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Phase 1b dose escalation and dose expansion study in patients with advanced or metastatic non-small cell lung cancer (NSCLC)

Submission date 11/05/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 04/08/2022	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 10/04/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
The purpose of this study is to learn about how the study drug, furmonertinib, works in participants with non-small cell lung cancer (NSCLC) who have a mutation in a specific gene and how it may help them. For participants with this type of NSCLC, the study will help researchers to learn how safe the study drug is, to learn how much of the study drug to give to patients, and to compare the effects, good or bad, of the study drug.

Globally, lung cancer is the second most commonly diagnosed cancer and the leading cause of cancer-related deaths among men and women, with an estimated 2.2 million new cancer cases and 1.8 million deaths reported in 2020. NSCLC is the predominant subtype of lung cancer, accounting for approximately 85% of all cases.

Who can participate?
Up to about 108 men and women (aged 18 years or over) with NSCLC may take part in this study. Patients that have NSCLC that has spread and has not responded to treatment or for which previous treatment was stopped because they could not tolerate the side effects would be eligible to take part.

What does the study involve?
This study has three parts:
1. Screening (to see if you are eligible for the study)
2. Treatment
3. Follow-up (to check on you after treatment is finished)

The study has a dose escalation phase, which will try to establish the maximum tolerated dose of the study drug, with up to 48 participants; and a dose expansion phase, which will collect further data on participants with different tumour mutations, with up to 60 participants.

The total time for a participant to be in the study will depend on how their lung cancer responds to treatment. This could range from 1 day to up to 48 months.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
As with all studies the drug treatment and other therapies may involve risks that are known as well as risks that are currently unknown. Participants will be carefully monitored for any side effects, however not all of the side effects that the study drug may have are known. Side effects may range from mild to serious, and in some cases side effects may be long-lasting or permanent or may even be life-threatening. Taking part in the study involves some risks and possible discomfort to participants, and this is explained in the Participant Information Sheet.

Where is the study run from?
Syneos Health UK Limited

When is the study starting and how long is it expected to run for?
May 2022 to December 2026

Who is funding the study?
ArriVent BioPharma, Inc. (USA)

Who is the main contact?
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-005831-22

Integrated Research Application System (IRAS)
1005456

Central Portfolio Management System (CPMS)
52527

Protocol serial number
FURMO-002

Study information

Scientific Title
A phase 1b dose escalation and dose expansion study evaluating the safety, pharmacokinetics, and antitumor activity of furmonertinib in patients with advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR or HER2 mutations, including exon 20 insertion mutations

Study objectives
- To evaluate the safety, tolerability, including estimation of the maximal tolerated dose (MTD), determination of the expansion dose, and characterization of dose limiting toxicities (DLTs) of escalating doses of furmonertinib administered daily to patients with locally advanced or metastatic NSCLC
- To make a preliminary assessment of the antitumor activity of furmonertinib
- To evaluate the safety and tolerability of furmonertinib at the expansion dose
- To characterize the pharmacokinetic (PK) properties of furmonertinib and its major metabolite (AST5902)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/07/2022, East Midlands - Leicester South Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8143; Leicestersouth.rec@hra.nhs.uk), ref: 22/EM/0118

Study design
Dose escalation study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Patients with Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) with mutations in a gene called epidermal growth factor receptor (EGFR) or human epidermal growth factor receptor 2 (HER2).

Interventions
All participants will receive the study drug. Depending on the dose group to which they e assigned, participants will take a dose consisting of 4, 6, or 8 pills of the study drug, furmonertinib (each pill is 40 mg strength), each day, at approximately the same time, on an empty stomach. The study drug is to be taken daily in treatment cycles of 21 days (one cycle = 21 days/3weeks)

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
Incidence and severity of adverse events (AEs) including DLTs, with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0) during the study

Key secondary outcome(s))
1. Confirmed objective response rate (ORR), defined as the percentage of patients with a confirmed complete response (CR) or partial response (PR) relative to the total number of patients. Confirmation of the response is based on two consecutive assessments, at least 28 days apart, as determined by investigator assessment and blinded independent central review (BICR) assessment using RECIST v1.1
2. Duration of response (DOR), disease control rate (DCR), progression-free survival (PFS), and

depth of response (DpR) evaluated by investigator assessment and by BICR per RECIST v1.1
3. Overall survival (OS)
4. Central nervous system (CNS) confirmed ORR (CNS ORR) and DOR (CNS DOR) via RECIST v1.1 by BICR
5. Change from baseline in safety-related clinical laboratory test results
6. Plasma concentrations of furmonertinib and its major metabolite (AST5902) at specified timepoints
7. Change from baseline in patient-reported symptoms and their impact on functioning and health-related quality of life, and the overall burden of side effects, as measured by the European Organization for Research and Treatment of Cancer Quality of Life Core 30 Questionnaire (EORTC QLQ-C30) and EORTC QLQ-LC13, and Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC SAQ)
8. Correlation of PK with primary, secondary, exploratory endpoints in patients treated with furmonertinib
9. Change in tumour tissue gene profile at baseline, during treatment, and at disease progression
10. Consistency and change of ctDNA gene profile in the peripheral blood at baseline, during treatment, and disease progression samples
11. EGFR mutation status in ctDNA in peripheral blood or possible changes in resistant gene profile at baseline, during treatment, and at disease progression

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Signed Informed Consent Form
2. Age ≥18 years at time of signing Informed Consent Form
3. Ability to comply with the study protocol, in the investigator’s judgment
4. Measurable disease per RECIST v1.1
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
6. Life expectancy of ≥ 12 weeks
7. Adequate hematologic and organ function within 14 days prior to initiation of study treatment
8. For women of childbearing potential (WOCBP): Agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agreement to refrain from donating eggs
9. For men who are not surgically sterile: Agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agreement to refrain from donating sperm
10. Patients with a history of treated CNS metastases or new asymptomatic CNS metastases detected at screening
11. Histologically or cytologically documented, locally advanced or metastatic NSCLC not amenable to curative surgery or radiotherapy
12. Consent to provide tumor tissue specimen (paraffin-embedded tissue block or 15 serial-cut slides)
13. Disease that has progressed after at least one available standard therapy; or for whom standard therapy has proven to be ineffective or intolerable; or for whom a clinical trial of an investigational agent is a recognized standard of care
14. Documented radiologic disease progression during or after the last systemic antitumor therapy before the first dose of the investigational product (furmonertinib)
15. For patients with EGFR mutations sensitive to osimertinib, the patient must have received osimertinib prior to study enrollment in regions where osimertinib is approved, including the US

Stage 1 Dose Escalation and Backfill Cohorts Inclusion Criteria:
16. Documented validated results from local testing of blood or tumor tissue confirming the presence of an EGFR Exon 20 insertion mutation, HER2 Exon 20 insertion mutation, or EGFR activating mutation (including Exon 19 and Exon 21 mutations such as G719X, Exon 19 deletion, L858R, L861Q) or EGFR T790M mutation
17. For patients with NSCLC with EGFR Exon 20 insertion mutations or HER2 Exon 20 insertion mutations, the patient must have experienced disease progression (during or after treatment) or have intolerance to treatment with platinum-based chemotherapy
18. For patients with NSCLC with EGFR activating mutations other than Exon 20 insertion mutations, the patient must have experienced disease progression (during or after treatment) with the standard of care EGFR TKI

Stage 2 Cohort 1 Inclusion Criteria:
19. Documented validated results from either local testing of blood or tumor tissue confirming the presence of EGFR Exon 20 insertion mutations
20. The patient must have experienced disease progression (during or after treatment) or have intolerance to treatment with platinum-based chemotherapy

Stage 2 Cohort 2 Inclusion Criteria:
21. Documented validated results from either local testing of blood or tumor tissue confirming the presence of HER2 Exon 20 Insertion Mutations
22. The patient must have experienced disease progression (during or after treatment) or have intolerance to treatment with platinum-based chemotherapy

Stage 2 Cohort 3 Inclusion Criteria:
23. Documented validated results from either local testing of blood or tumor tissue confirming the presence of an EGFR activating mutation (including Exon 19 and Exon 21 mutations such as G719X, Exon 19 deletion, L858R, L861Q) or EGFR T790M mutation
24. The patient must have experienced disease progression (during or after treatment) or have intolerance to treatment with the standard of care EGFR TKI

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
85 years

Sex
All

Total final enrolment
108

Key exclusion criteria

1. Inability or unwillingness to swallow pills
2. Inability to comply with study and follow-up procedures
3. Malabsorption syndrome or other condition that would interfere with enteral absorption
4. Pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures biweekly or more frequently
5. Severe acute or chronic infections
6. In the setting of a pandemic or epidemic, screening for active infections should be considered according to local or institutional guidelines or those of applicable professional societies
7. Previous interstitial lung disease (ILD), drug-induced interstitial lung disease, radiation pneumonitis requiring steroid therapy; or having the clinical manifestations of suspected ILD.
8. History of or active clinically significant cardiovascular dysfunction
9. Mean resting corrected QT interval (QTcF) > 470 msec, obtained from triplicate ECGs, using the screening clinic ECG machine derived QTcF value.
10. Clinically significant prolonged QT interval or other arrhythmia or clinical status considered by investigators that may increase the risk of prolonged QT interval or current use of the drugs that may lead to prolonged QT interval
11. Uncontrolled hypercalcemia (> 1.5 mmol/L ionized calcium or calcium > 12 mg/dL or corrected serum calcium ≥ ULN) or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy or denosumab.
12. Significant traumatic injury or major surgical procedure within 4 weeks prior to Day 1 of Cycle 1.
13. Patients with chronic diarrhea, short bowel syndrome or significant upper gastrointestinal surgery including gastric resection, a history of inflammatory bowel disease or any active bowel inflammation (including diverticulitis)
14. Any other diseases, active or uncontrolled pulmonary dysfunction, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of furmonertinib, that may affect the interpretation of the results, or renders the patients at high risk from treatment complications
15. Treatment with chemotherapy, immunotherapy, biologic therapy, or an investigational agent as anti-cancer therapy within 3 weeks or five half-lives prior to initiation of furmonertinib, whichever is shorter, or endocrine therapy within 2 weeks prior to initiation of furmonertinib
16. Radiation therapy (other than palliative radiation to bony metastases and radiation to CNS metastases as described above) as cancer therapy within 4 weeks prior to initiation of furmonertinib
17. Palliative radiation to bony metastases within 2 weeks prior to initiation of furmonertinib
18. Adverse events from prior anti-cancer therapy that have not resolved to Grade ≤ 1 except for alopecia or Grade ≤ 2 peripheral neuropathy
19. History of other malignancy within 3 years prior to screening, with the exception of patients with a negligible risk of metastasis or death and/or treated with expected curative outcome
20. Pregnant, breastfeeding, or intending to become pregnant during the study or within 60 days after the final dose of furmonertinib
21. Known or suspected allergy to furmonertinib or other components of its preparation
22. Use of a potent CYP3A4 inhibitor within 7 days prior to the first dose of investigational product or a potent CYP3A4 inducer within 21 days prior to the first dose of furmonertinib
23. Use of an herbal medicine within 2 weeks prior to the first dose of furmonertinib, or if herbal medicine is expected to be used during the study

In addition to the general exclusion criteria, patients who meet any of the additional criteria listed below will be excluded from entry into specific cohorts:
Stage 2 Cohort 3 Exclusion Criteria:

24. NSCLC patients with a documented EGFR Exon 20 insertion mutation by a local test (tumor tissue or blood)

Date of first enrolment
31/03/2022

Date of final enrolment
31/10/2023

Locations

Countries of recruitment
United Kingdom

Australia

Japan

Spain

Study participating centre
University College London Hospital
University College London Hospitals NHS Foundation Trust
250 Euston Road
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Sponsor information

Organisation
Syneos Health UK Limited

Funder(s)

Funder type
Industry

Funder Name
ArriVent BioPharma, Inc.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

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