

## Health Technology Briefing September 2023

### Pembrolizumab-vibostolimab for previously untreated non-small-cell lung cancer (NSCLC)

Company/Developer

Merck Sharp & Dohme Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 34690

NICE TSID: Not available

UKPS ID: 670337

#### Licensing and Market Availability Plans

Currently in phase III clinical trials

#### Summary

Pembrolizumab-vibostolimab is in development for treatment-naïve patients with metastatic non-small cell lung cancer (NSCLC). A metastatic NSCLC is an advanced stage of NSCLC (stage 4), where the cancer has spread from the lungs. NSCLC is the most common form of lung cancer, accounting for about 80 to 85 out of every 100 lung cancer cases. Lung cancer is one of the most frequently diagnosed cancers and the leading cause of cancer-related deaths worldwide. Several risk factors have been linked to lung cancer, including smoking, inhalation of radon, and exposure to certain chemicals. The main symptoms of lung cancer are chest infections, long-standing cough and coughing up blood, persistent breathlessness, pain when breathing or coughing, and unexplained weight loss. Most patients acquire resistance to existing treatment options over time. As vibostolimab affects immunoreceptors, the combination of pembrolizumab and vibostolimab may decrease such resistance and improve clinical outcomes.

Pembrolizumab-vibostolimab is a fixed-dose combination therapy (200mg pembrolizumab and 200mg vibostolimab) administered intravenously (through the vein), where both drugs are expected to work together to target specific proteins on the surfaces of metastatic NSCLC, resulting in a better treatment outcome. If licensed, pembrolizumab-vibostolimab may provide a new combination treatment option for patients with metastatic NSCLC.

#### Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Patients with treatment-naïve metastatic non-small cell lung cancer.<sup>1</sup>

## Technology

### Description

Pembrolizumab-vibostolimab (MK7684A) is an investigational monoclonal antibody fixed-dose combination therapy being developed for the treatment of metastatic non-small cell lung cancer (NSCLC).<sup>2</sup> Vibostolimab is an investigational monoclonal antibody that binds to the T cell immunoreceptor with immunoglobulin (Ig) and immunoreceptor tyrosine-based inhibitory motif (ITIM) domains (TIGIT) and inhibits interactions with its ligands.<sup>2</sup> Pembrolizumab is a monoclonal antibody that binds to the Programmed Cell Death Protein 1 (PD-1) receptor and blocks its interaction with Programmed Cell Death Ligand 1 (PD-L1) and Ligand 2 (PD-L2), releasing PD-1 pathway-mediated inhibition of the immune response.<sup>2</sup>

In a phase III clinical trial (NCT05226598) participants aged 18 years and above received an intravenous infusion of pembrolizumab-vibostolimab co-formulation (200mg pembrolizumab and 200mg vibostolimab), in addition to chemotherapy.<sup>1</sup>

### Key Innovation

Lung cancer patients are often diagnosed at an advanced stage, when multiple metastases would have already developed, making targeted therapy extremely difficult and systemic therapy less effective.<sup>3</sup> Checkpoint inhibition with PD-1/PD-L1 blockade has been a game changer in cancer treatment and has been widely used as a monotherapy or in combination with chemotherapy in the first-line setting in patients with advanced NSCLC.<sup>4,5</sup> However, most patients with advanced NSCLC acquired resistance over time.<sup>4,6</sup>

In preclinical models, TIGIT blockade has demonstrated modest antitumor activity as a monotherapy and enhanced effects when combined with a PD-1/PD-L1 inhibitor.<sup>7</sup> Hence, a co-formulation of pembrolizumab-vibostolimab may provide a more effective treatment for metastatic NSCLC. In a first-in-human phase 1 trial (MK-7684-001; NCT02964013), pembrolizumab-vibostolimab was well tolerated and demonstrated antitumor activity in patients with advanced solid tumours, including patients with advanced NSCLC.<sup>4</sup> If licensed, pembrolizumab-vibostolimab may provide a new combination treatment option for patients with metastatic NSCLC.

### Regulatory & Development Status

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

Vibostolimab as a monotherapy or in combination does not currently have Marketing Authorisation in the EU/UK for any indication.

Pembrolizumab has Marketing Authorisation in the EU/UK as:<sup>8</sup>

Monotherapy for:

- Breast cancer
- Classical Hodgkin lymphoma
- Head and neck squamous cell carcinoma
- Melanoma
- Microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer

- MSI-H or dMMR endometrial carcinoma
- MSI-H or dMMR gastric, small intestine, or biliary cancer
- Non-small cell lung cancer (monotherapy and combination)
- Renal cell carcinoma
- Urothelial carcinoma

Combination with chemotherapy for:

- Breast cancer
- Cervical cancer
- Endometrial cancer
- Head and neck squamous cell carcinoma
- Non-small cell lung cancer
- Oesophageal carcinoma
- Renal cell carcinoma

Pembrolizumab-Vibostolimab is also in phase II/III development for the following indications:<sup>9</sup>

- Uterine cervical neoplasms
- Endometrial neoplasms
- Squamous cell carcinoma of head and neck
- Hematological malignancies
- Melanoma
- Bladder cancer
- Gallbladder neoplasms
- Cholangiocarcinoma
- Esophageal neoplasms
- Triple negative breast neoplasms
- Hepatocellular carcinoma
- Ovarian neoplasms
- Stomach neoplasms

## Patient Group

### Disease Area and Clinical Need

Lung cancer is a type of cancer that starts from the lungs, windpipe (trachea) or the main airways (bronchus).<sup>10</sup> NSCLC is the most common form of lung cancer, accounting for about 80 to 85 out of every 100 lung cancer cases.<sup>11</sup> Metastatic NSCLC is an advanced stage of NSCLC (stage 4), where the cancer has spread from the lungs.<sup>12</sup> Several risk factors have been linked to lung cancer and these include; smoking, inhalation of radon, and exposure to certain chemicals and substances like arsenic, asbestos, cadmium, beryllium, coal and coke fumes, silica, and nickel.<sup>13</sup> There are usually no signs or symptoms of lung cancer in the early stages, however, symptoms develop as the condition progresses.<sup>14</sup> The following are the main symptoms of lung cancer; chest infections, long-standing cough and coughing up blood, persistent breathlessness, pain when breathing or coughing, unexplained weight loss.<sup>14</sup> About 2 in 5 people with lung cancer live for at least 1 year after they're diagnosed, and about 1 in 10 people live at least 10 years. However, survival rates vary widely, depending on how far the cancer has spread at the time of diagnosis.<sup>11</sup>

Lung cancer is one of the most frequently diagnosed cancers and the leading cause of cancer-related deaths worldwide with an estimated 2 million new cases and 1.76 million deaths per year.<sup>15</sup> In the UK, lung cancer is the third most common cancer, accounting for 13% of all new cancer cases (2016-2018).<sup>16</sup> More than 43,000 people are diagnosed with the condition yearly in the UK.<sup>11</sup> The age standardised incidence

rate for lung cancer in England is 88.4 and 67.4 per 100,000 amongst males and females respectively.<sup>16</sup> 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.<sup>17</sup> In England (2017), there were 38,888 patients diagnosed with malignant neoplasm of bronchus and lung (ICD-10 code C34) and 28,170 deaths registered where malignant neoplasm of bronchus and lung was the underlying cause.<sup>18</sup> For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year age-standardised survival rates for lung cancer were 40.6% and 16.2% respectively.<sup>19</sup>

### Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following therapies for the treatment of previously untreated metastatic NSCLC:

- Atezolizumab monotherapy<sup>20</sup>
- Atezolizumab combination therapy<sup>21</sup>
- Pembrolizumab monotherapy<sup>22</sup>
- Pembrolizumab with carboplatin and paclitaxel<sup>23</sup>
- Pembrolizumab with pemetrexed and platinum chemotherapy<sup>24</sup>
- Pemetrexed<sup>25</sup>

### Clinical Trial Information

<b>Trial</b>	<p><b>MK-7684A-007/KEYVIBE-007</b>; <a href="#">NCT05226598</a>, <a href="#">EudraCT 2021-004564-94</a>; A Randomized, Double-Blind, Phase 3 Study of MK-7684A Plus Chemotherapy Versus Pembrolizumab Plus Chemotherapy as First Line Treatment for Participants With Metastatic Non-Small Cell Lung Cancer.</p> <p><b>Phase III</b> – Active, not recruiting</p> <p><b>Location(s)</b>: Five EU countries, UK, US, and others</p> <p><b>Primary Completion date</b>: November 2025</p>
<b>Trial Design</b>	Randomised, parallel assignment, triple blinded
<b>Population</b>	N=700 (estimated); adults 18 years and older with a histologically or cytologically confirmed diagnosis of Stage IV squamous or non-squamous NSCLC, who have not received prior systemic treatment for metastatic NSCLC
<b>Intervention(s)</b>	Intravenous infusion of pembrolizumab-vibostolimab co-formulation (200mg pembrolizumab and 200mg vibostolimab) + chemotherapy
<b>Comparator(s)</b>	Intravenous infusion of pembrolizumab 200mg + chemotherapy
<b>Outcome(s)</b>	<p>Primary outcome measures:</p> <ul style="list-style-type: none"> <li>- Progression-Free Survival (PFS) [Time frame: up to approximately 33 months]</li> <li>- Overall Survival (OS) [Time frame: up to approximately 42 months]</li> </ul> <p>See trial record for a full list of other outcomes</p>
<b>Results (efficacy)</b>	-
<b>Results (safety)</b>	-

### Estimated Cost

The cost of pembrolizumab-vibostolimab is not yet known.

### 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 of issue to be confirmed
- NICE technology appraisal guidance in development. Amivantamab with lazertinib for previously untreated locally advanced or metastatic non-small-cell lung cancer. (GID-TA11279). Expected date of issue to be confirmed
- NICE technology appraisal guidance in development. Cemiplimab with chemotherapy for untreated advanced or metastatic non-small-cell lung cancer. (GID-TA10907). Expected date of issue to be confirmed
- NICE technology appraisal guidance in development. Durvalumab for untreated PD-L1-positive metastatic non-small-cell lung cancer. (GID-TA10633). Expected date of issue to be confirmed
- NICE technology appraisal guidance in development. Sugemalimab with chemotherapy for untreated metastatic non-small-cell lung cancer. (GID-TA10900). Expected date of issue 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 with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (TA683). March 2021
- NICE technology appraisal guidance. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (TA584). June 2019
- NICE technology appraisal guidance. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (TA531). July 2018
- NICE technology appraisal guidance. Pemetrexed for the first-line treatment of non-small-cell lung cancer (TA181). September 2009

#### 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

- Ettinger DS, Wood DE, Aisner DL *et al.* Non-Small Cell Lung Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. 2022.<sup>26</sup>
- Planchard D, Popat S, Kerr K, Novello S, *et al.* Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2018.<sup>27</sup>
- Scottish Intercollegiate Guideline Network (SIGN). Management of lung cancer. 2014.<sup>28</sup>
- London Cancer Alliance (LCA). Lung cancer clinical guidelines. 2013.<sup>29</sup>

### Additional Information

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