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AL8326 in advanced Small Cell Lung Cancer

Submission date 03/11/2023	**Recruitment status** Recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 02/04/2024	**Overall study status** Ongoing	
Last Edited 16/10/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
This is a multi-center, randomized, double-blind, placebo-controlled, phase III clinical trial to evaluate the efficacy and safety of AL8326 tablets in patients with advanced or recurrent small cell lung cancer (SCLC) after at least prior second-line treatment.

Who can participate?
Patients with advanced or recurrent small cell lung cancer (SCLC) after at least prior second-line treatment.

What does the study involve?
Eligible patients will be randomized in a 2:1 ratio to receive AL8326 tablets or placebo (dummy pill). AL8326 tablets and placebo will be administered orally once daily in 28-day as one cycle until intolerable toxicity, or confirmed disease progression, or death, or voluntary withdrawal or treatment for up to 12 months (approximately 13 cycles). Patients will have a final visit (28 days ± 7 days) after the last dose, or 12 months (approximately 13 cycles) of treatment (± 7 days), or before initiation of other antineoplastic therapy, or withdrawal, whichever came first. Patients then will enter the long-term follow-up period and will have telephone calls every 2-4 months for 1 year, then every 4-5 months for 2 years, and finally every 6-8 months for study survival follow-up.
Patients who have good response at the end of the treatment can remain on the study on blinded treatment on compassionate grounds.

What are the possible benefits and risks of participating?
According to the ongoing clinical trial program of AL8326 tablets and marketed drugs of the similar type, the possible common adverse reactions are: Hypertension, Proteinuria and nephrotoxicity, adverse changes in blood chemistry parameters (AST/ ALT, Lipase, amylase, Triglyceride, Bilirubin) Hand-foot syndrome, GI toxicity (Nausea, Vomiting, lower appetite, abdominal pain, diarrhea), GI haemorrhage, TSH increased or hypothyrodism, Hematologic Toxicity (Leukopenia, Neutropenia, Anemia, Thrombocytopenia. More detailed information is provided in the current Investigator 's Brochure. The investigator may adjust the dose of investigational product on a case-by-case basis in case of intolerance. Adverse events should be monitored closely during the clinical study

and dosing could be adjusted as needed to allow subjects to tolerate treatment. Adverse reactions caused by the investigational product can be managed by symptomatic treatment, discontinuation and/or dose adjustment.

Where is the study run from?
Solutions OP Ltd (UK)

When is the study starting and how long is it expected to run for?
November 2023 to December 2027

Who is funding the study?
Advenchen Pharmaceuticals (USA)

Who is the main contact?
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Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06247605

Integrated Research Application System (IRAS)
1008426

Central Portfolio Management System (CPMS)
55935

Protocol serial number
AL8326-GB-010 (PARSLUP)

Study information

Scientific Title
Phase III clinical study of AL8326 tablets in patients with advanced or recurrent small cell lung cancer after at least prior second-line treatment

Study objectives
Primary objective:
To evaluate the overall survival (OS) efficacy of AL8326 tablets as monotherapy in patients with recurrent or advanced small cell lung cancer after second-line or more systemic therapy.

Secondary objective:
To evaluate the progression free survival (PFS) and other efficacies of AL8326 tablets as monotherapy in patients with recurrent or advanced small cell lung cancer after second-line or more systemic therapy.

Safety objective:
To evaluate the safety of AL8326 tablets as monotherapy in patients with recurrent or progressed small cell lung cancer after second-line or greater systemic therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 28/03/2024, Wales Research Ethics Committee 2 Cardiff (Health and Care Research Wales, Castlebridge 5, 15-19 Cowbridge Road, East Cardiff, CF11 9AB, United Kingdom; +44 (0) 2922941119, (0)2922 940971, (0)2922 940959; Wales.REC2@wales.nhs.uk), ref: 23/WA/0329

Study design
Interventional randomized placebo controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Small Cell Lung Cancer

Interventions

This is a randomized, double-blind, 2:1 placebo-controlled Phase III Small Cell Lung Cancer trial conducted in multiple UK centres, looking into effect of AL8326 tablets in comparison to standard of care patients who completed at least two lines of anticancer treatment. AL8326 Tablets/Placebo treatment has oral administration, once daily for 28 consecutive days as a treatment cycle, starting at 60 mg each time. Subjects receive study drug (AL8326 tablets /placebo) at the time of investigational product treatment for up to 12 months (approximately 13 cycles) or disease progression during the study or may benefit from subsequent treatment as assessed by the investigator and may continue to receive subsequent blinded drug upon discussion between the investigator and the sponsor. Following completion of the final visit, subjects will be followed for OS. The research team will perform telephone calls every 2-4 months for 1 year after the final visit (whichever is last dose date if final visit is not performed), then every 4-5 months for 2 years, and finally every 6-8 months for study survival. Randomisation 2 (AL8326) to 1 (placebo) uses two stratification factors: Prior use of PD1/PD-L1 (Yes/No) and Brain metastases (Yes/No). The central randomization system will be used, and the randomization specialist completes the generation of the randomization table using SAS software and imports it into the central randomization system. After obtaining the sponsor’s approval, the investigator logs in the interactive web response system (IWRS) and enters the information of enrolled subjects. The system gives the corresponding medication number according to the randomization table. Site personnel will confirm that they have found the correct investigational product packaging by obtaining the number through the IWRS. Subject randomization numbers will be assigned sequentially according to the order in which subjects are enrolled. The start date of treatment should occur as soon as possible within 7 days of the subject 's randomization.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
[5-[2-[4-[4-fluoro-2-methyl-1H-indol-5-yloxy]-6-methoxyquinolin-7-yloxy]ethyl]-5-azaspiro[2,4]heptan-7-o, 5-[2-[4-[4-fluoro-2-methyl-1H-indol-5-yloxy]-6-methoxyquinolin-7-yloxy]ethyl]-5-azaspiro[2,4]heptan-7-ol

Primary outcome(s)
Overall survival: defined as the time from randomization to the date of death due to any cause.

Key secondary outcome(s))
1. Progression-free survival (PFS): Refers to the period of time from the date of randomization until the first observation of disease progression per RECIST 1.1 or death from any cause, whichever occurs earlier.
2. Objective response rate (ORR): the proportion of subjects who achieve CR and PR according to RECIST 1.1.
3. Duration of response (DOR): refers to the time from the first tumor assessment of CR or PR to the first tumor assessment of PD or death from any cause.
4. Disease Control Rate (DCR): The proportion of subjects who achieve CR, PR, and SD.
5. Safety will be evaluated by changes in AEs, ECOG score, body weight, physical examination, vital signs and laboratory tests (blood routine, blood biochemistry, coagulation function, urine

routine, thyroid function, stool routine, serum amylase, myocardial enzyme, etc.) and ECG
6. Sparse PK samples will be collected from all subjects who have received study drug (AL8326 tablets/placebo) for population pharmacokinetic analysis.

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. All subjects or legal representatives must sign by the Ethics Committee approved informed consent prior to the start of any screening procedures;
2. Age ≥ 18 years, male or female;
3. Histologically or cytologically confirmed small cell lung cancer patients who have recurrent or advanced disease after at least two lines of systemic regimen (including first-line platinum-based therapy, second-line monotherapy or other therapies *);
4. At least one measurable tumor lesion according to RECIST 1.1 *;
5. Previously received cytotoxic chemotherapy and/or immunotherapy, and the end of the last dose is at least 4 weeks apart from the first dose of study drug; the end of antitumor herb medicine is at least 14 days apart; the end of nitroso or mitomycin was at least 6 weeks apart, and tyrosine kinase inhibitors (TKIs) class molecular targeted drugs were at least 4 weeks apart; the treatment of brain metastases/bone metastases had to be at least 2 weeks apart; and had recovered to ≤ Grade 1 from the toxicity of previous treatment [except for the following: a. alopecia; b. long-term toxicity caused by radiotherapy, which could not be recovered in the judgment of the investigator; c. platinum-induced Grade 2 and the following neurotoxicity such as hearing impairment (according to the Common Terminology Criteria for Adverse Events CTCAE V5.0)];
6. Expected survival time of at least 12 weeks;
7. ECOG (PS) score of 0 to 2;
8. Subject has adequate organ and bone marrow function and meets the following laboratory criteria: a. Blood routine test, b. Liver function, c. Renal function, d. Coagulation function, e. Left ventricular ejection fraction (LVEF) > 50% at screening
9. Female subjects of childbearing potential must have a negative serum pregnancy test within 7 days prior to enrollment and agree to use a medically licensed contraceptive method (condom, contraceptive sponge, contraceptive gel, contraceptive membrane, intrauterine device, oral or injectable contraceptives, subcutaneous implants, etc.) during treatment and within 3 months after the end of treatment;
10. Capable and willing to comply with protocol requirements during the study and subsequent procedures.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Known uncontrollable hypersensitivity to AL8326 similar compounds;
2. Having previously used AL8326 tablets;
3. Having or had a history of leptomeningeal disease or leptomeningeal metastases at screening, or confirmed CNS metastases presenting with symptoms of uncontrolled brain metastases, spinal cord compression, or cancerous meningitis within 8 weeks of first dose, except for CNS metastases or spinal cord compression that are clinically stable and do not require corticosteroids and have an interval of greater than 2 weeks between screening and previous treatment (including radiation therapy or surgery);
4. Having or had other neoplasms unless radically treated and with no evidence of recurrence or metastasis within the past 2 years;
5. Having significant gastrointestinal history or current illness, such as inability to swallow, severe peptic ulcer, uncontrollable nausea and vomiting, and clinical difficulty in controlling chronic diarrhea, intestinal obstruction or other chronic gastrointestinal diseases in the past 3 months, which may affect the intake, transport or absorption of drugs as judged by the investigator, or who have previously undergone total gastrectomy;
6. Having other important primary diseases, such as single agent uncontrolled hypertension , arrhythmia requiring clinical intervention, abnormally prolonged arrhythmia caused by unstable coronary artery disease, decompensated congestive heart failure or myocardial infarction, unstable angina pectoris, ascites or pleural effusion with uncontrolled within 6 months before the administration of the IMP (CTCAE 5.0 ≥ 2), active autoimmune diseases, mental illness, symptomatic or interstitial lung disease requiring treatment, thyroid disease that may seriously affect the trial evaluation;
7. Had arterial thrombosis or severe venous thromboembolic events within 6 months before screening, such as cerebrovascular accident (including transient ischemic attack), deep venous thrombosis and pulmonary embolism;
8. Having imaging findings indicating that the tumor has invaded around important vessels at screening or the tumor is likely to invade important vessels and cause fatal massive hemorrhage during the subsequent study period as judged by the investigator;
9. Uncontrolled infection within 14 days prior to first dose;
10. Screening urine routine showed urine protein ≥ + +, and 24-hour urine protein > 1.0 g;
11. Having active bleeding within 3 months before screening or at high risk of bleeding as judged by the investigator;
12. Been receiving anticoagulants or vitamin K antagonists (e.g., warfarin, heparin, or their analogues) during the screening period [low-dose anticoagulants such as warfarin (no more than 1 mg daily orally), low-dose heparin (no more than 12,000 U daily), or low-dose aspirin (no more than 100 mg daily) were permitted for prophylactic purposes provided INR was ≤ 1.5];
13. Having positive test results for hepatitis C virus (HCV) antibody, treponema pallidum antibody, or human immunodeficiency virus (HIV) antibody, or active hepatitis B (defined as hepatitis B virus HBV DNA ≥ 2000 IU/mL or HBV DNA ≥ 10 ^ 4 copies);
14. Participated in other clinical trials (excluding observational or vitamin studies) within 4 weeks before informed consent;
15. Having received major surgical treatment within 6 weeks prior to screening (patients must be fully recovered and stable before the start of treatment) or serious unhealed wounds, ulcers or fractures at screening;
16. Having a history of organ transplantation or being prepared to undergo organ transplantation;

17. Other reasons that, in the discretion of the investigator, would make participation in this study inappropriate.

Date of first enrolment
30/11/2024

Date of final enrolment
30/10/2027

Locations

Countries of recruitment
United Kingdom

China

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Advenchen Pharmaceuticals, LLC

Funder(s)

Funder type
Industry

Funder Name
Advenchen Pharmaceuticals, LLC

Results and Publications

Individual participant data (IPD) sharing plan
Datasets generated during the study are not available other than to the commercial sponsor whose data is part of the intellectual property. Final data analysis / report will then be made publicly available via presentations , publications and recognised public databases.

IPD sharing plan summary

Data sharing statement to be made available at a later date