

Stereotactic body radiotherapy for the treatment of OPD

Submission date	Recruitment status	<input checked="" type="checkbox"/> Prospectively registered
31/07/2017	No longer recruiting	<input type="checkbox"/> Protocol
Registration date	Overall study status	<input type="checkbox"/> Statistical analysis plan
08/08/2017	Ongoing	<input type="checkbox"/> Results
Last Edited	Condition category	<input type="checkbox"/> Individual participant data
09/12/2025	Cancer	<input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-stereotactic-body-radiotherapy-with-targeted-drug-treatment-in-advanced-non-small-lung>

Contact information

Type(s)

Public

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

219505

ClinicalTrials.gov (NCT)

NCT03256981

Study information

Scientific Title

Targeted therapy with or without dose intensified radiotherapy for oligo-progressive disease in oncogene-Addicted Lung Tumours

Acronym

HALT

Study objectives

Current study hypothesis as of 25/10/2021:

The aim of this study is to determine whether in patients with mutation positive advanced NSCLC the use of SBRT to ≤5 sites of oligoprogressive disease (OPD) with continuation of TKI improves progression-free survival (PFS) compared with continuation of TKI alone.

Previous study hypothesis:

The aim of this study is to determine whether in patients with mutation positive advanced NSCLC the use of SBRT to ≤3 sites of oligoprogressive disease (OPD) with continuation of TKI improves progression-free survival (PFS) compared with continuation of TKI alone.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 10/07/2017, London - Fulham Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8021; fulham.rec@hra.nhs.uk), ref: 17/LO/0980

Study design

Randomized; Interventional; Design type: Treatment, Radiotherapy

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Lung cancer

Interventions

Current interventions as of 25/10/2021:

Eligible participants are randomised to receive either Stereotactic Body Radiotherapy (SBRT) or no SBRT at a ratio of 2:1 (SBRT : no SBRT), with all participants continuing to receive background treatment with TKI therapy as clinically indicated and as per standard care.

Participants allocated to TKI (tyrosine kinase inhibitor) alone arm continue on the same background TKI treatment as prior to trial entry.

Participants allocated to SBRT and TKI arm receive a dose and fractionation schedule dependent on the metastatic site and proximity to critical normal tissues. Patients continue to receive TKI treatment as prior to trial entry. Repeat SBRT is permissible upon development of subsequent OPD (oligopressive disease) lesions dependent on SBRT suitability and total progression lesion number at any one point remaining ≤ 5 .

All patients are seen eight weeks post-randomisation, then three monthly in line with routine care. Tumour imaging and toxicity assessment is assessed monthly every 3 months until disease progression. Quality of Life is assessed at baseline, eight weeks and at the first 3-month visit. Research bloods are collected at baseline, after the first SBRT fraction (treatment group), 8 weeks and 3 monthly until change in systemic therapy.

Previous interventions:

Eligible participants are randomised to receive either Stereotactic Body Radiotherapy (SBRT) or no SBRT at a ratio of 2:1 (SBRT : no SBRT), with all participants continuing to receive background treatment with TKI therapy as clinically indicated and as per standard care.

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Participants allocated to SBRT and TKI arm receive a dose and fractionation schedule dependent on the metastatic site and proximity to critical normal tissues. Patients continue to receive TKI treatment as prior to trial entry. Repeat SBRT is permissible upon the development of subsequent OPD (oligopressive disease) lesions dependent on SBRT suitability and total progression lesion number at any one point remaining ≤ 3 .

All patients are seen eight weeks post-randomisation, then three monthly in line with routine care. Tumour imaging and toxicity assessment is assessed monthly every 3 months until disease progression. Quality of Life is assessed at baseline, 8 weeks and at the first 3-month visit. Research bloods are collected at baseline, after the first SBRT fraction (treatment group), 8 weeks and 3 monthly until change in systemic therapy.

Intervention Type

Other

Primary outcome(s)

Current primary outcome measures as of 25/10/2021:

Progression-free survival defined as the time from randomisation to the first of one of the following events or death from any cause:

- 1.1. Clinically symptomatic progression requiring palliative tumour-specific oncological intervention (e.g. change in systemic therapy or localised non-SBRT radiotherapy) as determined by the treating physician
- 1.2. New or existing intra-cranial lesions not amenable to radical surgery or SRS
- 1.3. Development of new extra-cranial lesions or progression of existing extra-cranial lesions not meeting the criteria for SBRT treatment (e.g. size > 7 cm)
- 1.4. Development of > 5 new or progressing extra-cranial lesion at any one point in time (i.e. widespread progression)

Previous primary outcome measures:

Progression-free survival defined as the time from randomisation to the first of one of the following events or death from any cause:

- 1.1. Clinically symptomatic progression requiring palliative tumour-specific oncological intervention (e.g. change in systemic therapy or localised non-SBRT radiotherapy) as determined by the treating physician.
- 1.2. New or existing intra-cranial lesions not amenable to radical surgery or SRS.
- 1.3. Development of new extra-cranial lesions or progression of existing extra-cranial lesions not meeting the criteria for SBRT treatment (e.g. size >5cm)
- 1.4. Development of >3 new or progressing extra-cranial lesion at any one point in time (i.e. widespread progression)

Key secondary outcome(s)

Current secondary outcome measures as of 25/10/2021:

1. Time to next line of systemic therapy or palliative care – time from randomisation to change in therapy or referral to palliative care due to clinical progression as determined by the treating physician, or death.
2. Overall survival is measured from the time of randomisation until death from any cause.
3. Patterns of disease progression are identified using CT scans to further document natural history of oncogene-addicted NSCLC at 3 monthly intervals.
4. Radiotherapy toxicities (acute and late) assessed using CTCAE v4.0 (clinician and patient versions where available). Acute events are defined as ≤90 days post SBRT start date (applicable for each subsequent course of SBRT where relevant); late events > 90 days.
5. Quality of Life is assessed using EQ-5D-5L and the EORTC QLQ-C30 at baseline, 8 weeks and at the first 3-month visit.
6. Measurement of resistant sub-clones in ctDNA is from blood samples collected at baseline, 8 weeks post-randomisation and 3-monthly during follow-up.
7. Time to failure of next line treatment is measured from the time of randomisation to disease progression on the next line of active systemic therapy.

Previous secondary outcome measures:

1. Time to next line of systemic therapy or palliative care – time from randomisation to change in therapy or referral to palliative care due to clinical progression as determined by the treating physician, or death.
2. Overall survival is measured from the time of randomisation until death from any cause.
3. Patterns of disease progression are identified using CT scans to further document natural history of oncogene-addicted NSCLC at 3 monthly intervals
4. Radiotherapy toxicities (acute and late) assessed using CTCAE v4.0 (clinician and patient versions (where available)) and RTOG. Acute events are defined as ≤ 90 days post SBRT start date (applicable for each subsequent course of SBRT where relevant); late events > 90 days.
5. Quality of Life is assessed using EQ-5D-5L and the EORTC QLQ-C30 at baseline, 8 weeks and at the first 3-month visit
6. Measurement of resistant sub-clones in ctDNA is from blood samples collected at baseline, 8 weeks post-randomisation and 3-monthly during follow-up
7. Time to failure of next line treatment is measured from the time of randomisation to disease progression on the next line of active systemic therapy

Completion date

31/12/2026

Eligibility

Key inclusion criteria

Current inclusion criteria as of 25/10/2021:

1. Male or female, ≥ 16 years of age
2. Established histological diagnosis of advanced NSCLC, not suitable for radical treatment, with defined actionable mutation receiving targeted TKI therapy
3. Clinical and/or radiologically confirmed response to TKI therapy (assessed locally usually 2-3 months post commencing TKI)
4. Confirmed OPD defined as ≤ 5 extracranial sites of progressive disease. All sites must be visible, imaging defined targets and suitable for treatment with SBRT as determined by the virtual MDT and in accordance with the HALT Radiotherapy planning and delivery guidance document.
5. Adequate baseline organ function to allow SBRT to all relevant targets
6. Predicted life expectancy ≥ 6 months
7. Karnofsky Index $\geq 60\%$ and ECOG 0-2
8. Provision of written informed consent

Previous inclusion criteria:

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2. Established histological diagnosis of advanced NSCLC, not suitable for radical treatment, with defined actionable mutation receiving targeted TKI therapy
3. Clinical and/or radiologically confirmed response to TKI therapy (assessed locally usually 2-3 months post commencing TKI)
4. Confirmed OPD defined as ≤ 3 extracranial sites of progressive disease. All sites must be visible, imaging defined targets and suitable for treatment with SBRT as determined by the virtual MDT and in accordance with the HALT Radiotherapy planning and delivery guidance document.
5. Adequate baseline organ function to allow SBRT to all relevant targets
6. Predicted life expectancy ≥ 6 months
7. Karnofsky Index $\geq 60\%$ and ECOG 0-2
8. Provision of written informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

16 years

Upper age limit

99 years

Sex

All

Total final enrolment

113

Key exclusion criteria

Current exclusion criteria as of 25/10/2021:

1. >5 extracranial sites of progressive disease
2. Progressing or newly diagnosed brain metastases identified at the time of trial entry, not amenable to radical surgery or SRS. Previously treated brain metastases (i.e palliative radiotherapy or systemic therapy) which have remained clinically and radiologically stable for ≥ 6 months are permissible.
3. Prior radiotherapy near the oligopressive lesion precluding ablative SBRT
4. Co-morbidities considered clinically to preclude safe use of SBRT e.g. IPF in patients with an oligopressive lung lesion, inflammatory bowel disease in patients with an oligopressive pelvic lymph node
5. Any psychological, sociological or geographical issue potentially hampering compliance with the study
6. Pregnancy

Previous exclusion criteria:

1. >3 extracranial sites of progressive disease
2. Brain metastases not amenable to radical surgery or SRS
3. Prior radiotherapy near the oligopressive lesion precluding ablative SBRT
4. Co-morbidities considered clinically to preclude safe use of SBRT e.g. IPF in patients with an oligopressive lung lesion, inflammatory bowel disease in patients with an oligopressive pelvic lymph node
5. Any psychological, sociological or geographical issue potentially hampering compliance with the study
6. Pregnancy

Date of first enrolment

01/10/2017

Date of final enrolment

17/07/2023

Locations

Countries of recruitment

United Kingdom

England

France

Italy

Spain

Switzerland

Study participating centre
The Royal Marsden Hospital
Downs Road
Sutton
England
SM2 5PT

Study participating centre
The Royal Marsden Hospital
Fulham Road
Chelsea
London
England
SW3 6JJ

Study participating centre
The Christie Hospital
Wimslow Road
Withington
Manchester
England
M20 4BX

Study participating centre
Weston Park Hospital
Whitham Road
Sheffield
England
S10 2SJ

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

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham

England
NG5 1PB

Study participating centre
St Bartholomew's Hospital
West Smithfield
London
England
EC1A 7BE

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
Scotland
G12 0YN

Study participating centre
Guy's Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Belfast City Hospital
Lisburn Road
Belfast
Northern Ireland
BT9 7AB

Study participating centre

Clatterbridge Cancer Centre

Clatterbridge Road

Wirral

England

CH63 4JY

Study participating centre

University College London Hospital

250 Euston Road

London

England

NW1 2PG

Study participating centre

Churchill Hospital

Old Road

Headington

Oxford

England

OX3 7LE

Study participating centre

Leicester Royal Infirmary

Infirmary Square

Leicester

England

LE1 5WW

Study participating centre

Bristol Haematology and Oncology Centre

Horfield Road

Bristol

England

BS2 8ED

Study participating centre

Castle Hill Hospital

Castle Road

Cottingham

England

HU16 5JQ

Study participating centre

Western General Hospital

Crewe Road South

Edinburgh

Scotland

EH4 2XU

Study participating centre

Addenbrookes

Addenbrookes Hospital

Hills Road

Cambridge

England

CB2 0QQ

Sponsor information

Organisation

Institute of Cancer Research

ROR

<https://ror.org/043jzw605>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from halt-icrcts@icr.ac.uk

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary		28/06/2023	No	No	
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes