TRACERx

TRAcking non small cell lung Cancer Evolution through therapy (Rx)

STUDY DESIGN

A prospective observational cohort study of patients with non-small cell lung cancer (NSCLC), in which translational research is the fundamental aspect of the study.

OBJECTIVES

Primary Objectives:

- Define the relationship between intratumour heterogeneity and clinical outcome following surgery and adjuvant therapy (including relationships between intratumour heterogeneity and clinical disease stage and histological subtypes of NSCLC).
- Establish the impact of adjuvant platinum-containing regimens upon intratumour heterogeneity in relapsed disease.

Key Secondary Objective:

- Development and validation of intratumour heterogeneity (ITH) ratio index (I_{TB}) as a prognostic and predictive biomarker in relation to DFS and OS.

PRIMARY ENDPOINTS

- Intratumour heterogeneity quantified by the ratio index I_{TB}
- Disease-free survival
- Overall survival

TARGET ACCRUAL

A minimum target recruitment of 750 eligible patients, with an upper limit of 842 eligible patients, of which 270 are expected to have a first recurrence and agree to provide a biopsy of the site of local recurrence/metastases. Patients will be followed up for a maximum of 5 years.

PARTICIPATING SITES

Hospitals: 15-20 sites

Central Laboratories:

- Translational Cancer Therapeutics Laboratory – UCL
- Department of Cancer Studies and Molecular Medicine – University of Leicester
- CEP GCLP laboratories – University of Manchester

Please see protocol for a list of additional collaborating translational research laboratories.

KEY ELIGIBILITY CRITERIA

Inclusion Criteria:

- Written Informed consent
- Patients ≥18 years of age, with early stage IIA-IIIB disease (according to TNM 8th edition) who are eligible for primary surgery.
- Histopathologically confirmed NSCLC, or a strong suspicion of cancer on lung imaging necessitating surgery (e.g. diagnosis determined from frozen section in theatre)
- Primary surgery in keeping with NICE guidelines planned
- Agreement to be followed up at a TRACERx site
- Performance status 0 or 1
- Suspected tumour at least 15mm in diameter on pre-operative imaging to allow for sampling of at least two tumour regions

Exclusion Criteria:

- Any other current malignancy or malignancy diagnosed or relapsed at any time, which is currently being treated (including by hormonal therapy).
- Any other* current malignancy or malignancy diagnosed or relapsed within the past 3 years**

*Exceptions are non-melanomatous skin cancer, stage 0 melanoma in situ, and in situ cervical cancer.
**An exception will be made for malignancies diagnosed or relapsed more than 2, but less than 3, years ago only if a pre-operative biopsy of the lung lesion has confirmed a diagnosis of NSCLC.

- Psychological condition that would preclude informed consent
- Treatment with neo-adjuvant therapy for current lung malignancy deemed necessary
- Post-surgery staging is not IIA-IIIB
- Known Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) or syphilis infection
- Sufficient tissue, i.e. a minimum of two tumour regions, is unlikely to be obtained for the study based on pre-operative imaging

TISSUE AND BLOOD SAMPLES

- Multi-region tissue sampling (including DNA and RNA sequencing & immunological analyses) at primary surgery, at first recurrence (biopsy/metastasectomy) and possibly at progression
- Blood samples for germline DNA, circulating free tumour DNA (cfDNA), circulating tumour cells (CTC) and immunology

Please refer to the TRACERx protocol, trial specific procedures and samples summary for full eligibility criteria and further details.

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