IDEAL-CRT

A phase I/II trial of concurrent chemoradiation with dose-escalated radiotherapy in patients with stage II or stage III Non-Small Cell Lung Cancer

ISOTOXIC **D**OSE **E**SCALATION AND **A**CCELERATION IN **L**UNG CANCER **C**HEMO**R**ADIO**T**HERAPY

RATIONALE

- A phase I/II study of radiotherapy dose escalation & acceleration for good performance status patients with inoperable stage II or III NSCLC.
- Aim is to investigate the toxicity, feasibility and potential clinical effectiveness of dose-escalated RT with concurrent chemotherapy.
- The method of dose escalation will be through an individual patient-based model. Each patient will be treated to the dose that, based on the optimised distribution of radiation of his/her treatment plan, is calculated to be associated with an acceptable level of grade three toxicity (from oesophagus or lung).
- Potential experimental arm for a future UK randomised phase III trial

PRIMARY SAFETY ENDPOINTS

- Acute Oesophagitis during RT or within 3 months from the first dose of RT
- Early Radiation Pneumonitis occurring within 6 months from the first dose of RT

SECONDARY SAFETY ENDPOINTS

- Chronic Oesophageal Stricture rate from 3 months post RT
- Pneumonitis from 6 or more months after end of RT
- Changes from baseline in Pulmonary Function Tests
- Any Grade 2-5 pulmonary toxicity from start of RT to death

OTHER SAFETY ENDPOINTS

- Cardiac Toxicity based on submission of ECG & symptom reporting on CRFs

EFFICACY ENDPOINTS

- Tumour Response
- Progression Free Survival
- Overall Survival
- Local Control (Local Progression Free Survival)

SAMPLE SIZE

- 39 patients
  - ARM 1 – 23 patients
  - ARM 2 - 16 patients

ELIGIBILITY CRITERIA - Summarised

- Histologically or cytologically confirmed NSCLC
- Stages: II & III
- Inoperable disease as assessed by a Lung Cancer Multi-Disciplinary Team (MDT); or operable but MDT agrees that chemoRT is a suitable alternative to surgery; or operable but the patient refuses surgery
- RT dose constraints consistent with minimum prescription dose of 63Gy in 30 fractions.
- No prior thoracic radiotherapy
- No prior lobectomy / pneumonectomy
- No prior systemic chemotherapy
- Patients not presenting with a collapsed lung or collapse of an entire lobe
- Adequate Pulmonary Function Test (PFT) results:FEV1 ≥ 40% of predicted OR ≥ 1L / DCLO ≥ 40% of predicted
- WHO Performance status 0 or 1
- Baseline bloods suitable for cisplatin / vinorelbine chemotherapy
- Renal function adequate for chemotherapy ≥60ml/min.

CURRENT TRIAL STATUS

- Ethics approval granted
- NCRI approved trial
- Activated and recruiting patients

CONTACT DETAILS

- Trial Coordinator – Laura Hughes
  - Email: l.hughes@ucl.ac.uk
  - Tel: 020 7679 9284
- Senior Trial Coordinator – Yenting Ngai
  - Email: y.ngai@ucl.ac.uk
- Chief Investigator – Dr David Landau (Guy's & St Thomas' Hospital)
  - Email: david.landau@kcl.ac.uk

Conducted by Cancer Research UK & UCL Cancer Trials Centre, 90 Tottenham Court Road, London W1T 4TJ

IDEAL-CRT

TRIAL DESIGN

Eligible Patients (Stage II & III NSCLC) consented and registered

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Planned for Radiotherapy

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Calculate **total *pneumonitis dose*** (which predicts a 10% Grade 3+ pneumonitis risk) & must be within a **range of 63-73Gy**
Dose reduced if exceeds spinal cord or cardiac dose-limits

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Calculate the ***maximum oesophageal dose*** associated with the total *pneumonitis dose*
Check with CTC for the current TRIAL *maximum oesophageal doses for both ARM 1 & ARM 2 and which ARM 2 cohorts are open*
Is the TRIAL (ARM 2) *maximum oesophageal dose* or the PATIENT maximum *oesophageal dose* higher?

TRIAL Higher → **n=23**

PATIENT Higher → **n=16**

ARM 1

- Radiotherapy given in 30 fractions over 5 weeks with one day per week of twice daily fractionation (not on chemotherapy administration days)
- Prescribed dose (range 63-73Gy)
- Start of trial ARM 1 maximum oesophageal dose = 63Gy
- Chemotherapy (vinorelbine and cisplatin) given concurrently

ARM 2 (Oesophagus Dose Escalation Arm)

- Radiotherapy given in 30 fractions with one day per week of twice daily fractionation (not on chemotherapy administration days)
- Prescribed dose (range 63-73Gy)
- Pt maximum oesophageal dose is adjusted to fit the current trial maximum oesophageal dose.
- Start of trial ARM 2 maximum oesophageal dose = 65Gy

Cohort 1 65Gy	**Cohort 2** 68Gy	**Cohort 3** 71Gy

- Chemotherapy (vinorelbine and cisplatin) given concurrently

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FOLLOW - UP