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A randomised, multicentre trial of primary treatment chemotherapy/immunotherapy and radiotherapy for patients with non-small cell lung cancer

Submission date
19/08/2024

Recruitment status
Recruiting

Registration date
21/08/2024

Overall study status
Ongoing

Last Edited
07/04/2025

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Radiotherapy of the chest area is widely used in the treatment of lung cancer. Its use in stage IV non-small cell lung cancer (NSCLC) has evolved across the world based on local experience, as doctors attempt to ease symptoms, maintain/improve quality of life, and prolong survival while minimising side effects. The way radiotherapy is being used is based on older evidence, and there is a need for new research to figure out the best timing and dosing of radiotherapy when used alongside current systemic treatments.
The aims of this study are:
1. To work out the effect of early high-dose radiotherapy on the chest area on symptoms, disease progression, length, and quality of life
2. To assess the side effects of early high-dose radiotherapy on the chest area
3. To work out the cost-effectiveness of this type of radiotherapy
4. To identify potential barriers, evaluate and explain the treatment and outcomes and highlight issues from a patient, carer, and health care professional's point of view.

Who can participate?
Patients aged 16 years and older with stage IV NSCLC who are fit for chemotherapy and/or immunotherapy and high-dose radiotherapy to the chest area, without symptoms requiring immediate radiotherapy.

What does the study involve?
Following consent, patients will undergo screening tests to ensure they are eligible. Once screened eligible, patients are randomly allocated to one of the two treatment groups. The two treatment groups are:
Control group: chemotherapy and/or immunotherapy
Radiotherapy group: chemotherapy and/or immunotherapy AND radiotherapy that will start within 12 weeks of randomisation and between cycle 1 and 4 of the chemotherapy and/or immunotherapy

A patient is just as likely to receive either of the treatment groups. If allocated to the radiotherapy group, patients will have a radiotherapy planning session with a CT scan. Patients will attend usual clinic visits, at weeks 4, 6, 8, 10, 12, and 14, months 4, 6, 9, 12, 15, 18, and 21 for study assessments. The study assessments will vary depending on the visit but can include weight, asking about how the patient has been feeling and any health issues, asking about any changes to medication and level of self-care/daily activity/physical ability, and completing questionnaires. At months 4, 6, 9, 12, 15 and 21 a CT chest/abdomen/pelvis scan will be done. For the visits, if a patient is unable to attend the clinic, a member of the research team will contact them by telephone for assessments that can be done over the telephone.

What are the possible benefits and risks of participating?
There may or may not be a direct medical benefit from taking part in the trial. This trial will help to further our knowledge of how to treat stage IV NSCLC and this may benefit others with the same condition in the future.
There may be some unpleasant side effects. There could be risks to your child if you become pregnant, or are breastfeeding. As part of the trial, there is a brain CT scan during the screening process. There are also CT chest/abdomen/pelvis scans throughout the trial totalling up to about seven scans, throughout the screening, treatment, and follow-up phases. The number of scans in the trial is similar to standard of care. CT scans and radiotherapy use ionising radiation that may cause cancer many years or decades after exposure. The chance of cancer being caused by ionising radiation associated with imaging or radiotherapy is very small in these patients.

Where is the study run from?
The Christie NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
April 2023 to December 2027

Who is funding the study?
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC) (UK)

Who is the main contact?
tourist-prince@soton.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-when-to-give-radiotherapy-for-advanced-lung-cancer-prince

Study website
https://www.southampton.ac.uk/ctu/trialportfolio/listoftrials/tourist.page

Contact information

Type(s)
Public, Scientific

Contact name
Mrs Izabela Eberhart

Contact details
Southampton Clinical Trials Unit, MP131
Southampton General Hospital

Tremona Road
Southampton
United Kingdom
SO16 6YD
+44 (0)23 8120 5154
tourist-prince@soton.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
334993

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NIHR133518, CPMS 61676, IRAS 334993

Study information

Scientific Title
PRINCE: Prospective, randomised, multicentre trial of first line systemic treatment and radiotherapy in stage IV non-small cell lung cancer

Acronym
PRINCE (TOURIST Platform)

Study objectives
The PRINCE trial will test the hypothesis that early high-dose palliative thoracic radiotherapy is clinically effective in health utility for patients with stage IV non-small cell lung cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/05/2024; South Central - Oxford C Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048144, oxfordc.rec@hra.nhs.uk), ref: 24/SC/0133

Study design
Randomized parallel-group controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, Medical and other records, Telephone

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Stage IV non-small cell lung cancer

Interventions
PRINCE is a randomised control trial in the TOURIST Platform. Patients may be identified at any point after the diagnosis of stage IV NSCLC by their usual care team. To permit timely randomisation and minimise treatment delays potentially eligible patients should be identified at the thoracic multidisciplinary team meeting prior to their first oncology appointment.

PRINCE includes the addition of early high-dose palliative thoracic radiotherapy in patients receiving standard of care (SoC) first-line systemic treatment (chemotherapy, immunotherapy, or a combination of both) to assess if improvement in local disease control results in improved quality of life (QoL)/survival for patients. Once written informed consent has been gained, all screening and baseline procedures have been completed and the patient is confirmed eligible, they will be randomised (1:1) at the start of their systemic treatment to one of two study arms: Control Arm - SoC systemic therapy, Radiotherapy Arm - SoC systemic therapy and radiotherapy. Patients will have equal chances of receiving one of the two arms. There will be either 12 or 13 visits for radiotherapy, depending on clinician decision. Radiotherapy will begin anytime within 84 days after randomisation and between cycles 1 and 4 of systemic therapy.

Patients will be followed up to Month 21, follow-up assessments include:
1. Adverse event, toxicity and medication assessment
2. Quality of life questionnaires
3. Smoking habit questions
4. Weight
5. CT with contrast chest/abdo/pelvis
6. Eastern Cooperative Oncology Group (ECOG) performance status

When all patients have completed all of their study visits, survival and disease progression data will be collected directly from the hospital sites.

An economic evaluation to measure the quality-adjusted life years at 21 months will be performed. A process evaluation using interviews (over the phone or using an online meeting system e.g. Zoom), diaries and a PPI questionnaire to identify issues for implementation from patients, patient carers and Health Care Professionals.
15 patients - individual interview and a diary to complete
All patients - PPI QoL questionnaire completion
15 patient-carers - individual interview
10 health care professionals (across two trials in the TOURIST Platform) – individual interview

Intervention Type
Procedure/Surgery

Primary outcome measure
Health utility measured using EORTC QLU-C10D Area Under the Curve (AUC; using trapezoidal rule) to derive a health utility score per year. Questionnaires completed: Screening/Baseline, week 4, week 6, week 8, week 12, week 14, month 4, month 6, month 9, month 12, month 15, month 18, month 21.

Secondary outcome measures
1. Overall survival (OS), defined as time from randomisation to death from any cause. Censored at the last follow-up if event-free
2. Progression-free survival (PFS), defined as time from randomisation to disease progression (RECIST v1.1) or death from any cause. Censored at last follow-up if event-free
3. Quality of life using EORTC QLQ-C30 and EQ-5D-5L. Questionnaires completed: Screening /Baseline, month 4, month 6, month 9, month 12, month 15, month 21
4. Lung cancer symptoms using EORTC QLQ-LC13. Questionnaire completed: Screening /Baseline, month 4, month 6, month 9, month 12, month 15, month 21
5. Acute and late toxicity as assessed using NCI CTCAE v5.0. From informed consent to end of study

Overall study start date
01/04/2023

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. >=16 years of age
2. Stage IV non-small cell lung cancer (NSCLC) (radiological diagnosis confirmed at multidisciplinary team [MDT] as a minimum) (additionally see #6 trial-specific requirement below)
3. Thoracic disease amenable to radiotherapy
4. Provision of written informed consent
5. For women of childbearing potential: a negative urine or serum pregnancy test within 7 days of trial entry into the main trial
6. Histologically or cytologically confirmed NSCLC
7. At least T2 and/or N1 disease
8. ECOG Performance Status (0-2)
9. The patient is deemed fit to receive a minimum of four cycles of systemic anti-cancer treatment according to local guidelines and assessment
10. Fit to receive high-dose palliative radiotherapy with acceptable pulmonary function according to local guidelines and assessment

Participant type(s)
Patient

Age group

Mixed

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 472; UK Sample Size: 472

Key exclusion criteria
1. The need for palliative radiotherapy to the thorax prior to randomisation
2. Co-morbidities which are considered a contraindication to radiotherapy by the treating clinical team, including interstitial lung disease and active connective tissue disorders
3. History of prior malignant tumours likely to interfere with the protocol treatment or comparisons
4. Leptomeningeal disease
5. Women who are pregnant or breastfeeding
6. Women of child-bearing potential who are not able or unwilling to use a highly effective method of contraception
7. Patients who, in the judgment of the investigator, will be unlikely or unable to comply with the requirements of the protocol
8. Primary targeted systemic therapy for NSCLC with a driver mutation (EGFR, ALK, ROS-1, BRAF)
9. Prior treatments for this NSCLC*
10. Patients participating in a clinical trial of an investigational medicinal product
*Cycle 1 of standard-of-care systemic therapy for this NSCLC may be delivered prior to randomisation

Date of first enrolment
30/07/2024

Date of final enrolment
30/03/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Weston Park Hospital
Witham Road
Sheffield
United Kingdom
S10 2SJ

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Kings Mill Hospital
Mansfield Road
Sutton-in-Ashfield
United Kingdom
NG17 4JL

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
The Christie Hospital
550 Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
Leighton Hospital
Leighton
Crewe
United Kingdom
CW1 4QJ

Study participating centre
Queen's Hospital
Barking, Havering and Redbridge University Hospitals NHS Trust, Rom Valley Way

Romford, Essex
United Kingdom
RM7 0AG

Study participating centre
Royal Devon and Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Clatterbridge Cancer Centre
The Clatterbridge Cancer Centre NHS Foundation Trust
65 Pembroke Place
Liverpool
United Kingdom
L7 8YA

Study participating centre
Colchester Hospital
Turner Road
Colchester
United Kingdom
CO4 5JL

Study participating centre
Royal Surrey County Hospital
Egerton Road
Guildford
United Kingdom
GU2 7XX

Study participating centre
University College London Hospital
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Guy's and St Thomas' Hospital
Guy's and St Thomas' NHS Foundation Trust
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Sponsor information

Organisation
The Christie NHS Foundation Trust

Sponsor details
550 Wilmslow Road
Withington
Manchester
England
United Kingdom

M20 4BX
-
the-christie.sponsoredresearch@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.christie.nhs.uk/

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2028

Individual participant data (IPD) sharing plan
The current data-sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date