ISRCTN14634058 https://doi.org/10.1186/ISRCTN14634058

# PARIS-Pembrolizumab in combination with radiotherapy in locally advanced non-small cell lung cancer (NSCLC)

| | | |
|---|---|---|
| **Submission date**<br>17/07/2017 | **Recruitment status**<br>Stopped | [X] Prospectively registered<br>[ ] Protocol<br>[ ] Statistical analysis plan<br>[ ] Results<br>[ ] Individual participant data<br>[ ] Record updated in last year |
| **Registration date**<br>19/07/2017 | **Overall study status**<br>Stopped | |
| **Last Edited**<br>21/06/2019 | **Condition category**<br>Cancer | |

**Plain English summary of protocol**
-

## Contact information

**Type(s)**
Public

**Contact name**
Miss Erin Peat

**Contact details**
Clinical Trials Research Unit
University of Leeds
Leeds
United Kingdom
LS2 9JT

## Additional identifiers

**EudraCT/CTIS number**
2017-000444-17

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**
34452

# Study information

### Scientific Title
A Phase I Study of Pembrolizumab anti PD-1 monoclonal antibody in combination with Radiotherapy in locally advanced Non-Small Cell Lung Cancer (NSCLC)

### Acronym
PARIS

### Study objectives
The aim of this study is to determine the recommended phase II dose of pembrolizumab, in combination with a standard dose of radical thoracic radiotherapy, in patients with locally advanced non-small cell lung cancer (NSCLC), in order to be used in future phase II trials. The safety and toxicity of the combination of pembrolizumab (at the recommended dose) and radiotherapy are also be investigated.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
North West - Greater Manchester South Research Ethics Committee, 22/05/2017, rec: 17/NW /0242

### Study design
Non-randomised; Interventional; Design type: Treatment, Drug, 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 below to request a patient information sheet

### Health condition(s) or problem(s) studied
Lung Cancer

### Interventions
Participants receive the first dose of pembrolizumab two weeks before the start of radiotherapy. Pembrolizumab is subsequently delivered every three weeks, starting on the first day of radiotherapy and are continued after completion of radiotherapy for up to 12 months. Participants receive radiotherapy for up to six and a half weeks.

As this combination of treatment has not been given before, participants are registered initially into a dose finding phase where dose limiting toxicities (DLTs) is monitored during and for 12 weeks after completion of combined pembrolizumab and thoracic radiotherapy at each dose level in order to confirm the recommended phase II dose. Participants are given a different dose of pembrolizumab treatment depending on the group or 'cohort' they are recruited into.

The starting dose of pembrolizumab for the first patients are 200 mg (dose level 1). This dose may be reduced to a dose of 100 mg (dose level -1) if unacceptable numbers of dose limiting toxicities are experienced at dose level 1. A maximum of 12 participants are treated in the dose finding part of the study aiming to establish the recommended phase II dose (RP2D).

Once the recommended phase II dose is found, an expanded cohort of 13 participants are treated at this dose of pembrolizumab to obtain further safety data.

During radiotherapy treatment the patient are seen weekly for follow-up.

After completion of combination pembrolizumab and radiotherapy treatment, patient visits are scheduled at these time-points:
1. Weekly visits until toxicity resolved to grade 0-1 after radiotherapy. Patients in the dose finding cohort will also be seen weekly to week four regardless of toxicity.
2. Patients on maintenance Pembrolizumab: Three weekly visit up to 12 months
3. Patients not on maintenance Pembrolizumab: Monthly visits for up to four months post RT and then at months six, nine and 12.
4. CT scan assessment within a month of completing RT, three, six and 12 months (following RT)
Thereafter, follow-up visits are scheduled according to host institution protocol.

All participants, including those withdrawn due to toxicity, are followed up for adverse reactions and serious adverse reactions until death, withdrawal of consent, or the end of the study (whichever occurs first).

## Intervention Type
Other

## Phase
Phase I

## Primary outcome measure
1. Recommended phase II dose is measured using the amount of participants in the dose finding phase experiencing dose limiting toxicity (DLT) in the time period during and for 12 weeks after treatment with combined Pembrolizumab and thoracic radiotherapy
2. Dose limiting toxicity is measured using toxicities experienced from the start of treatment to 12 weeks post combination therapy

## Secondary outcome measures
1. Safety profile of Pembrolizumab combined with thoracic RT (acute and late toxicity) is measured by assessing the occurrence of SAEs, SARs, and SUSARs until 90 days after the participant has stopped trial treatment. The toxicity profile is measured by assessing the occurrence of adverse events until 30 days after the participant has stopped trial treatment.
2. Treatment compliance of Pembrolizumab combined with thoracic RT is measured by recording dose reductions, delays, omissions, and withdrawals throughout each participant's treatment on the study

3. Best overall response to Pembrolizumab combined with thoracic RT is measured using the RECIST criteria from the start of treatment until disease progression/recurrence (taking as reference for progressive disease the smallest measurements recorded since the treatment started)
4. Best overall response to Pembrolizumab combined with thoracic RT measured according to immune-related response criteria (irRC) is measured as the best confirmed irRC overall response over the study as a whole, recorded between the date of first dose until the last tumour assessment before subsequent therapy (except for local palliative radiotherapy for painful bone lesions) for the individual participant
5. Progression-free survival is measured using date of registration to first documented evidence of disease progression or death
6. Overall survival is measured from participant records from date of registration to death

### Overall study start date
01/10/2016

### Completion date
31/12/2020

## Eligibility

### Key inclusion criteria
1. Histologically or cytologically confirmed NSCLC
2. Unresectable stage III NSCLC not suitable for concurrent chemoradiotherapy i.e;
2.1. Patient unsuitable for cisplatin (eg poor renal function);
2.2. Large volume of disease with predicted dose to thoracic organs at risk that are likely to exceed the constraints for concurrent chemoradiotherapy, in the opinion of a clinical oncologist specialised in lung cancer
3. Stage IV NSCLC with dominant chest symptoms and low burden of metastatic disease who may benefit from thoracic RT
4. Patient considered suitable for radical radiotherapy
5. If chemotherapy has been given previously, the maximum interval between the last day of chemotherapy and the start of radiotherapy must be 6 weeks. The minimum interval between the last day of chemotherapy and the start of Pembrolizumab must be one week
6. Age ≥ 18
7. Life expectancy estimated to be greater than 6 months
8. Performance status (ECOG) 0 or 1 (see Appendix 1)
9. MRC dyspnoea score < 3 (see Appendix 2)
10. FEV1 ≥ 40% predicted and DLCO ≥ 40% predicted; Lung V20 ≤ 30% in the dose finding part of the study and ≤ 35% in the expanded cohort
11. No prior thoracic radiotherapy (excluding patients that have had RT for Breast cancer providing that the overlap is minimal as per local investigators discretion or as discussed and agreed by CI as required) or T cell modulating antibodies (including anti-PD-1, anti-PD-L1, PD-L2, anti-CD137 and anti-CTLA4, including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways)
12. Measurable disease based on RECIST 1.1
13. Patient willing to undergo a repeat biopsy post RT
14. Written informed consent must be given according to GCP and national regulations.
15. Adequate organ function within 7 days of study treatment as defined in the protocol

### Participant type(s)

Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
Planned Sample Size: 25; UK Sample Size: 25

### Key exclusion criteria
1. Mixed non-small cell and small cell tumours
2. Participation in a study of an investigational agent or using an investigational device within 4 weeks prior to the anticipated start of treatment.
3. Current or previous malignant disease within 3 years except CIN, non-melanoma skin cancer and low grade, low stage prostate cancer found as incidental finding and not requiring treatment
4. History of interstitial pneumonitis
5. Presence of brain metastases confirmed by CT or MR brain (unless suitable for local treatment such as SRS or Neurosurgery)
6. History of autoimmune disease requiring steroids or immunosuppressive medication
7. Uncontrolled hypothyroidism or hyperthyroidism
8. Other diseases requiring immunosuppressive therapy greater than 28 days prior to the anticipated first dose of trial treatment.
9. Other diseases requiring systemic glucocorticoid (doses < = 10 mg prednisolone or equivalent) prior to the first dose of trial treatment.
10. Received a prior autologous or allogeneic organ or tissue transplantation.
11. Chronic GI disease likely to interfere with protocol treatment.
12. Testing positive for human immunodeficiency virus, active hepatitis B or C infection.
13. Treatment with live vaccine within 30 days prior to the first dose of trial treatment.
14. Patients of reproductive potential who are unable to comply with effective contraception if sexually active during the study and for up to 120 days after the last dose of Pembrolizumab
15. Women who are pregnant or breastfeeding. Women of childbearing potential must have a negative serum or urine pregnancy test
16. Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial

### Date of first enrolment
01/08/2017

### Date of final enrolment
01/02/2020

## Locations

### Countries of recruitment

England

United Kingdom

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

### Study participating centre
**St James's University Hospital**
Beckett Street
Leeds
United Kingdom
LS9 7TF

### Study participating centre
**Royal Marsden Hospital**
Downs Road
Sutton
Surrey
United Kingdom
SM2 5PT

## Sponsor information

### Organisation
The Christie NHS Foundation Trust

### Sponsor details
550 Wilmslow Road
Withington
Manchester
England
United Kingdom
M20 4BX

### Sponsor type
Hospital/treatment centre

**ROR**
https://ror.org/03v9efr22

# Funder(s)

**Funder type**
Government

**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**
Planned publication in a high-impact peer reviewed journal and presentation of results at a relevant conference around one year after the end of the study.

**Intention to publish date**
01/02/2021

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

**IPD sharing plan summary**
Data sharing statement to be made available at a later date

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |