

NCRI Lung Clinical Studies Group

Introduction

During the reporting period we have further improved the trials development pathway. There was a fallow period after the departure of our first portfolio co-ordinator, Shelagh Bonner-Shand, who left for personal reasons after only a few months. Ms Nicky Gower nobly stepped back into the breach until Ms Natalie Billington started work as our full time project officer in May 2009. Natalie has already made an impact on the speed of the development process and the accuracy and completeness of Lung CSG records. Nicky Gower continues to oversee Natalie's work which provides vital day-to-day advice and support.

We now expect in the next reporting period to have the trials development pathway fully functional. It is now time we turn our attention to raising the profile of the group and its portfolio of studies as well as monitoring and assisting the work of the networks around the country.

Membership and structure

The membership of the group has now entered a relatively stable period although there has been some further rotation of the Subgroup chairs. Mick Peake stood down as chair of the SCEPTRE subgroup to free up time for his work with the Department of Health and NICE. Mick remains a valued member of the group. Rob Rintoul has taken over as the chair of SCEPTRE.

Natalie Billington joined the group ex officio as described in the introduction. We have cross-representation on relevant groups including the Primary Care CSG, the Complementary Therapies CSG, the Correlative Science CSG, the Consumer Liaison Group, the EORTC lung group, the newly formed European Thoracic Oncology Platform (ETOP), the London Lung Cancer Group (LLCG), the British Thoracic Oncology Group (BTOG) and the Mesothelioma Interest Group (MIG).

Portfolio & accrual

The group's portfolio of studies is summarised under each of the relevant subgroups. 1886 patients were recruited in 2008-9 representing 5.0% of incidence cases, 3.7% to RCTs and 1.3% to non-RCTs.

Accrual figures for individual studies can be found in appendix 1.

SCEPTRE (Chair: Robert Rintoul)

The key tasks for this subgroup are to re-examine the possibility of screening trials and to develop smoking cessation studies.

Key achievements in the year included securing funding for a pilot study to investigate lung screening in the UK by LD-CT. Professor John Field is CI of the UK Lung Screening Study (UKLS).

The subgroup has studies in lung epidemiology, early diagnosis and molecular biology and is also conducting and developing novel studies in pre-malignant disease such as an investigation of the incidence and behaviour of pre-malignant lesions (Lung SEARCH, CI: Professor Stephen Spiro) and the use of Tyrosine Kinase Inhibitors to treat pre-malignant lesions (TIDAL, CI: Professor Tim Eisen).

Acronym	Title	PI(s)	Status
CLUB	Cancer of the Lung Biomarkers	Dr Aiman Alzetani	Open
Lung-SEARCH	A randomised controlled trial of surveillance for the early detection of lung in an at risk group	Professor Stephen Spiro	Open
ReSoLuCENT	Resource for the Study of Lung Cancer Epidemiology in North Trent	Professor Penella Woll	Open
MEDLUNG	Early detection of lung cancer: metabolic biomarkers for high risk screening	Dr Paul Lewis	Open
Early Lung Cancer Study	The use of molecular biomarkers in early lung cancer detection	Professor John Field	Closed
MUSICAL	Mediastinal endoscopic UltraSound In the diagnosis and staging of CArcinoma of the Lung	Dr Steve Pereira	Closed

Rare Tumours (Chair: Professor Mike Lind)

This Subgroup has discussed study designs for neuroendocrine lung tumours at some length. There are many difficulties in defining the disease population which is a necessary prerequisite to a clinical study. The Subgroup aims to develop a study in this area before going on to investigate bronchioloalveolar carcinoma and thymoma. There are no active protocols at present.

Translational Research (Chair: Professor John Field)

The particular roles of this sub-group will be to ensure that we maximise the translational potential of trials in the portfolio and to conduct observational studies such as those noted below.

A number of trials are in development including a study into molecularly directed treatment (ET study: PI Dr Siow-Ming Lee), Predictive epigenomics derived from circulating plasma DNA in NSCLC (PI Dr Peter Schmid) and a proposal for a UK Lung Cancer Consortium to work with OnCore to maximize sample collection (PI Professor John Field).

Acronym	Title	PI(s)	Status
CLUB	Cancer of the Lung Biomarkers	Professor Nicholas James	Open
LLP	LLP Liverpool Lung Project	Professor John Field	Open

Clinical Trials Subgroup (Chair: Mr Jim Paul)

This subgroup advises on design and conduct of trials working in the trials development pathway. It does not have a portfolio of its own.

Mesothelioma (Chair: Mr David Waller)

This Subgroup is working on the challenge of developing new systemic therapy trials (MESO-2 and MESO-3). During the year MARS completed accrual.

Acronym	Title	PI(s)	Status
MALCS	A population based case-control study of mesothelioma and lung cancer in relation to occupation among British men and women under the age of 60	Professor Julian Peto	Open
MESOVATS	Prospective randomised controlled trial of video-assisted thoracoscopic (VATS) cytoreductive pleurectomy compared to talc pleurodesis in patients with suspected or proven malignant mesothelioma.	Dr Robert Rintoul	Open
ADMIN-M	A randomised phase II trial of single agent ADI-PEG 20 (pegylated arginine deaminase) in patients with malignant pleural mesothelioma	Dr Peter Szlosarek	In Set up
MARS	Mesothelioma and Radical Surgery trial. MARS pilot study - to determine the feasibility and acceptability of performing a randomised trial comparing extra-pleural pneumonectomy (EPP) against no EPP surgery within the context of trimodality therapy (chemotherapy, surgery, post-operative radiotherapy).	Professor Julian Peto, Mr David Waller, Professor Tom Treasure	Closed

Loco-Subregional Disease (LORD, NSCLC I-IIIa & SCLC LD) (*Chair: Dr Matthew Hatton*)

This group focuses on treatments with radical intent. The group has a strategy of developing a portfolio of radiotherapy feasibility trials before proceeding to large scale radiotherapy trials in the light of difficulties with a number of RT trials which have failed to recruit satisfactorily.

Studies in development include Lung ART (EORTC study of adjuvant RT for N2 disease) and ISTART (Isotoxic dose escalation for 6-week radical RT).

Acronym	Title	PI(s)	Status
Lung Boost	New pathway with Bronchoscopic or Oesophageal Ultrasound for Lung Cancer Diagnosis and Staging: A Randomised Controlled Trial	Dr Sam Janes	Open
NCRN 014	A multi-centre, randomised, double-blind, placebo-controlled, phase III study of single-agent Tarceva® (erlotinib) following complete tumour resection with or without adjuvant chemotherapy in patients with stage IB-IIIa non-small-cell lung carcinoma who have EGFR-positive tumours	Adopted industry trial (OSI- 774-3020)	Open
NCRN019	A double-blind randomised, placebo-	Adopted Industry	Open

MAGRIT	controlled Phase III study to assess the efficacy of rec-MAGE-A3 + As15 as adjuvant therapy in patients with resectable MAGE-A3+ve NSCLC	trial (GSK 109493)	
CONVERT	Concurrent once-daily versus twice-daily radiotherapy for limited stage SCLC	Dr Corinne Faivre-Finn	Open
ASTER	Assessment of Surgical sTaging versus Endoscopic ultrasound in lung cancer: a Randomised controlled trial	Dr Robert Rintoul	Closed
SOCCAR	A randomised phase III trial of sequential chemotherapy followed by radical radiotherapy versus concurrent chemoradiotherapy followed by chemotherapy in patients with inoperable stage III non-small cell lung cancer and good performance status.	Dr Joe Maguire	Closed

Advanced Disease (NSCLC IIIB/IV & SCLC ED) (Chair: Dr Marianne Nicolson)

There are several trial ideas in development and increasing contact with pharmaceutical companies with consequent adoption of high quality sponsored trials into the Lung CSG portfolio. BTOG2 is nearing completion of accrual and the group has 2 more large scale studies (FRAGMATIC and ET) to maintain its record of accruing to important studies which may not necessarily be of direct interest to pharma.

A number of studies are being developed as part of the AZ-NCRN initiative.

Acronym	Title	PI(s)	Status
BTOG2	British Thoracic Oncology Group (BTOG) phase III trial of gemcitabine plus cisplatin at 80 mg/m ² vs gemcitabine plus cisplatin at 50mg/m ² gemcitabine plus carboplatin AUC 5 in stage IIIB/IV non small cell lung cancer (NSCLC)	Professor David Ferry	Open
FRAGMATIC	A randomised phase III clinical trial investigating the effect of FRAGMin Added to standard Therapy In patients with lung Cancer	Dr Fergus MacBeth	Open
LLP	LLP Liverpool Lung Project	Professor John Field	Open
LungStar	A multicentre phase III randomised double blind placebo controlled trial of pravastatin added to first-line standard chemotherapy in patients with small cell lung cancer	Professor M J Seckl	Open
QUARTZ	A phase III multicentre randomised controlled trial to assess whether optimal supportive care (including dexamethasone) alone is as effective as optimal supportive care (including	Dr Paula Mulvenna	Open

	dexamethasone) and whole brain radiotherapy (WBRT) in the treatment of patients with inoperable brain metastases from non-small cell lung cancer.		
TACTIC	A randomised phase II double cline placebo controlled trial of Whole Brain Radiotherapy (WBRT) and Tarceva (OSI-774, erlotinib) in patients with advanced non-small cell lung cancer (NSCLC) with multiple brain metastases	Dr Siow Ming Lee	Open
Topical	Tarceva or placebo in clinically advanced non-small cell lung cancer	Dr Siow Ming Lee	Closed
NCRN017	A multicentre, randomised, double-blind, controlled Phase III efficacy and safety study of erlotinib with or without sunitinib in the treatment of advanced NSCLC	Adopted Industry trial (Pfizer A6181087)	On hold

Meetings

We held a meeting adjacent to the International Lung Cancer Meeting in Liverpool in July 2008. Whilst the attendance did not reach our goal of 100 delegates, we did have a lively discussion which helped to raise the profile of the group and to provide confirmation of our strategic direction. We also held a meeting with international speakers on anti-angiogenic therapies in a variety of malignancies including lung cancer at the NCRI meeting in October 2008. This meeting was very well attended.

Collaborations

We are collaborating with the Primary Care CSDG on several SCEPTRE projects, with the Radiotherapy CSG now Clinical and Translational Radiobiology and radiotherapy Working Group on QUARTZ and other RT issues and with the Colorectal CSG on a study into metastasectomy.

We collaborate with the EORTC Lung Group and have several joint members. We plan to enhance this relationship over the next review period.

We collaborate with the BTS, BTOG, LLCG and other interested groups and this is particularly facilitated by having several joint members.

We are developing our relationship with industry, particularly in the field of advanced disease. Initially we plan to demonstrate our capacity as a recruitment organization and go on to be more influential at earlier stages of trial design and conduct.

Other activities

Members and former members take an active role in Health Technology Assessments for lung cancer. We submitted a joint report with other organisations coordinated by the Royal College of Physicians.

During 2008/09 we surveyed the best-performing and worst-performing quartiles of UK cancer research networks and are analyzing responses at present both for examples of best practice and reasons for poor recruitment.

3-year strategy

We think that our existing structure will succeed in maintaining and widening the portfolio with consequent increase in accrual to NCRI Lung CSG trials.

There are specific areas where we wish to place a particular emphasis at the main group level to help achieve this goal. These areas are studies involving radiotherapy and loco-regional disease, screening for lung cancer and adopting interesting industrial trials into the portfolio. Work continues in all of these areas.

We aim to extract significant translational data from all of our studies and this is the primary role of the Translational Subgroup which reviews all trials proposals selected for further development.

Priorities for next year

Our priorities for next year are to:

- Maximize the efficiency of the trials development pathway monitored by our project officer
- Improve contacts with clinical and research staff across the country
- Raise the profile of our portfolio and hence to improve accrual to clinical trials

Professor Tim Eisen, Chair

Appendix 1

NCRI Lung CSG portfolio with recruitment figures – June 2009

Study Title	Chief Investigator	Email	CTU	Tumour Type	Subgroup	Target accrual	Actual accrual*	Approx. start date	Estimate closure date
BTOG 2	Dr Cindy Billingham	l.j.billingham@bham.ac.uk	Birm	NSCLC	Advanced	1350	1200	Apr-05	Sep-09
LungStar	Prof Michael Seckl	m.seckl@imperial.ac.uk	UCL	SCLC	Advanced	1300	293	Jan-07	Sep-09
RIB	Prof Peter Hoskin	peterhoskin@nhs.net	UCL	NSCLC & SCLC	Advanced	580	523	Apr-03	Dec-09
Quartz	Dr Paula Mulvenna	paula.mulvenna@nuth.nhs.uk	MRC	NSCLC	Advanced	1000	92 pts 72 carers	Mar-07	Mar-10
LLP	Prof John Fields	j.k.field@liv.ac.uk	L'pool	NSCLC & SCLC	Advanced	10000	10200	Jan-98	Jun-10
Modafinil for fatigue	Dr Bee Wee	Bee.wee@hmc.ox.ac.uk	Oxford	NSCLC	Advanced	206	0	Jun-09	Sept-10
Tactic	Dr Ming Lee	siow-ming.lee@uclh.nhs.uk	UCL	NSCLC	Advanced	144	23	Jan-08	Dec-10
Fragmatic	Dr Fergus Macbeth	fergus.macbeth@velindre-tr.wales.nhs.uk	Wales	NSCLC & SCLC	Advanced	2200	640	Aug-07	Jan-11
Lung Boost	Dr Sam Janes	sam.janes@uclh.nhs.uk	UCL	NSCLC	LORD	168	48	Apr-08	Oct-10
Convert	Dr Corinne Faivre-Finn	Corinne.Finn@christie.nhs.uk	Christie	SCLC	LORD	532	33	Apr-08	Jan-12
Experience of mesothelioma	Dr Anne Arber	a.arber@surrey.ac.uk	Surrey	MESO	Mesothelioma	10	8	May-08	Jun - 09
Mesovats	Dr Robert Rintoul	robert.rintoul@papworth.nhs.uk	Papworth	MESO	Mesothelioma	196	92	Sep-03	Dec-09
MALCS	Prof Julian Peto	julian.peto@icr.ac.uk	ICR	All	Mesothelioma	3000	450	Jan-01	Jun-15
Club Trial	Prof Nick James	N.D.James@bham.ac.uk	Birm	NSCLC & SCLC	SCEPTRE	600	429	Jan-05	Jun-10
Resoluent	Prof Penella Woll	p.i.woll@sheffield.ac.uk	Weston	NSCLC & SCLC	SCEPTRE	500 cases/ 500 controls	268/ 241	Apr-06	Dec-10
Medlung	Dr Paul Lewis	p.d.lewis@swansea.ac.uk	Swansea	NSCLC & SCLC	SCEPTRE	350	n/k	Jul-06	Jun-11
Lung Search	Dr Stephen Spiro	stephen.spiro@uclh.nhs.uk	UCL	All	SCEPTRE	1300	598	Aug-07	Spring 2010

Study Title	
RIB	A multicentre randomised trial of single dose Radiotherapy compared to Ibandronate for localised metastatic bone pain
Modafinil for fatigue	Modafinil for the treatment of fatigue in lung cancer: a multicentre, randomised, double-blinded, placebo controlled trial
Experience of mesothelioma	Patients' experience during the first three months following a diagnosis of mesothelioma

* Accrual figures are approximate as of 22/06/2009

ADVANCED
LORD
MESO
SCEPTRE

Industry Adopted Trials

Study Title	Pharma	Tumour Type	Subgroup	Target accrual
NCRN 014 Radiant	OSI	NSCLC – Ib-IIIa	LORD	945
NCRN 019 MAGRIT	GSK	NSCLC – IB, II or IIIA	LORD	2270
<i>NCRN 017¹</i>	<i>Pfizer</i>	<i>NSCLC – adv/mets</i>	<i>Advanced</i>	<i>1100</i>
NCRN 032	Eli Lilly	NSCLC - III	Advanced	800
NCRN 051	Pfizer	NSCLC – Adv	Advanced	130
NCRN 053	Pfizer	NSCLC – Adv	Advanced	600

¹Trial on hold.

Accrual figures for industry adopted trials currently not available

Appendix 1

NCRI Lung CSG 2008/09 Publications and abstracts report

Di Bernardo MC, Matakidou A, Eisen T, Houlston RS; GELCAPS Consortium. Lung Cancer. 2008 Dec 29. [Epub ahead of print] Plasminogen activator inhibitor variants PAI-1 A15T and PAI-2 S413C influence lung cancer prognosis. *PMID: 19117638 [PubMed - as supplied by publisher]*

Wang Y, Broderick P, Webb E, Wu X, Vijayakrishnan J, Matakidou A, Qureshi M, Dong Q, Gu X, Chen WV, Spitz MR, Eisen T, Amos CI, Houlston RS. Common variants influence lung cancer risk. *Nat Genet.* 2008 Dec;40(12):1407-9. Epub 2008 Nov 2. *PMID: 18978787 [PubMed - indexed for MEDLINE]*

Relat Lee SM, James LE, Qian W, Spiro S, Eisen T, Gower NH, Ferry DR, Gilligan D, Harper PG, Prendiville J, Hocking M, Rudd RM. Comparison of gemcitabine and carboplatin versus cisplatin and etoposide for patients with poor-prognosis small cell lung cancer. *Thorax.* 2009 Jan;64(1):75-80. Epub 2008 Sep 11.

Liu P, Vikis HG, Wang D, Lu Y, Wang Y, Schwartz AG, Pinney SM, Yang P, de Andrade M, Petersen GM, Wiest JS, Fain PR, Gazdar A, Gaba C, Rothschild Familial aggregation of common sequence variants on 15q24-25.1 in lung cancer. *PMID: 18786981 [PubMed - indexed for MEDLINE]*

H, Mandal D, Coons T, Lee J, Kupert E, Seminara D, Minna J, Bailey-Wilson JE, Wu X, Spitz MR, Eisen T, Houlston RS, Amos CI, Anderson MW, You M. Identification of low penetrance alleles for lung cancer: the GEnetic Lung CAncer Predisposition Study (GELCAPS). *J Natl Cancer Inst.* 2008 Sep 17;100(18):1326-30. Epub 2008 Sep 9. *PMID: 18780872 [PubMed - indexed for MEDLINE]*

Eisen T, Matakidou A, Houlston R; GELCAPS Consortium. *BMC Cancer.* 2008 Aug 20;8:244. *PMID: 18715499 [PubMed - indexed for MEDLINE]*

Eisen T, Thatcher N, Leyvraz S, Miller WH Jr, Couture F, Lorigan P, Lüthi F, Small D, Tanovic A, O'Brien M. Phase II study of weekly plitidepsin as second-line therapy for small cell lung cancer. *Lung Cancer.* 2009 Apr;64(1):60-5. Epub 2008 Aug 9. *PMID: 18692272 [PubMed - in process]*

