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Stereotactic body radiotherapy for the treatment of OPD

Submission date 31/07/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 08/08/2017	**Overall study status** Ongoing	
Last Edited 19/06/2025	**Condition category** Cancer	

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 ≥60% and ECOG 0-2
8. Provision of written informed consent

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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 ≤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 ≥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
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Study participating centre
The Royal Marsden Hospital
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EC1A 7BE

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Study participating centre
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Study participating centre
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Barcelona
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08036

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Seville
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Study participating centre
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Rome
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Study participating centre
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Addenbrookes Hospital

Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
Institute of Cancer Research

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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