio and industry sponsored studies	Group	Ongoing
	<p>Key research priority areas include -</p> <p>Brian mets</p> <p>Palliative radiotherapy</p> <p>SCLC</p> <p>Living with and beyond</p>	<p>MOB</p> <p>MH</p> <p>FB</p> <p>LC</p>	Outline proposals to Group and Annual Trials Meeting
UK researcher engagement new trial development	<p>Promote opportunities for investigators to present study outline through Annual Trials Meeting, BTOG and Subgroup meetings</p> <p>Define a new trial development process across the Group and subgroups with scoring systems for new trial ideas</p> <p>Ensure supportive environment for honest feedback to those proposing studies</p>		Ongoing

	Advise on future-proofing trials in light of the fast moving changes in of standard of care treatments for lung cancer		
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	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		
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 Subgroup		

	<p>Rotation of Subgroup chair</p> <p>Review and update membership</p> <p>Screening</p> <p>Engage with the UK National Screening Committee (UKNSC)</p> <p>Identify research opportunities around implementation of a national screening program eg database integration, smoking cessation, biological samples.</p> <p>Screening for other high risk groups e.g. lymphoma radiation exposure</p> <p>Identification of a biomarker for early detection</p> <ul style="list-style-type: none"> • Loco-Regional Disease <p>Review and update membership</p> <p>Work with screening subgroup to consider management studies for the cohort of patients identified through a national screening program.</p> <p>Work with Roche on their virtual MDT platform to document treatment decisions in stage III disease.</p> <p>Explore research opportunities for the next adjuvant international trial.</p> <p>Consider the LWBC research priorities and their applications to improve fitness for radical treatment.</p> <p>Management of patients with driver mutations presenting with loco-regional disease given the new generation of active TKIs.</p> <ul style="list-style-type: none"> • Advanced Disease <p>Review and update membership</p>	<p>PC</p> <p>FS /</p> <p>MOB</p> <p>FB</p>	<p>Feb 2019</p> <p>Apr 2019</p> <p>Apr 2019</p> <p>Apr 2019</p>
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	<p>Nurture the development of studies /platforms for SCLC, palliative radiotherapy and brain metastasis.</p> <p>Mesothelioma</p> <p>Review and update membership.</p> <p>Work to maintain and update the current trials portfolio</p> <p>Develop a platform for early phase studies in mesothelioma</p>	<p>PS</p> <p>DF</p>	<p>Apr 2019</p>
Industry engagement	<p>Continue engagement with Phama/biotech companies and explore opportunities to extend this to the subgroup level.</p> <p>Monitor impact of mesothelioma compensation claims to fund access drugs being tested in portfolio studies.</p>		
next generation of researchers	<p>Appoint and Mentor Trainee Group members to subgroups</p> <p>Engage younger scientists and physicians through BTOG and other national meetings</p> <p>Work with Royal Colleges and other training bodies</p>	<p>MA, MR</p>	
Consumer involvement	<p>Continue to involve consumers across the work of the Group to encourage their input at an early stage in all new trial proposals</p> <p>Ensure Subgroup has consumer involvement</p>	<p>TH</p> <p>MH/ND</p>	
International	<p>Maintain strong links with international research groups</p> <p>Identify Group leads to link to BTOG,</p>		

	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: <ul style="list-style-type: none"> • Primary Care Group • SPED Advisory Group • CTRad • Supportive and Palliative Care Group • CM-Path 	FS FM AW 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 eg UK Oncology Forum		

	<p>Engagement with CRN subspecialty leads through The main Group and/ or Subgroup meetings.</p> <p>Use Lung Cancer Awareness month to highlight lung cancer research.</p>		
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B – Advanced Disease Subgroup Strategy

Aims

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

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

	ARROW	Protocol under development
	TOURIST	Protocol under development
SCLC Extensive Disease	Study 15	Actively Recruiting
	DISCOVER SCLC	Protocol under development

C – Loco-Regional Disease (LORD) Subgroup Strategy

- Continue to expand research in early stage lung cancer, particularly related to new radiotherapy combinations (immunotherapy and targeted agents) and support protocol development and funding applications – 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 2

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	Group involvement in the trial
<p>Joshi, K., Robert de Massy, M., Ismail, M. <i>et al.</i> Spatial heterogeneity of the T cell receptor repertoire reflects the mutational landscape in lung cancer. <i>Nat Med</i> 25, 1549–1559 (2019). https://doi.org/10.1038/s41591-019-0592-2</p> <p>Chemi, F., Rothwell, D.G., McGranahan, N. <i>et al.</i> Pulmonary venous circulating tumor cell dissemination before tumor resection and disease relapse. <i>Nat Med</i> 25, 1534–1539 (2019). https://doi.org/10.1038/s41591-019-0593-1</p> <p>Biswas, D., Birkbak, N.J., Rosenthal, R. <i>et al.</i> A clonal expression biomarker associates with lung cancer mortality. <i>Nat Med</i> 25, 1540–1548 (2019). https://doi.org/10.1038/s41591-019-0595-z</p>	<p>TRACERx. These three 2019 publications have increased our understanding of the development and spread of lung cancer giving important insights which can be used to develop future treatments.</p>	<p>Contributions to the development, recruitment and management of study have been made by a number of past and present members of the Group who is acknowledged as authors in their publications.</p>
<p>The UK at the Forefront of Innovative Drug-Radiotherapy Combination Clinical Trials: Introducing the CONCORDE Platform. Faivre-Finn C, Brown S, Ryan A, Greystoke A; CONCORDE Investigators.</p>	<p>CONCORDE has been developed as a unique platform that will test new drug radiotherapy combinations. The lessons learnt during its development are being shared with the wider</p>	<p>This study has been developed through a Lung Research Group Short Term Working Party.</p>

Clin Oncol. 2020 doi: 10.1016/j.clon.2020.02.003.	community through publications such as this.	
Kyte, D., Retzer, A., Ahmed, K., Keeley, T., Armes, et.al. (2019). Systematic evaluation of Patient-Reported Outcome protocol content and reporting in cancer trials. <i>Journal of the National Cancer Institute</i> , 111(11), 1170-1178. DOI: 10.1093/jnci/djz038	Work establishing methodology for Patient reported outcomes in cancer trials.	Contributions to the development and management of study have been made by members of the Group who is acknowledged as authors in the publication.
PA Crosbie, H Balata, M Evison, M Atack, et.al. Implementing lung cancer screening: baseline results from a community-based ‘Lung Health Check’ pilot in deprived areas of Manchester. <i>Thorax</i> (2019) 74:405-409.	The Manchester Lung Health Check pilot took lung cancer screening into deprived communities – resulting in high levels of early stage lung cancer detection and curative intent treatment. This model was included in the NHS Long Term plan and secured £70M funding from NHS England for a national targeted lung cancer screening pilot.	First Author is chair of the Screening and Early Detection sub-group.
S Page, C Milner-Watts, M Perna, U Janzic et.al Review: Systemic treatment of brain metastases in non-small cell lung cancer. <i>European Journal of Cancer</i> 132, 2020, 187-198. https://doi.org/10.1016/j.ejca.2020.03.006	A review to the current state of knowledge of treatment of brain metastases. Part of the workup for the EDAM trial proposal.	First author is one of our young investigators, support by members of the Group.

Group involvement with NICE appraisals

NICE appraisal	Appraisal outcome	Group involvement with NICE appraisal
ID1468, Brigatinib, 1 st line, ALK + ve NSCLC	In process	<p>The Group is consulted as a recognised Stakeholder for all lung cancer appraisals</p> <p>The ones listed here have the nominated experts contributing to the appraisal drawn from the Group / Subgroups</p>
ID1328, Loratinib, 2 nd line, ALK + ve NSCLC	Recommended treatment, final appraisal, May 2020	
ID1559, Nivolumab, 2 nd line, squamous NSCLC(CDF Review TA483)	In process	
ID1572, Nivolumab, 2 nd line, non-squamous NSCLC(CDF Review TA484)	In process	
ID1675, Nivolumab / Ipilimumab, 1 st line PD-L1 + ve NSCLC	Suspended	
<i>ID1504</i> Atezolizumab / Chemotherapy, 1 st line SCLC	Not funded at 1 st meeting; in process	
ID1302 - osimertinib 1 st line EGFR +ve NSCLC	In process, approved for CDF during COVID 19 epidemic	
ID1577 - osimertinib 2 nd line EGFR +ve (T790+ve) NSCLC (CDF review TA416) and 2L respectively.	In process	
ID1512 Entrectinib line for NTRK fusion + ve		

ID 1541 Entrectinib for ROS1 + ve NSCLC	In process	
ID 1504 Atezolizumab with chemo, SCLC 1 st line.	In process	
ID1683 Pembrolizumab with carboplatin and paclitaxel 1 st line squam NSCLC	In process	
ID1495 Atezolizumab with Carboplatin or Cisplatin and Pemetrexed non squam NSCLC	In process	
TA584 Atezolizumab with chemo NSCLC, 1 st line	Suspended	
ID1618 Durvalumab SCLC 1 st line	Approved June 2019	
ID1175 Durvalumab NSCLC after concurrent chemo-XRT	In process	
	Approved	