NCRI
National
Cancer
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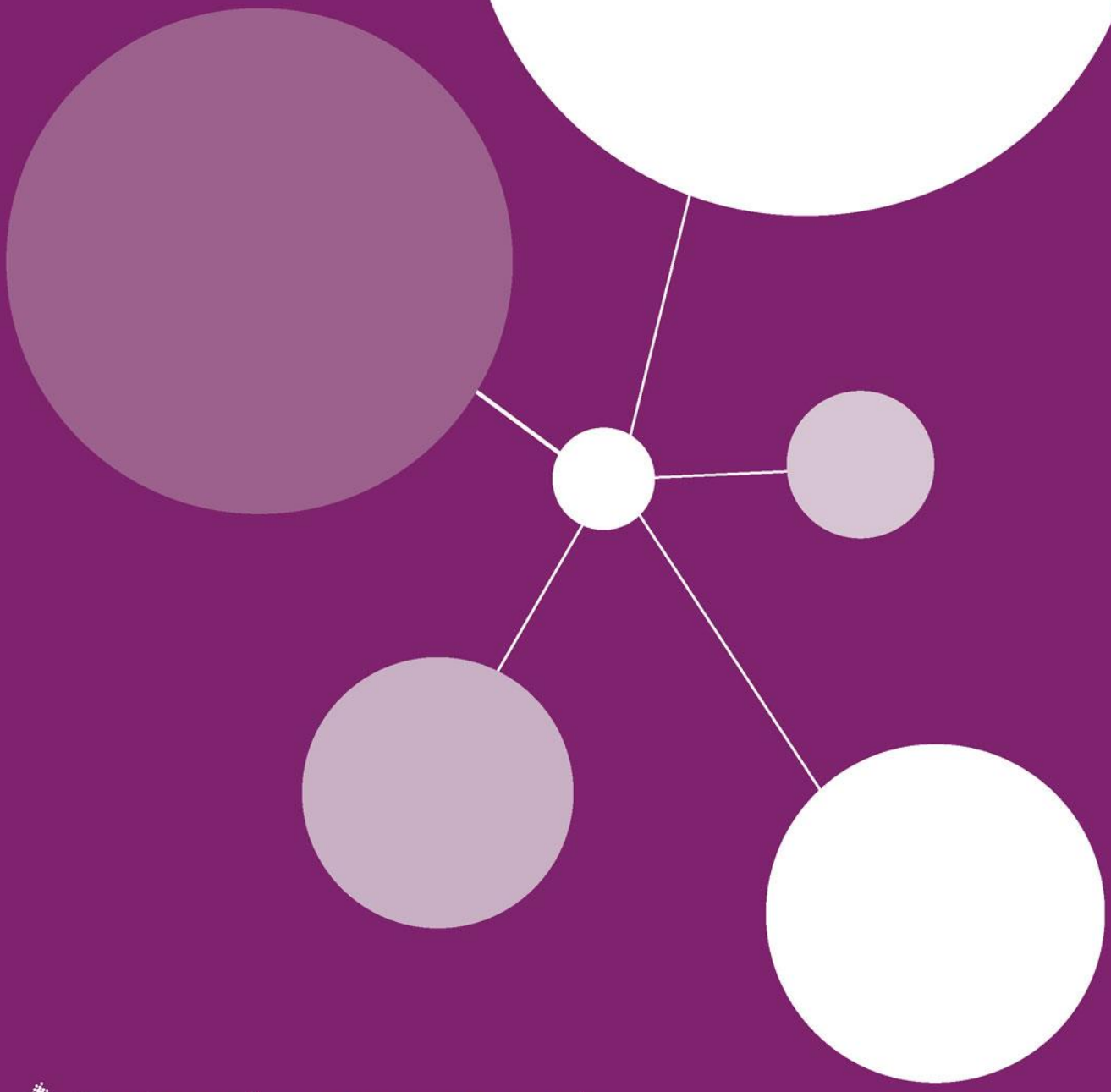
Institute

NCRI Lung Cancer Clinical Studies Group

Annual Report 2015-16



Partners in cancer research

NCRI Lung Cancer CSG Annual Report 2015-16

1. Executive Summary (including top 3 achievements in the year)

The work of the Lung CSG continues to result in an increased number of patients accessing the trials portfolio with a particularly pleasing increase in the numbers entering interventional studies. International collaboration with EORTC, ETOP, IMIG increases and we have become founder members of TACT (International lung cancer trials group collaboration) as we look to enhance the international recognition of the NCRI CSG as a successful trials organisation. CSG members have regularly volunteered to offer their expert support to the NICE evaluations of new drug applications considered for funding. Our public involvement representatives continue to excel ensuring the wider engagement and relevance of the lung group.

Members of the Lung CSG has been involved in the development of a number of studies that are at the forefront internationally, these include the Stratified Medicine Programme (SMP) 2, MATRIX and TRACERx which have been recruiting steadily undoubtedly raise the profile of the UK lung cancer research portfolio.

NRCI Lung CSG strategy meeting was held in November 2015 and agreed on the key research areas and develop a program that works with sub-speciality leads and other research groups to deliver trials in these areas. The meeting also agreed to raise the profile of the CSG through the reinstatement of its Annual Meeting and the national badging of UK investigator lead studies. Planning is advanced for 2016 Annual Meeting will be held jointly with BTOG while the CSG workshops will continue to be an integral part of the annual BTOG meeting. This will increase the opportunities for investigators to meet and allow more feedback to the engaged research teams while the CSG will continue to develop other forums and offer workshops to encourage new investigators to bring proposals for discussion.

2. Structure of the Group

The number of CSG core members has been maintained and the membership refreshed as members complete their terms. Members have responded to requests for expert reviews from bodies such as NICE which continue to generate a significant extra (voluntary) workload. The four Subgroups – Screening / Early Diagnosis, LocoRegional Disease (LORD), Advanced Disease and Mesothelioma continue to review and develop trial protocols and there is a good record of new members applying for positions in the Subgroup and an expansion of non-core membership is planned to facilitate engagement with all interested in lung cancer research.

3. CSG & Subgroup strategies

Main CSG

The appointment of three new Subgroup Chairs and the ongoing refreshment of the membership with its mix of new and experienced researchers will re-energise the Lung CSG while maintaining the existing links with international research groups. An important goal is to develop strong links with other (cross cutting) CSGs and the subspecialty leads for lung cancer over the coming year to encourage and facilitate access to local NCRI budgets for clinical trials. The development of the Lung CSG members' link with their network leads should inform on any problematic issues that stifle trials locally.

Working with BTOG we are developing a more comprehensive timetable of meetings and workshops to develop trial outlines. The annual meeting has been reinstated and areas where we would expect to develop some broad based studies that improve overall recruitment to lung cancer trials are immune therapies, radiotherapy, mesothelioma and fitness for treatment.

The CSG strategy looks to embedded smoking cessation, supportive care and follow up sub-studies into trials that are being developed and will work with SPED, the Primary Care and the Supportive and Palliative Care CSGs to achieve this. We also plan to work with key clinical and scientific groups to develop a multi-modality database and translational research platform for lung cancer, one goal being studies that investigate possible use of blood and urine markers as we continue to struggle with the amount of information required from small biopsies.

Links with other CSGs and international groups will by necessity be solidified/increased through communication and collaboration via Lung CSG members. Further worldwide recruiting translational, phase II and III studies participation for even rare genetic subgroups worldwide will be developed, led and supported by the Lung CSG.

Mesothelioma Subgroup (Chair, Dr Peter Szlosarek)

The Mesothelioma Subgroup is organised virtually and meets annually at BTOG. Several new trials are in set up or in development and overall 2015/2016 has witnessed a record increase in the trial portfolio reflecting the high burden of MPM in the UK. Several commercial Phase II/III trials supported by the NCRN have recently closed: (1) DETERMINE, assessing the CTLA4 antagonist tremelimumab vs placebo in second and third line patients with MPM, which was presented at ASCO 2015 and failed to show an improvement over placebo in this setting; and (2) the COMMAND trial, assessing the role of the FAK inhibitor, defactinib versus placebo as maintenance therapy following 4-6 cycles of standard chemotherapy in MPM in the first-line setting. Phase I commercial trials in MPM have also been well represented, meso 2 (ganetspib + standard chemotherapy) and TRAP-MPM cohort, with the latter proceeding to a phase II/III trial called ATOMIC–meso (CI: Szlosarek) in patients with biphasic and sarcomatoid MPM. Consistent with the James Lind Alliance Initiative, several academic immunotherapy trials are proceeding with support of the NCRN: PROMISE-ETOP (CI: Popat) and CONFIRM (CI: Fennell) with additional phase I trials due to launch in 2016 (FAK+pembrolizumab, Glasgow, Leicester and Southampton). Finally, the CSG is supportive of pemetrexed retreatment with a revised trial design (CI: Shah).

Advanced Disease Subgroup (Chair, Dr Sanjay Popat)

The Advanced Disease Subgroup interacts mainly virtually, with one physical meeting annually during the BTOG annual meeting. The Subgroup will be participating in the National Trials Meeting to critique and prioritize trials for further development.

The Subgroup hosts a varied portfolio of trials for advanced NSCLC and SCLC many are commercial but there is a range from the complex biomarker-directed trials to single CRN observational studies.

The NSCLC academic portfolio is challenged (as is the case globally) by the dominance of commercial trials. However, the SMP2 molecular pre-screening study paired with the National Lung MATRIX trial (developed and delivered in collaboration with Industry and CRUK) have recruited well and better than other International genotype-directed umbrella studies. These remain flagship studies for the CSG and Subgroup.

In SCLC, the completion of recruitment on time and target to the STOMP 1st line maintenance randomized phase II trial has been a particular success. These results are eagerly anticipated and will be important in determining the strategy for PARP inhibition in SCLC.

In NSCLC, the QUARTZ trial (CI Mulvenna) reported at ASCO 2015 and has markedly changed UK practice. The ETOP-sponsored-NIHR co-delivered BELIF trial (UK CI: Popat) reported at ESMO 2016 and resulted in an extension to the EMA label for bevacizumab.

LocoRegional Disease (LORD) Subgroup (Chair, Dr Yvonne Summers)

Dr Yvonne Summers has taken over as Chair of the LORD Subgroup and continued the strong focus on academic radiotherapy studies, with several experienced Pi's on the Subgroup who continue to develop high quality trials. There are three new investigator led studies in set up (REPLICA, SARON and ADSCaN) and full CTAAC applications have been invited for IDEAL-2 (Landau) and PRINCE (Hatton) with newer investigators developing and submitting proposals (HALT, MacDonald).

The role of immunotherapy following chemo-radiotherapy in stage III NSCLC was also addressed in the PACIFIC trial, which has successfully completed recruitment and after two years with no adjuvant studies open to recruitment on the portfolio the PEARLS study has opened and address the important question of whether immunotherapy can improve outcomes for patients with surgically resected NSCLC.

The key portfolio CRUK funded CONVERT study completed recruitment in 2015, was presented by Prof Faivre-Finn in an oral presentation at ASCO 2016. The trial will influence practice demonstrating that twice daily radiotherapy maintains clinical outcomes while halving treatment time for SCLC patients.

The national workshop organised by the LORD Subgroup was well attended and new trial proposals will be explored at the Annual Trial Meeting on 16 June, with further surgical proposals anticipated. An additional strategic aim is to develop smoking cessation studies; though sadly the most recent proposal was unsuccessful in securing funding.

Screening/Early Diagnosis Subgroup (Chair, Dr Neal Navani)

Dr Navani took on the role of Subgroup chair in June 2015 from Dr Rintoul. The Screening/Early Diagnosis Subgroup has 16 open trials on its portfolio with 3 in set-up including the PEARL trial – which is the world's first randomised trial of treating pre-invasive airway lesions to prevent lung cancer and recently funded by CRUK. Trials have generally recruited well with key publications expected from the SEARCH and UKLS screening trials in 2016 and 2017. A key publication from the UKLS trial has already set out a potential plan for lung cancer screening in the UK. The recently opened Lung Screen uptake trial will seek to establish the best method for recruiting lung cancer screening participants.

The Subgroup conducted an extremely well attended meeting at BTOG in Jan 2016. The Subgroup recognises that several studies within the portfolio have an aspect of smoking cessation research embedded, however there are no current trials to examine interventions to reduce harm from tobacco. Applications supported jointly with the Primary Care CSG have been encouraged and have resulted in new submissions for funding in June 2016.

4. Task groups/Working parties

In February 2016, CTRad and Lung CSG ran a workshop in Glasgow to develop a UK research program for radiotherapy new drug combinations in NSCLC. A lung CSG short term working party will be established to develop the ideas put forward for phase I trials in stage IV NSCLC and phase II studies in locally advanced disease.

5. Patient recruitment summary for last 5 years

In the Lung Cancer CSG portfolio, 29 no. of trials closed to recruitment and 24 opened.

Table 1 Summary of patient recruitment by RCT/Non-RCT

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	4537	2442	2032	1716	5.4	4.6

Table 2 Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	2744	4445	2028	1171	4.8	2.8
2013/2014	3036	992	2665	942	6.3	2.2
2014/2015	3396	1236	3074	1236	7.3	2.9
2015/2016	3541	1724	3270	1724	7.76	4.09

Lung cancer has the third largest number of commercial trials in all the CSGs portfolios, behind breast cancer and haematological oncology. Lung cancer has the sixth largest non-commercial portfolio. In the Lung Cancer CSG portfolio over the course of 2015–16 there were 29 trials closing to recruitment with 24 new studies opening.

Currently there are 54 trials open to recruitment in the portfolio and a further 6 in set-up which is too many for a full description of each one. From these, 6 trials are commercially sponsored with a further 48 non-commercial trials in the portfolio, of which 6 are in set-up. The regularly updated portfolio maps (Appendix 4b) - provided by the NCRI CSGs Secretariat, assisted by CSG members are being refined and hopefully will prove of greater use to current and potential investigators as well as lung cancer specialist and research nurses who are using them regularly.

6. Links to other CSGs, international groups and network subspecialty leads

Many international lung cancer research groups are standing agenda items with updates from CSG members, for example, Dr O'Brien (immediate past Chair of the EORTC lung group), Dr Popat (BTOG Chair) and Professor Fennell (IMIG chair and co-ordinator of their very successful 2016 Annual Meeting in the UK). The new TACT (International lung cancer trials group collaboration) has Dr Nicholson on its steering committee has the NCRI Lung CSG as a recognised partner and contributor to this developing organisation that is likely to have a large impact on development of trials especially for rare patient subgroups with lung cancer.

David Baldwin has been appointed Chair of the Screening, Prevention and Early Diagnosis (SPED) Advisory Group and we are developing close links with the Supportive & Palliative Care CSG (Chair, Professor Ahmedzai) and the Primary Care CSG (Chair, Professor Neal) with complimentary attendance at the CSG meetings. Developing links with the new network subspecialty leads (SSLs) remains an important objective over the coming year, using the Chair and local members as essential contacts.

The CSG has representation in the EORTC Lung Group hosting the immediate past president (O'Brien) and other active lung group members (O'Brien, PEARLS trial; Popat, GEM study; Danson SPLENDOUR study). The CSG reports back functioning of the ITMIG group in which members are represented (POPAT, Regional ITMIG Champion, Research group member). The CSG is a member of ETOP, and hosts and co-develops ETOP studies (BELIEF, PROMISE-Meso studies; Popat was elected onto the ETOP Foundation Council). The UK recruited to the BELIEF trial, which led to extension of the EMA bevacizumab label. The CSG is a member of the TACT global trials alliance.

7. Funding applications in last year

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
IDEAL CRT: Randomised PhII Trial of standard concurrent chemoradiation versus isotoxic, dose escalated chemoradiation in stage III NSCLC	Outline application	Dr David Landau	Full application invited
A randomised phase 2 trial of FAK inhibitor (vs6063) vs placebo in patients who have had complete macroscopic resection of mesothelioma	Feasibility application	Professor Dean Fennell	Not funded
A Phase II, multicentre, randomised trial comparing combination gemcitabine/carboplatin and hydroxychloroquine with Carboplatin/etoposide therapy alone in extensive stage small cell lung cancer (SCLC)	Feasibility application *Amendment*	Professor Siow-Ming Lee	Approved (no cost)

December 2015			
The PEARL trial: Photodynamic therapy for the prevention of Lung Cancer	Full application	Professor Sam Janes	Funded
DARWIN2: Deciphering Anti-tumour Response and Resistance With INtratumour heterogeneity		Professor Allan Hackshaw	Endorsed
HALT: Ablative Radiotherapy for Oligo-Progressive Disease (OPD) in Oncogene Addicted Lung Tumours	Outline application	Professor Judith Bliss	Full application invited
PRINCE: A randomised phase II / III study of Primary Chemo-Radiotherapy In stage IV Non-small CEll Lung cancer	Outline application	Dr Matthew Hatton	Full application invited
A phase III clinical trial of pembrolizumab versus placebo in patients with relapsed malignant pleural mesothelioma	Outline application	Professor Dean Fennell	Full application invited
May 2016			
IDEAL-2: Randomised PhII/III Trial of standard concurrent chemoradiation versus isotoxic, dose escalated chemoradiation in stage III NSCLC	Full application	Dr David Landau & Dr John Fenwick	Not funded
CheckpOiNt blockade For Inhibition of Relapsed Mesothelioma: A Phase III trial to evaluate the efficacy of MEDI4736	Full application	Professor Dean Fennell & Professor Gareth Griffiths	Funded
PRINCE: A randomised phase II / III study of Primary Chemo-Radiotherapy In stage IV Non-small CEll Lung cancer	Full application	Dr Matthew Hatton & Claire Lawless	Not funded
HALT: Ablative Radiotherapy for Oligo-Progressive Disease (OPD) in Oncogene Addicted Lung Tumours	Full application	Professor Fiona McDonald	Funded
A trial to assess the relationship between tumour burden and detection of oncogenic mutations in plasma of patients with EGFR or KRAS mutant adenocarcinoma of the lung	Full application	Dr Matthew Krebs	Not funded
National Lung Matrix Trial: Multi-drug, genetic marker-directed, non-comparative, multi-centre, multi-arm phase II trial in non-small cell lung cancer	Full application	Professor Gary Middleton	Funded through SEB Strategic Reserve

8. Collaborative partnership studies with industry

The Combination Alliance that seeks to develop the phase I/II new trial trials portfolio across the UK is a standing item on the CSG agenda and currently 6 trials on the portfolio are commercially sponsored and lung cancer has the third largest number of commercial trials in all the CSGs portfolios, behind breast cancer and haematological oncology.

The other key industry relationships come via the CRUK Stratified Medicine Phase II study and Lung MATRIX trial where CSG members are key advisors to the programme. In the SMP2 study collaborations exist with Illumina for the genotyping platform and in MATRIX AstraZeneca and Pfizer are collaborating with CRUK and the CSG for a proof-of-principle genotype-driven umbrella-design open label multi-cohort phase II trial. Lung CSG members involved as key investigators include: CI (Middleton), TMG Chair (Popat) and arm Lead Clinicians (Yap, Summers, Mulatero,

Popat, Spicer, Middleton). Discussions with existing and additional industry partners for new IMP arms are ongoing.

There are a large number of commercial trials on the portfolio though many are for small sub-sets of NSCLC patients with a mutation (e.g. the < 7% with EML-ALK translocation). CSG members are invited to comment during the adoption process for commercial trials and try to avoid competing trials arriving on the portfolio in these rare patient populations. However, warning may not always be heeded leaving an ongoing risk of failure to recruit to time and to target with the current system.

The CSG's key industry relationships are via CRUK with the National Lung MATRIX trial and the CRUK Stratified Medicine Phase II study (SMP2). In the SMP2 study collaborations exist with Illumina for the genotyping platform, allele calling for which has been developed in collaboration. CSG members are key advisors to the programme. In the MATRIX trial, AstraZeneca and Pfizer are collaborating with CRUK and the CSG for a proof-of-principle genotype-driven umbrella-design open label multi-cohort phase II trial. CSG (main-group and subgroup) members are involved as key investigators in the trial: CI (Middleton), TMG Chair (Popat), Arm Lead Clinicians (Yap, Summers, Mulatero, Popat, Spicer, Middleton). Discussions with existing and additional industry partners for new IMP arms are ongoing.

9. Impact of CSG activities

Our flagship studies (TRACERx /DARWIN and SMP2/MATRIX) are now recruiting well with the expectation that the basis science data that will come out of these studies will inform the thinking and design for future studies over the next decade.

The presentation of CONVERT at ASCO 2016 adds to the series of radiotherapy studies over the past ten years where the Lung CSG has made significant contributions to the trial which have defined international practice.

In addition, it is an exciting time for lung cancer treatment with industry bringing a number of new targeted treatments and immunotherapy drugs onto the market. This has led to NICE initiating 15 Single Technological Appraisals with the involvement of members of the CSG as expert commentators. In addition to the more 'routine' horizon scanning, review of funding applications to CTAAC, HTA and YCR is regularly performed by CSG members.

10. Consumer involvement

Consumer representation changed mid-year as Mat Baker's term ended after many years' contribution. He continued on LORD subgroup and Consumer Forum. His contribution is appreciated. Tom Haswell, an experienced consumer familiar to the CSG and cancer research community, replaced him. Janette Rawlinson continued during the review period.

All have supported the CSG's work at practical and strategic levels and the NCRI Consumer Forum. Practically, they reviewed and responded to trial proposals, guidelines, consultations and other documents. Strategically they contributed to discussions including screening, early diagnosis, consideration of smoking cessation and surgical trials for the portfolio, the importance of collaborating with other CSGs and patient recruitment experiences. They participated in the CSG's Lung Strategy day.

They attended NCRI, BTOG, NAEDI, Britain against Cancer, Lung Cancer Centre of Excellence, Royal Marsden Lung Cancer and NCIN conferences. Tom and Janette spoke at LC Centre of Excellence and Royal Society of CardioThoracic Surgery conferences. Mat jointly authored another NCPES poster presented at the NCRI Conference 2015 on demographic and cancer type variations in patients' cancer research participation, ending this phase of NCRN supported work. Janette submitted two posters to BTOG with one awarded a prize. Tom and Janette judged posters at NAEDI.

Mat contributed as Research Advisor to a DH funded project at Health Services Research Unit at University of Oxford developing a PROM to elicit perceptions of those with Long Term Conditions sensitive to changes associated with adaptive capacity over time. Its development is very relevant to cancer research.

All are involved in PPI development in cancer research and contribute widely – highlights include:

- LC awareness day aimed at primary care.
- TORCH workshop on the importance of early consumer involvement within research design and embedding such involvement.
- Precision Medicine showcase at Houses of Parliament to raise awareness of the UK as a centre for precision medicine, showcasing Stratified Medicine Programme with Genomics England, CRUK and Ministers.
- Membership of a patient group for European Lung Foundation, attended European Respiratory Congress in Amsterdam and contributed to two EORTC workshops in Brussels.
- Various cancer research advisory boards, committees, groups and panels in Scotland, England, UK and Europe.
- NCRI conference organising committee and Early Diagnosis expert review panel.

Wider involvement included board membership of NIHR HS&DR Programme and a large CCG (HSJ CCG of the Year 2015), advisory work with a DoH Research Unit, and advisory and joint applicant roles on several studies. Both are members of NCRSA's (formerly NCIN) lung Clinical Reference Group. Such additional roles provide opportunities to connect ideas and people and potentially offer greater collaboration as opportunities develop on patient focused themes within Departmental policies. Refreshing the sub groups and CSG strategy may offer further consumer involvement opportunities.

11. Open meetings/annual trials days/strategy days

The strategy day was held on 27 November and the outcomes are detailed in the Strategy Milestones document in Appendix 2. These outcomes include reinstating the Annual Trials meeting and preparation are advanced for this to happen on 27 July 2016.

12. Priorities and challenges for the forthcoming year

Priorities for the Lung Cancer CSG are:

- Develop and maintain the Annual Trials Meeting and other collaborative and workshops to extend the trials portfolio.
- Improving links with sub-speciality leads, other CSGs and international groups through communication and collaboration via CSG and Subgroup members.

- Raising the profile of the Lung Cancer CSG through badging of investigator lead study and developing a presence with social media.

Challenges for the Lung Cancer CSG are:

- Ensuring research remains core to NHS service and is recognised in all job plans.
- The changing landscape of molecular subtyping makes treatment studies more focused on small populations of patients and having adequate delivery resource at CRN level to deliver complex biomarker-directed studies.
- Funding for academic studies with increasing pressures from commercial studies for limited trial infrastructure.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG Strategy
B – Mesothelioma Subgroup Strategy
C – Advanced Disease Subgroup Strategy
D – LOcoRegional Disease (LORD) Subgroup Strategy
E – Screening/Early Diagnosis Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Appendix 6 – Strengths & Weaknesses from the Lung Cancer CSG 2015 Progress Review

Dr Matthew Hatton (Lung Cancer CSG Chair)

Appendix 2

Membership of the Lung Cancer CSG

Name	Specialism	Location
Professor Pieter Postmus	Clinical Oncologist	Liverpool
Dr Tim Yap*	Clinical Scientist	London
Mr Tom Haswell	Consumer	Glasgow
Mrs Janette Rawlinson	Consumer	Tipton
Dr Doris Rassl	Histopathologist	Cambridge
Dr Matthew Hatton	Clinical Oncologist	Sheffield
Dr David Landau	Clinical Oncologist	London
Dr Noelle O'Rourke	Clinical Oncologist	Glasgow
Dr Lynn Calman	Senior Research Fellow	Manchester
Dr Martin Forster	Medical Oncologist	London
Dr Mary O'Brien	Medical Oncologist	Sutton
Dr Thomas Newsom-Davis	Medical Oncologist	London
Dr Marianne Nicolson (Chair)	Medical Oncologist	Aberdeen
Dr Sanjay Popat	Medical Oncologist	London
Dr Riyaz Shah	Medical Oncologist	Kent
Dr Yvonne Summers	Medical Oncologist	Manchester
Dr Peter Szlosarek	Medical Oncologist	London
Mr John McPhelim	Nurse	Lanarkshire
Dr Anand Devaraj	Radiologist	London
Professor David Baldwin	Respiratory Physician	Nottingham
Dr Neal Navani	Respiratory Physician	London
Professor Lucinda Billingham	Statistician	Birmingham
Mr Babu Naidu	Surgeon	Birmingham

*denotes trainee member

Membership of the Subgroups

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

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

Advanced Disease Subgroup		
Name	**Specialism**	**Location**
Dr Jason Lester	Clinical Oncologist	Cardiff
Dr Hannah Lord	Clinical Oncologist	Dundee
Professor Allan Hackshaw	Epidemiologist	London
Dr Fiona Blackhall	Medical Oncologist	Manchester
Dr Sarah Danson	Medical Oncologist	Sheffield
Dr Gary Middleton	Medical Oncologist	Birmingham
Dr Sanjay Popat (Chair)	Medical Oncologist	London
Dr Clive Mulatero	Medical Oncologist	Leeds
Dr Riyaz Shah	Medical Oncologist	Kent
Dr James Spicer	Medical Oncologist	London
Professor Charles Swanton	Medical Oncologist	London

Screening/Early Diagnosis Subgroup		
Name	**Specialism**	**Location**
Professor Paul Aveyard	Behavioural Medicine	Oxford
Professor John Field	Clinical Oncologist	Liverpool
Dr Sam Janes	General Medicine	London
Professor Richard Neal	General Practitioner	Wrexham
Professor David Weller	General Practitioner	Edinburgh
Professor Tim Eisen	Medical Oncologist	Cambridge
Professor Fergus Gleeson	Radiologist	Oxford
Professor David Baldwin	Respiratory Physician	Nottingham
Dr Neal Navani (Chair)	Respiratory Physician	London
Dr Mick Peake	Respiratory Physician	Leicester
Dr Robert Rintoul	Respiratory Physician	Cambridge

*denotes trainee member
**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Lung Cancer CSG Strategy: January 2016 – December 2018

This strategy timeline has been produced to define the Lung Cancer Research Strategy Plan and its implementation and will be reviewed and updated at each CSG meeting (ND supported by All)
The document is composed of the following:

Page 2 – 6: NCRI Lung CSG Strategy: plan of implementation, containing agreed strategic objectives (1-6), specific actions, CSG leads and proposed deadlines.

Lung Cancer CSG Members		Responsibility
MH	Matthew Hatton	CSG chair
SP	Sanjay Popat	Advanced disease Subgroup Chair
NN	Neal Navani	Early diagnosis Subgroup Chair
YS	Yvonne Summers	LORD Subgroup Chair
PS	Peter Szlosarek	Mesothelioma Subgroup Chair
DB	David Baldwin	SPED chair / representative
JE	John Edwards	Surgical studies
LB	Lucinda Billingham	Statistics Lead
AD	Anand Devaraj	Radiology Lead
DR	Doris Rassl	Pathology / Transitional research
DL	David Landau	Radiotherapy / Transitional research
DF	Dean Fennell	Medical Oncology / Transitional research
MN	Marianne Nicolson	Medical Oncology studies
MF	Martin Forster	Medical Oncology studies
RS	Riyaz Shah	Medical Oncology Studies
TN-D	Tom Newsom-Davis	Medical Oncology / Supportive care Lead
GM	Gary Middleton	Medical Oncology / Matrix CI
NOR	Noelle O Rourke	Radiotherapy studies
JM	John McPhelim	Nursing / PAM Research Lead
TY	Tim Yap	Junior Clinician Lead
JR	Janette Rawlinson	PPI Lead
TH	Tom Haswell	PPI Lead
ND	Nanita Dalal	PA
NK	Nicola Keat	NCRI Exec

PAM - Professions Allied to Medicine

Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Establish a set of priorities for the development and set up of studies that takes account of the NIHR portfolio, international agenda, available funding opportunities and clinical need	ALL	Document key priorities at Strategy Day 27 Nov15 Review May 2016	Review Portfolio priorities 6-monthly at CSG meetings
1b. Portfolio development – Advanced disease	Ensure cohesive strategy of advanced disease clinical trials, taking into account: - Opportunities within the international agenda, avoiding competition with key Pharma studies - The need for a high recruiting study open at all times - Balance between late and early phase studies - Multicentre studies with good regional coverage - All disease stages - Supportive care studies - Transitional subgroups - Interaction with CRN subspecialty leads	SP MN, GM, TY, JR JM,LB, DR	Identified at Strategy Day 27 Nov 15 Progress review 6 monthly at CSG meetings	Annual meeting / workshops to identify new studies / leads to fill gaps in portfolio. Immunotherapy, PS 2 patients, cerebral mets.
1c. Portfolio development LORD	Secure new studies for •SCLC •Surgery / adjuvant treatment •Radiotherapy - Follow up studies - Transitional subgroups - Interaction with CRN subspecialty leads	YS DL, TN-D, JE, TH JM,LB, DR	Identified at Strategy Day 27 Nov 15 Progress review 6 monthly at CSG meetings	Annual meeting / workshops to identify new studies / leads to fill gaps in portfolio.
1d. Portfolio development Early Diagnosis	Develop the early detection, screening and prevention portfolio •Early detection application of risk scores, biomarkers , •Interventions to increase presentation to primary care •Screening •Prevention, smoking cessation - Engage with other interested Group – SPED, BTS, Primary care - Transitional subgroups - Interaction with CRN subspecialty leads	NN DB, AD, NOR, MF, JR JM,LB, DR	Identified at Strategy Day 27 Nov 15 Progress review 6 monthly at CSG meetings	Annual meeting / identify new studies / leads to fill gaps in portfolio Working Group to engage with other interested groups

Strategic objective	Action	CSG Lead	Date	Outcomes
1e. Portfolio development – Meso subgroup	Ensure cohesive strategy for meso thelioma clinical trials, taking into account: - Opportunities within the international agenda, - Balance between late and early phase studies - Multicentre studies with good regional coverage - All disease stages - Transitional subgroups - Supportive care studies - Interaction with CRN subspecialty leads	PS MN, GM, TY, JR JM,LB, DR	Identified at Strategy Day 27 Nov 15 Progress review 6 monthly at CSG meetings	Annual meeting / workshops to identify new studies / leads to fill gaps in portfolio. Radical third line treatment
1f. Interaction with (inter)national research groups	Identify leads within the CSG to link with the following research groups: IMIG EORTC ETOP BTOG ITMIG TACT	DF SP MN	Mar 2016	To keep under review at 6 monthly CSG meeting
1g. Interaction with Cross Cutting groups	Identify leads within the CSG to link with the following cross cutting CSGs and advisory groups: •Primary Care CSG •Screening, Prevention and Early Diagnosis (SPED) Advisory Group •CTRAD •Supportive and Palliative Care CSG	DB MF	Mar 2016	To keep under review at 6 monthly CSG meeting
1h. National Cancer Intelligence Network (NCIN)	Establish clear link with Lung Cancer Clinical Reference Group Maintain clear links with NCIN the use of data to inform study design and take over long term follow-up	NN / ALL	Report 6 monthly at CSG meeting	Invite NCIN Lung Cancer CRG Chair to attend next CSG meeting

Strategic objective	Action	CSG Lead	Date	Outcomes
2. Key research priority areas	**Surgery: / Radiotherapy** • Improving fitness for radical treatment. • Embed follow up randomisations in radical treatment trials **Early phase:** • Work with ECMCs to build on MATRIX / Tracer X to increase the availability of early phase studies for lung cancer patients **Advance disease :** • Establish further studies for brain mets pts • Establish high recruiting immunotherapy study **Translational:** •Work with key clinical and scientific groups to develop a multi-modality database and translational research platform •Engage with collaborative working steering group form CR-UK Cancer Imaging Centre Network •Embed smoking cessation research into treatment protocols •Add supportive care sub-studies questions into future protocols	MH / JE GM SP DL AD All All	May 2016 Ongoing End 2016 May 2016 End 2016 May 2016	Outline proposal to CSG Nov 16 Outline proposal to CSG Nov 2016 May 2016 update on progress 6 monthly CSG meeting s
3a. Raising awareness and profile	Regular dissemination of study recruitment activity and outcomes through newsletters, annual meetings and Annual Report and submission of meeting abstracts Restart dedicated annual NCRI lung cancer trials meeting Communications about new studies with CRN subspecialty leads Start and NCRI Lung CSG account to use Lung Cancer Awareness month to highlight lung cancer research	PC/ND/SA MH, SP, All TY JR	Ongoing 2016 2016	MH / ND to feedback Participate in future NCRI Subspecialty leads / CSG meetings Discuss next CSG meeting May 2016

Strategic objective	Action	CSG Lead	Date	Outcomes
3b. Ensuring successful delivery of studies through integration with NIHR CRN: Cancer	CSG members to commit to delivering studies developed by the CSG Interaction with LCRN Subspecialty Leads to determine placement of new studies and address barriers to actively recruiting patients Monitor recruitment to portfolio studies, esp those developed by the CSG to ensure delivery to time and target Contribute as far as possible to NIHR CRN: Cancer Speciality Objectives so they reflect what LCRNs need to deliver to ensure lung cancer patients can access the full portfolio of studies within UK	ALL MH / ND ALL ALL	Ongoing Ongoing Ongoing Ongoing	Recruit CSG-led studies to time and target Good regional placement of studies Meet NIHR CRN Speciality Objectives
3c. Maximise output from clinical trials	Establish working groups for new studies within 6 weeks of funding award to facilitate swift set up, including representation from CI, CRCTU, NIHR CRN: Cancer	CI/CTUs	Ongoing	
4. Strengthen UK wide and international working	Refine prioritisation process for international clinical trials to be submitted for funding to optimise the timing and success of applications Identify UK selling points for lung cancer research to identify and promote the flagships studies on the portfolio Work to badge academically sponsored NCRI CSG studies as 'UK Lung study XX' Work to ensure research remains core to NHS service and is recognised in all job plans .	All All MH / ND dialogue with NIHR cancer CRN	Ongoing Ongoing May 2016 May 2016	Update at six monthly CSG meetings

Strategic objective	Action	CSG Lead	Date	Outcomes
5. CSG structure and function	Establish Early Screening Working Party to work with SPED /Primary Care CSG Consider case for improving fitness for treatment Working Party Consider case for Translational Research Working Party Identify mentors for future trainee registrars in the CSG / subgroups Identify mentors for new PPI members in CSG / subgroups	NN MH DL MH / ND MH / ND	May 2016 May 2016 May 2016 May 2016	
6. Patient and Public Involvement and Impact	Ensure consumers remain associated with the development of every new study at an early stage Consider developing research studies to address key questions of concern to PPI representatives and other consumers	All JR / TH to bring questions to the group	Ongoing Ongoing	

B – Mesothelioma Subgroup Strategy

1. To support high quality biomarker driven studies in MPM.
2. To deliver on trial recruitment by co-ordinating recruiting centres.
3. To encourage greater involvement by all sectors of the mesothelioma community.

C – Advanced Disease Subgroup Strategy

Priorities:

1. Brain metastases studies.
2. Academic immunotherapy studies.
3. Studies in the PS2 population.

Challenges:

1. Funding for academic studies.
2. Potential for poor recruitment due to competition from commercial studies for same limited delivery resource.
3. Having adequate delivery resource at CRN level to deliver complex biomarker-directed studies.

D – LOcoRegional Disease (LORD) Subgroup Strategy

1. Secure new studies for
    - SCLC
    - Surgery/adjuvant treatment
    - Radiotherapy
2. Develop follow-up studies for when studies are closing.
3. Interact with transitional subgroups.
4. Interact with CRN subspecialty leads to fill gaps in the portfolio.

E – Screening/Early Diagnosis Subgroup Strategy

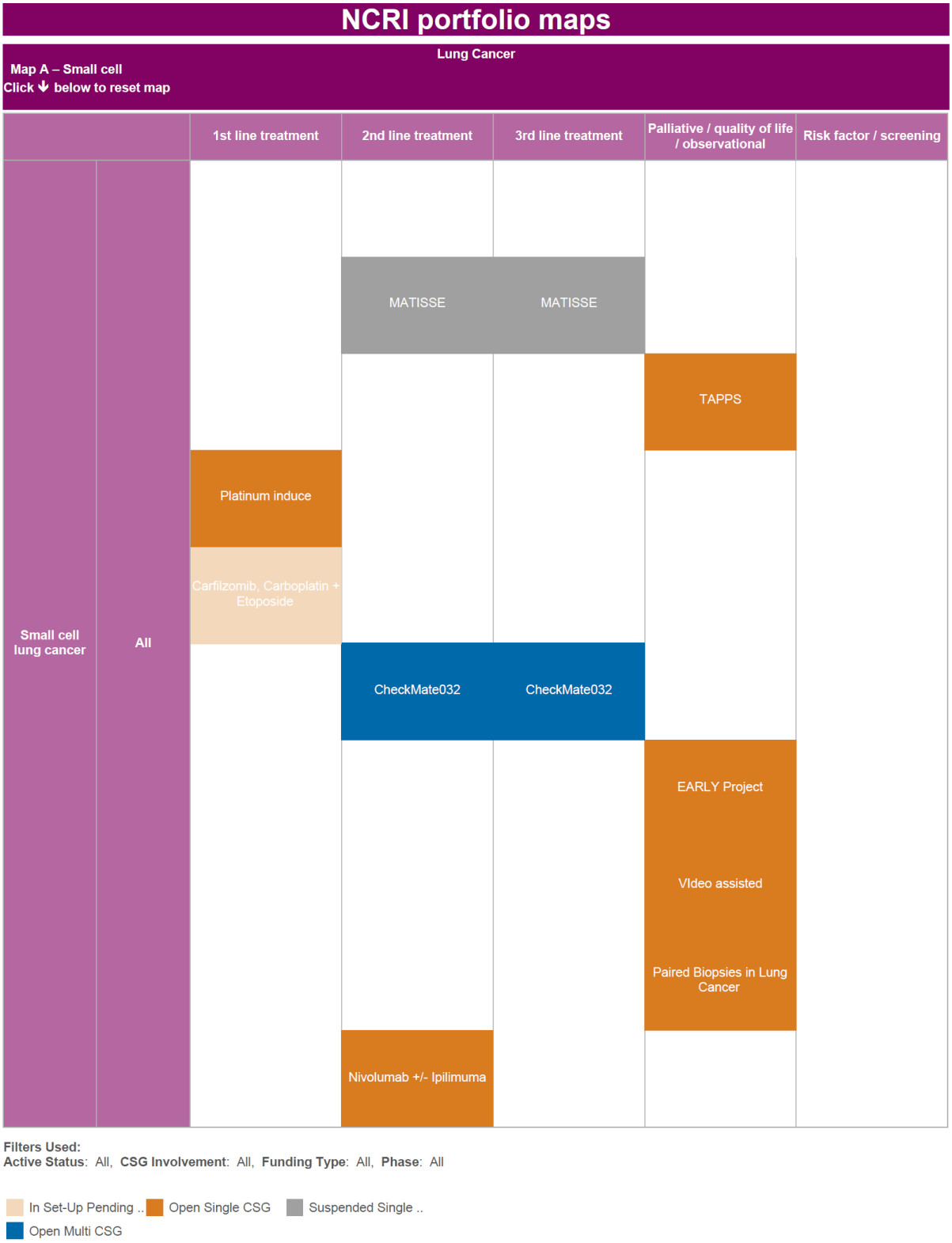
The strategy for research into the early diagnosis and screening of lung cancer will necessarily be shaped by a decision on lung cancer screening by the national screening committee. An initial opinion on this is expected in late 2016. In addition, the research landscape will be shaped by the results of the influential NELSON randomised trial of CT screening for lung cancer expected in 2016/17.

There are several key strategic aims in the coming years:

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

Appendix 3

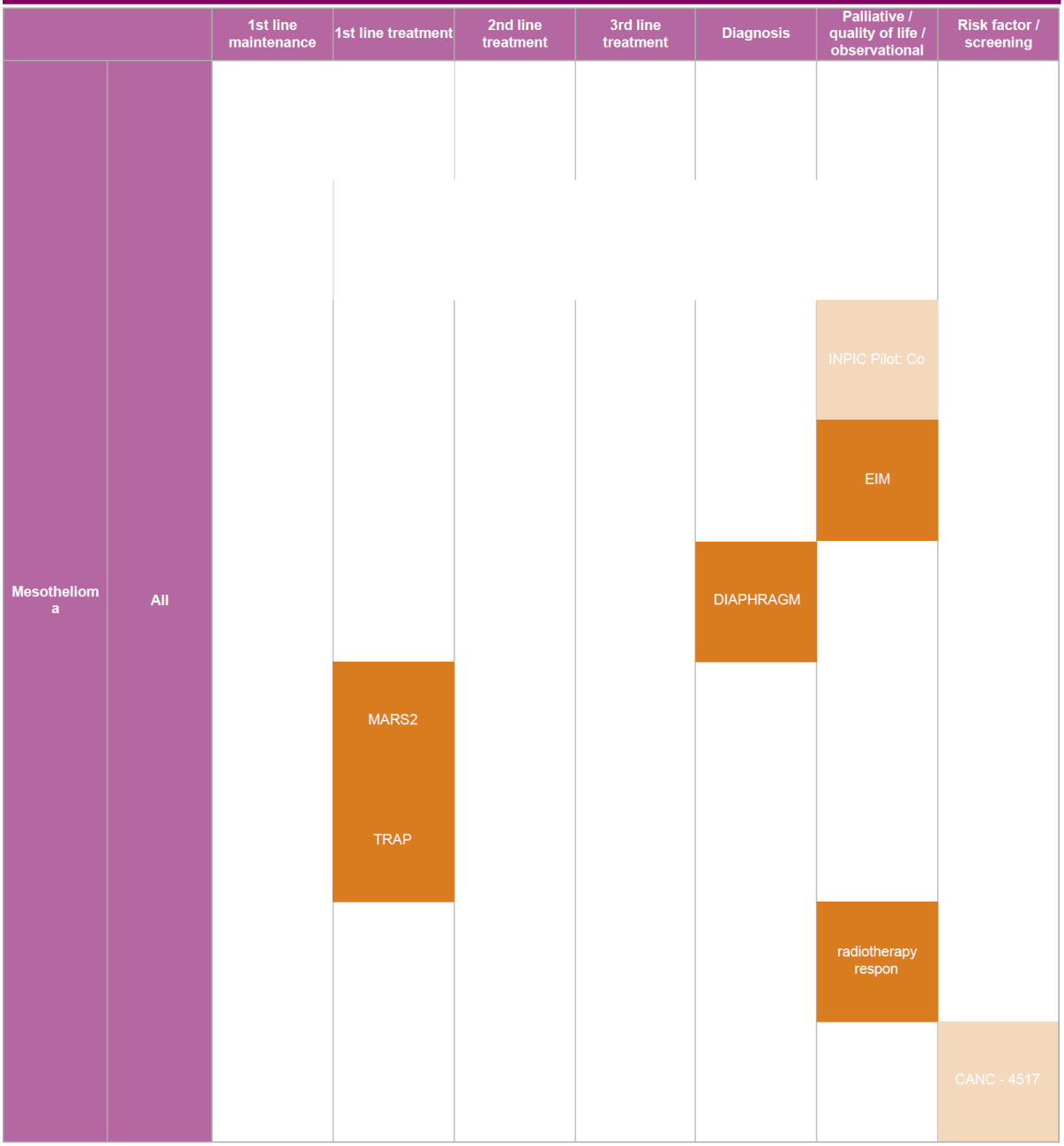
Portfolio maps



NCRI portfolio maps

Lung Cancer

Map B – Mesothelioma
Click ⬇ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. In Set-Up NHS Per..
Open Single CSG Null

NCRI portfolio maps

Lung Cancer

Map C – Non-small cell
Click ↓ below to reset map

		Null	1st line maintenance	1st line treatment	2nd line treatment	3rd line treatment	Adjuvant / neoadjuvant	Supportive care / observational
Biomarker selected	Alk			ASCEND IV	PF 06463922 AP26113 ASCEND 7	PF 06463922 ASCEND 7		GEM
	EGFR	[18F]FLT-PET		9291 vs. SOC EGFR Video assisted JVCY CAURAL IncyteNSCLC DARWIN1	National Lung Matrix Open Label, Mul ibitor INC280 alone	National Lung Matrix TIGER 3 Open Label, Mul		EGF GEM MAGENTA Tumourigenicity LUCID CANC - 4658
	KRas				National Lung Matrix	National Lung Matrix		GEM
	Other		PACIFIC	VESTA h II Met/Adv. NSCL INCB039110 L3280A Vs Gem+C 0718C) versus plati 209-116 TREATME	FGFR Study Docetaxel MEDI4736 National Lung Matrix CheckMate 171 ABOUND.2L	FGFR Study MEDI4736 h II Met/Adv. NSCL ARCTIC National Lung Matrix		GEM Imaging biomark
Non-biomarker selected	All types		PIN - Olaparib Checkmate 227	R'therapy+ BKM120 Isotoxic IMRT Platinum induce SABRTOOTH LungTech Stereo Checkmate 227	VanSel1 R'therapy+ BKM120 TORCMEK	VanSel1 R'therapy+ BKM120 TORCMEK	Lung ART ABLE Trial EORTC 1217 PEARLS	REPLICA SPLENDOUR SPECIAL TARGET Trial OPTIMUM Trial
	Non-squam..							GEM
	Squamous			CEDAR RTFORCE PET Bo				

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG Suspended Single ..
Open Multi CSG Null

NCRI portfolio maps

Lung Cancer

Map D – Non-treatment
Click ↓ below to reset map

		Post-diagnosis	Pre-diagnosis
Biomarkers	All	LLP	LLP
		CLUB	
		Tumour Angiogen	
		Magnitude of up	
		Lenvatinib (E7080) vs. Sorafenib	
		FREELUNG v4.0	
		TRACERx	
		Quant of neutrophil	Quant of neutrophil
		REQUITE	
		Developing A BI	
		Predicting drug	
Data collection	All	LungCAST	
			CANDID
			ECLS
		TargetLung	
		PEACE	
		RCRT: Feasibili	
Diagnosis / imaging	All		Pleural effusion
		CR UK Stratifie	CR UK Stratifie
		Streamline L	
			UKALL60+
			EARLY Project
			Peripheral Blood Transcriptome Study
Quality of life / symptom control	All	HYPREL	
		Rehabilitation	
		TAPPS	
		The efficacy of	
		Exercise Regime	
		Effect of skin rash	
		SIMPLE	
		RETROSPECTIVE CHART REVIEW	
Risk factor / screening	All	ReSoLuCENT	
			MEDLUNG
			Study1a
			Lung Screen Uptake Trial v1.0

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

In Set-Up Pending .. Open Single CSG In Set-Up Pending ..
Open Multi CSG In Set-Up NHS Per.. In Set-Up Pending ..

Appendix 4

Publications in the reporting year

CHART-ED

Continuous Hyperfractionated Accelerated RadioTherapy – Escalated Dose (CHART-ED): A Phase I study, Hatton M, Hill R, Fenwick J, Morgan S, Wilson P, Atherton P, Dickson J, Murray K, Paul J, Radiotherapy Oncology, 2016;118:471-77

Isotoxic Intensity Modulated Radiotherapy (IMRT) in Stage III Non Small Cell Lung Cancer (NSCLC) - A Feasibility Study

Protocol for the Isotoxic Intensity Modulated Radiotherapy (IMRT) in stage III non-small cell lung cancer (NSCLC) - A feasibility study. Kate Haslett K, Franks K, Hanna G, Harden S, Hatton M, Harrow S, McDonald F, Ashcroft L, Falk S, Driscoll H, Groom N, Harris C, McCloskey P, Whitehurst P, Bayman N, Faivre-Finn C, Accepted BMJ Open, Jan 2016

LungStar trial

A multicentre phase III randomised double-blind placebo-controlled trial of pravastatin added to first-line chemotherapy in patients with non-small cell lung cancer, Hackshaw A et al., Setting up non-commercial clinical trials takes too long in the UK: findings from a prospective study Soc Med. 2008Jun;101(6): 299-304.

Appendix 5

Major international presentations in the reporting year

LungART

Quality of Resection in Pathological N2 NSCLC in the Phase 3 Lung Adjuvant Radiotherapy Trial (Lung ART): An Important Factor, presented at 16th World Conference on Lung Cancer (International Association for the Study of Lung Cancer), Sept 2015:, awarded Dan Idhe Lectureship Award (Medical Oncology). Journal of Thoracic Oncology • Volume 10, Number 9, Supplement 2, S181; Abstract ORAL05.02,

ADSCaN

A Randomised Phase II study of Accelerated, Dose escalated, Sequential Chemo-radiotherapy in Non-Small Cell Lung Cancer (NSCLC)

Hatton M, et.al, Presented : NCRI National Cancer Research Meeting, Liverpool, 2015

14th British Thoracic Oncology Group Meeting, Dublin, 2016. Abstract: Lung Cancer 91 Suppl 1 S68:188

Isotoxic Intensity Modulated Radiotherapy (IMRT) in stage III Non-Small Cell Lung Cancer (NSCLC) – A Feasibility Study

Groom N, Tsang Y, Hatton M, Hanna G, Franks K, Harden S, McDonald F, Harrow S, Faivre-Finn C

Presented: 14th British Thoracic Oncology Group Meeting, Dublin, 2015. Abstract: Lung Cancer 91 Suppl 1 S69:191

Appendix 6

Strengths & weaknesses from the Lung Cancer CSG 2015 Progress Review

Strengths

- A good menu of trials
- The growth in the number of trials since the last review
- Some excellent innovative academically lead trials such as TRACERx, MATRIX, FREELUNG, DIAPHRAGM
- High success rate with funding committees
- A significant number of trials in set up
- The standardisation of RT across trials
- The recruitment of a number of clinical oncologists since the last review and the engagement of this group of researchers in clinical research
- Excellent consumer involvement
- A very good publication record
- Active engagement with young investigators, although this might be more formalised
- Some good ideas for trials in prevention and early diagnosis

The panel also identified a number of issues which need to be addressed:

For the CSG

- Developing a clear strategy for the CSG and for each of the subgroups which pulls the research community together, identifies the UK's unique selling points and clear priorities for the Group
- Building strong relationships with the networks, CTUs, local clinical research network subspecialty leads for lung and those engaged in preclinical work
- Ensuring that the work of the Mesothelioma Subgroup is more fully integrated into that of the rest of the CSG
- Addressing heterogeneous recruitment across the country
- Filling the gaps in the portfolio e.g. in advanced/metastatic NCSLC, SCLC and third line treatment
- Developing large scale biologically driven or immunotherapy driven trials
- Formally spelling out the Group's vision for bringing on trainees and young investigators

For the NCRI

- Following up the lack of analysis and publication of the BTOG2 trial