A randomized, double-blind, international multicenter, phase III study to evaluate the anti-tumor efficacy and safety of HLX10 (recombinant humanized anti-PD-1 monoclonal antibody injection) or placebo in combination with chemotherapy (carboplatin/cisplatin-etoposide) and concurrent radiotherapy in patients with limited-stage small cell lung cancer (LS-SCLC)

Published: 08-12-2022
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This study has been transitioned to CTIS with ID 2024-515047-31-00 check the CTIS register for the current data. Primary objective:- To evaluate the anti-tumor efficacy of HLX10 in combination with chemotherapy and concurrent radiotherapy in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON53822

Source
ToetsingOnline

Brief title
HLX10-020-SCLC302

Condition

- Respiratory tract neoplasms

Synonym
Lung cancer - Limited-stage small cell lung cancer (LS-SCLC)

Research involving
Human

Sponsors and support

Primary sponsor: Shanghai Henlius Biotech, Inc.
Source(s) of monetary or material Support: Shanghai Henlius Biotech Inc.

Intervention

Keyword: Limited-Stage Small Cell Lung Cancer (LS-SCLC), Recombinant Humanized Anti-PD-1 Monoclonal Antibody

Outcome measures

Primary outcome

Overall survival (OS): OS is defined as a period from randomization through

death from any cause.

Secondary outcome

- Progression-free survival (PFS): PFS is defined as a period from

randomization initiation through the first objective PD or death (on account of

any cause without PD) as assessed by the investigator per RECIST v1.1

- Objective response rate (ORR): ORR is defined as the proportion of subjects

who have the best response of complete response (CR) or partial response (PR)

as assessed by the investigator according to RECIST 1.1.

- Duration of remission (DOR): DOR is defined as the period from the first

recording of response (CR or PR) to the first recording of progressive disease

or death (whichever occurs first) as assessed by the investigator according to

RECIST 1.1. Response termination date should be consistent with the date of PD or death from any cause for the PFS endpoint as assessed per RECIST v1.1

- Adverse events (AE) (including serious adverse events (SAE)), laboratory tests (hematology, blood chemistry, coagulation function, urinalysis, thyroid function, and cardiac function), 12-lead electrocardiogram (12-lead ECG), vital signs, and physical examination

- Quality of life assessment

- Serum HLX10 concentration

- HLX10 anti-drug antibody/neutralizing antibody (ADA/NAb)

- Relationship between PD-L1 expression in tumor tissuesand efficacy

Study description

Background summary

Small cell lung cancer (SCLC) is a kind of the lung cancer and accounts for about 15-20% of lung cancer. The disease progresses rapidly with SCLC. SCLC is divided into two stages, including limited-stage (LS-SCLC) and extensive-stage (ES-SCLC) small cell lung cancer. Currently, surgery, chemotherapy and radiotherapy are the primary treatment for LS-SCLC. However, surgery is only applicable for a few patients with early SCLC. For patients with inoperable LS-SCLC, concurrent chemotherapy and radiotherapy is the standard treatment regimen.
Based on the considerable benefits of PD-1/PD-L1 inhibitors in patients with tumors, Shanghai Henlius Biotech, Inc. independently developed an innovative PD-1 targeted monoclonal antibody, HLX10. Existing clinical data demonstrates that HLX10 is confirmed safe and tolerable by the first-in-human phase I study for patients with advanced solid tumors and other clinical studies for patients with malignant solid tumors. Preliminary efficacy of HLX10 was observed in some patients with advanced solid tumors in the first-in-human phase I clinical study (HLX10-001). The safety and efficacy of HLX10 will be further evaluated in clinical studies.
Based on the existing pre-clinical and clinical study results, Shanghai Henlius Biotech, Inc. intends to conduct a phase III clinical study in patients with LS-SCLC who have never received any treatment for LS-SCLC, to evaluate the

efficacy and safety of HLX10 in combination with chemotherapy (carboplatin/cisplatin-etoposide) and concurrent radiotherapy.

Study objective

This study has been transitioned to CTIS with ID 2024-515047-31-00 check the CTIS register for the current data.

Primary objective:
- To evaluate the anti-tumor efficacy of HLX10 in combination with chemotherapy and concurrent radiotherapy in subjects with LS-SCLC

Secondary objectives:
- To evaluate the safety of HLX10 in combination with chemotherapy and concurrent radiotherapy in subjects with LS-SCLC
- To evaluate the pharmacokinetics (PK), immunogenicity, and biomarkers

Study design

This study is a randomized, double-blind, placebo-controlled, phase III clinical study to evaluate the anti-tumor efficacy and safety of HLX10 in combination with chemotherapy and concurrent radiotherapy in subjects with LS-SCLC.

Subjects will be randomized 1:1 to Arm A or Arm B:
- Arm A (HLX10): HLX10 + chemotherapy (carboplatin/cisplatin-etoposide) + radiotherapy
- Arm B (control): placebo + chemotherapy (carboplatin/cisplatin-etoposide) + radiotherapy

The 4 stratification factors include ECOG PS (0 or 1), staging (I/II or III), radiation fraction (bid or qd), and region (Asia or non-Asia).

After screening, subjects meeting the inclusion criteria and not meeting the exclusion criteria will be enrolled. All enrolled subjects will receive HLX10 or placebo in combination with chemotherapy Q3W and concurrent radiotherapy.

Prophylactic cranial radiotherapy after chemoradiotherapy is highly recommended for patients with CR/PR, SD at the discretion of the investigator.
The said regimen should be continued until progressive disease (determined by the investigator according to RECIST1.1), toxicity intolerance, withdrawal of informed consent, death, loss to follow-up, or other reasons specified in the protocol (whichever occurs first). Subjects who discontinue the study treatment will immediately enter the follow-up period

This study is divided into three stages: screening (28 days), treatment (until

disease progression, intolerable toxicity, withdrawal of informed consent, death, loss to follow-up or other reasons specified in the protocol, whichever occursfirst), and follow-up (including safety follow-up period and survival follow-up period).

Intervention

One treatment cycle lasts for 3 weeks (21 days). The patient will be treated on Day 1 of the first 4 cycles with study medication (HLX10) or placebo in combination with chemotherapy for up to 16 months. The patient will receive concurrent radiotherapy starting on Day 1 of cycle 2, HLX10 or placebo alone (without chemotherapy) will be administrated since Day 1 of cycle 5 and following cycles. The route of administration for HLX10 and placebo is intravenous infusion and the dose of HLX10 is 300 mg. Administration of the investigational drug or placebo will be completed within 30 to 90 min.

For this study, we will have 2 groups:
- Group 1 (the experiment group). The people in this group will get HLX10 in combination with chemotherapy and concurrent radiotherapy.
- Group 2 (the control group). The people in this group will get placebo in combination with chemotherapy and concurrent radiotherapy.

A draw will decide which treatment the patient is given. The chances of receiving HLX10 or placebo in combination with chemotherapy and concurrent radiotherapy are 50% (1 in 2).

Study burden and risks

The schedule of activities, which summarizes the frequency and timing of the various measurements, can be found in the protocol (pages 25-31).

Discomforts and risks associated with participation:

Medicinal product /
Side effects whereof the investigator should be immediately notified: hypersensitivity, encephalitis, myocarditis, polymyositis, rhabdomyolysis, toxic epidermal necrolysis, Stevens-Johnson syndrome and renal failure.
The following side effects are common: Skin toxicity (mainly rashes and pruritus (30-40%)), Diarrhea and/or colitis (8-19%), Fatigue (16-24%), Immune-related hepatitis (liver inflammation) (5%), Hypothyroidism (4-10%), Hyperthyroidism (increased secretion of thyroid hormones) (4%), Hypophysitis (pituitary gland inflammation) (1%), Type I diabetes mellitus (carbohydrate metabolism disorder), Immune-related pneumonitis (pulmonary inflammation), Sarcoidosis (a chronic disease with unknown cause that is characterized by nodules in the lungs, liver, lymph nodes, and salivary glands) and Rheumatoid arthritis (joint inflammation).

The following side effects are less frequent: cardiovascular adverse events, nephritis, encephalopathy, leukodystrophy, posterior reversible encephalopathy syndrome, peripheral motor and sensory neuropathy, uveitis, episcleritis, blepharitis, blurred vision, acute cholangitis and acute pancreatitis.
The medicinal product can also have side effects that are not known about at the moment.

The side effects of carboplatin include:
- Hematologic toxicity, including myelosuppression (decreased bone marrow activity, resulting in reduced blood cell production).
- Gastrointestinal toxicity, including nausea, vomiting, abdominal pain, diarrhea, constipation, and decreased appetite.
- Nephrotoxicity, including blood urea nitrogen and creatinine increased (two markers used to measure renal functions).
- Hypersensitivity, including rashes, fever, pruritus, urticaria (a skin disease characterized by red itchy or white protruding plaques), erythema, bronchospasms (sudden contraction of bronchial wall muscles, resulting in dyspnea), and hypotension (blood pressure decreased).
- Ototoxicity, including hearing loss and tinnitus (buzzing, hissing, or roaring sounds in ears).
- Neurotoxicity, including weakened deep tendon reflexes (sudden uncontrollable muscle movements) and paresthesia (abnormal or uncomfortable sensations in the organs, body parts, or skin).
- Others, including hepatic function abnormal, hypogeusia (decreased sense of taste), alopecia (hair loss), fever, and chills. Side effects occur in the respiratory system, cardiovascular system, mucosa and skin, genitourinary system, and musculoskeletal system.

The side effects of cisplatin include:
- Nephrotoxicity, including blood urea nitrogen and creatinine increased, hematuria.
- Gastrointestinal toxicity, including decreased appetite, nausea, vomiting, diarrhea.
- Hematologic toxicity, including white blood cell count decreased and platelet count decreased.
- Ototoxicity, including tinnitus and hearing loss.
- Neurotoxicity, including peripheral nerve damage, manifested as ataxia, myalgia, paresthesia in extremities.
- Anaphylaxis, including increased heart rate, blood pressure decreased, dyspnea, facial edema.
- Others, muscle cramps, hypomagnesemia, cardiac arrhythmias, and so on.

The side effects of etoposide include:
- Myelosuppression, including platelet count decreased and white blood cell count decreased.
- Decreased appetite, nausea, vomiting, and stomatitis (oral inflammation).
- Hypersensitivity, including hypotension and laryngospasm (closure of the

larynx, blocking air flow into the lungs).

The side effects of radiotherapy include:
- Radiation pneumonitis.
- Radiation esophagitis.
- Decreased appetite, nausea, and vomiting.
- Myelosuppression, including platelet count decreased and white blood cell count decreased.
- Pigmentation.
- Dermatitis and skin damage.

Pregnancy and breastfeeding:
Women who are pregnant or breastfeeding cannot take part in this study. Women should also not get pregnant during the study and for at least 6 months after the last administration of the investigational product. Males with a female partner need to make sure that she cannot become pregnant with his child for at least 6 months after the last administration of the investigational product.

Blood sampling: Discomfort (including pain), bleeding, or bruises, small blood scabs, or swelling (including redness) at the site for blood sampling may be experienced. In rare cases, lipothymia or localised infection may occur.

Tumor biopsy: If a tumor biopsy is necessary as part of the screening, discomfort or pain during the procedure may be felt. Bleeding or temporary discomfort may occur at the tumor biopsy site. If anesthesia is performed during tumor biopsy, anesthetic complications may occur.

Electrocardiography: During the examination, the patient is required to lie flat for 5-10 minutes. The investigator will place several electrodes on the skin of the chest, wrists, and ankles to record the electrophysiological activities of the heart. The patient may feel cold or mild discomfort on the skin when the electrodes are placed and removed.

Echocardiography: During the examination, the patient is required to lie flat for 10-15 minutes. The investigato will place an echocardiography probe on the skin surface in front of the heart. The patient may feel cold once the probe is placed on the skin surface and mild discomfort from the compression of the chest wall. A very small minority of people may be allergic to the coupling agent on the ultrasonic probe.

Blood pressure: After the patient has rested for 10 minutes in a sitting position, an inflatable cuff will be placed on the arm and a device will be used to measure the blood pressure. The patient may experience mild discomfort in the arm when the cuff is inflated.

Imaging examination (CT or MRI): CT uses X-rays for scanning and image acquisition. While as a consequence of repeated CT scans, radiation accumulates

over time, and long-term accumulation of low-dose radiation may result in cancer. However, the dosage and frequency at which CT scanning poses a health risk remain unclear, and no method is available for accurate prediction. Magnetic resonance imaging (MRI) uses extremely strong magnets to excite atoms in the human body. The excited atoms can be detected by a scanner to produce an image of the scanned object. The patient cannot have an MRI if (s)he has a ferromagnetic metal implant that may be displaced or heated by magnetism. Similarly, the patient should not undergo an MRI if (s)he has an implanted pacemaker. In addition, the patient may feel uncomfortable when required to lie in a semi-enclosed space in the device for an extended period of time (about 30 to 40 minutes) during the MRI scan.

Bone scan: During the scan, a contrast agent is injected into the vein to help identify the lesions. The discomfort and risks related to contrast agent injection in the bone scan are similar to those in the CT scan.

Contrast agent used for imaging examination: The contrast agent may cause such side effects as nausea, vomiting, headache, pruritus, skin redness, rashes, or welts, asthma, abnormal heart rhythm, blood pressure increased or decreased, and shortness of breath. In rare cases, it may cause dyspnea, standstill cardiac, laryngeal edema or swelling in other body sites, convulsions, significant hypotension, or even death in severe circumstances. The contrast agent may cause deterioration of renal functions in patients with renal insufficiency. A radioactive contrast agent is required during a bone scan. The bone scan involves a small dose of radiation from the contrast agent, and your risk of exposure to radiation is low.

Contacts

Public
Shanghai Henlius Biotech, Inc.

Kagnan Road, Pilot Free Trade Zone, PRC No 220, Complex Building, Room 330
Shanghai 200233
CN
Scientific
Shanghai Henlius Biotech, Inc.

Kagnan Road, Pilot Free Trade Zone, PRC No 220, Complex Building, Room 330
Shanghai 200233
CN

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients must be willing to voluntarily participate in this clinical study and provide written ICF
- Male or female aged >=18 years
- Histologically diagnosed with SCLC
- Diagnosed with LS-SCLC (Stage I-III of the AJCC 8th edition of the cancer staging) which can be safely treated with curative radiation doses
- At least one measurable lesion as assessed by an investigator as per RECIST v1.1 within 4 weeks prior to randomization
- Patient must provide tumor tissues that met requirements for assay of PD-L1 expression
- ECOG PS 0 or 1
- Expected survival of at least 6 months
- Laboratory tests verified sufficient organ and marrow function without abnormalities in haematopoietic function or cardiac, hepatic or renal function or immunodeficiency within 7 days prior to randomization
- Women of childbearing potential must be tested negative for serum/urine pregnancy test within 7 days prior to randomization and must agree to use contraception methods with an annual failure rate of < 1% or to remain abstinent from signing ICF to at least 6 months after last dose of study drug
- Male patients must agree to remain abstinent or take contraceptions measures during study treatment and for at least 6 months after last dose of the drug
- Previous non-systematic anti-tumor treatment should be completed >= 2 weeks prior to initiation of the study medication and treatment related AEs have returned to <= grade 1 based on CTCAE 5.0 (except alopecia grade 2)

Exclusion criteria

- Histologically or cytologically confirmed mixed SCLC
- Subjects suitable for surgery
- previously received systematic anti-tumor treatments for small cell lung cancer
- Patients with other active malignancies within 5 years or at the same time (except localized tumors that have been cured)
- Patients preparing for or have received an organ or bone marrow transplant
- Patients with pleural, pericardial effusions, or ascites requiring clinical intervention
- Patients wtih myocardial infarction and poorly controlled arrhytmia within 6 months prior to the first dose of the IMP
- Class III to IV cardiac insufficiency according to NYHA classification or a left ventricular ejection fraction < 50% by cardiac color Doppler
- Subject within uncontrolled or symptomatic hypercalcemia
- Patients with peripheral neuropathy >= grade 2 by CTCAE
- Patients with HIV infection and HIV antibody test results are positive
- Patients with active pulmonary tuberculosis
- Subjects with previous and current interstitial pneumonia, pneumoconiosis, radiation pneumonitis, drug-related pneumonitis and sever impaired pulmonary function that may interfere with the detection and management of suspected drug-related pulmonary toxicity as judged by the investigator.
- Hepatitis B or Hepatitis C (patient with hepatitis B who are stable on antiviral therapy can be enrolled)
- Subjects with known active or suspected autoimmune diseases. Patients in a stable state with no need for systemic immunosuppressant therapy are allowed to be enrolled.
- Have received treatment with live vaccines within 28 days prior to first administration
- subjects requiring treatment with systemic corticosteroids or other immunosuppressive drugs within 14 days prior to first dose or during the study (in absence of active autoimmune disease, subjects are allowed to use topical or inhaled glucocorticosteroids and <= 20 mg./day therapeutic dose of prednosine for adrenal glucocorticoid replacement therapy).
- Any active infection requiring systemic anti-infective treatment within 14 days prior to the administration of IMP
- have received any major surgery within 28 days prior to the first dose of the IP
- the subject has previously received other antibodies/drugs against immune checkpoints, such as PD-1, PD-L1, CTLA4, etc.
- Participation in any other ongoing interventional clinical study less than 28 days from the end of the previous study treatment to the start of this trial
- Subjects with known anaphylaxis to carboplatin/cisplatin or etoposide
- Pregnant or lactating women
- Subjects with a known history of psychotropics substance abuse or drug abuse
- in the judgment of the investigator, subjects who have any other factors that may lead to a premature discontinuation
- Subjects expected to require surgical resection during the study

- Primary tumor/lymph node too large for planned radiotherapy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-04-2024
Enrollment:	10
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	/
Generic name:	Serplulimab Injection

Ethics review

Approved WMO

Date:	08-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-02-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-515047-31-00
EudraCT	EUCTR2022-002226-27-NL
ClinicalTrials.gov	NCT05353257
CCMO	NL82997.056.22