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HEALTH TECHNOLOGY BRIEFING MARCH 2021

Cemiplimab in combination with chemotherapy for advanced or metastatic non-small cell lung cancer – first-line

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Developer/Company	Sanofi	**UKPS ID**	654274

Licensing and market availability plans	Currently in phase III clinical trials

SUMMARY

Cemiplimab in combination with chemotherapy is in clinical development for the treatment of advanced or metastatic non-small cell lung cancer (NSCLC). NSCLC makes up the majority of lung cancers in the UK and at the metastatic stage (stage IV), the disease has already spread from the lungs to other sites. Symptoms of lung cancer include a persistent cough, shortness of breath, coughing up blood, aches and pains in the chest or shoulder, loss of appetite, weight loss and fatigue. Most patients with NSCLC are diagnosed at the advanced/metastatic stage where curative treatment with surgery is unsuitable. Advanced NSCLC is not usually curable; there is therefore the need for additional treatment options.

Cemiplimab is a type of protein called an antibody, which can bind to PD-1 (a protein found on immune cells) and prevent it interacting with PD-L1 (a protein, often found on tumour cells, that can bind to PD-1). Therefore, it allows the T-cells (a type of white blood cells) to attack the cancer cells. Cemiplimab is administered by intravenous infusion. If licenced, cemiplimab in combination with chemotherapy, would offer an additional treatment option for patients with advanced NSCLC regardless of PD-L1 status.

PROPOSED INDICATION

First-line therapy for adult patients with advanced or metastatic NSCLC regardless of histology or programmed death-ligand 1 (PD-L1) status (with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) aberrations).[a]

TECHNOLOGY

DESCRIPTION

Cemiplimab (Libtayo, REGN2810) is a fully human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with its ligands PD-L1 and PD-L2. Engagement of PD-1 with its ligands PD-L1 and PD-L2, which are expressed by antigen presenting cells and may be expressed by tumour cells and/or other cells in the tumour microenvironment, results in inhibition of T cell function such as proliferation, cytokine secretion, and cytotoxic activity. Cemiplimab potentiates T cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands.[1]

In a phase III study, EMPOWER 3 (NCT03409614), cemiplimab 350mg is administered every 3 weeks plus up to four cycles of chemotherapy.[2]

INNOVATION AND/OR ADVANTAGES

Most patients with NSCLC present with advanced disease at the time of diagnosis. Until recently, platinum-based doublet chemotherapy regimens were the standard of care first-line treatment for patients with advanced NSCLC whose tumours lack an EGFR, ALK, or ROS1 mutation. Despite chemotherapy, patients with metastatic NSCLC have poor overall survival.[2]

Cemiplimab has exhibited antitumour activity and safety in a phase I trial of advanced malignancies including NSCLC. Based on their unique modes of action, combining cemiplimab with platinum-based chemotherapy has the potential for a synergistic effect in patients with advanced NSCLC of both histologies and irrespective of PD-L1 expression.[2]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

In the UK/EU, cemiplimab is licensed as monotherapy for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma (mCSCC or laCSCC) who are not candidates for curative surgery or curative radiation.[1] Cemiplimab is not licensed in the UK/EU in combination.

Common or very common side effects associated with cemiplimab include: arthralgia; arthritis; asthenia; colitis; diarrhoea; hepatic disorders; hyperthyroidism; hypothyroidism; infusion related reaction; myalgia; pain; pneumonitis; skin reactions; stomatitis.[1]

Cemiplimab in combination with chemotherapy is not currently in phase II/III clinical development for any other indications.[3] As a monotherapy, cemiplimab is currently in phase III trials for cervical cancer and as adjuvant treatment in cutaneous squamous cell carcinoma.[4]

[a] Information provided by Sanofi on UK PharmaScan

PATIENT GROUP

DISEASE BACKGROUND

Lung cancer is one of the most common and serious types of cancer. There are usually no signs or symptoms in the early stages of lung cancer, but many people with the condition eventually develop symptoms such as a persistent cough, coughing up blood, persistent breathlessness, unexplained tiredness and weight loss, and/or an ache or pain when breathing or coughing.[5]

Smoking cigarettes is the single biggest risk factor for lung cancer and is responsible for more than 70% of cases. Other risk factors include passive smoking, radon (a radioactive gas), and exposure to chemicals such as arsenic, asbestos, beryllium, cadmium, coal/coke, silica and nickel.[6]

There are three main types of NSCLC:[7]

- Adenocarcinoma – starts in the mucus making gland cells in the lining of airways
- Squamous cell cancer – develops in the flat cells that cover the surface of the airways
- Large cell carcinoma – the cancer appears large and round under the microscope

In addition to being diagnosed by type of lung cancer, patients will also have the cancer graded. Grading is based on how cells look under a microscope, and gives an estimate of how quickly or slowly the cancer is growing, and whether it is likely to spread.[8] Advanced lung cancer means that the cancer has spread from where it started in the lung. It is also called metastatic cancer. Advanced cancer cannot usually be cured, but treatment can control it, help symptoms and improve quality of life.[9]

CLINICAL NEED AND BURDEN OF DISEASE

Primary lung cancer remains the most common malignancy after non-melanoma skin cancer, and deaths from lung cancer exceed those from any other malignancy worldwide.[10]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases in 2017. There are around 48,000 new lung cancer cases in the UK yearly. Incidence rates for lung cancer in the UK are highest in people aged 85 to 89 (2015-2017). Incidence rates for lung cancer are projected to fall by 7% in the UK between 2014 and 2035, to 88 cases per 100,000 people by 2035.[11]

In 2019/20 there were 111,188 hospital admissions with primary diagnosis malignant neoplasm of bronchus and lung (ICD-10 code C34), and 132,969 finished consultant episodes (FCEs), resulting in 243,883 FCE bed days.[12] According to the National Cancer Registration and Analysis Service (NCRAS), there were 18,213 diagnosed cases of stage IV lung cancer in 2017, this represents 47% of the overall number of lung cancer cases diagnosed for that year.[13] In the UK it is estimated that up to 85% of lung cancer cases are NSCLC, applying this figure to the number of stage IV lung cancer cases diagnosed in 2017, it can be estimated that approximately 15,481 cases diagnosed with stage IV in 2017 were NSCLC.[7]

In England between 2013 and 2017, the age-standardised net lung cancer survival for stage IV was 19.3% at one year and 2.9% at five years.[14] There are around 35,100 lung cancer deaths in the UK every year (based on data from 2016-2018). Mortality rates for lung cancer are projected to fall by 21% in the UK between 2014 and 2035.[15] In England and Wales in 2019 there were 29,463 deaths with malignant neoplasm of bronchus and lung (ICD-10 codes C34) recorded as the underlying cause.[16]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Treatment of NSCLC depends on the stage of the cancer and the general health of the patient. The main treatment options for stage I, II and III NSCLC are surgery, chemotherapy and radiotherapy. At advanced stage III disease, where patients are not candidates for surgical resection or definitive chemoradiation and stage IV metastatic disease, treatment aims to control the cancer for as long as possible and help with symptoms. Treatment generally include chemotherapy, targeted drugs, radiotherapy and symptom control treatment.[17]

CURRENT TREATMENT OPTIONS

Current first-line treatment for adults with advanced non-squamous NSCLC with PD-L1 under 50% are:[18]

- Atezolizumab combination
- Pembrolizumab with pemetrexed and platinum chemotherapy
- Pemetrexed with cisplatin

Current first-line treatment for adults with advanced non-squamous NSCLC with PD-L1 over 50% are:[19]

- Pembrolizumab
- Pembrolizumab with pemetrexed and platinum chemotherapy

Current first-line treatment for adults with advanced squamous NSCLC with PD-L1 under 50% are:[20]

- Pembrolizumab with carboplatin and paclitaxel

Current first-line treatment for adults with advanced squamous NSCLC with PD-L1 over 50% are:[21]

- Pembrolizumab
- Pembrolizumab with carboplatin and paclitaxel

PLACE OF TECHNOLOGY

If licensed, cemiplimab in combination with chemotherapy will offer an additional first-line treatment for patients with advanced or metastatic NSCLC, irrespective of their PD-L1 status.

CLINICAL TRIAL INFORMATION

Trial	**EMPOWER-LUNG 3;** NCT03409614; 2017-001311-36; A Two-Part Randomised, Phase 3 Study of Combinations of Cemiplimab (Anti-PD-1 Antibody) and Platinum-based Doublet Chemotherapy in First-line Treatment of Patients With Advanced or Metastatic Non-Small Cell Lung Cancer **Phase III** – active, not recruiting **Location(s):** US, EU (incl. UK), China, Thailand, Republic of Korea and Malaysia **Primary completion date:** May 2023
Trial design	Randomised, placebo controlled.
Population	N = 790; 18 years and older; patients with histologically or cytologically documented squamous or non-squamous NSCLC with stage IIIB or IIIC disease who are not candidates for treatment with definitive concurrent chemoradiation or

	patients with stage IV disease if they have not received prior systemic treatment for recurrent or metastatic NSCLC
Intervention(s)	Cemiplimab + platinum-based doublet chemotherapy – intravenous injection (IV) – 35mg plus up to 4 cycles of chemotherapy[2]
Comparator(s)	• Platinum-based doublet chemotherapy (IV) • Platinum-based doublet chemotherapy + placebo (IV)
Outcome(s)	Overall survival] and Progression Free Survival See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

ESTIMATED COST

The estimated cost of cemiplimab 350mg/7ml is £4650.00.[22]

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (TA600). September 2019.
- NICE technology appraisal. Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (TA557). January 2019.
- NICE technology appraisal. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (TA531). July 2018.
- NICE technology appraisal. Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (TA428). January 2017.
- NICE technology appraisal. Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (TA192). July 2010.
- NICE technology appraisal. Pemetrexed for the first-line treatment of non-small-cell lung cancer (TA181). September 2009.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.
- NICE quality standard. Lung cancer in adults (QS17). March 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

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- European Society for Medical Oncology. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2016.[10]

- European Society for Medical Oncology. ESMO Consensus Guidelines: Non-small-cell lung cancer first-line/second and further lines in advanced disease. 2014.[24]
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ADDITIONAL INFORMATION

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