

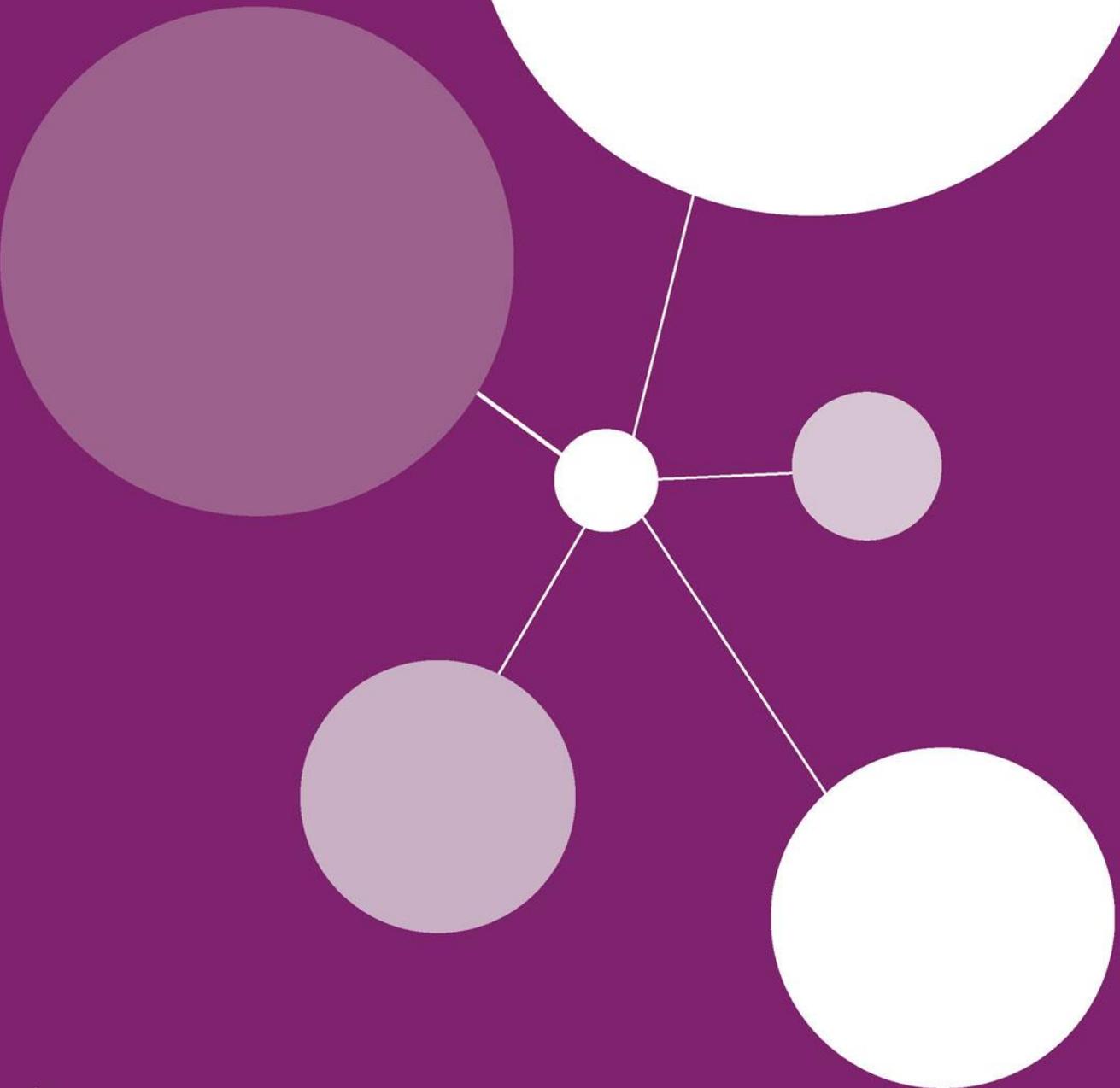


**NCRI**

National  
Cancer  
Research  
Institute

# **NCRI Lung Cancer Clinical Studies Group**

**Annual Report 2016-17**



Partners in cancer research





## NCRI Lung Cancer CSG Annual Report 2016-17

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

The work of the Lung CSG has maintained the number of patients accessing the trials portfolio and it is particularly pleasing to see the numbers entering interventional studies continues to increase. Members of the Lung CSG have been involved in the development of a number of new study ideas and continue to contribute to those open studies that are at the forefront internationally, e.g. the Stratified Medicine Programme (SMP) 2, MATRIX and TRACERx, which have been recruiting steadily and raising the profile of the UK lung cancer research portfolio. Our consumer representatives continue to excel ensuring the wider engagement and relevance of the Group.

The CSG, working closely with the British Thoracic Oncology Group, reinstated the Annual Lung Cancer Trials Meeting in June 2016 and offered a forum and workshops that encouraged new investigators to bring proposals for discussion. The CSG will continue to run and develop this meeting over the coming years as part of a portfolio that will increase the opportunities for investigators to meet and allow more feedback to engaged research teams.

The Group has formed a short term task group following the Glasgow workshop to develop a UK research program for radiotherapy new drug combinations in NSCLC. Two study platforms are being developed for stage III NSCLC (CONCORDE) and stage IV disease (SPITFIRE) which aim to submit funding applications later this year.

Members maintain strong links with a number of international groups (e.g. EORTC, ETOP, IMIG, TACT) and contribute to the development of a number of their trial protocols enhancing the international recognition of the NCRI CSG as a successful trials organisation. CSG members also continue to regularly volunteer and offer their expert support to NICE evaluations of new drug and applications considered for funding.

### 2. Structure of the Group

The CSG currently has one vacancy as we look to replace our pathology representative. New members have maintained a good balance of senior and junior researchers and brought palliative care and psychosocial oncology expertise, thus strengthening our ability to develop studies in these areas and improving ties with the cross-cutting CSGs. The individual Subgroups continue to review and develop trial protocols and a short term Working Party has been formed to develop trials for new drug/radiotherapy combinations. This continued expansion of membership

has given us good geographical coverage across the UK, facilitating engagement with all interested in lung cancer research.

### **3. CSG & Subgroup strategies**

#### **Main CSG**

The refreshment of Lung CSG membership including a mix of new and experienced researchers will re-energise the Group and will allow us to replace two Subgroup Chairs who rotate off the CSG at the end of this year. These changes maintain the existing links with international research groups and strengthen links with other cross-cutting CSGs.

We will continue to develop a more comprehensive timetable of meetings and workshops to develop trial outlines. In addition to the Annual Trials meeting and BTOG workshops, we will be adding an annual workshop (TORCH) that will help investigators develop their research ideas into outlines to take forward for funding. The CSG will also continue to organise themed workshops following on from the success of the Glasgow meeting on cardio-pulmonary toxicity from radiotherapy. Gaps in the trials portfolio will be areas for future workshops, starting with a joint meeting with the Brain CSG focused on cerebral metastasis management which is planned for the autumn.

The CSG will continue supporting the short term task group in the development of trial platforms (CONCORDE and SPITFIRE) to study new drug radiation combinations in NSCLC and progressing the strategy that looks to embed smoking cessation, supportive care and follow up sub-studies into trials being developed.

The Lung CSG members will continue to increase the profile of the group on social media and aims to develop a system to badge the non-commercial academic studies on the portfolio to further raise the profile of UK lung cancer research.

The CSG will continue to engage with the subspecialty leads for lung cancer over the coming year to encourage and facilitate access to local NCRI budgets for clinical trials. In addition to personal invitations to the Annual meeting a joint meeting of the CSG and the Leads is planned for the autumn.

#### **Mesothelioma Subgroup (Chair, Dr Peter Szlosarek)**

The reporting year has been productive for the Mesothelioma Subgroup. Several studies have completed recruitment in the portfolio as follows: (1) ARTMEIS, a randomized, double-blind, placebo-controlled study of amatumixab with pemetrexed and cisplatin in subjects with unresectable mesothelioma, (2) completion of the phase II component of the nintedanib in combination + (pemetrexed / cisplatin) followed by nintedanib versus placebo + pemetrexed / cisplatin followed by placebo for the treatment of patients with unresectable mesothelioma, (3) completion of TRAP study in ASS1-deficient patients with mesothelioma assessing the safety and efficacy of ADI-PEG 20 combined with cisplatin and pemetrexed, (4) the Epizyme study of tazemetostat in patients with recurrent mesothelioma after first line cisplatin and pemetrexed; and (5) MESO-2, a surgical feasibility study assessing the role of chemotherapy ± surgical pleurectomy.

The next year promises to be an equally active period with a number of new studies opening across the UK in the first and second line treatment setting.

### **Advanced Disease Subgroup (Chair, Dr Sanjay Popat)**

The Subgroup has a busy portfolio of commercial studies that dominate recruitment nationally. UK recruitment to these commercial studies includes Keynote024 which led to the licensing of pembrolizumab, a NEJM publication with UK co-authorship. CSG members continue to strongly influence the design and delivery of industry-sponsored trials.

The Subgroup continues to deliver academic trials with European Groups, e.g. the ETOP-BELIEF trial was published in the Lancet Respiratory Medicine supporting the expansion of the EMA licensing of bevacizumab. The ETOP-EORTC SPLENDOUR trials continue to recruit well and the UK-led EORTC-GEM study has now closed.

The portfolio hosts a number of key academic studies, mostly phase II signal-generating studies. Our flagship studies, led by the UK National Lung MATRIX trial supported by the CRUK Stratified Medicine part 2 (SMP2), continue to recruit well. The SMP2 study is expanding sites to maximize UK NGS genotyping penetrance and arms on the MATRIX trial have met their recruitment totals and closed. Additional arms have been submitted to CRUK for consideration of funding and the SMP2 panel has been broadened to account for new targets.

Brain metastases, immunotherapy, and small cell lung cancer remain key targets for academic studies with a number of initiatives and proposals in development for these indications and have been discussed at various fora. The CONVOLUTE study investigating duration of immunotherapy has been submitted for consideration of funding.

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

The LORD Subgroup has refreshed its membership with several new members from respiratory medicine, clinical oncology and radiology. The portfolio of studies continues to focus on translational research, surgery, radiotherapy and adjuvant therapy.

Our flagship translational study, TRACERx, has continued to recruit well (over 500 patients enrolled) and the first academic outputs from the programme will be published in May 2017 in Nature and New England Journal of Medicine.

Investigator led radiotherapy studies continue to thrive with SARON, recently opened, and ADSCaN which is opening Q2 2017. The existing surgical study, VIOLET, recruits to target with new studies focusing on patient reported outcome measures following VATS surgery or SABR (LILAC) and rehabilitation for patients with thoracic cancer entering the portfolio.

Collaborative links with the EORTC are maintained with joint studies LungART, LUNGTECH and PEARLS recruiting steadily. The practice changing CONVERT study of radiotherapy in SCLC reported at ASCO and is accepted for publication in Lancet Oncology. The portfolio gap for this group of patients has been filled by STIMULI, a study of immunotherapy after concurrent CRT in LS-SCLC being run with ETOP/EORTC.

New investigators have been supported to develop studies of radiotherapy new drug combinations in NSCLC (CONCORDE) and HALT (ablative radiotherapy for oligo-progressive disease) has been funded by CRUK.

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

The Screening/Early Diagnosis Subgroup is organised virtually and meets annually at BTOG. The Subgroup has 12 open studies and several 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 was funded by CRUK.

The Subgroup has reviewed several high quality applications to funding bodies. The Yorkshire Cancer Research charity has invested >£5M into early diagnosis of lung cancer (including the Yorkshire Lung Screening Trial) and prioritisation of lower socioeconomic classes for early detection initiatives. These studies have involved close collaboration between primary and secondary care and are pending portfolio adoption.

The Subgroup is working on the backdrop of the possibility of lung cancer screening implementation. Key research questions, however, remain such as improving risk criteria for lung cancer detection, the use of biomarkers and avoiding over diagnosis.

The Subgroup has encouraged applications to the BTOG/NCRI clinical trials workshop in June 2017.

#### 4. Task groups/Working parties

##### **NSCLC Radiotherapy-Drug Consortium Working Party (Workstream leads, Dr Alastair Greystoke, Dr Martin Forster, Dr Fiona McDonald and Dr Gerry Hanna)**

A Lung CSG short term Working Party (WP) has been established to develop a UK research program for radiotherapy new drug combinations in NSCLC (non-small cell lung cancer) with the input of CTRad.

The WP has developed an outline from two platform studies: in stage III NSCLC, we will focus on the addition of new drugs to radical radiotherapy fractionations in stage III disease (Concorde) and in stage IV disease to explore immunotherapy/stereotactic radiation combinations (Spitfire). It is envisaged that both studies will be jointly funded through Cancer Research UK and pharmaceutical companies, with funding applications to be submitted in the autumn. Trial Management Groups with membership from clinical and medical oncology have been established with draft protocols been taken to the 19<sup>th</sup> MCCR workshop in Methods in Clinical Cancer Research (Zeist, Netherlands) by trainees for further development.

#### 5. Patient recruitment summary for last 5 years

In the Lung Cancer CSG portfolio, 31 trials closed to recruitment and 50 opened.

**Table 1 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
2016/2017	5593	2384	5123	2337	12.15	5.54

There has been a further increase in recruitment to lung cancer portfolio studies with the continued increase to interventional studies being particularly pleasing. Currently there are 88 trials open (29 commercial and 59 non-commercial) to recruitment in the portfolio and a further 28 in set-up (18 commercial and 10 non-commercial). The regularly updated portfolio maps (Appendix 3), provided by the NCRI CSG team and assisted by CSG members, are being refined and will hopefully prove of greater use to current and potential investigators, as well as lung cancer specialists and research nurses who are using them regularly.

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

The CSG has representation in the EORTC Lung Group hosting the immediate past president (Dr O'Brien) and other active lung group members (O'Brien: PEARLS trial; Popat: GEM study; Danson: SPLENDOUR study). The CSG reports back on the functioning of the ITMIG group and is represented by Dr Popat, Regional ITMIG Champion and research group member. The CSG has steering group representation on ETOP and TACT enabling the Group to host and co-develop studies, notable examples include BELIEF and PROMISE-Meso.

Nationally, Dr Navani is the Clinical Lead for the National Lung Cancer Audit and there are close links with the SPED Advisory Group (Chaired by Professor Baldwin, previous Lung CSG member), Supportive & Palliative Care CSG (Chair, Professor Ahmedzai), Primary Care CSG (Chair, Professor Neal), CTRad (Dr Macdonald) and the Psychosocial Oncology & Survivorship CSG (Dr Calman), with complimentary attendance at the CSG meetings. Four CSG members also serve as lung Sub-speciality Leads (SSLs) facilitating the communication between the Group and the networks.

## 7. Funding applications in last year

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

<b>Cancer Research UK Clinical Research Committee (CRUK CRC)</b>			
<b>Study</b>	<b>Application type</b>	<b>CI</b>	<b>Outcome</b>
<b>May 2016</b>			
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
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
Ablative Radiotherapy for Oligo-Progressive Disease (OPD) in Oncogene Addicted Lung Tumours	Full application	Dr Fiona McDonald & Professor Judith Bliss	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
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
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
<b>November 2016</b>			
CAR MI: Dynamic imaging of regional CAR T-cell immunotherapy of mesothelioma, combined with immunomodulation of the tumour microenvironment	EMPA Outline	Dr John Maher	Not invited to full
<b>Other committees</b>			
<b>Study</b>	<b>Committee &amp; application type</b>	<b>CI</b>	<b>Outcome</b>
Yorkshire Lung Screening Trial	YCR	Dr Matt Callister	Funded

## 8. Collaborative partnership studies with industry

The Group's key industry relationships are via CRUK with the National Lung MATRIX trial and the CRUK Stratified Medicine Phase II study (SMP2). In this study, collaborations exist with Illumina for the genotyping platform, and CSG members are key advisors to the programme. In the MATRIX trial, AstraZeneca and Pfizer are collaborating for a proof-of-principle genotype-driven umbrella design, open label, multi-cohort phase II trial. CSG members are involved as key investigators in the trial (CI: Middleton), TMG Chair (Popat) and arm lead clinicians (Summers, Popat, Spicer, Middleton). Discussions with existing and additional Industry partners for new IMP arms are ongoing, as are discussions to develop the arms for the radiotherapy new drug combinations study platforms.

There are a large number of commercial trials on the portfolio, though many are for small subsets 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. In addition, the ECMC 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.

## 9. Impact of CSG activities

Our flagship studies (TRACERx, DARWIN and SMP2/MATRIX) are recruiting well with the expectation that the basic science data that will come out of these studies will inform the design for future studies. TRACERx has submitted manuscripts for publication in high impact journals and some arms are reaching their recruitment target so there will be outcomes reported shortly. We are also pleased to report a manuscript of the BTOG 2 study has been submitted for publication.

Follow-up presentations of CONVERT has emphasized the series of radiotherapy studies over the past 10 years where the Lung CSG has made significant contributions to radiotherapy trials that are defining 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 the involvement

of Group members as expert commentators in 17 NICE initiated Single Technological Appraisals during 2016–17. Additionally, members have regularly contributed to the more ‘routine’ horizon scanning and review of funding applications to CRC, HTA and YCR.

## 10. Consumer involvement

Both consumer members, Tom Haswell and Janette Rawlinson, have made valuable contributions to the Group and the wider lung cancer research community’s work.

They have attended CSG meetings, the NCRI Consumer Forum and responded to trial proposals and consultations. Strategic discussions they have been involved in include the Annual Trials meeting, meetings on branding/marketing, screening, early diagnosis, quality of life, treatment modes/combinations, patient participation and potential collaboration with other CSGs.

Conferences attended include the NCRI Conference, BTOG, Early Diagnosis, IMIG, Precision Medicine Congress, ERS International Congress, Festival of Genomics, RSM LC and PHE Cancer Outcomes. Janette exhibited a consumer related poster at the NCRI Conference whilst Tom judged posters at the Early Diagnosis Conference. Both spoke as panel members at AMRC/ABPI Patients First Conference and Precision Medicine Forum, participated in Stratified Medicine Programme expert meetings in roles on SMP board and Lung Matrix Trial Management Group.

Consumer highlights include:

- Both advised pharma delegations (Johnson & Johnson) regarding the risk of developing lung cancer and screening.
- Janette is a panel member of the All Party Parliamentary Group meeting on Precision Medicine at the House of Lords and speaker at APP Cancer Campaigning Group meeting on ‘the Third sector’s role in the Cancer Strategy – ‘One Year on’.
- Janette is a member of the Patient Advisory Group for European Lung Foundation and attended the European Respiratory Congress to launch a multilingual lung cancer website.
- Tom is a member of the International LC Patient Advisory Group (Boehringer) and Early Diagnosis expert review panel member.
- Tom is the consumer member on NCRI’s CM-Path Initiative and organised a local involvement day at the Bio Depository/Pathology Department.
- Janette was part of the cancer awareness day by the Sandwell & West Birmingham Cancer Steering Group.
- Both are involved in various cancer research advisory boards, committees and groups.
- Advisory and joint applicant roles on several studies (both)

Wider involvement includes:

- NIHR HSDR and CCG board membership.
- NCRAS’s lung Clinical Reference Group.
- Contributing locally, nationally and internationally to lung cancer research.

Their broad involvement offers future collaboration and development opportunities.

## **11. Open meetings/annual trials days/strategy days**

The CSG held a Strategy Day on 27 November 2015 and the outcomes are detailed in the Strategy Milestones document in Appendix 2. The Lung Annual Trials meeting in June 2016 was moderately well attended with very positive feedback for delegates and it is hoped that this year's meeting will see an increase in attendance as we use the relationship we have built up with BTOG to increase awareness of the meeting. In addition, the CSG organised a one day trials meeting on 'Radiotherapy related cardiopulmonary toxicity in thoracic malignancies' in Glasgow in February that was well attended by cardiologists, respiratory physicians, oncologists and physicists interested in generating trial proposals in this area.

## **12. Priorities and challenges for the forthcoming year**

### **Priorities**

- Maintain the Annual Trials Meeting and develop other collaborative workshops and meetings to extend the trials portfolio.
- Finding a thoracic pathologist to serve on the CSG and consider ways of building up the basic science representation on the Group.
- Raising the profile of the Lung Cancer CSG through badging of investigator lead study and developing a presence with social media.

### **Challenges**

- 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

**Dr Matthew Hatton (Lung Cancer CSG Chair)**

## Appendix 1

### Membership of the Lung Cancer CSG

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

\* denotes trainee member

## Membership of the Subgroups

<b>LOCoRegional Disease (LORD) Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
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

<b>Mesothelioma Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
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 James Entwisle	Radiologist	Leicester
Mr John Edwards	Surgeon	Sheffield
Professor Andrew Ritchie	Surgeon	Gloucester
Mr David Waller	Surgeon	Leicester

<b>Advanced Disease Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
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

<b>Screening/Early Diagnosis Subgroup</b>		
<b>Name</b>	<b>Specialism</b>	<b>Location</b>
Professor Paul Aveyard	Behavioral 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

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

## **B – Mesothelioma Subgroup Strategy**

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

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

### **Aims**

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

## **C – Advanced Disease Subgroup Strategy**

### **Aims**

- To develop academically-led studies in Brain Metastasis – a Workshop planned autumn 2017.
- Continue to work with international groups (ETOP, EORTC) collaboratively on key academic research questions to address other gaps in the portfolio, e.g. SCLC, the PS2 population.
- To continue rotation of membership through the Subgroup including succession planning for the Chair.

### **Challenges**

- Funding for the pragmatic academic studies.
- Maintaining a balanced portfolio that can meet recruitment targets particularly in areas of high commercial interest.

## **D – LocoRegional Disease (LORD) Subgroup Strategy**

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

- Encourage and support translational research with all projects – TRACERx is the exemplar project where translational research will generate many clinical research questions.

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

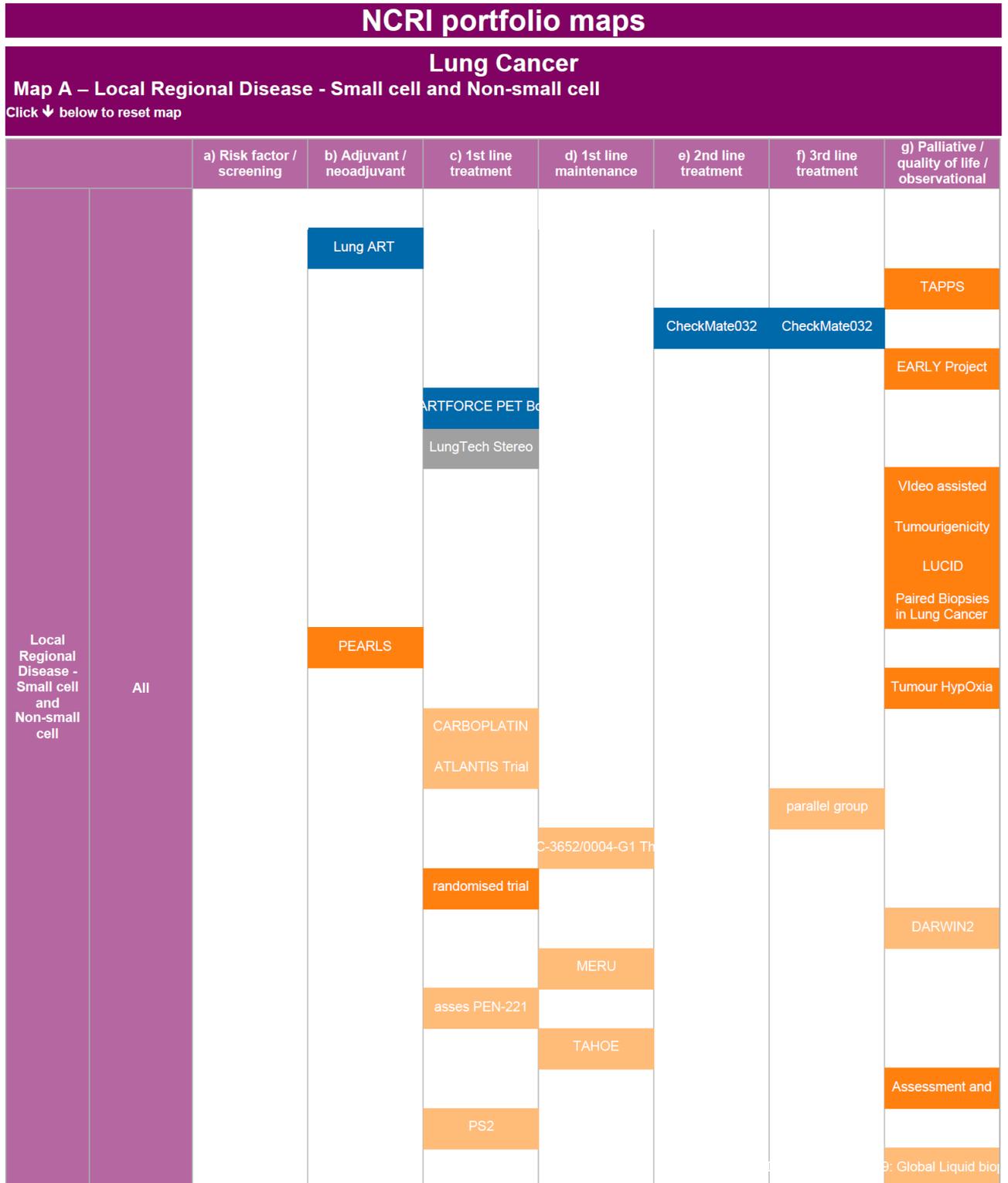
The research landscape will be shaped by the results of the influential NELSON randomised trial of CT screening for lung cancer expected in 2017 and research strategy will then be shaped by a decision on lung cancer screening by the national screening committee.

The key strategic aims in the coming years remain:

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

# Appendix 3

## Portfolio maps



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

- Open Multi CSG
- Open Single CSG
- In Setup, Waiting ..
- In Setup, HRA Ap..
- Suspended Single..
- In Setup, Waiting ..

# NCRI portfolio maps

## Lung Cancer

### Map B – Mesothelioma

Click ↓ below to reset map

		a) Risk factor / screening	b) Diagnosis	c) 1st line treatment	d) 1st line maintenance	e) 2nd line treatment	f) 3rd line treatment	g) Palliative / quality of life / observational
Mesothelioma	All	ZOLA trial		MARS2 TRAP Amatuximab + Pemetrexed + Cisp Mesothelioma				EIM
				CA209-743 (phase III) Pleural Mesothelioma				MesoTRAP feasibility study
					CONFIRM	VIM		
								SYSTEMS/2
								ASSESS-meso

Filters Used:

Active Status: All, CSG Involvement: All, Funding Type: All, Phase: All

Open Multi CSG

Open Single CSG

Null

In Setup, HRA Ap..

In Setup, Waiting ..

# NCRI portfolio maps

## Lung Cancer

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

Click ↓ below to reset map

		a) 1st line treatment	b) 1st line maintenance	c) 2nd line treatment	d) 3rd line treatment	e) Supportive care / observational	
Non-biomarker selected	All types			VanSel1	VanSel1		
				R'therapy+ BKM120	R'therapy+ BKM120		
			PIN / Olaparib				REPLICA
					MEDI4736	MEDI4736	
							SPLENDOUR
					TORCMEK	TORCMEK	
							Imaging biomark
							TARGET Trial
							OPTIMUM Trial
							Radiosensitising agents in NSCLC
		(MSB0010718C) versus					
		pembrolizumab in NSCLC PS2 patients combination of					
		ATOMIC-Meso Phase 2/3 Study					
		PANORAMA					
		Tolerability Study of					
		Anti PD-1 LUC1001					
						Support Needs of	
		IN PATIENTS WITH NY-ESO-1c259T in Advanced NSCLC					
		CheckMate 568				quantitation -	
		Non-squamous			Avelumab Vs docetaxel in NSCLC		
	MPDL3280A in Stage IV Non/Squamous NSCLC chemotherapy versus						
				Nivolumab + Ipilimumab ED/SCLC			
	KEYNOTE/189						
	ATEZOLIZUMAB						
	Squamous						
		SPINET					
		evaluate nab174;/paclitaxe					
		N3					

Filters Used:

Active Status: All, CSG Involvement: All, Funding Type: All, Phase: All

- Open Multi CSG
- In Setup, HRA Ap..
- In Setup, Waiting ..
- Suspended Single..
- Open Single CSG
- In Setup, HRA Ap..
- In Setup, Waiting ..

# NCRI portfolio maps

## Lung Cancer

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

Click ↓ below to reset map

		Null	a) 1st line treatment	b) 1st line maintenance	c) 2nd line treatment	d) 3rd line treatment	e) Supportive care / observational	
Biomarker	Alk		Brigatinib v Crizotinib				and safety of 450	
							Combination with	
	EGFR		in IIIb/IV biomarker Patritumab + Erlotinib in NSCLC			National Lung Matrix	National Lung Matrix	MAGENTA
			Ramucirumab or DARWIN1 Erlotinib or Gefitinib					
					T790M/NSCLC after ABOUND.2L INC280 alone/+ m/k inhibitor of MET, AXL, FGFR	m/k inhibitor of MET, AXL, FGFR		
					ELUXA 2 patients with EGFR			
					National Lung Matrix	National Lung Matrix		
	KRas	Endometry Duo-1			National Lung Matrix	National Lung Matrix		
	Other				FGFR Study	FGFR Study		
				National Lung Matrix /adenocarcinoma	National Lung Matrix			
		Patients with Ia/m						
				INC280 in adult				

Filters Used:

Active Status: All, CSG Involvement: All, Funding Type: All, Phase: All

- Open Multi CSG
- In Setup, Waiting ..
- In Setup, Waiting ..
- Open Single CSG
- In Setup, NHS Per..
- In Setup, Waiting ..

# NCRI portfolio maps

## Lung Cancer

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

Click ↓ below to reset map

		Post-diagnosis	Pre-diagnosis
Biomarkers	All	LLP	LLP
		CLUB	
		Tumour Angiogen	
		Pleural effusion biomarker study	
		Lenvatinib (E7080) vs. Sorafenib	
		FREELUNG v4.0	
		TRACERx	
		Quant of neutrophil	Quant of neutrophil
		REQUITE	
		Developing A BI	
		Predicting drug	
		Methodology to Select Tumor/Specific Neo/Antigen	
Data collection/observational	All	LungCAST	
			CANDID
		TargetLung	
		PEACE	
		Respiratory Distress Symptom Intervention (RDSI)	
		Exploring RATS for lung cancer V1	
Diagnosis / imaging	All	EARL	
		CR UK Stratife	CR UK Stratife
			EARLY Project
		VOCs in Lung ca	
Quality of life / Supportive..	All	CORE Trial	
		Rehabilitation	
		TAPPS	
		Exercise Regime	
		SIMPLE	
		The MENAC Trial	
		ThIRSTY	
		Survivorship in lung cancer, implementing the recovery package	
		FACT: Effect on Patient Reported Outcomes of Surgery and SABR (V...	
		Integrated short term rehabilitation for thoracic cancer	
Phase IV EORTC study to validate new LC29 module			
FACT: Factors Associated with lung Cancer Trial			
Risk factor / screening	All		Study1a
			Lung Screen Uptake Trial v1.0
		The LUCAS Study	
			NAVIGATE
		CURVE	
		SPECTALung (EORTC 1335)	
	LUSH (Lung Symptom awareness and Health)		

Filters Used:

Active Status: All, CSG Involvement: All, Funding Type: All, Phase: All

■ Open Multi CSG    ■ Null    ■ In Setup, Waiting ..    ■ In Setup, Waiting ..  
■ Open Single CSG    ■ In Setup Single C..    ■ In Setup, Waiting ..    ■ Suspended Single..

## Appendix 4

### Publications in the reporting year

Study	Reference
<b>LUME-MESO: 1199.93</b>	Scagliotti GV, Gaafar R, Nowak AK, Reck M, Tsao AS, van Meerbeeck J, Vogelzang NJ, Nakano T, von Wangenheim U, Velema D, Morsli N, Popat S. LUME-Meso: Design and Rationale of the Phase III Part of a Placebo-Controlled Study of Nintedanib and Pemetrexed/Cisplatin Followed by Maintenance Nintedanib in Patients with Unresectable Malignant Pleural Mesothelioma Clinical Lung Cancer (in press)
	Grosso F, Steele N, Novello S, Nowak A, Popat S, Greillier L, John T, Leighl N, Reck M, Taylor P, Pavlakis N. OA22. 02 Nintedanib plus Pemetrexed/Cisplatin in Patients with MPM: Phase II Findings from the Placebo-Controlled LUME-Meso Trial. J Thorac Oncol (2017) Jan 31;12(1):S329-30
	Scagliotti GV, Gaafar R, Nowak A, Vogelzang NJ, Von Wangenheim U, Morsli N, Velema D, Popat S. P2.01: LUME-MeSO: Phase II/III Study of Nintedanib + Pemetrexed/Cisplatin in Patients With Malignant Pleural Mesothelioma: Track: SCLC, Mesothelioma, Thymoma. J Thorac Oncol (2016) Oct;11(10S):S216
<b>FGFR study</b>	Pearson A, Smyth E, Babina IS, Herrera-Abreu MT, Tarazona N, Peckitt C, Kilgour E, Smith NR, Geh C, Rooney C, Cutts R, Campbell J, Ning J, Fenwick K, Swain A, Brown G, Chua S, Thomas A, Johnston SR, Ajaz M, Sumpter K, Gillbanks A, Watkins D, Chau I, Popat S, Cunningham D, Turner NC. High-level clonal FGFR amplification and response to FGFR inhibition in a translational clinical trial. Cancer Discov (2016) 6(8):838-51.
	Smyth EC, Turner NC, Pearson A, Peckitt C, Chau I, Watkins DJ, Starling N, Rao S, Gillbanks A, Kilgour E, Sumpter KA, Smith NR, Cutts R, Rooney C, Thomas AL, Ajaz MA, Chua S, Brown G, Popat S, Cunningham D. Phase II study of AZD4547 in FGFR amplified tumours: Gastroesophageal cancer (GC) cohort pharmacodynamic and biomarker results. J Clin Oncol (2016) 34:Suppl (February 1), 154
<b>LUX-Lung 8</b>	Popat S, Felip E, Cobo M, Fulop A, Dayen C, Trigo JM, Gregg R, Waller CF, Gordon J, Lorence R., line afatinib vs erlotinib in patients with advanced squamous cell carcinoma (SCC) of the lung: patient-reported outcome (PRO) data from the global LUX-Lung 8 (LL8) Phase III trial. Eur J Canc (2015) 51: S626-S627
<b>BELIEF</b>	Rosell R, Dafni U, Felip E, Curioni-Fontecedro A, Gautschi O, Peters S, Massutí B, Palermo R, Ponce Aix S, Carcereny E,

	Früh M, Pless M, Popat S, Kotsakis A, Cuffe S, Bidoli P, Favaretto A, Froesch P, Reguart N, Puente J, Coate L, Barlesi F, Rauch D, Thomas M, Camps C, Gómez-Codina J, Majem M, Porta R, Shah R, Hanrahan E, Kammler R, Ruepp B, Rabaglio M, Kassapian M, Karachaliou N, Tam R, Shames DS, Molina MA, Stahel RA, for the BELIEF collaborative group. Phase II trial of erlotinib and bevacizumab in patients with advanced non-small cell lung cancer and activating EGFR mutations (BELIEF). <i>Lancet Respir Med</i> (in press)
<b>LUX-LUNG 5</b>	Schuler M, Yang JC, Park K, Kim JH, Bennouna J, Chen YM, Chouaid C, De Marinis F, Feng JF, Grossi F, Kim DW, Liu X, Lu S, Strausz J, Vinnyk Y, Wiewrodt R, Zhou C, Wang B, Chand VK, Planchard D; LUX-Lung 5 Investigators (Popat S). Afatinib beyond progression in patients with non-small-cell lung cancer following chemotherapy, erlotinib/gefitinib and afatinib: phase III randomized LUX-Lung 5 trial. <i>Ann Oncol</i> (2016) 27:417-423
<b>LUX-LUNG 3</b>	Schuler M, Wu YL, Hirsh V, O'Byrne K, Yamamoto N, Mok T, Popat S, Sequist LV, Massey D, Zazulina V, Yang JCH. First-line Afatinib Versus Chemotherapy in Non-Small-Cell Lung Cancer Patients with Common Epidermal Growth Factor Receptor Mutations and Brain Metastases. <i>J Thoracic Oncol</i> (2016) 11:380-390
<b>NP28761</b>	Yang JC, Ou SH, De Petris L, Gadgeel S, Gandhi L, Kim DW, Barlesi F, Govindan R, Dingemans AM, Crinò L, Léna H, Popat S, Ahn JS, Dansin E, Golding S, Bordogna W, Balas B, Morcos PN, Zeaiter A, Shaw A. P3. 02a-016 Pooled Efficacy and Safety Data from Two Phase II Studies (NP28673 and NP28761) of Alectinib in ALK+ Non-Small-Cell Lung Cancer (NSCLC): Topic: ALK Clinical. <i>J Thorac Oncol</i> (2017) Jan 31;12(1):S1170-1
<b>TIMELY</b>	Popat S, Hughes L, O'Brien M, Ahmad T, Lewanski C, Dervede U, Jankowska P, Mulatero C, Shah R, Hicks J, Geldart T, Cominos M, Gray G, Spicer J, Bell K, Ngai Y, Hackshaw A. P3. 02b-046 Afatinib Benefits Patients with Confirmed/Suspected EGFR Mutant NSCLC, Unsuitable for Chemotherapy (TIMELY Phase II Trial): Topic: EGFR Clinical. <i>J Thorac Oncol</i> (2017) Jan 31;12(1):S1215-6
<b>CHECKMATE 171</b>	Felip E, Van Meerbeeck J, Wolf J, Ardizzoni A, Li A, Srinivasan S, Popat S. CheckMate 171: A multicenter phase 2 trial of nivolumab (nivo) in patients (pts) with stage IIIB/IV squamous cell (SQ) NSCLC who have received $\geq 1$ prior systemic treatment. <i>J Thorac Oncol</i> (2016) Apr;11(4 Suppl):S141.
<b>FREELung</b>	Pender A, Rana S, Izquierdo Delgado E, Proszek P, Garcia-Murillas I, Bhosle J, O'Brien M, Palma JF, Turner NC, Popat S, Downward J, Gonzalez D. EGFR mutant circulating tumour DNA detection in advanced lung adenocarcinoma: optimising

	the application of a ctDNA diagnostic to real world clinical practice. Lung Cancer (2016) 91:S2
<b>CONVERT</b>	<p>An international randomised trial of concurrent chemo-radiotherapy (cCRT) comparing twice-daily (BD) and once-daily (OD) radiotherapy schedules in patients with limited stage small cell lung cancer (LS-SCLC) and good performance status (PS), ASCO 2016 Conference (oral presentation of the results of the study) – June 2016</p> <p>An international randomised trial of concurrent chemo-radiotherapy (cCRT) comparing twice-daily (BD) and once-daily (OD) radiotherapy schedules in patients with limited stage small cell lung cancer (LS-SCLC) and good performance status (PS), NCRI 2016 Conference (oral presentation of the results of the study at the Clinical Trials Showcase session &amp; poster) – November 2016</p> <p>Circulating Tumour Cells in CONVERT patients, World Lung 2016 Conference - December 2016</p> <p>Compliance and outcome of elderly patients treated in the Concurrent ONce-daily VERSus twice-daily RadioTherapy (CONVERT) trial World Lung 2016 Conference - December 2016</p>
	<p>An international randomised trial of concurrent chemo-radiotherapy (cCRT) comparing twice-daily (BD) and once-daily (OD) radiotherapy schedules in patients with limited stage small cell lung cancer (LS-SCLC) and good performance status (PS), British Thoracic Oncology Group Conference (abstract &amp; poster) – January 2017</p> <p>An international randomised trial of concurrent chemo-radiotherapy (cCRT) comparing twice-daily (BD) and once-daily (OD) radiotherapy schedules in patients with limited stage small cell lung cancer (LS-SCLC) and good performance status (PS), Sharing the Vision for World Class Radiotherapy Symposium (abstract &amp; poster) – March 2017</p>
<b>PEARL</b>	Study of Pembrolizumab (MK-3475) vs Placebo for Participants With Non-small Cell Lung Cancer After Resection With or Without Standard Adjuvant Therapy (MK-3475-091/KEYNOTE-091), presented at ASCO 2016.
<b>TracerX</b>	<p>“Phylogenetic circulating tumour DNA analysis depicts early stage lung cancer evolution” C Abosh et al. Nature DOI:10.1038/nature22364</p> <p>“Tracking the Evolution of Non-Small Cell Lung Cancer” M Jamal-Hanjani et al. NEJM DOI: 10.1056/NEJMoa1616288</p>

## Appendix 5

### Major international presentations in the reporting year

Study	Conference details
<b>CONVERT</b>	An international randomised trial of concurrent chemo-radiotherapy (cCRT) comparing twice-daily (BD) and once-daily (OD) radiotherapy schedules in patients with limited stage small cell lung cancer (LS-SCLC) and good performance status (PS), ASCO 2016 Conference (oral presentation of the results of the study) – June 2016