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Newcastle University

Health Technology Briefing
July 2023

Pembrolizumab-vibostolimab with etoposide and platinum chemotherapy for previously untreated extensive-stage small cell lung cancer

Company/Developer	Merck Sharp & Dohme Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 34689	NICE ID: Not available	UKPS ID: 670338

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Pembrolizumab-vibostolimab with etoposide and platinum chemotherapy is in clinical development for the first-line treatment of extensive stage small cell lung cancer (SCLC). Extensive stage SCLC is when cancer cells form in the tissues of the lung and spread beyond the lung to other places in the body. Symptoms include chest pain, a cough that does not go away or gets worse, coughing up blood, and breathlessness. Smoking is the biggest risk factor for SCLC. Extensive-stage SCLC is a challenging disease to treat and despite improvements in the treatment of the disease, most patients will have disease progression within 6 months.

Pembrolizumab-vibostolimab is a co-formulated medicinal product containing fixed doses of pembrolizumab and vibostolimab. Pembrolizumab is a humanised blood protein, the binding of which to a receptor called programmed death-1 (PD-1) on the surface of cells increases the immune response to tumour cells. Vibostolimab is also a humanised blood protein that binds to a molecule called TIGIT on immune cells and this interaction can activate an immune response that that contributes to the destruction of tumour cells. Preclinical and clinical data suggest that vibostolimab offers promising antitumor activity when combined with pembrolizumab in patients with lung cancer. The medicinal product will be administered by intravenous (IV) infusion. If licensed, this combination will add an alternative treatment option for first-line treatment of extensive-stage SCLC.

Proposed Indication

For the first-line treatment of adult patients with extensive-stage (stage IV) small cell lung cancer (SCLC).[1]

Technology

Description

Pembrolizumab co-formulated with vibostolimab (MK-7684A) contains fixed doses of the two monoclonal antibodies vibostolimab and pembrolizumab, with potential immune checkpoint inhibitory and antineoplastic activities. Vibostolimab is an antibody against the immune checkpoint inhibitor T-cell immunoglobulin (Ig) and immunoreceptor tyrosine-based inhibitory motif (ITIM) domains (TIGIT; T-cell immunoreceptor with Ig and ITIM domains; T-cell immunoglobulin and ITIM domain). Upon administration of pembrolizumab-vibostolimab, the binding of vibostolimab to TIGIT that is expressed on various immune cells, particularly on tumour-infiltrating T lymphocytes (TILs) and natural killer (NK) cells, prevents the interaction of TIGIT with its ligands CD112 and CD155, which are expressed on T cells, NK cells and certain cancer cells. The blocking of the interaction of CD112 and CD155 with TIGIT leads to enhanced interaction of the two ligands with the costimulatory receptor CD226, which is expressed on immune cells, such as NK cells and CD8+ T cells, thus activating CD226-mediated signalling, which in turn triggers the immune system to exert a T-cell-mediated immune response against cancer cells. TIGIT has a key role in the suppression of T-cell proliferation and activation, and tumour cell immune evasion. Pembrolizumab, an antibody directed against human cell surface receptor PD-1 (programmed death-1 or programmed cell death-1) targets and binds to PD-1, an inhibitory signalling receptor expressed on the surface of activated T cells and blocks the binding to and activation of PD-1 by its ligands, which results in the activation of T-cell-mediated immune responses against tumour cells. The ligands for PD-1 include programmed cell death ligand 1 (PD-L1), which is overexpressed on certain cancer cells, and programmed cell death ligand 2 (PD-L2), which is primarily expressed on antigen presenting cells (APCs). Activated PD-1 negatively regulates T-cell activation and has a key role in in tumour evasion from host immunity.[2]

Pembrolizumab-vibostolimab in combination with etoposide and platinum chemotherapy is in clinical development for the first-line treatment of extensive stage SCLC. In the phase III clinical trial (NCT05224141), pembrolizumab-vibostolimab is administrated by intravenous (IV) infusion as fixed-dose co-formulation of 200 mg pembrolizumab and 200 mg vibostolimab every 3 weeks (Q3W) in combination with 100 mg/m^2 etoposide, and platinum (Area Under the Curve (AUC) 5 mg/mL/min carboplatin or 75 mg/m^2 cisplatin) chemotherapy Q3W for a total of approximately 12 weeks. This will be followed by additional cycles of pembrolizumab-vibostolimab Q3W until any of the conditions for discontinuation are met.[1]

Key Innovation

Extensive stage SCLC is a therapeutically challenging disease and despite immunotherapeutic advancements in the first-line treatment of the disease, most patients will have disease progression within 6 months.[3] Current standard of care immunotherapy plus chemotherapy options for first-line extensive stage SCLC are associated with modest improvements in median overall survival (OS) and progression-free survival (PFS). Preclinical and clinical data suggest that blocking the interaction between the T-cell immunoreceptor with immunoglobulin and TIGIT and its ligands CD112 and CD155 with the anti-TIGIT humanised monoclonal antibody vibostolimab yields promising antitumor activity when combined with pembrolizumab, with or without chemotherapy, including in patients with lung cancer.[4] If licensed,

pembrolizumab-vibostolimab in combination with chemotherapy will offer an additional front-line treatment option for patients with extensive stage SCLC.

Regulatory & Development Status

Pembrolizumab-vibostolimab fixed-dose combination does not have Marketing Authorisation in the EU/UK for any indication.

Pembrolizumab-vibostolimab is currently in phase II/III clinical trials for the following indications:[5]

- Haematological Malignancies
- Melanoma
- Lung Neoplasms
- Non-Small-Cell Lung Carcinoma
- Bladder Cancer
- Solid tumours
- Colorectal Cancer
- Metastatic Castration-Resistant Prostate Cancer
- Metastatic Urothelial Carcinoma
- Renal cell carcinoma

Patient Group

Disease Area and Clinical Need

SCLC is a malignant epithelial tumour arising from cells lining the lower respiratory tract.[6] Malignant (cancer) cells form in the tissues of the lung in SCLC. About 15% to 20% of all lung cancers are SCLC.[7] SCLC is an aggressive cancer and approximately two-thirds of patients have evidence of distant metastasis at presentation. In extensive-stage SCLC, 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. Smoking cigarettes, pipes, or cigars is the biggest factor for lung cancer. Other risk factors include family history of lung cancer, and being exposed to irritants, such as second-hand smoke, asbestos, arsenic, chromium, beryllium, nickel, soot or tar in the workplace, radiation, and air pollution. Most common presenting symptoms are cough, chest pain, haemoptysis (coughing up blood), dyspnoea, and weight loss.[6,8]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2016-2018).[9] Extensive-stage SCLC is a form of lung cancer accounting for 1 in 8 lung cancer cases in the UK.[10] 48,549 new cases of lung cancer were diagnosed annually on average between 2016 and 2018 in the UK.[9] According to these statistics, it can be estimated that an average of 6,068 cases of extensive-stage SCLC are diagnosed in the UK every year.[9,10]

Recommended Treatment Options

Currently, the National Institute for Health and Care Excellence (NICE) recommended options for the first-line treatment of extensive-stage SCLS are:

- Platinum-based combination chemotherapy.[11]
- Atezolizumab in combination with carboplatin and etoposide.[12]

Clinical Trial Information

Trial	**KEYVIBE-008**; NCT05224141; 2021-005034-42; A Phase 3, Randomised, Double-Blind Study of MK-7684A in Combination with Etoposide and Platinum Followed by MK-7684A vs Atezolizumab in Combination with Etoposide and Platinum Followed by Atezolizumab for the First-Line Treatment of Participants with Extensive-Stage Small Cell Lung Cancer **Phase III**- Active – not recruiting **Location(s):** 14 countries in EU, UK, USA, Canada, and other countries **Primary completion date:** May 2025
Trial Design	Randomised, Parallel Assignment, Double-masked
Population	N=450 (estimated); histologically or cytologically confirmed diagnosis of extensive-stage SCLC in need of first-line therapy; aged 18 years and older.
Intervention(s)	Pembrolizumab 200 mg plus vibostolimab 200 mg fixed dose co-formulation administered via IV infusion Q3W on day 1 of each cycle until discontinuation criteria are met. In combination with Etoposide 100 mg/m^2 administered via IV infusion Q3W on Days 1 2, 3 of each cycle for up to 4 cycles, Cisplatin 75 mg/m^2 administered via IV infusion Q3W on Day 1 of each cycle for up to 4 cycles, and Carboplatin AUC 5 mg/mL/min administered via IV infusion Q3W on Day 1 of each cycle for up to 4 cycles.
Comparator(s)	1200 mg atezolizumab Q3W, in combination with 100 mg/m^2 etoposide and platinum chemotherapy
Outcome(s)	**Primary outcome measures:** • Overall Survival (OS) [Time Frame: Up to approximately 37 months] See trial record for full list of other outcomes/
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of pembrolizumab-vibostolimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Tislelizumab with platinum-based chemotherapy and etoposide for untreated extensive-stage small-cell lung cancer (TA11094). Expected date of issue to be confirmed.
- NICE technology appraisal guidance. 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 2023.
- NICE guideline. Suspected cancer: recognition and referral (NG12). December 2021.
- NICE quality standard. Lung cancer in adults (QS17). December 2019.
- NICE quality standard. Suspected cancer (QS124). December 2017.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- National Comprehensive Cancer Network (NCCN). Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. December 2021.[13]
- European Society for Medical Oncology (ESMO). Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. July 2021.[14]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2019.[15]
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Additional Information

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.