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Newcastle University

Health Technology Briefing
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Vibostolimab-pembrolizumab for previously untreated PD-L1-positive metastatic non-small cell lung cancer

Company/Developer	Merck Sharp & Dohme Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

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Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Vibostolimab-pembrolizumab is currently in clinical development for previously untreated programmed cell death 1 ligand 1 (PD-L1) positive metastatic non-small cell lung cancer (NSCLC). NSCLC is the most common form of lung cancer. Elevated levels of PD-L1 expression are observed on the cell surface of different types of cancer cells, including NSCLC. It is believed that PD-L1 expression allows cancer cells to avoid the immune response. Metastatic cancer refers to cancer that has spread from the part of the body where it started to other parts of the body. Lung cancer remains the leading cause of cancer deaths, and there is need for more treatment options to prolong survival and preserve quality of life.

Vibostolimab-pembrolizumab contains fixed doses of two proteins (monoclonal antibodies) administered by intravenous infusion. Pembrolizumab is designed to bind to a receptor called programmed death-1 (PD-1) and stops the cancer switching off these immune cells, thereby increasing the immune response to tumour cells. Vibostolimab binds to a molecule called TIGIT on immune cells and this interaction can activate an immune response that contributes to the destruction of tumour cells. Preclinical and clinical data suggest that vibostolimab offers promising antitumour activity when combined with pembrolizumab in patients with lung cancer. If licensed, vibostolimab-pembrolizumab will offer an additional treatment option for patients with PD-L1-positive metastatic NSCLC.

Proposed Indication

First-line treatment of adults with programmed cell death 1 ligand 1 (PD-L1) positive metastatic non-small cell lung cancer (NSCLC) for which epidermal growth factor receptor (EGFR)-, anaplastic lymphoma kinase (ALK)-, or reactive oxygen species proto-oncogene 1 (ROS1)-directed therapy is not indicated as primary therapy.[1]

Technology

Description

Vibostolimab-pembrolizumab (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). Pembrolizumab is 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.[2]

Upon administration of vibostolimab-pembrolizumab, the binding of vibostolimab to TIGIT, which 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.

Vibostolimab-pembrolizumab is in clinical development for previously untreated PD-L1 positive metastatic NSCLC. In the phase III clinical trial (MK-7684A-003, KEYVIBE-003; NCT04738487), vibostolimab-pembrolizumab is administrated by intravenous (IV) infusion as fixed-dose co-formulation of 200 mg pembrolizumab and 200 mg vibostolimab every 3 weeks for up to 35 administrations (up to approximately 2 years).[1]

Key Innovation

The importance of TIGIT in regulating immune cell function in the tumour microenvironment and its role as a potential therapeutic target has been highlighted in the field of lung cancer. In a previous study, vibostolimab as a TIGIT-inhibitor, combined with pembrolizumab, yielded favourable tolerance and showed efficacy in the anti-PD-1/PD-L1-naïve population.[3] If licensed, vibostolimab-pembrolizumab will offer an additional treatment option for patients with PD-L1 positive metastatic NSCLC.

Regulatory & Development Status

Vibostolimab-pembrolizumab fixed-dose combination does not currently have Marketing Authorisation in the EU/UK for any indication.

Vibostolimab-pembrolizumab is currently in phase II and III clinical development for other indications such as:[4]

- melanoma
- haematological malignancies
- lung neoplasms
- bladder cancer
- colorectal cancer
- metastatic castration-resistant prostate cancer
- metastatic urothelial carcinoma
- renal cell carcinoma
- solid tumours

Patient Group

Disease Area and Clinical Need

NSCLC is the most common form of lung cancer. Around 80 to 85% of lung cancer cases in the UK are NSCLC. The three main types are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[5] Metastatic cancer refers to cancer that has spread from the part of the body where it started to other parts of the body.[6] PD-L1 is a type 1 transmembrane protein that belongs to the B7 ligands family. Expression of PD-L1 on tumour cells promotes down-regulation and self-tolerance of the immune system from rejecting the tumour by supressing T-cell inflammatory activity through binding the regulatory T-cell receptor, PD-1.[7] Risk factors for lung cancer include smoking, second-hand smoke, exposure to workplace chemicals, radiation exposure, air pollution and family history of lung cancer.[8] Symptoms of lung cancer include a persistent cough, repeated chest infections, breathlessness, unexplained pain, weight loss or tiredness. However, lung cancer may not always have symptoms early on.[9]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2016-2018).[10] Between 2017 and 2019 in the UK, there were 34,771 deaths due to lung cancer; the age-standardised mortality rate was 55.5 per 100,000.[11] In England, 2021-22, there were 119,396 finished consultant episodes (FCE) and 99,551 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34) which resulted in 206,640 FCE bed days and 75,969 day cases.[12]

Recommended Treatment Options

Treatment for lung cancer includes surgery, chemotherapy, radiotherapy, immunotherapy, and other targeted therapy drugs. Patients may be offered one or more different treatments depending on the stage, histology and type of lung cancer as well as their general health.[13]

The National Institute for Health and Care Excellence (NICE) currently recommends:[14-16]

- pembrolizumab monotherapy for untreated PD-L1-positive metastatic NSCLC in adults whose tumours express PD-L1 (with at least a 50% tumour proportion score) and have no epidermal growth factor receptor- or anaplastic lymphoma kinase-positive mutations

- pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous NSCLC in adults whose tumours express PD-L1 with a tumour proportion score of 0% to 49%, or the tumours express PD-L1 with a tumour proportion score of 50% or more and they need urgent clinical intervention
- atezolizumab monotherapy for untreated metastatic NSCLC in adults whose tumours have PD-L1 expression on at least 50% of tumour cells or 10% of tumour-infiltrating immune cells, and do not have epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) mutations

Clinical Trial Information

Trial	**MK-7684A-003, KEYVIBE-003;** NCT04738487;EudraCT 2020-004049-35 ; A Phase 3, Multicenter, Randomized, Double-Blind Study of MK-7684 With Pembrolizumab as a Coformulation (MK-7684A) Versus Pembrolizumab Monotherapy as First Line Treatment for Participants With PD-L1 Positive Metastatic Non-Small Cell Lung Cancer **Phase III -** Recruiting **Location(s):** 3 EU countries, Canada, USA, and other countries **Primary completion date:** April 2026
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N (estimated)=1246; aged 18 years or older; subjects with histologically or cytologically confirmed diagnosis of Stage IV: M1a, M1b, or M1c NSCLC
Intervention(s)	Coformulation of pembrolizumab (MK-3475) 200mg and vibostolimab (MK-7684) 200mg (IV) every 3 weeks for up to 35 administrations (up to approximately 2 years)
Comparator(s)	Pembrolizumab monotherapy 200 mg IV every 3 weeks for up to 35 administrations (up to approximately 2 years)
Outcome(s)	Primary outcome measures: • Overall Survival (OS) in Participants with Programmed Cell Death Ligand 1 (PD-L1) Tumour Proportion Score (TPS) ≥50% [Time Frame: Up to ~59 months] • OS in Participants With PD-L1 TPS ≥1% [Time Frame: Up to ~59 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of vibostolimab-pembrolizumab is currently unknown.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Avelumab for untreated PD-L1 positive recurrent or metastatic non-small-cell lung cancer (GID-TA10250) Expected date to be confirmed.
- NICE technology appraisal guidance. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (TA770). February 2022.
- NICE technology appraisal guidance. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (TA705). June 2021.
- NICE technology appraisal guidance. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (TA531). July 2018.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019. Updated July 2023.
- NICE quality standard. Lung cancer in adults (QS17). March 2012. Updated December 2019.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- European Society for Medical Oncology (ESMO). Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. September 2020.[17]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2019.[18]
- London Cancer Alliance. LCA Lung Cancer Clinical Guidelines. March 2016.[19]

Additional Information

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