

# A CR-UK phase I study of BKM120 in patients with non-small cell lung cancer (NSCLC) receiving thoracic radiotherapy

<b>Submission date</b> 25/01/2013	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 29/01/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 24/06/2019	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/cancer-help/trials/a-study-looking-adding-biological-therapy-to-radiotherapy-non-small-cell-lung-cancer-bkm120>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2012-003762-40

### ClinicalTrials.gov (NCT)

NCT02128724

**Protocol serial number**

13615

## Study information

**Scientific Title**

A CR-UK phase I dose escalation study of BKM120 in patients with non-small cell lung cancer (NSCLC) receiving thoracic radiotherapy

**Acronym**

BKM120

**Study objectives**

This study will be a single-centre, open-label, 3+3 cohort, dose escalation phase I study of the use of BKM120 in combination with thoracic radiotherapy. Patients with incurable NSCLC requiring palliative thoracic radiotherapy will be eligible for entry.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

NRES Committee South Central - Oxford B, 07/01/2013, ref: 12/SC/0674

**Study design**

Non-randomised open-label 3+3 cohort dose-escalation phase I study

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Topic: National Cancer Research Network; Subtopic: Lung Cancer; Disease: Lung (non-small cell)

**Interventions**

BKM120 Cohort 1, 50 mg OD (days 1-14). 20 Gy in 5 fractions (days 8-14)

BKM120 Cohort 2, 80 mg OD (days 1-14). 20 Gy in 5 fractions (days 8-14)

BKM120 Cohort 3, 100 mg OD (days 1-14). 20 Gy in 5 fractions (days 8-14)

BKM120 Cohort 4, At maximum tolerated dose (MTD) (days 1 to 28). 20 Gy in 5 fractions (days 22 - 28)

**Intervention Type**

Drug

**Phase**

Phase I

**Drug/device/biological/vaccine name(s)**

BKM120

## Primary outcome(s)

The safety, dose-limiting toxicity (DLT) and MTD of BKM120 with radiotherapy

## Key secondary outcome(s)

Current secondary outcome measures as of 19/07/2016:

1. To evaluate Akt phosphorylation as a predictive marker of response to BKM120; Timepoint(s): Determine phosphorylation status of Akt in peripheral blood mononuclear cells (PBMC) at baseline, during BKM120 treatment and following BKM120 + RT treatment
2. To investigate potential biomarkers that correlate with response to BKM120; Timepoint(s): Measure tumour pAkt and Phosphatase and tensin homolog (PTEN) levels and then identify mutation status of RAS, PI3K and EGFR by PCR
3. To investigate whether BKM120 alters tumour hypoxia and perfusion; Timepoint(s): Changes in 18F-Misonidazole uptake as detected by PET-CT scans. Changes in blood flow as detected by perfusion CT

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2. To investigate potential biomarkers that correlate with response to BKM120; Timepoint(s): Measure tumour pAkt and Phosphatase and tensin homolog (PTEN) levels and then identify mutation status of RAS, PI3K and EGFR by PCR
3. To investigate whether BKM120 alters tumour hypoxia and perfusion; Timepoint(s): Changes in 18F-Misonidazole uptake as detected by PET-CT scans

## Completion date

17/10/2017

## Eligibility

### Key inclusion criteria

Current inclusion criteria as of 02/03/2017:

1. Evidence of histologically confirmed NSCLC of any stage
2. Thoracic lesion requiring palliative radiotherapy and which has been identified on a scan within eight weeks of starting the trial
3. Male or female, age  $\geq 18$  years at the day of consenting to the study
4. Life expectancy of at least 16 weeks
5. Eastern Cooperative Oncology Group (ECOG) performance score of 0-2
6. Patient is able to swallow and retain oral medication
7. The patient is willing to provide written informed consent and is likely to comply with the protocol for the duration of the study, and scheduled follow-up visits and examinations
8. Haematological and biochemical indices within the ranges shown below:
  - 8.1. Haemoglobin (Hb)  $\geq 9.0$  g/dL
  - 8.2. Absolute neutrophil count  $\geq 1.5 \times 10^9/L$
  - 8.3. Platelet count  $\geq 100 \times 10^9/L$
  - 8.4. International Normalised Ratio (INR)  $\leq 1.5$
  - 8.5. Potassium, calcium and Magnesium Within normal range
  - 8.6. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) not above normal range or  $\leq 3.0$  times ULN if liver metastases are present
  - 8.7. Total serum bilirubin not above normal range, or  $\leq 1.5$  times ULN if liver metastases are

present or total bilirubin  $\leq 3.0$  times ULN if the chief investigator is satisfied that the patient has well documented Gilbert's disease and absence of other contributing disease process at the time of diagnosis

8.8. Creatinine  $\leq 1.5 \times$  ULN

8.9. Fasting plasma glucose (FPG)  $\leq 120$ mg/dL [6.7 mmol/L]

Previous inclusion criteria from 19/07/2016 to 02/03/2017:

1. Evidence of histologically confirmed NSCLC of any stage

2. Thoracic lesion requiring palliative radiotherapy and which has been identified on a scan within eight weeks of starting the trial

3. Male or female, age  $\geq 18$  years at the day of consenting to the study

4. Life expectancy of at least 16 weeks

5. Eastern Cooperative Oncology Group (ECOG) performance score of 0-1

6. Patient is able to swallow and retain oral medication

7. The patient is willing to provide written informed consent and is likely to comply with the protocol for the duration of the study, and scheduled follow-up visits and examinations

8. Haematological and biochemical indices within the ranges shown below:

8.1. Haemoglobin (Hb)  $\geq 9.0$  g/dL

8.2. Absolute neutrophil count  $\geq 1.5 \times 10^9$ /L

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8.7. Total serum bilirubin not above normal range, or  $\leq 1.5$  times ULN if liver metastases are present or total bilirubin  $\leq 3.0$  times ULN if the chief investigator is satisfied that the patient has well documented Gilbert's disease and absence of other contributing disease process at the time of diagnosis

8.8. Creatinine  $\leq 1.5 \times$  ULN

8.9. Fasting plasma glucose (FPG)  $\leq 120$ mg/dL [6.7 mmol/L]

Original inclusion criteria:

1. Evidence of histologically confirmed NSCLC of any stage

2. Thoracic lesion requiring palliative radiotherapy and which has been identified on a scan within eight weeks of starting the trial

3. Male or female, age  $\geq 18$  years at the day of consenting to the study

4. Life expectancy of at least 16 weeks

5. Eastern Cooperative Oncology Group (ECOG) performance score of 0-1

6. Patient is able to swallow and retain oral medication

7. The patient is willing to provide written informed consent and is likely to comply with the protocol for the duration of the study, and scheduled follow-up visits and examinations

8. Haematological and biochemical indices within the ranges shown below:

8.1. Haemoglobin (Hb)  $\geq 9.0$  g/dL

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diagnosis

8.8. Creatinine  $\leq 1.5 \times$  ULN

8.9. Fasting plasma glucose (FPG)  $\leq 120$ mg/dL [6.7 mmol/L]

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Total final enrolment**

21

### **Key exclusion criteria**

1. Previous chemotherapy or biological therapy within four weeks of starting study treatment
2. Treatment with any other investigational agent, or participation in another interventional clinical trial within 28 days prior to enrolment
3. Patient has not recovered to grade 1 or better (except alopecia) from related side effects of any prior antineoplastic therapy
4. Treatment at the start of study treatment with any drugs known to be moderate or strong inhibitors or inducers of isoenzyme CYP3A4, and the treatment cannot be discontinued or switched to a different medication prior to starting study drug.
5. Presence of active uncontrolled or symptomatic CNS metastases. Patients with asymptomatic CNS metastases may participate in this trial. Any prior local treatment for CNS metastases must have been completed treatment  $\geq 28$  days prior to enrolment in the trial (including surgery and radiotherapy).
6. Patient has poorly controlled diabetes mellitus (HbA1c  $> 8\%$ )
7. Previous exposure to PI3K, mTOR, or AKT inhibitor
8. Patient has a known hypersensitivity to any of the excipients of BKM120
9. Previous thoracic radiotherapy treatment
10. Any previous extra-thoracic radiotherapy within 28 days prior to enrolment
11. Medically documented history of or active major depressive episode, bipolar disorder, obsessive-compulsive disorder, schizophrenia, a history of suicidal attempt or ideation, or risk of doing harm to others
12. Patient meets the cut-off score of  $\geq 12$  in the PHQ9 or a cut-off of  $\geq 15$  in the GAD7 mood scale, respectively, or selects a positive response of '1, 2, or 3' to question number 9 regarding potential for suicidal thoughts ideation in the PHQ9 (independent of the total score of the PHQ9)
13. Patient has  $\geq$ CTCAE grade 3 anxiety
14. Other psychological, social or medical condition, physical examination finding or a laboratory abnormality that the Investigator considers would make the patient a poor trial candidate or could interfere with

protocol compliance or the interpretation of trial results.

15. Patient has a concurrent malignancy or has had any malignancy (other than NSCLC) in the last 3 years prior to start of study treatment (with the exception of adequately treated basal or squamous cell carcinoma or cervical carcinoma in situ)

16. Patient has had major surgery within 14 days of starting the study drug.

17. Patient has any other concurrent severe, and/or uncontrolled medical condition that would, in the investigator's judgement contraindicate patient participation in the clinical study (e.g. chronic pancreatitis, chronic active hepatitis).

18. Patient has impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of BKM120.

19. Patients who are known to be serologically positive for Hep B, Hep C or HIV.

20. Patient has active cardiac disease including any of the following:

20.1. LVEF < 50% as determined by MUGA scan or ECHO

20.2. QTc > 480 msec on screening ECG (using the QTcF formula)

20.3. Patient is taking a medication that has a known risk of causing QT interval prolongation or inducing Torsades de Pointes, and the treatment cannot be discontinued or switched to an alternative medication.

20.4. Angina pectoris that requires the use of antianginal medication

20.5. Ventricular arrhythmias except for benign premature ventricular contractions

20.6. Any other cardiac arrhythmia not controlled with medication

20.7. Supraventricular and nodal arrhythmias requiring a pacemaker or not controlled with medication

20.8. Conduction abnormality requiring a pacemaker

20.9. Valvular disease with documented compromise in cardiac function

20.10. Symptomatic pericarditis

20.11. History of myocardial infarction within 6 months of entering the trial

20.12. History of congestive heart failure (New York Heart Association functional classification III-IV)

20.13. Documented cardiomyopathy

21. Pregnant or breastfeeding women, or women of childbearing potential unless effective methods of contraception are used. Women of childbearing potential must use highly effective methods of contraception. Oral contraception, injected or implanted hormonal methods are not allowed as BKM120 potentially decreases the effectiveness of hormonal contraceptives.

Acceptable methods of contraception are either:

21.1. True abstinence

21.2. Surgical sterilization

21.3. Male partner sterilization

Or use of a combination of any two of the following (a+b):

a) Placement of an IUD or IUS

b) Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository. Female patients must use acceptable methods of contraception must continue to use contraception for at least 4 weeks after completing BKM120. Male patients (and their female partners) will need to continue to use use contraception for at least 16 weeks after completing BKM120. Women of childbearing potential must have a negative serum pregnancy test  $\leq$  72 hours prior to initiating treatment

**Date of first enrolment**

31/03/2013

**Date of final enrolment**

31/08/2017

# Locations

## Countries of recruitment

United Kingdom

England

## Study participating centre

**Churchill Hospital**

Oxford

United Kingdom

OX3 7LE

# Sponsor information

## Organisation

University of Oxford (UK)

## ROR

<https://ror.org/052gg0110>

# Funder(s)

## Funder type

Charity

## Funder Name

Cancer Research UK (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

## Funder Name

Oxford Cancer Imaging Centre (UK)

# 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 Sarah Pearson (octo-enquiries@oncology.ox.ac.uk).

Type of data: PET imaging data

When the data will become available and for how long: Currently available, no specific limit on duration at present.

By what access criteria will be shared: Internal/external researchers will have to complete a data sharing form (available on request) specifying amongst other details the motivation of their request, background, rationale, details of funding and approvals and also agree to specific conditions of data sharing. There is no specific restriction on the types of analyses at present and upon approval data will be transferred using a secure method.

Consent: Consent not specifically obtained but the data is completely anonymised including scan dates. This is in compliance with the MRC's Good Practice Principles for Sharing Individual Participant Data From Publicly Funded Clinical Trials V1.0 4.2.2.

Ethical/legal restrictions: The researchers would expect the research to be ethically approved where required and for legal compliance as appropriate.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/05/2019	19/06/2019	Yes	No
<a href="#">Basic results</a>		18/10/2018	18/10/2018	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No