ISRCTN12569958 https://doi.org/10.1186/ISRCTN12569958

A trial using blood tests to detect cancer cells after standard treatment to trigger additional treatment in early stage triple negative breast cancer patients

Submission date 08/05/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/06/2017	**Overall study status** Completed	
Last Edited 10/10/2023	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-whether-ctdna-can-help-doctors-know-who-risk-breast-cancer-coming-back-pembroluzimab-reduces-ctdna-ctraktn

Study website
https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/our-research/clinical-trials/c-trak-tn

Contact information

Type(s)
Public

Contact name
Ms Katie Goddard

Contact details
The Institute of Cancer Research
Royal Cancer Hospital
237 Fulham Road
London
United Kingdom
SW3 6JB
+44 208 722 4614
c-trak-tn-icrctsu@icr.ac.uk

Additional identifiers

EudraCT/CTIS number
2017-000508-92

IRAS number

ClinicalTrials.gov number
NCT03145961

Secondary identifying numbers
33825

Study information

Scientific Title
c-TRAK TN: A randomised trial utilising ctDNA mutation tracking to detect minimal residual disease and trigger intervention in patients with moderate and high risk early stage triple negative breast cancer

Acronym
c-TRAK TN

Study objectives
Study aims:
1. To assess whether ctDNA screening can be used to predict which patients are at highest risk of relapse, and identify patients that have microscopic or minimal residual disease (MRD), that is not visible on imaging
2. In patients that have MRD (as detected by a positive ctDNA blood test) following completion of treatment, to assess the potential effectiveness of treatment with pembrolizumab, assessed as the sustained clearance of ctDNA

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford C Research Ethics Committee, 05/04/2017, ref: 17/SC/0090

Study design
Randomised; Both; Design type: Treatment, Screening, Immunotherapy, Active Monitoring, Cohort study

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
Breast cancer

Interventions
Current interventions as of 04/01/2023:
Patients registered to c-TRAK TN underwent ctDNA blood tests every 3 months. If the patient had a positive ctDNA result during the 'active' ctDNA surveillance period, they were allocated centrally by the ICR-CTSU. Prior to the implementation of protocol v6.0; the randomised component of the trial; ctDNA surveillance was blinded and patients were randomised on a 2:1 basis via a minimisation algorithm to either pembrolizumab treatment or observation. Following the implementation of protocol version 6.0; the non-randomised component of the trial; all patients were then allocated to treatment intervention.

Pembrolizumab treatment group: Patients will be informed and asked to re-consent to confirm they want to receive treatment. They will then undergo eligibility assessments to ensure it is safe for them to start treatment. If the patient consents and is eligible to start treatment, they will receive 200mg pembrolizumab as a 30-minute intravenous infusion every 3 weeks for up to 12 months. A ctDNA blood test will be done at every cycle and will be blinded. For 12 months after the completion of pembrolizumab, patients will continue with ctDNA blood tests every 3 months. After this, patients will be followed up every 6 months until disease recurrence, or until centres are informed no further follow-up is required, unless the patient withdraws consent.

Observation group: Patients and their treating team will not be informed of the randomisation and will continue to have ctDNA blood tests every 3 months up to 24 months after commencing ctDNA screening. They will be followed up every 6 months until disease recurrence, or until centres are informed no further follow-up is required, unless the patient withdraws consent.

Previous interventions:
Patients will be registered to c-TRAK TN, and undergo blinded ctDNA blood tests every 3 months. Neither the patient nor their treating team will be informed of the blood test results. If the patient has a positive ctDNA result within 12 months of commencing ctDNA screening, the patient will be randomised centrally by the ICR-CTSU on a 2:1 basis via a minimisation algorithm, to either pembrolizumab treatment or observation.

Pembrolizumab treatment group: Patients will be informed and asked to re-consent to confirm they want to receive treatment. They will then undergo eligibility assessments to ensure it is safe for them to start treatment. If the patient consents and is eligible to start treatment, they will receive 200mg pembrolizumab as a 30-minute intravenous infusion every 3 weeks for up to 12 months. A ctDNA blood test will be done at every cycle and will remain blinded. For 12 months after the completion of pembrolizumab, patients will have blinded ctDNA blood tests done every 3 months. After this, patients will be followed up every 6 months until disease recurrence, or until centres are informed no further follow-up is required, unless the patient withdraws consent.

Observation group: Patients and their treating team will not be informed of the randomisation and will continue to have ctDNA blood tests every 3 months up to 24 months after commencing ctDNA screening. They will be followed up every 6 months until disease recurrence, or until centres are informed no further follow-up is required, unless the patient withdraws consent.

Intervention Type
Other

Primary outcome measure
Current primary outcome measure as of 31/10/2019:
1. ctDNA positivity in blood by 12 months, as assessed by digital PCR on the blood sample taken at that time point
2. ctDNA positivity in blood by 24 months as assessed by digital PCR on the blood sample taken at that time point
3. Removal of ctDNA in the blood by 6 months (24 weeks) after starting pembrolizumab, measured by digital PCR on the blood sample collected 6 months (24 weeks) after commencing pembrolizumab
4. Absence of disease recurrence by 6 months (24 weeks) after starting pembrolizumab, measured by the recurrence assessment carried out 6 months (24 weeks) after commencing pembrolizumab

Previous primary outcome measure:
1. The proportion of patients with ctDNA positivity by 12 or 24 months as assessed by the blood sample taken at 12 months and 24 months
2. The proportion of patients without either detectable ctDNA or disease recurrence 12 months after starting pembrolizumab, measured by the blood sample and recurrence assessment carried out 12 months after commencing pembrolizumab

Secondary outcome measures
Current secondary outcome measures as of 31/10/2019:
1. The time from entry into ctDNA screening to first positive ctDNA detection, assessed using ctDNA screening blood samples taken every 3 months from baseline up to a maximum of 12 months after starting ctDNA screening
2. The proportion of patients randomised to receive pembrolizumab that are found to have metastatic disease, visible and diagnosed via imaging, at the time of first ctDNA detection which is assessed using ctDNA blood samples taken every 3 months from baseline up to a maximum of 12 months after starting ctDNA screening
3. The time between randomisation to the therapeutic aspect of the trial (either to pembrolizumab treatment or observation group) and first confirmed detection of recurrent disease.
4. Proportion of patients without detectable ctDNA or disease recurrence 6 months after randomisation to observation group
5. Safety and tolerability of pembrolizumab treatment, assessed by NCI CTCAE v4.0 classification of adverse events and the proportion of patients reporting a dose reduction or delay
6. The proportion of patients randomised to receive pembrolizumab who start the therapy, assessed at the point of commencement or non-commencement of treatment, up to 8 weeks following randomisation

Exploratory Outcome Measures:
1. Descriptive differences in time between ctDNA detection and disease recurrence, and disease

free survival, between patients in the pembrolizumab and the observation groups, assessed as the time between first ctDNA detection and documented recurrence or disease free survival event, whichever comes first, expected to occur up to 5 years
2. To explore predictors of sustained ctDNA clearance on pembrolizumab
3. To explore potential predictors of relapse and ctDNA detection, and alternative definitions of ctDNA clearance. Assess the relationship between lead time and clinical/biological factors using standard statistical techniques for time to event data.
4. Association between ctDNA clearance and time to recurrence in the pembrolizumab group, assessed using standard statistical techniques for time to event data

Previous secondary outcome measures:
1. The time from entry into ctDNA screening to first positive ctDNA detection, assessed using ctDNA screening blood samples taken every 3 months from baseline up to a maximum of 12 months after starting ctDNA screening
2. The proportion of patients randomised to receive pembrolizumab that are found to have metastatic disease, visible and diagnosed via imaging, at the time of first ctDNA detection which is assessed using ctDNA blood samples taken every 3 months from baseline up to a maximum of 12 months after starting ctDNA screening
3. Review of the lead time between first detection of ctDNA and confirmed recurrent disease assessed by comparing the date of randomisation to recurrence detection, expected to occur up to 5 years
4. The proportion of patients without detectable ctDNA or disease recurrence 12 months after randomisation to observation group
5. Safety and tolerability of pembrolizumab assessed using NCI CTCAE v4.0, and the proportion of patients reporting dose reductions or delays, assessed throughout pembrolizumab treatment, up to 12 months
6. The proportion of patients randomised to receive pembrolizumab who start the therapy, assessed at the point of commencement or non-commencement of treatment, up to 8 weeks following randomisation

Exploratory Outcome Measures:
1. Descriptive differences in time between ctDNA detection and disease recurrence, and disease free survival, between patients in the pembrolizumab and the observation groups, assessed as the time between first ctDNA detection and documented recurrence or disease free survival event, whichever comes first, expected to occur up to 5 years
2. The relationship between sustained clearance of ctDNA on pembrolizumab and biological markers up to 12 months after commencing pembrolizumab
3. Relationship between lead time of detection of ctDNA and disease relapse and measurement of potential predictive clinical and biological factors will be assessed using standard statistical techniques for time to event data up to 5 years

Overall study start date
01/07/2015

Completion date
31/03/2024

Eligibility

Key inclusion criteria

Current inclusion criteria as of 31/10/2019:
1. Signed Informed Consent Form for Registration
2. Male or female patients ages 16 years or older
3. ECOG performance status 0, 1 or 2
4. Histologically proven primary triple negative breast cancer as defined as oestrogen receptor (ER) negative, progesterone receptor (PgR) negative (if available, otherwise PgR unknown), (as defined by Allred score 0/8 or 2/8 or stain in <1% of cancer cells) and HER2 negative (immunohistochemistry 0/1+ or negative by in situ hybridization) as determined by local laboratory
5. Availability of tissue from two archival tumour tissue samples (either from diagnostic biopsy, and/or primary surgery). If only one tumour sample is available, the site should inform the ICR-CTSU who will discuss eligibility with the Chief Investigator (or designated TMG member). Patients who have tumours previously sequenced outside the c-TRAK TN trial must provide one archival tumour tissue sample and the report that confirms the mutations detected
6. Patients with moderate or high-risk early-stage triple-negative breast cancer according to the following risk of relapse criteria:
6.1. Neoadjuvant chemotherapy (no adjuvant chemotherapy planned):
6.1.1. High-risk criteria - Residual microscopic or macroscopic invasive cancer in the axillary nodes after chemotherapy
6.1.2. Moderate risk criteria - Residual invasive cancer in the breast, and axillary lymph node negative after chemotherapy
6.2. Adjuvant chemotherapy:
6.2.1. High-risk criteria - Tumour size >50mm and node positive OR ≥4 nodes positive regardless of primary tumour size
6.2.2. Moderate risk criteria - Tumour size >20mm AND/OR involved axillary macroscopic lymph node
6.3 Both neoadjuvant and adjuvant chemotherapy:
Patients who have received both neoadjuvant chemotherapy and further adjuvant chemotherapy must fulfil only the adjuvant chemotherapy risk criteria to be eligible. They can fulfil the criteria on either clinical staging prior to neoadjuvant chemotherapy or pathological staging at surgery
7. Patients must be registered according to the following criteria for timing of registration:
7.1. Neoadjuvant chemotherapy (no adjuvant chemotherapy planned):
Patients must be registered within 6 weeks of surgery. Patients may be registered before or during radiotherapy and should be registered as early as possible
7.2. Adjuvant chemotherapy (no neoadjuvant chemotherapy received):
Patients must be registered before, or on the day of, the 3rd cycle of adjuvant chemotherapy and should be registered as early as possible
7.3. Both neoadjuvant and adjuvant chemotherapy
Patients must be registered within 6 weeks of surgery. Patients may be registered before or during radiotherapy. Patients must register before starting capecitabine
8. Consent to provide research blood samples
9. Patients with bilateral tumours can be included if both are triple negative and if two archival tissues samples can be provided per tumour.
10. Patients must have had surgery achieving clear margins (as per local guidelines).
11. Female and male patients of reproductive potential must be willing to use an adequate method of contraception, for the first year of the trial and if randomised to pembrolizumab, for the duration of treatment through to 120 days after the last dose of pembrolizumab (see appendix 2). Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the patient.
12. Patients must be willing to have frequent blood tests (every 3 months for 2 years in ctDNA screening and 3 weekly if subsequently allocated pembrolizumab) and receive a 12 month

course of pembrolizumab if randomised to pembrolizumab treatment on ctDNA detection.
13. No evidence of distant metastatic disease on staging scans conducted at any time since initial diagnosis

Previous inclusion criteria as of 26/10/2018:
1. Signed Informed Consent Form for Registration
2. Male or female patients ages 16 years or older
3. ECOG performance status 0, 1 or 2
4. Histologically proven primary triple negative breast cancer as defined as oestrogen receptor (ER) negative, progesterone receptor (PgR) negative (if available, otherwise PgR unknown), (as defined by Allred score 0/8 or 2/8 or stain in <1% of cancer cells) and HER2 negative (immunohistochemistry 0/1+ or negative by in situ hybridization) as determined by local laboratory.
5. Availability of tissue from two archival tumour tissue samples (either from diagnostic biopsy, and/or primary surgery). If only one tumour sample is available, the site should inform the ICR-CTSU who will discuss eligibility with the Chief Investigator (or designated TMG member). Patients who have tumours previously sequenced outside the c-TRAK TN trial must provide one archival tumour tissue sample and the report that confirms the mutations detected
6. Patients with moderate or high risk early stage triple negative breast cancer according to the following risk of relapse criteria:
High risk criteria:
6.1.1. Neoadjuvant chemotherapy – residual invasive cancer in the axillary nodes after chemotherapy, defined as at least microscopic residual disease (>0.2mm) by histology, OR OSNA macroscopic, OR OSNA microscopic with residual invasive cancer in the breast.
6.1.2. Adjuvant chemotherapy – tumour size >50mm and node positive OR ≥4 nodes positive regardless of primary tumour size.
Moderate risk criteria:
6.2.1. Neoadjuvant chemotherapy – residual invasive cancer in the breast and axillary lymph node negative after chemotherapy
6.2.2. Adjuvant chemotherapy – tumour size >20mm AND/OR involved axillary macroscopic lymph node defined as ≥2mm by histology or OSNA macroscopic.
Note: Patients who have received both neoadjuvant chemotherapy and further adjuvant chemotherapy must fulfill the adjuvant chemotherapy risk criteria to be eligible on either clinical staging prior to neoadjuvant chemotherapy or pathological staging at surgery.
7. Patients registered according to following criteria for timing of registration
Neoadjuvant chemotherapy:
Patients must be registered within 3 months of surgery or within 6 weeks of completing adjuvant radiotherapy if indicated, whichever occurs later. Patients may be registered before or during radiotherapy and should be registered as early as possible.
Adjuvant chemotherapy:
Patients must be registered within 3 months of the last cycle of adjuvant chemotherapy, or within 6 weeks of completing adjuvant radiotherapy, whichever occurs later. Patients may register during adjuvant chemotherapy or radiotherapy and should be registered as early as possible.
8. Consent to provide research blood samples
9. Patients with bilateral tumours can be included if both are triple negative and if two archival tissues samples can be provided per tumour.
10. Patients must have had surgery achieving clear margins (as per local guidelines).
11. Female and male patients of reproductive potential must be willing to use an adequate method of contraception, for the first year of the trial and if randomised to pembrolizumab, for the duration of treatment through to 120 days after the last dose of pembrolizumab (see appendix 2). Note: Abstinence is acceptable if this is the usual lifestyle and preferred

contraception for the patient.
12. Patients must be willing to have frequent blood tests (every 3 months for 2 years in ctDNA screening and 3 weekly if subsequently allocated pembrolizumab) and receive a 12 month course of pembrolizumab if randomised to pembrolizumab treatment on ctDNA detection.
13. No evidence of distant metastatic disease on staging scans conducted at any time since initial diagnosis

Previous inclusion criteria as of 03/05/2018:
1. Signed Informed Consent Form for Registration
2. Male or female patients ages 16 years or older
3. ECOG performance status 0, 1 or 2
4. Histologically proven primary triple negative breast cancer as defined as oestrogen receptor (ER) negative, progesterone receptor (PgR) negative (if available, otherwise PgR unknown), (as defined by Allred score 0/8 or 2/8 or stain in <1% of cancer cells) and HER2 negative (immunohistochemistry 0/1+ or negative by in situ hybridization) as determined by local laboratory.
5. Availability of tissue from two archival tumour tissue samples (either from diagnostic biopsy, and/or primary surgery). If only one tumour sample is available, the site should inform the ICR-CTSU who will discuss eligibility with the Chief Investigator (or designated TMG member). Patients who have tumours previously sequenced outside the c-TRAK TN trial must provide one archival tumour tissue sample and the report that confirms the mutations detected
6. Patients with moderate or high risk early stage triple negative breast cancer according to the following risk of relapse criteria:
High risk criteria:
6.1.1. Neoadjuvant chemotherapy – residual invasive cancer in the axillary nodes after chemotherapy, defined as at least microscopic residual disease (>0.2mm) by histology, OR OSNA macroscopic, OR OSNA microscopic with residual invasive cancer in the breast.
6.1.2. Adjuvant chemotherapy – tumour size >50mm and node positive AND/OR ≥4 nodes positive regardless of primary tumour size.
Moderate risk criteria:
6.2.1. Neoadjuvant chemotherapy – residual invasive cancer in the breast and axillary lymph node negative after chemotherapy
6.2.2. Adjuvant chemotherapy – tumour size >20mm AND/OR involved axillary macroscopic lymph node defined as ≥2mm by histology or OSNA macroscopic.
Note: Patients who have received both neoadjuvant chemotherapy and further adjuvant chemotherapy must fulfill the adjuvant chemotherapy risk criteria to be eligible on either clinical staging prior to neoadjuvant chemotherapy or pathological staging at surgery.
7. Patients registered according to following criteria for timing of registration
Neoadjuvant chemotherapy:
Patients must be registered within 3 months of surgery or within 4 weeks of completing adjuvant radiotherapy if indicated, whichever occurs later. Patients may be registered before or during radiotherapy and should be registered as early as possible.
Adjuvant chemotherapy:
Patients must be registered within 3 months of the last cycle of adjuvant chemotherapy, or within 4 weeks of completing adjuvant radiotherapy, whichever occurs later. Patients may register during adjuvant chemotherapy or radiotherapy and should be registered as early as possible.
8. Consent to provide research blood samples
9. Patients with bilateral tumours can be included if both are triple negative and if two archival tissues samples can be provided per tumour.
10. Patients must have had surgery achieving clear margins (as per local guidelines).
11. Female and male patients of reproductive potential must be willing to use an adequate

method of contraception, for the first year of the trial and if randomised to pembrolizumab, for the duration of treatment through to 120 days after the last dose of pembrolizumab (see appendix 2). Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the patient.
12. Patients must be willing to have frequent blood tests (every 3 months for 2 years in ctDNA screening and 3 weekly if subsequently allocated pembrolizumab) and receive a 12 month course of pembrolizumab if randomised to pembrolizumab treatment on ctDNA detection.
13. No evidence of distant metastatic disease on staging scans conducted at any time since initial diagnosis

Previous inclusion criteria:
1. Signed Informed Consent Form for Registration
2. Male or female patients ages 16 years or older
3. ECOG performance status 0 or 1
4. Histologically proven primary triple negative breast cancer as defined as oestrogen receptor (ER) negative, progesterone receptor (PgR) negative (if available, otherwise PgR unknown), (as defined by Allred score 0/8 or 2/8 or stain in <1% of cancer cells) and HER2 negative (immunohistochemistry 0/1+ or negative by in situ hybridization) as determined by local laboratory.
5. Provision of tissue from two archival tumour tissue samples (either from diagnostic biopsy, and/or primary surgery, or where available residual disease post-neoadjvuant chemotherapy). If only one tumour sample is available, the site should inform the ICR-CTSU who will discuss eligibility with the Chief Investigator or if unavailable the designated TMG member. Patients who have tumours previously sequenced outside the c-TRAK TN trial must provide one archival tumour tissue sample and the report that confirms the mutations detected.
6. Patients with moderate or high risk early stage triple negative breast cancer according to the following risk of relapse criteria:
High risk criteria:
6.1.1. Neoadjuvant chemotherapy – residual invasive cancer in the axillary nodes after chemotherapy, defined as at least microscopic residual disease (>0.2mm) by histology, OR OSNA macroscopic, OR OSNA microscopic with residual invasive cancer in the breast.
6.1.2. Adjuvant chemotherapy – tumour size >50mm and node positive AND/OR ≥4 nodes positive regardless of primary tumour size.
Moderate risk criteria:
6.2.1. Neoadjuvant chemotherapy – residual invasive cancer in the breast and axillary lymph node negative after chemotherapy
6.2.2. Adjuvant chemotherapy – tumour size >20mm AND/OR involved axillary macroscopic lymph node defined as ≥2mm by histology or OSNA macroscopic.
Note: Patients who have received both neoadjuvant chemotherapy and further adjuvant chemotherapy must fulfill the adjuvant chemotherapy risk criteria to be eligible on either clinical staging prior to neoadjuvant chemotherapy or pathological staging at surgery.
7. Patients registered according to following criteria for timing of registration
Neoadjuvant chemotherapy:
Patients must be registered within 3 months of surgery or within 4 weeks of completing adjuvant radiotherapy if indicated, whichever occurs later. Patients may be registered before or during radiotherapy and should be registered as early as possible.
Adjuvant chemotherapy:
Patients must be registered within 3 months of the last cycle of adjuvant chemotherapy, or within 4 weeks of completing adjuvant radiotherapy, whichever occurs later. Patients may register during adjuvant chemotherapy or radiotherapy and should be registered as early as possible.
8. Provision of blood samples for germline DNA analysis and exploratory ctDNA analysis.

9. Patients with bilateral tumours can be included if both are triple negative and if two archival tissues samples can be provided per tumour.
10. Patients must have had surgery achieving clear margins (as per local guidelines).
11. Female and male patients of reproductive potential must be willing to use an adequate method of contraception, for the first year of the trial and if randomised to pembrolizumab, for the duration of treatment through to 120 days after the last dose of pembrolizumab (see appendix 2). Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the patient.
12. Patients must be willing to have frequent blood tests (every 3 months for 2 years in ctDNA screening and 3 weekly if subsequently allocated pembrolizumab) and receive a 12 month course of pembrolizumab if randomised to pembrolizumab treatment on ctDNA detection.
13. No evidence of distant metastatic disease on staging scans conducted at any time since initial diagnosis

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 150; UK Sample Size: 150

Total final enrolment
208

Key exclusion criteria
Current exclusion criteria as of 26/10/2018:
1. Any concurrent or planned treatment for the current diagnosis of breast cancer other than surgery, locoregional adjuvant radiotherapy, standard adjuvant chemotherapy, or a bisphosphonate/denosumab
2. Prior treatment with a PDL1, PD1, or other immunomodulatory therapy
3. Prior diagnosis of cancer including prior diagnosis of breast cancer in the previous 5 years, other than for basal cell carcinoma of the skin or cervical carcinoma in situ
4. Patients previously entered into a therapeutic trial during or after neoadjuvant chemotherapy where experimental therapy is continued post-surgery
5. Treatment with an unlicensed or investigational product within 4 weeks of trial entry
6. Active autoimmune disease requiring systemic therapy in the last two years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of such systemic treatment
7. Diagnosis of immunodeficiency or receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of pembrolizumab
8. Known history of active TB (Tuberculosis Bacillus)
9. Known history of Human Immunodeficiency Virus (HIV)

10. Known active Hepatitis B or Hepatitis C
11. Known history of, or any evidence of active, non-infectious pneumonitis
12. Active infection requiring systemic therapy
13. Previous solid organ transplantation or allogenic stem cell transplantation
14. Females who are pregnant or breastfeeding
15. Presence of any systemic illness incompatible with participation in the clinical trial or inability to provide written informed consent
16. A pathological complete response (pCR) to neoadjuvant chemotherapy (added 31/10/2019)

Previous exclusion criteria as of 03/05/2018:
1. Any concurrent or planned treatment for the current diagnosis of breast cancer other than surgery, locoregional adjuvant radiotherapy, standard adjuvant chemotherapy, or a bisphosphonate/denosumab
2. Prior treatment with a PDL1, PD1, or other immunomodulatory therapy
3. Prior diagnosis of cancer including prior diagnosis of breast cancer in the previous 5 years, other than for basal cell carcinoma of the skin or cervical carcinoma in situ
4. Patients previously entered into a therapeutic trial during or after neoadjuvant chemotherapy where experimental therapy is continued post-surgery
5. Treatment with an unlicensed or investigational product within 4 weeks of trial entry
6. Active autoimmune disease requiring systemic therapy in the last two years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of such systemic treatment
7. Diagnosis of immunodeficiency or receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of pembrolizumab
8. Known history of active TB (Tuberculosis Bacillus)
9. Known history of Human Immunodeficiency Virus (HIV)
10. Known active Hepatitis B or Hepatitis C
11. Known history of, or any evidence of active, non-infectious pneumonitis
12. Active infection requiring systemic therapy
13. Previous solid organ transplantation
14. Females who are pregnant or breastfeeding
15. Presence of any systemic illness incompatible with participation in the clinical trial or inability to provide written informed consent

Previous exclusion criteria:
1. Any concurrent or planned treatment for the current diagnosis of breast cancer other than surgery, locoregional adjuvant radiotherapy, standard adjuvant chemotherapy, or a bisphosphonate/denosumab
2. Prior treatment with a PDL1, PD1, or other immunomodulatory therapy
3. Prior diagnosis of cancer including prior diagnosis of breast cancer in the previous 5 years, other than for basal cell carcinoma of the skin or cervical carcinoma in situ
4. Patients previously entered into a therapeutic trial during or after neoadjuvant chemotherapy where experimental therapy is continued post-surgery. Patients involved in clinical trials involving experimental drugs prior to primary standard treatment (i.e. window of opportunity trials) can be considered for entry into c-TRAK TN
5. Treatment with an unlicensed or investigational product within 4 weeks of trial entry
6. Active autoimmune disease requiring systemic therapy in the last two years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of such systemic treatment
7. Diagnosis of immunodeficiency or receiving systemic steroid therapy or any other form of

immunosuppressive therapy within 7 days prior to the first dose of pembrolizumab
8. Known history of active TB (Tuberculosis Bacillus)
9. Known history of Human Immunodeficiency Virus (HIV)
10. Known active Hepatitis B or Hepatitis C
11. Known history of, or any evidence of active, non-infectious pneumonitis
12. Active infection requiring systemic therapy
13. Females who are pregnant or breastfeeding
14. Presence of any systemic illness incompatible with participation in the clinical trial or inability to provide written informed consent

Date of first enrolment
21/12/2018

Date of final enrolment
06/12/2019

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

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

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

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road

Glasgow
United Kingdom
G12 0YN

Study participating centre
The Christie
550 Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
Clatterbridge Cancer Centre
Clatterbridge Health Park
Clatterbridge Road
Birkenhead
Wirral
United Kingdom
CH63 4JY

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

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

Study participating centre
Royal Bournemouth Hospital
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW

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

Study participating centre
University College Hospital
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Velindre Hospital
Velindre Road
Whitchurch
Cardiff
United Kingdom
CF14 2TL

Study participating centre

St Bartholomew's Hospital
W Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LJ

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

Study participating centre
Maidstone Hospital
Maidstone
United Kingdom
ME16 9QQ

Sponsor information

Organisation
Institute of Cancer Research

Sponsor details
Royal Cancer Hospital
237 Fulham Road
London
United Kingdom
SW3 6JB
+44 208 722 4040
c-trak-tn-icrctsu@icr.ac.uk

Sponsor type
Research organisation

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Industry

Funder Name
Merck Sharp and Dohme

Alternative Name(s)
MSD United Kingdom, Merck Sharp & Dohme, Merck Sharp & Dohme Corp., MSD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

The main trial results will be published in a peerreviewed journal, on behalf of all collaborators. It is the aim that this will be published around 1 year after the overall trial end date.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request (c-trak-tn-icrctsu@icr.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 6.0	16/06/2020	04/01/2023	No	No
Results article		21/11/2022	04/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			10/10/2023	No	Yes