NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
July 2023

Serplulimab with chemotherapy for treating previously untreated extensive stage small-cell lung cancer

Company/Developer	Shanghai Henlius Biotech Inc

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30372	NICE ID: N/A	UKPS ID: N/A

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Serplulimab with chemotherapy is currently in clinical development as a first-line treatment for extensive-stage small-cell lung cancer (SCLC). SCLC is a very aggressive form of cancer that forms in the tissues of the lungs and often goes undiagnosed until it's more advanced, so the survival rate tends to be low. Extensive stage SCLC (ES-SCLC) is when the cancer cells spread beyond the lungs to other places in the body. Symptoms include chest discomfort or pain, a cough that does not go away or gets worse, trouble breathing and wheezing. Smoking is the biggest risk factor.ES-SCLC is a challenging disease to treat, and resistance eventually develops relatively quickly in most patients suggesting a clinical need for more effective treatments.

Serplulimab is a monoclonal antibody administered by intravenous infusion and acts by binding to a protein called PD-1 found on the T cells. Binding to this protein can lead to the activation of the body's immune system to enable it to fight the cancer cells. Detailed epitope analysis showed that serplulimab has a unique way of recognising and binding to different epitopes in PD-1 compared to other clinically approved PD-1 antibodies. If approved, this combination will add an alternative treatment option for first-line treatment of ES-SCLC.

Proposed Indication

First-line treatment of adult patients with extensive stage small-cell lung cancer (ES-SCLC).[1]

Technology

Description

Serplulimab (Hansizhuang) is a fully humanised IgG4 monoclonal antibody, a type of protein that has been designed to attach to programmed cell death protein 1 (PD-1), a receptor found on T cells. Cancer cells can produce programmed death-ligand 1 (PD-L1) and PD-L2 on their surface. These also attach to the PD-1 receptor and, by doing so, switch off the activity of the T cells. Serplulimab binds to the PD-1 receptors on T cells without switching off their activity. This blocks the PD-1 receptor so PD-L1 and PD-L2 on the surface of the cancer cells can no longer attach and switch off the T cells. This may help to restore immune function through the activation of T cells against tumour cells.[2]

Serplulimab with chemotherapy is currently in development for the first-line treatment of ES-SCLC. In the phase III trial (NCT04063163) patients with ES-SCLC who had not received prior systemic therapy were randomized to receive serplulimab 4.5 mg/kg (n = 389) or placebo (n = 196) intravenously once every 3 weeks; all patients received carboplatin and etoposide intravenously once every 3 weeks for up to four cycles.[3,4]

Key Innovation

ES-SCLC is a therapeutically challenging disease. After more than two decades without clinical progress, the addition of PD-1 axis blockade to platinum-based chemotherapy has demonstrated sustained overall survival (OS) benefit and represents the current standard of care in the first-line setting. Despite this benefit, resistance emerges relatively rapidly in virtually all patients.[5]

Serplulimab has been shown to, increase functional activities of human T cells and showed in vitro and anti-tumour activity in several tumour models. Detailed epitope analysis showed that serplulimab has a unique mode of recognition compared to the other clinically approved PD-1 antibodies. Serplulimab binds to different epitopes in PD-1 and also exhibited a higher affinity to human PD-1 along with greater potency to block PD-L1 and PD-L2 compared with other PD-1 inhibitors .[6]

Serplulimab with chemotherapy as first-line treatment provided significant benefits and a manageable safety profile compared with chemotherapy alone in ES-SCLC patients. In a global phase 3 study (NCT04063163) , OS benefits were demonstrated with a PD-1 inhibitor among previously untreated ES-SCLC patients.[7] If licensed, serplulimab with chemotherapy will offer an additional treatment therapy for ES-SCLC patients.

Regulatory & Development Status

Serplulimab does not currently have Marketing Authorisation in the EU/UK for any indication.

Serplulimab has the following designations/awards granted.[2,8]

- an orphan drug designation in the EU in December 2022 for the treatment of SCLC
- an orphan drug in the USA in April 2022 for the treatment of SCLC

Serplulimab is currently in phase II and III clinical trials as combination therapy for various cancer indications including:[9]

- Non-small cell lung cancer
- Colorectal cancer
- Renal cell carcinoma
- Gastric cancer
- Cervical cancer
- Oesophageal squamous cell carcinoma
- Rectal cancer
- Neuroendocrine carcinoma

Patient Group

Disease Area and Clinical Need

SCLC is a disease in which malignant cells form in the tissues of the lung. In extensive-stage, cancer has spread beyond the lung or the area between the lungs or the lymph nodes above the collarbone to other places in the body.[10] SCLC represents one of the most lethal forms of cancer, with limited successful therapeutic options and consequently presenting striking low survival rates in late stages.[11] Smoking is a major risk factor for SCLC while other risk factors include being exposed to second-hand smoke, being exposed to radiation, living where there is air pollution and family history of lung cancer. Signs and symptoms of small cell lung cancer include coughing and shortness of breath, blood in sputum, hoarseness, and loss of appetite. Certain factors affect prognosis (chance of recovery) and treatment options. For most patients with SCLC, current treatments do not cure the cancer.[10]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2016-2018). Between 2016-2018, 48,549 new cases of lung cancer were diagnosed annually on average in the UK.[12] ES-SCLC is a form of lung cancer accounting for 1 in 8 lung cancer cases in the UK..[13] Using the above statistics, it can be estimated that an average of 6,068 cases of ES-SCLC are diagnosed in the UK every year.[12,13] In England (2021-22), there were 119,396 finished consultant episodes (FCEs) and 99,551 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34), which resulted in 75,969 day cases and 206,640 FCE bed days.[14] In England (2017), there were 38,888 patients diagnosed with malignant neoplasm of bronchus and lung and 28,170 deaths registered had malignant neoplasm of bronchus and lung as the underlying cause.[15]The 5 year overall survival rate for SCLC patients is less than 10%.[16]

Recommended Treatment Options

Currently the only treatment recommended by the National Institute for Health and Care Excellence (NICE) for untreated ES-SCLC is atezolizumab with carboplatin and etoposide.[17]

Clinical Trial Information

Trial	NCT05468489; A Randomised, Open-label Study of HLX10 Plus Chemotherapy (Carboplatin-Etoposide) in Comparison with Atezolizumab Plus Chemotherapy in Previously Untreated US Patients with Extensive Stage Small Cell Lung Cancer (ES-SCLC) **Phase III:** Recruiting **Location(s):** USA **Primary completion date:** June 2024
Trial Design	Randomised, parallel assignment, open label

Population	N=200 (estimated); patients histologically or cytologically diagnosed with ES-SCLC; no prior systemic therapy for ES-SCLC; aged 18 years and older.
Intervention(s)	Serplulimab + chemotherapy (carboplatin-etoposide)
Comparator(s)	Atezolizumab + chemotherapy (carboplatin-etoposide)
Outcome(s)	**Primary outcome measure:** • Overall survival (OS) [Time frame: A period from randomization through death regardless of causality (approximately up to 24 months).] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	NCT04063163; 2019-003063-21; A Randomised, Double-Blind, Multicentre, Phase III Study to Compare Clinical Efficacy and Safety of HLX10 (Recombinant Humanized Anti-PD-1 Monoclonal Antibody Injection) in Combination With Chemotherapy (Carboplatin-Etoposide) in Previously Untreated Patients With Extensive Stage Small Cell Lung Cancer (ES-SCLC) **Phase III:** Active, not recruiting **Location(s):** 1 EU country, China, Georgia, Russia, Turkey and Ukraine **Primary completion date:** October 2021
Trial Design	Randomised, parallel assignment, quadruple-masked
Population	N=585 (actual); patients histologically or cytologically diagnosed with ES-SCLC; no prior systemic therapy for ES-SCLC; 18 years and older
Intervention(s)	Serplulimab + chemotherapy (carboplatin-etoposide)
Comparator(s)	Placebo + chemotherapy (carboplatin-etoposide)
Outcome(s)	**Primary outcome measure:** • Overall survival (OS) [Time frame: A period from randomization through death regardless of causality (approximately up to 24 months).] See trial record for full list of other outcomes.
Results (efficacy)	Among the 585 patients who were randomized (mean age, 61.1 [SD, 8.67] years; 104 [17.8%] women), 246 (42.1%) completed the trial and 465 (79.5%) discontinued study treatment. All patients received study treatment and were included in the primary analyses. As of the data cut-off (October 22, 2021) for this interim analysis, the median duration of follow-up was 12.3 months (range, 0.2-24.8 months). The median overall survival was significantly longer in the

	serplulimab group (15.4 months [95% CI, 13.3 months-not evaluable]) than in the placebo group (10.9 months [95% CI, 10.0-14.3 months]) (hazard ratio, 0.63 [95% CI, 0.49-0.82]; P < .001). The median progression-free survival (assessed by an independent radiology review committee) also was longer in the serplulimab group (5.7 months [95% CI, 5.5-6.9 months]) than in the placebo group (4.3 months [95% CI, 4.2-4.5 months]) (hazard ratio, 0.48 [95% CI, 0.38-0.59]).[18]
Results (safety)	Treatment-related adverse events that were grade 3 or higher occurred in 129 patients (33.2%) in the serplulimab group and in 54 patients (27.6%) in the placebo group.[18]

Estimated Cost

The cost of serplulimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Tislelizumab with platinum-based chemotherapy and etoposide for untreated extensive-stage small-cell lung cancer. [GD-TA11094]. Expected publication date to be confirmed.
- NICE technology appraisal. Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer. [TA638]. July 2020
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.
- NICE quality standards. Lung cancer in adults (QS17). December 2019.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.

Other Guidance

- National Comprehensive Cancer Network (NCCN). Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. 2021.[19]
- European Society for Medical Oncology (ESMO). Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2021.[16]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2019.[20]
- Scottish Intercollegiate Guideline Network (SIGN). Management of lung cancer. 2014.[21]

Additional Information

Shanghai Henlius Biotech Inc did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge

pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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