

## HEALTH TECHNOLOGY BRIEFING OCTOBER 2020

### Durvalumab in addition to platinum based chemoradiation therapy for treating non-small-cell lung cancer.

<b>NIHRIO ID</b>	24204	<b>NICE ID</b>	10297
<b>Developer/Company</b>	AstraZeneca UK Ltd	<b>UKPS ID</b>	659009

#### Licensing and market availability plans

Currently in phase III clinical trials.

### SUMMARY

Durvalumab in addition to platinum-based chemoradiation therapy (CRT) is in development for patients with unresectable, locally advanced non-small cell lung cancer (NSCLC). Locally advanced (stage III) lung cancer refers to when the cancer has spread to lymph nodes and tissues near the lung that was initially affected but not to other areas of the body. The prognosis for unresectable, stage III NSCLC remains poor so there is a need for additional treatment options to improve overall survival rates.

Durvalumab is given by intravenous infusion and works by blocking an immune protein called programmed cell death ligand-1 (PD-L1). PD-L1 expression enables cancer cells to avoid recognition by the immune system. By blocking PD-L1, durvalumab allows the immune system to recognise and target the cancer cells. Addition of durvalumab to the current CRT treatment is thought to be more effective and improve overall survival rates compared to CRT alone. If licenced, durvalumab in addition to CRT may provide an additional treatment option for patients with unresectable, locally advanced NSCLC.

*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 unavailable to comment.*

## PROPOSED INDICATION

First line treatment of patients with locally advanced, unresectable stage III non-small cell lung cancer (NSCLC).<sup>1</sup>

## TECHNOLOGY

### DESCRIPTION

Durvalumab (Imfinzi, MEDI4736) is an Fc optimized monoclonal antibody directed against programmed cell death-1 ligand 1 (PD-L1), with potential immune checkpoint inhibitory and antineoplastic activities. Upon intravenous administration, durvalumab binds to PD-L1, thereby blocking its binding to and activation of its receptor programmed death (PD-1) expressed on activated T cells. This may reverse T-cell inactivation and activate the immune system to exert a cytotoxic T-lymphocyte (CTL) response against PD-L1- expressing tumour cells. PD-L1, a member of the B7 protein superfamily, is overexpressed on certain tumour cell types and on various tumour-infiltrating immune cells. PD-L1 binding to PD-1 on T cells suppresses the immune system and results in increased immune evasion. The Fc region of durvalumab is modified in such a way that it does not induce either antibody-dependent cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC).<sup>2,3</sup>

Durvalumab in addition to platinum-based chemoradiation is in clinical development for the treatment of locally advanced, unresectable stage III NSCLC. In the phase III trial PACIFIC2 (NCT03519971), participants are given durvalumab by intravenous infusion in concurrence with platinum-based chemoradiation therapy (CRT) which consists of 5 radiation fractions per week for around 6 weeks ( $\pm 3$  days) in addition to one of the following standard of care platinum-based chemotherapy options; cisplatin/etoposide, carboplatin/paclitaxel, pemetrexed/cisplatin or pemetrexed/carboplatin.<sup>1</sup>

### INNOVATION AND/OR ADVANTAGES

The prognosis for unresectable stage III NSCLC remains poor, with five-year overall survival rates of approximately 15%.<sup>4</sup> There is an unmet need for treatment options for locally advanced unresectable NSCLC.<sup>5</sup>

Results from the phase III PACIFIC study showed that when durvalumab was given 1-42 days after completion of definitive concurrent CRT there was significantly improved progression-free survival compared to placebo. Increasing evidence suggests additional benefit when anti-PD-1/PD-L1 therapies are administered alongside concurrent CRT.<sup>6</sup>

### DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Durvalumab as a monotherapy is licensed in the EU/UK for the treatment of locally advanced, unresectable NSCLC in adults whose tumours express PD-L1 on  $\geq 1\%$  of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy.<sup>7</sup>

Very common ( $\geq 10\%$ ) side effects of durvalumab monotherapy include: upper respiratory tract infections, hypothyroidism, cough/productive cough; diarrhoea; abdominal pain; rash; pruritus and pyrexia.<sup>7</sup>

Durvalumab is currently in 366 phase II/III studies for several oncology indications such as:<sup>8</sup>

- Hepatocellular carcinoma
- Non-invasive muscle bladder cancer
- Squamous cell carcinoma of the head and neck
- Solid tumours
- NSCLC stage IV
- Pancreatic cancer

## PATIENT GROUP

### DISEASE BACKGROUND

Lung cancer is classified into two main types: small-cell lung cancer (SCLC) or NSCLC. NSCLC comprises approximately 80 to 85% of lung cancers in the UK. There are three common types of NSCLC; adenocarcinoma (the most common type which starts in the mucus making glands lining of the airways), squamous cell cancer (develops in the flat cells that cover the surface of the airways and tends to grow near the centre of the lung) and large cell carcinoma (cancer cells which appear large and round under the microscope).<sup>9</sup> The stage of a cancer refers to how large it is and whether it has spread. Stage III NSCLC is referred to as locally advanced disease. Stage III has two subtypes; if the cancer has spread only to lymph nodes on the same side of the chest where the cancer started it is stage IIIA, if the cancer has spread to the lymph nodes on the opposite side of the chest or above the collar bone, it is called stage IIIB.<sup>10</sup> Unresectable NSCLC cannot be removed by surgery.<sup>11</sup>

Symptoms of lung cancer include a persistent cough that doesn't go away after 2 or 3 weeks, chest infections that keep coming back, coughing up blood, an ache or pain when breathing or coughing, persistent breathlessness, persistent tiredness or lack of energy, loss of appetite or unexplained weight loss.<sup>12</sup>

A person's risk of developing lung cancer depends on many factors including age, genetics and exposure to risk factors. The greatest risk factor is long-term tobacco smoking, which increases a person's risk of developing lung cancer 25-fold. Other risk factors include exposure to air pollution, radon, asbestos, certain metals and chemicals, or second hand smoke; long-term use of hormone replacement therapy for menopause; and a history of lung diseases such as tuberculosis, emphysema, or chronic bronchitis. A history of lung cancer in closely related family members is also an important risk factor; however, it is unclear whether the increased risk is the result of genetic factors or exposure to second-hand smoke.<sup>13</sup>

### CLINICAL NEED AND BURDEN OF DISEASE

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.<sup>14</sup>

In 2019/20 there were 111,188 hospital admissions with a primary diagnosis malignant neoplasm of bronchus and lung (ICD-10 code C34) resulting in 132,969 finished consultant episodes (FCEs) and 243,883 FCE bed days.<sup>15</sup> According to the National Cancer Registration and Analysis Service (NCRAS) there were 7,564 diagnosed cases of stage III lung cancer in 2017. In the UK it is estimated that 85% of lung cancers are NSCLC, applying this figure to

the number of stage III lung cancer cases diagnosed in 2017, it can be estimated that approximately 6,429 were stage III NSCLC.<sup>9,16</sup>

Survival rates for lung cancer depend on the stage at which the cancer is identified.<sup>17</sup> In England, between 2013 and 2017, the age-standardised net lung cancer survival for stage III was 48.7% at one year and 2.9% at five years.<sup>18</sup> Lung cancer survival has not shown much improvement in the last 40 years in the UK. Lung cancer survival is correlated with age; almost half of people in England diagnosed with lung cancer aged 15-39 survive their disease for five years or more compared with 5 in 100 people diagnosed aged 80 and over (2009-2013).<sup>17</sup> In England and Wales in 2017 there were 30,131 deaths with malignant neoplasm of bronchus and lung (ICD-10 codes C34) recorded as the underlying cause.<sup>19</sup>

## PATIENT TREATMENT PATHWAY

### TREATMENT PATHWAY

Treatment for lung cancer is managed by multidisciplinary team who consist of specialists from different departments to provide the best treatment.<sup>20,21</sup> Treatment of NSCLC depends on where the cancer is, how far it has grown or spread (the stage), how abnormal the cells look under a microscope (the grade) and the general health and level of fitness of the patient. Possible treatment options for stage III NSCLC include; chemoradiotherapy followed by surgery, surgery followed by chemotherapy, chemoradiotherapy followed by immunotherapy or a targeted cancer drug.<sup>21</sup>

### CURRENT TREATMENT OPTIONS

The only treatment option currently recommended by NICE for patients with unresectable, locally advanced NSCLC is giving durvalumab following platinum based chemoradiation therapy.<sup>5</sup>

### PLACE OF TECHNOLOGY

If licenced, durvalumab in combination with platinum based chemoradiation therapy will offer an additional first line treatment option for patients with unresectable stage III NSCLC.<sup>1</sup>

## CLINICAL TRIAL INFORMATION

<b>Trial</b>	<b>PACIFIC2, <a href="#">NCT03519971</a></b> ; A phase III, Randomized, Placebo-controlled, Double-blind, Multi-center, International Study of Durvalumab Given Concurrently with Platinum-based Chemoradiation Therapy in Patients With Locally Advanced, Unresectable NSCLC (Stage III) <b>Phase III</b> – Active, not recruiting <b>Location(s)</b> : 3 EU countries (not incl UK) and other countries <b>Primary completion date</b> : August 2021
<b>Trial design</b>	Randomised, placebo-controlled, double-blind, parallel assignment

<b>Population</b>	N=328; adults aged 18 years to 130 years; histologically or cytologically documented NSCLC; locally advanced, unresectable (Stage III)
<b>Intervention(s)</b>	Durvalumab (intravenous infusion) in addition to radiation therapy and one of the following platinum-based standard of care chemotherapy options: <ul style="list-style-type: none"> <li>- cisplatin/etoposide</li> <li>- carboplatin/paclitaxel</li> <li>- pemetrexed/cisplatin</li> <li>- pemetrexed/carboplatin</li> </ul>
<b>Comparator(s)</b>	Placebo (intravenous infusion) in addition to radiation therapy and one of the following platinum-based standard of care chemotherapy options: <ul style="list-style-type: none"> <li>- cisplatin/etoposide</li> <li>- carboplatin/paclitaxel</li> <li>- pemetrexed/cisplatin</li> <li>- pemetrexed/carboplatin</li> </ul>
<b>Outcome(s)</b>	Primary outcome measure: <ul style="list-style-type: none"> <li>• Progression-free survival (PFS) [ Time Frame: From date of randomisation until the date of objective disease progression or death assessed, up to 4 years]</li> </ul> <p>See trial record for full list of outcomes</p>
<b>Results (efficacy)</b>	-
<b>Results (safety)</b>	-

## ESTIMATED COST

1 vial of durvalumab 120mg/2.4ml concentrate for solution for infusion costs £592.  
1 vial of durvalumab 500mg/10ml concentrate for solution for infusion costs £2466.00.<sup>22</sup>

## RELEVANT GUIDANCE

### NICE GUIDANCE

- NICE technology appraisal. Durvalumab for treating locally advanced unresectable non-small-cell lung cancer after platinum-based chemoradiation (TA578). May 2019.
- 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: Radiotherapy (All Ages). B01/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

## OTHER GUIDANCE

- European Society of Medical Oncology (ESMO). Pan-Asian adapted ESMO Clinical Practice Guidelines for the Management of Patients with Locally-Advanced Unresectable Non-Small-Cell Lung Cancer. 2020.<sup>23</sup>
- National Comprehensive Cancer Network (NCCN). Non-Small Cell Lung Cancer, Version 5.2017, NCCN Clinical Practice Guidelines in Oncology. 2017.<sup>24</sup>
- Scottish Intercollegiate Guidelines Network. Management of lung cancer (SIGN 137). 2014.<sup>25</sup>

## ADDITIONAL INFORMATION

## REFERENCES

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