

Stereotactic body radiotherapy for the treatment of OPD

Submission date 31/07/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 08/08/2017	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 19/06/2025	Condition category Cancer	<input type="checkbox"/> Individual participant data <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>

Study website

<https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/clinical-trials/halt>

Contact information

Type(s)

Public

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

219505

ClinicalTrials.gov number

NCT03256981

Secondary identifying numbers

CPMS 34870, IRAS 219505

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)

London – Fulham Research Ethics Committee, 10/07/2017, ref: 17/LO/0980

Study design

Randomized; Interventional; Design type: Treatment, Radiotherapy

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

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

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 (oligoprogressive 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.

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 the development of subsequent OPD (oligoprogressive 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 measure

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)

Secondary outcome measures

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

Overall study start date

01/01/2017

Completion date

31/12/2025

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

Age group

Adult

Lower age limit

16 Years

Sex

Both

Target number of participants

Planned Sample Size: 110; UK Sample Size: 110

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 oligoprogressive lesion precluding ablative SBRT
4. Co-morbidities considered clinically to preclude safe use of SBRT e.g. IPF in patients with an oligoprogressive lung lesion, inflammatory bowel disease in patients with an oligoprogressive 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 oligoprogressive lesion precluding ablative SBRT
4. Co-morbidities considered clinically to preclude safe use of SBRT e.g. IPF in patients with an oligoprogressive lung lesion, inflammatory bowel disease in patients with an oligoprogressive 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**

England

France

Italy

Spain

Switzerland

United Kingdom

Study participating centre

The Royal Marsden Hospital

Downs Road

Sutton

United Kingdom

SM2 5PT

Study participating centre

The Royal Marsden Hospital

Fulham Road

Chelsea

London

United Kingdom

SW3 6JJ

Study participating centre

The Christie Hospital

Wimslow Road

Withington

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M20 4BX

Study participating centre

Weston Park Hospital

Whitham Road

Sheffield

United Kingdom

S10 2SJ

Study participating centre

Royal Surrey County Hospital

Egerton Road

Guildford
United Kingdom
GU2 7XX

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

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

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

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

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
S016 6YD

Study participating centre

Belfast City Hospital

Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre

Clatterbridge Cancer Centre

Clatterbridge Road
Wirral
United Kingdom
CH63 4JY

Study participating centre

University College London Hospital

250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre

Churchill Hospital

Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre

Leicester Royal Infirmary

Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre

Bristol Haematology and Oncology Centre

Horfield Road

Bristol
United Kingdom
BS2 8ED

Study participating centre
Castle Hill Hospital
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HU16 5JQ

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EH4 2XU

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10043

Study participating centre
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Carrer de Villarroel 170
Barcelona
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08036

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Study participating centre
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Villejuif
Paris
France
94800

Study participating centre
Policlinico Universitario Campus Bio-Medico
Via Alvaro del Portillo
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Rome
Italy
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Study participating centre
Addenbrookes
Addenbrookes Hospital

Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation

Institute of Cancer Research

Sponsor details

Royal Cancer Hospital
237 Fulham Road
London
United Kingdom
SW3 6JB
+44 208 722 4554
halt-icrctsu@icr.ac.uk

Sponsor type

Research organisation

ROR

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

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

The main trial results will be published in a peer-reviewed journal, on behalf of all collaborators. Study results will aim to be published within 1 year after trial ends.

Intention to publish date

31/12/2025

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-icrctsu@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