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National Lung Matrix Trial: multi-drug phase II trial in non-small cell (NSC) lung cancer

Submission date
10/06/2015

Recruitment status
No longer recruiting

Registration date
10/06/2015

Overall study status
Completed

Last Edited
02/07/2025

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-different-drugs-for-non-small-cell-lung-cancer-national-lung-matrix-trial

Contact information

Type(s)
Scientific

Contact name
Dr Joshua Savage

ORCID ID
https://orcid.org/0000-0003-0599-0245

Contact details
Cancer Research UK Clinical Trials Unit (CRCTU)
Institute of Cancer and Genomic Sciences
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 415 8421
lungmatrix@trials.bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2014-000814-73

ClinicalTrials.gov (NCT)

NCT02664935

Protocol serial number
CPMS 17746

Study information

Scientific Title
National Lung Matrix Trial: multi--drug, genetic marker-directed, non--comparative, multi--centre, multi--arm phase II trial in non-small cell lung cancer

Acronym
NLMT

Study objectives
The trial consists of a series of parallel multi-centre single arm Phase II trial arms, each testing an experimental targeted drug in a population stratified by multiple pre-specified actionable target putative biomarkers. The primary objective is to evaluate whether there is a signal of activity in each drug-(putative)biomarker cohort separately. A Bayesian adaptive design is adopted to achieve this objective. The trial is primarily an enrichment putative biomarker design, including patients who are positive for at least on of the actionable targets included in the trial. Patients who are positive for just one putative biomarker will receive the experimental targeted drug specific for that putative biomarker. Putative biomarkers within each drug cohort have been chosen such that in the majority of cases it is not expected that patients will be positive for two or more putative biomarkers within the same drug. In the rare situation that patients are positive for two or more putative biomarkers relevant across different drugs, treatment will be allocated in accordance with the following strategy:
1. All amplifications and rearrangements will be treated with targeted agent appropriate to them irrespective of concomitant mutations. This will yield crucial predictive biomarker information.
2. For concomitant mutations decisions will be made by the Chief Investigator on a case-by-case basis and based on close consideration of pathway preference and likely dominance of one signal pathway over another together with any pre-clinical efficacy studies that address the activity of the drugs in the presence of concomitant mutations.
A secondary objective of the trial is to provide the opportunity for industrial partners to test novel agents in the cohort of patients who are not positive for any of the actionable targets in the trial, referred to as the no actionable genetic change arm.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central – Oxford C Research Ethics Committee, 18/12/2014, ref: 14/SC/1346

Study design
Non-randomized; Interventional; Design type: Not specified, Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Non-small cell lung cancer

Interventions
Current intervention as of 12/06/2019:
1. Arm A - FGFR Inhibitor; AZD4547 - closed to recruitment
2. Arm B - MTORC1/2 Inhibitor; Vistusertib (AZD2014)
3. Arm C - CDK4/6 Inhibitor; Palbociclib
4. Arm D - ALK Inhibitor; Crizotinib
5. Arm E - MEK inhibitor in combination with Docetaxel; Selumetinib and Docetaxel
6. Arm F – AKT Inhibitor; AZD5363 - closed to recruitment
7. Arm G – EGFR mutation positive T790M+ Inhibitor; Osimertinib (AZD9291) - closed to recruitment
8. Arm H – Sitravatinib - closed to recruitment
9. Arm NA - Anti-PDL1; Durvalumab (MEDI4736) - closed to recruitment
10. Arm J - AZD6738 + Durvalumab (MEDI4736)

Previous intervention as of 14/03/2019:
1. Arm A - FGFR Inhibitor; AZD4547
2. Arm B - MTORC1/2 Inhibitor; Vistusertib (AZD2014)
3. Arm C - CDK4/6 Inhibitor; Palbociclib
4. Arm D - ALK Inhibitor; Crizotinib
5. Arm E - MEK inhibitor in combination with Docetaxel; Selumetinib and Docetaxel
6. Arm F – AKT Inhibitor; AZD5363
7. Arm G – EGFR mutation positive T790M+ Inhibitor; Osimertinib (AZD9291)
8. Arm H – Sitravatinib
9. Arm NA - Anti-PDL1; Durvalumab (MEDI4736)

Previous intervention as of 21/09/2016:
1. Arm A - FGFR Inhibitor; AZD4547
2. Arm B - MTORC1/2 Inhibitor; Vistusertib (AZD2014)
3. Arm C - CDK4/6 Inhibitor; Palbociclib
4. Arm D - ALK Inhibitor; Crizotinib
5. Arm E - MEK inhibitor in combination with Docetaxel; Selumetinib and Docetaxel
6. Arm F – AKT Inhibitor; AZD5363
7. Arm G – EGFR mutation positive T790M+ Inhibitor; Osimertinib (AZD9291)
8. Arm NA Cohort NA1 - Anti-PDL1; Durvalumab (MEDI4736)
Study Entry : Registration only

Initial:
1. AZD2014, Arm B - MTORC1/2 Inhibitor; AZD4547
2. Arm A - FGFR Inhibitor; Crizotinib
3. Arm D - ALK Inhibitor; MEDI4736
4. Arm NA Cohort NA1 - Anti-PDL1; Palbociclib
5. Arm C - CDK4/6 Inhibitor; Selumetinib and Docetaxel
6. Arm E - MEK inhibitor in combination with Docetaxel
Study Entry : Registration only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
AZD4547, vistusertib (AZD2014), palbociclib, crizotinib, selumetinib, docetaxel, durvalumab (MEDI4736), AZD5363, osimertinib (AZD9291), sitravatinib (MGCD516), AZD6738

Primary outcome(s)
Current primary outcome measures as of 14/03/2019; updated 12/06/2020 to add Arm J:
1. Objective response (OR) – Arms A, B, D, E, F, G, H, NA, J
2. Durable clinical benefit (DCB) – Arms A, B, D, E, F, H, NA, J
3. Progression-free survival time (PFS) – Arm C

Previous primary outcome measures:
Best objective response (BOR); Timepoint(s): Patients will have CT scans every 6 weeks from baseline until disease progression

Key secondary outcome(s))
Current secondary outcome measures as of 14/03/2019:
1. Best percentage change in sum of target lesion diameters (PCSD)
2. Time to Progression (TTP)
3. Overall survival time (OS)
4. Adverse events (AE)

Previous secondary outcome measures:
1. Best percentage change in sum of target lesion diameters (PCSD)
2. Overall survival time (OS)
3. Progression-free survival time (PFS)
4. Time to Progression (TTP)
5. Adverse events

Added 14/02/2017:
6. Durable clinical benefit (DCB)

Completion date
31/03/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/03/2019:
Core inclusion criteria are presented below. Additional inclusion criteria apply to each arm and are presented in the relevant arm supplement in the trial protocol.
1. Prior anti-cancer treatment:
1.1. Patients who refuse any standard-of-care first-line therapy are eligible to receive National Lung Matrix Trial treatment as first-line therapy, providing they explicitly consent to this effect
1.2. Patients who have previously consented to and received standard-of-care first-line therapy must have completed all standard-of-care therapy that the treating oncologist thinks is

appropriate. As a minimum patients must have failed one or more lines of treatment (either radiological documentation of disease progression or due to toxicity). Patients whose disease has increased in size but is not classed as progressive disease as per RECIST criteria, will be eligible. Patients with no change at all in dimension of disease (i.e. true stability) after first-line therapy will not be eligible.
1.3. Patients who have progressed after surgical resection and adjuvant therapy will be eligible for entry without the need for the administration of first-line metastatic therapy
1.4. Patients will also be eligible without the necessity for first line regimen if they have relapsed within 6 months of completion of definitive chemoradiation
2. Consented and provided an adequate specimen to adequately characterise the molecular genotype of the tumour in the molecular pre-screening according to the molecular exclusion rules
3. Histological or cytologically confirmed NSCLC stage III (not suitable for radical radiotherapy or surgery) or stage IV. This includes patients who may have abnormal histology, but IHC strongly support either squamous cell carcinoma (p63 positivity) or adenocarcinoma (Thyroid transcription factor 1 [TTF1] positivity). If a physician and pathologist are convinced after multi-disciplinary review that the patient has stage III or IV NSCLC but where all the IHC is negative and the morphology does not distinguish a specific sub-type, these patients will be eligible for non-histology specific cohorts.
4. CT or MRI scan of head, chest and abdomen within 28 days of treatment demonstrating measurable disease as per RECIST version 1.1. (The same imaging modality must be used throughout treatment).
5. Adequate haematological function within 7 days of treatment:
5.1. Haemoglobin ≥90 g/l
5.2.Absolute neutrophil count (ANC) ≥1.5 x 10(9)/l
5.3. Platelets ≥100 x 10(9)/l
6. Adequate hepatic function within 7 days of treatment in patients with no liver metastasis (see arm-specific entry criteria for adequate hepatic function in patients with liver metastases):
6.1. Total serum bilirubin ≤1.5 x upper limit of normal (ULN). (Note that this will not apply to patients with confirmed Gilbert's syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of evidence of haemolysis or hepatic pathology), who may be allowed inclusion at the discretion of the local Investigator).
6.2. Alanine transferase (ALT) ≤2.5 x ULN
6.3. Aspartate transferase (AST) ≤2.5 x ULN
7. Adequate renal function within 7 days of treatment:
7.1. Creatinine clearance (CLcr) >50 ml/min (measured or calculated by Cockcroft and Gault equation). If calculated CLcr is <50 ml/min a direct measurement of glomerular filtration rate (GFR) such as EDTA may be performed. If the value is >50 ml/min the patient is eligible.
8. Aged ≥18 years
9. Females must agree to use adequate contraceptive measures, should not be breast feeding and must have a negative pregnancy test prior to start of dosing if of child-bearing potential or must have evidence of non-child-bearing potential by fulfilling one of the following criteria at screening:
9.1.Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments
9.2. Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation
9.3. Women aged under 50 years old would be consider postmenopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and with luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in the post-menopausal range for the institution
10. Provision of signed and dated, written informed consent prior to any study specific

procedures, sampling and analyses

Previous inclusion criteria as of 12/12/2016:
1. Patients must have completed all standard of care therapy that the treating oncologist thinks is appropriate. As a minimum patients must have failed one or more lines of treatment (either radiological documentation of disease progression or due to toxicity)
2. Patients who have progressed after surgical resection and adjuvant therapy will be eligible for entry without the need for the administration of first line metastatic therapy
3. Patients will also be eligible without the necessity for first line regimen if they have relapsed within 6 months of completion of definitive chemoradiation
4. Consented and provided an adequate specimen to completely characterise the molecular phenotype of the tumour in the molecular pre-screening (SMP2) according to the molecular exclusion rules
5. Histological or cytologically confirmed NSCLC stage III (not suitable for radical radiotherapy or surgery) or stage IV. This includes patients who may have abnormal histology, but IHC strongly support either squamous cell carcinoma (p63 positivity) or adenocarcinoma (Thyroid transcription factor 1 [TTF1] positivity). If a physician and pathologist are convinced after multi-disciplinary review that the patient has stage III or IV NSCLC but where all the IHC is negative and the morphology does not distinguish a specific sub-type, these patients will be eligible for non-histology specific cohorts
6. CT scan of head, chest and abdomen within 28 days of treatment demonstrating measurable disease as per RECIST version 1.1
7. Adequate haematological function within 7 days of treatment
7.1. Haemoglobin ≥ 90 g/L
7.2. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L.
7.3. Platelets ≥ 100 x 109/L
8. Adequate hepatic function within 7 days of treatment in patients with no liver metastasis (see arm specific entry criteria for adequate hepatic function in patients with liver metastases)
8.1. Total serum bilirubin ≤ 1.5 x upper limit of normal (ULN). (Note that this will not apply to patients with confirmed Gilbert's syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of evidence of haemolysis or hepatic pathology), who may be allowed inclusion at the discretion of the local Investigator)
8.2. Alanine transferase (ALT) ≤ 2.5 x ULN
8.3. Aspartate transferase (AST) ≤ 2.5 x ULN
9. Adequate renal function within 7 days of treatment.
9.1. Creatinine <1.5 times ULN concurrent with creatinine clearance (CLcr) >50 ml/min (measured or calculated by Cockcroft and Gault equation). If calculated CLcr is <50 ml/min a direct measurement of glomerular filtration rate (GFR) such as EDTA may be performed. If the value is ≥50 ml/min the patient is eligible
10. Age ≥ 18 years
11. Females must agree to use adequate contraceptive measures (as defined in Section 6.3), should not be breast feeding and must have a negative pregnancy test prior to start of dosing if of child-bearing potential or must have evidence of non-child-bearing potential by fulfilling one of the following criteria at screening:
11.1. Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments
11.2. Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation
11.3. Women aged under 50 years old would be consider postmenopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and with luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in the post-menopausal range for the institution.

12. Provision of signed and dated, written informed consent prior to any study specific procedures, sampling and analyses

Previous inclusion criteria from 02/09/2015 to 12/12/2016:
1. Patients must have completed all standard of care therapy that the treating oncologist thinks is appropriate. As a minimum patients must have failed one or more lines of treatment (either radiological documentation of disease progression or due to toxicity)
2. Patients who have progressed after surgical resection and adjuvant therapy will be eligible for entry without the need for the administration of first line metastatic therapy, if they have progressed within 6 months of completing their adjuvant treatment
3. Patients will also be eligible without the necessity for first line regimen if they have relapsed within 6 months of completion of definitive chemoradiation
4. Consented and provided an adequate specimen to completely characterise the molecular phenotype of the tumour in the molecular pre-screening (SMP2) according to the molecular exclusion rules
5. Histological or cytologically confirmed NSCLC stage III (not suitable for radical radiotherapy or surgery) or stage IV. This includes patients who may have abnormal histology, but IHC strongly support either squamous cell carcinoma (p63 positivity) or adenocarcinoma (Thyroid transcription factor 1 [TTF1] positivity). If a physician and pathologist are convinced after multi-disciplinary review that the patient has stage III or IV NSCLC but where all the IHC is negative and the morphology does not distinguish a specific sub-type, these patients will be eligible for non-histology specific cohorts
6. CT scan of head, chest and abdomen within 28 days of treatment demonstrating measurable disease as per RECIST version 1.1
7. Adequate haematological function within 7 days of treatment
7.1. Haemoglobin ≥ 90 g/L
7.2. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L.
7.3. Platelets ≥ 100 x 109/L
8. Adequate hepatic function within 7 days of treatment in patients with no liver metastasis (see arm specific entry criteria for adequate hepatic function in patients with liver metastases).
8.1. Total serum bilirubin ≤ 1.5 x upper limit of normal (ULN)
8.2. Alanine transferase (ALT) ≤ 2.5 x ULN
8.3. Aspartate transferase (AST) ≤ 2.5 x ULN
9. Adequate renal function within 7 days of treatment.
9.1. Creatinine <1.5 times ULN concurrent with creatinine clearance (CLcr) >50 ml/min (measured or calculated by Cockcroft and Gault equation)
10. Age ≥ 18 years
11. Females must agree to use adequate contraceptive measures (as defined in Section 6.3), should not be breast feeding and must have a negative pregnancy test prior to start of dosing if of child-bearing potential or must have evidence of non-child-bearing potential by fulfilling one of the following criteria at screening:
11.1. Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments
11.2. Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation
11.3. Women aged under 50 years old would be consider postmenopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and with luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in the post-menopausal range for the institution.
12. Provision of signed and dated, written informed consent prior to any study specific procedures, sampling and analyses

Original inclusion criteria:
1. Patients must have completed all standard of care therapy that the treating oncologist thinks is appropriate. As a minimum patients must have failed one or more lines of treatment (either radiological documentation of disease progression or due to toxicity)
2. Consented and provided an adequate specimen to completely characterise the molecular phenotype of the tumour in SMP2
3. Histological or cytologically confirmed NSCLC stage III (not suitable for radical radiotherapy or surgery) or stage IV. This includes patients who may not have clear morphology, but IHC strongly support either squamous cell carcinoma (p63 positivity) or adenocarcinoma (Thyroid transcription factor 1 [TTF1] positivity). If a physician and pathologist are convinced after multi-disciplinary review that the patient has stage III or IV NSCLC but where all the IHC is negative and the morphology does not distinguish a specific sub-type, these patients will be eligible for non-histology specific cohorts.
4. CT scan of head, chest and abdomen within 28 days of treatment demonstrating measurable disease as per RECIST version 1.1
5. Eastern Cooperative Oncology Group (ECOG) Performance Status =1 with no deterioration over the previous 2 weeks
6. Adequate haematological function within 7 days of treatment
6.1. Haemoglobin = 90 g/L
6.2. Absolute neutrophil count (ANC) = 1.5 x 109/L
6.3 Platelets = 100 x 109/L
7. Adequate hepatic function within 7 days of treatment
7.1. Total serum bilirubin = 1.5 x upper limit of normal (ULN)
7.2. Alanine transferase (ALT) = 2.5 x ULN
7.3. Aspartate transferase (AST) = 2.5 x ULN
8. Adequate renal function within 7 days of treatment
8.1. Creatinine <1.5 times ULN concurrent with creatinine clearance (CLcr) >50 ml/min (measured or calculated by Cockcroft and Gault equation)
9. Age at least 18 years
10. Provision of signed and dated, written informed consent prior to any study specific procedures, sampling and analyses
11. Target Gender: Male & Female

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
423

Key exclusion criteria

Current exclusion criteria as of 14/03/2019:
Core exclusion criteria are presented below. Additional exclusion criteria apply to each arm and are presented in the relevant arm supplement in the trial protocol.
1. Major surgery (excluding placement of vascular access) within 4 weeks prior to treatment
2. Nausea, vomiting, chronic gastrointestinal diseases (e.g. inflammatory bowel disease) that would preclude adequate absorption
3. Any psychological, familial, sociological or geographical condition hampering protocol compliance
4. Concurrent malignancies or invasive cancers diagnosed within past 3 years except for adequately treated basal cell carcinoma of the skin and in situ carcinoma of the uterine cervix
5. Judgement by the local Investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions and requirements
6. Any unresolved toxicity of grade 2, 3 or 4 from previous treatment (excluding alopecia) at Registration (see CTCAE Toxicity Criteria Gradings)
7. Patients who have previous symptomatic brain metastases or spinal cord compression are excluded unless they have had adequate treatment, no evidence of progression or symptoms, and have had no requirement for steroid treatment in the previous 28 days before commencement of trial treatment
8. Patients with asymptomatic brain metastases picked up at screening CT scan are not excluded providing that in the view of the local Investigator they do not require immediate radiotherapy or surgical intervention, and have had no requirement for steroid treatment in the previous 28 days before commencement of trial treatment
9. As judged by the local Investigator, any evidence of severe or uncontrolled systemic diseases, including active bleeding diatheses, or active infection including hepatitis B, hepatitis C and human immunodeficiency virus. Screening for chronic conditions is not required.
10. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to registration)

Cardiac exclusion criteria, performance status and prior treatment washout periods are detailed within the National Lung Matrix Trial arm-specific eligibility criteria.

Previous exclusion criteria as of 12/12/2016:
1. Major surgery (excluding placement of vascular access) within 4 weeks prior to treatment
2. Nausea, vomiting, chronic gastrointestinal diseases (e.g. inflammatory bowel disease) that would preclude adequate absorption
3. Any psychological, familial, sociological or geographical condition hampering protocol compliance.
4. Concurrent malignancies or invasive cancers diagnosed within past 3 years except for adequately treated basal cell carcinoma of the skin and in situ carcinoma of the uterine cervix
5. Judgement by the local investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions and requirements
6. Any unresolved toxicity of grade 2, 3 or 4 from previous treatment (excluding alopecia) at Registration.
7. Patients who have previous symptomatic brain metastases or spinal cord compression are excluded unless they have had adequate treatment, no evidence of progression or symptoms, and have had no requirement for steroid treatment in the previous 28 days before commencement of trial treatment
8. Patients with asymptomatic brain metastases picked up at screening CT scan are not excluded providing that in the view of the local investigator they do not require immediate radiotherapy or surgical intervention, and have had no requirement for steroid treatment in the previous 28

days before commencement of trial treatment
9. As judged by the local investigator, any evidence of severe or uncontrolled systemic diseases, including active bleeding diatheses, or active infection including hepatitis B, hepatitis C and human immunodeficiency virus. Screening for chronic conditions is not required
10. Pregnant or breast-feeding women

Cardiac exclusion criteria, performance status and prior treatment washout periods are detailed within The National Lung Matrix Trial arm-specific eligibility criteria.

Previous exclusion criteria from 02/09/2015 to 12/12/2016:
1. Major surgery (excluding placement of vascular access), chemotherapy, radiotherapy, any investigational agents or other anti-cancer therapy within 4 weeks prior to treatment
2. Nausea, vomiting, chronic gastrointestinal diseases (e.g. inflammatory bowel disease) that would preclude adequate absorption
3. Any psychological, familial, sociological or geographical condition hampering protocol compliance.
4. Concurrent malignancies or invasive cancers diagnosed within past 3 years except for adequately treated basal cell carcinoma of the skin and in situ carcinoma of the uterine cervix
5. Judgement by the investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions and requirements
6. Any unresolved toxicity of grade 2, 3 or 4 from previous treatment (excluding alopecia) at Registration.
7. Patients who have previous symptomatic brain metastases or spinal cord compression are excluded unless they have had adequate treatment, no evidence of progression or symptoms, and have had no requirement for steroid treatment in the previous 28 days before commencement of trial treatment
8. Patients with asymptomatic brain metastases picked up at screening CT scan are not excluded providing that in the view of the investigator they do not require immediate radiotherapy or surgical intervention, and have had no requirement for steroid treatment in the previous 28 days before commencement of trial treatment
9. As judged by the investigator, any evidence of severe or uncontrolled systemic diseases, including active bleeding diatheses, or active infection including hepatitis B, hepatitis C and human immunodeficiency virus. Screening for chronic conditions is not required
10. Pregnant or breast-feeding women

Cardiac exclusion criteria and performance status eligibility criteria are detailed within The National Lung Matrix Trial arm-specific eligibility criteria.

Original exclusion criteria:
1. Major surgery (excluding placement of vascular access), chemotherapy, radiotherapy, any investigational agents or other anti-cancer therapy within 4 weeks prior to treatment.
2. Nausea, vomiting, chronic gastrointestinal diseases (e.g. inflammatory bowel disease) that would preclude adequate absorption
3. Any psychological, familial, sociological or geographical condition hampering protocol compliance.
4. Concurrent malignancies or invasive cancers diagnosed within past 5 years except for adequately treated basal cell carcinoma of the skin and in situ carcinoma of the uterine cervix
5. Judgement by the investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions and requirements
6. Any unresolved toxicity of grade 2, 3 or 4 from previous treatment (excluding alopecia) at Registration
7. Spinal cord compression or brain metastases unless asymptomatic, treated and stable and not

requiring steroids for at least 28 days prior to registration
8. As judged by the investigator, any evidence of severe or uncontrolled systemic diseases, including active bleeding diatheses, or active infection including hepatitis B, hepatitis C and human immunodeficiency virus. Screening for chronic conditions is not required
9. Patients and patients with partners of childbearing potential not willing to use effective contraception during the trial period and for at least 90 days after completion of treatment
10. Female patients of child bearing potential should be using adequate contraceptive measures, should not be breast feeding and must have a negative pregnancy test prior to registration
11. Female patients of non-child-bearing potential are excluded unless they fulfil one of the following criteria at screening:
11.1 Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments
11.2 Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation
11.3 Women aged under 50 years old would be consider postmenopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and with luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in the post-menopausal range for the institution

Date of first enrolment
31/03/2015

Date of final enrolment
31/10/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cancer Research UK Clinical Trials Unit
Institute of Cancer and Genomic Sciences
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Cancer Research 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
Pfizer

Alternative Name(s)

Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen, Pfizer Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Mirati Therapeutics

Results and Publications

Individual participant data (IPD) sharing plan
For NLMT data, scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. Requests should be made by returning a completed Data Sharing Request Form and curriculum vitae of the lead applicant and statistician to newbusiness@trials.bham.ac.uk. The Data Sharing Request Form captures information on the specific requirements of the research, the statistical analysis plan, and the intended publication schedule. The request will be reviewed independently by the Cancer Research UK Clinical Trials Unit (CRCTU) Directors at University of Birmingham in discussion with the Chief Investigator and relevant Trial Management Group and independent Trial Steering Committee. In making their decision the Director's Committee will consider the scientific validity of the request, the qualifications of the Research Group, the views of the Chief Investigator, Trial Management Group and Trial Steering Committee, consent arrangements, the practicality of anonymizing the requested data and contractual obligations. Where the CRCTU Directors and appropriate Trial Committees are supportive of the request, and where not already obtained, consent for data transfer will be sought from the Sponsor of the trial before notifying the applicant of the outcome of their request. It is anticipated that applicants will be notified of a decision within 3 months of receipt of the original request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		15/07/2020	25/11/2021	Yes	No
Results article		11/03/2025	13/03/2025	Yes	No
Protocol article		01/12/2015		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			02/07/2025	No	Yes

Study website	Study website	11/11/2025	11/11/2025	No	Yes