

# Health Technology Briefing

## January 2022

### Durvalumab for limited stage small-cell lung cancer after 1 therapy

Company/Developer

AstraZeneca UK Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 33506

NICE ID: 10743

UKPS ID: 663173

#### Licensing and Market Availability Plans

Currently in phase III clinical trials

#### Summary

Durvalumab is in clinical development for the treatment of adults with limited stage small-cell lung cancer (LS-SCLC) whose cancer has not worsened since receiving concurrent chemoradiation therapy (cCRT). SCLC is a form of lung cancer characterised by the appearance of the tumour cells under a microscope. Limited stage SCLC occurs when the cancer is only seen on one side of the chest and is small in size. Symptoms may include cough, difficulty breathing chest pain, hoarseness, fatigue and weight loss. LS-SCLC treatment, which includes cCRT and preventative radiotherapy of the brain, is an area of unmet need and the standard of care has not changed in decades.

Durvalumab is a type of protein (monoclonal antibody) administered by intravenous (IV) infusion to increase the ability of the immune system to kill cancer cells. Durvalumab is currently used to treat extensive stage SCLC and a different form of lung cancer known as non-small cell lung cancer (NSCLC). If licensed, durvalumab could provide a further treatment option for LS-SCLC patients whose disease has not worsened following cCRT.

## Proposed Indication

Treatment of adults with LS-SCLC who have not progressed following cCRT<sup>1</sup>

## Technology

### Description

Durvalumab (Imfinzi) is a fully human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that selectively blocks the interaction of programmed cell death ligand-1 (PD-L1) with PD-1 and CD80. Expression of PD-L1 protein is an adaptive immune response that helps tumours evade detection by the immune system. Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation.<sup>2</sup>

Durvalumab is currently in phase III clinical development for the treatment of adults with LS-SCLC who have not progressed following cCRT. In the phase III clinical trial (ADRIATIC, NCT03703297) patients were administered durvalumab 1500mg via intravenous (IV) infusion in combination with placebo saline solution via IV infusion once every 4 weeks for up to 4 doses/cycles. Patients were then administered monotherapy durvalumab, or in combination with tremelimumab (75mg), 1500mg via IV infusion once every 4 weeks, 4 weeks after initial dosing.<sup>1</sup>

### Key Innovation

Durvalumab already has a Marketing Authorisation in the UK for the treatment of extensive stage small-cell lung cancer (ES-SCLC).<sup>2</sup> It has also shown positive treatment outcomes in the treatment of NSCLC following cCRT. LS-SCLC is an area of unmet need where standard of care treatment, which includes cCRT and prophylactic brain irradiation, has not changed for several decades. Treatment outcomes for LS-SCLC are poor. If approved, durvalumab may offer a novel treatment approach for LS-SCLC patients following cCRT.<sup>3</sup>

### Regulatory & Development Status

Durvalumab has a Marketing Authorisation in the UK for the monotherapy 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 and in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with ES-SCLC.<sup>2</sup>

Durvalumab as a monotherapy and in addition to various other medicinal products is being developed for numerous indications in phase II and phase III clinical trials, including bladder, cervical and renal cancers.<sup>4</sup>

## Patient Group

### Disease Area and Clinical Need

SCLC is a form of lung cancer in which malignant cells form in the lung which appear small when viewed under a microscope. SCLC may be small cell carcinomas or combined small cell carcinomas.<sup>5</sup> The most common SCLC symptoms may include cough, dyspnoea, chest pain, hoarseness, fatigue and weight loss.<sup>6</sup> LS-SCLC occurs when the cancer is only present one side of the chest and is small enough to be treated with a single port of radiation therapy.<sup>7</sup> The major risk factor associated with SCLC is smoking.<sup>5</sup>

Approximately 15% of lung cancers diagnosed are SCLC.<sup>8</sup> In 2016-18, there were an average of 48,549 cases of lung cancer each year in the UK.<sup>9</sup> It can therefore be estimated that on average there are approximately 7,282 cases of SCLC diagnosed yearly in the UK. In England in 2020-21 there were 86,043 hospital admissions for malignant neoplasm of bronchus and lung (ICD10 C34).<sup>10</sup> The 5 year overall survival rate for SCLC patients is less than 10%.<sup>11</sup>

### Recommended Treatment Options

The only treatment recommended by NICE for second line treatment of SCLC is topotecan. Topotecan is recommended in patients for whom re-treatment with the first line chemotherapy regimen is not appropriate and the combination of cyclophosphamide, doxorubicin and vincristine (CAV) is contraindicated.<sup>12</sup>

### Clinical Trial Information

<b>Trial</b>	<b>ADRIATIC, <a href="#">NCT03703297, 2018-000867-10</a></b> ; A Phase III, Randomized, Double-blind, Placebo-controlled, Multi-center, International Study of Durvalumab or Durvalumab and Tremelimumab as Consolidation Treatment for Patients With Limited Stage Small Cell Lung Cancer Who Have Not Progressed Following Concurrent Chemoradiation Therapy (ADRIATIC) <b>Phase III</b> – Active, not recruiting <b>Locations:</b> EU, UK, USA, Canada and other countries <b>Primary completion date:</b> May 2024
<b>Trial Design</b>	Randomised, parallel assignment, triple masking
<b>Population</b>	N=728; adults aged 18 years and older with LS-SCLC (stage I-III); received 4 cycles of cCRT
<b>Intervention(s)</b>	Durvalumab (IV) + placebo (IV) – participants received durvalumab 1500mg/m <sup>2</sup> once every 4 weeks in combination with placebo saline solution for up to 4 cycles, followed by durvalumab 1500mg/m <sup>2</sup> monotherapy 4 weeks following the combination therapy  Durvalumab (IV) + tremelimumab (IV) – participants received durvalumab 1500mg/m <sup>2</sup> and tremelimumab 75mg once every 4 weeks for up to 4 cycles, followed by durvalumab 1500mg/m <sup>2</sup> monotherapy 4 weeks following the combination therapy
<b>Comparator(s)</b>	Placebo (IV) – participants received two consecutive placebo saline solutions once every 4 weeks for up to 4 cycles followed by a single placebo saline solution 4 weeks following the combination therapy
<b>Outcome(s)</b>	<b>Primary outcome measures:</b>  Progression-free survival (PFS) [Time frame: approximately 4 years]  Overall survival (OS) [Time frame: approximately 6 years]  See trial record for a full list of other outcomes
<b>Results (efficacy)</b>	-

Results (safety)

-

### Estimated Cost

Durvalumab is already marketed in the UK for various indications; a 120mg/2.4ml concentrate for solution for infusion vial costs £592.00 and a 500mg/10ml concentrate for solution for infusion vial costs £2466.00.<sup>13</sup>

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal. Topotecan for the treatment of relapsed small-cell lung cancer (TA184). November 2009.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.

#### NHS England (Policy/Commissioning) Guidance

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

#### Other Guidance

- Ganti AKP, Loo Jr BW, Bassetti M, Blakely C, Chiang A et al. Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. 2021.<sup>14</sup>
- Dingemans AMC, Fruh M, Ardizzoni A, Besse B, Faivre-Finn C et al. Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2021.<sup>11</sup>
- Simone II CB, Bogart JA, Cabrera AR, Daly ME, DeNunzio NJ et al. Radiation Therapy for Small Cell Lung Cancer: An ASTRO Clinical Practice Guideline. 2020.<sup>15</sup>
- Scottish Intercollegiate Guidelines Network. SIGN 137 – Management of lung cancer. 2014.<sup>16</sup>

### Additional Information

### References

- 1 Clinicaltrials.gov. *Study of Durvalumab + Tremelimumab, Durvalumab, and Placebo in Limited Stage Small-Cell Lung Cancer in Patients Who Have Not Progressed Following Concurrent Chemoradiation Therapy (ADRIATIC)*. Trial ID: NCT03703297. 2018. Status: Active, not recruiting. Available from: <https://clinicaltrials.gov/ct2/show/NCT03703297?term=NCT03703297&draw=2&rank=1> [Accessed 10 December 2021].
- 2 Electronic Medicines Compendium (emc). *Imfinzi 50 mg/mL concentrate for solution for infusion*. 2021. Available from: <https://www.medicines.org.uk/emc/product/9495> [Accessed 10 December 2021].
- 3 Senan S, Shire N, Mak G, Yao W, Jiang H. ADRIATIC: A phase III trial of durvalumab &#xb1; tremelimumab after concurrent chemoradiation for patients with limited stage small cell

- lung cancer. *Annals of Oncology*. 2019;30:ii25. Available from: <https://doi.org/10.1093/annonc/mdz071.007>.
- 4 Clinicaltrials.gov. *Durvalumab - Phase II and III clinical trials*. 2021. Available from: [https://clinicaltrials.gov/ct2/results?cond=&term=Durvalumab&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age\\_v=&gndr=&intr=&titles=&outc=&spons=AstraZeneca&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd\\_s=&strd\\_e=&prcd\\_s=&prcd\\_e=&sfpd\\_s=&sfpd\\_e=&rfpd\\_s=&rfpd\\_e=&lupd\\_s=&lupd\\_e=&sort=](https://clinicaltrials.gov/ct2/results?cond=&term=Durvalumab&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=&titles=&outc=&spons=AstraZeneca&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=) [Accessed 10 December 2021].
- 5 National Cancer Institute. *Small Cell Lung Cancer Treatment (PDQ®)–Patient Version*. 2021. Available from: <https://www.cancer.gov/types/lung/patient/small-cell-lung-treatment-pdq> [Accessed 10 December 2021].
- 6 National Cancer Institute. *Small Cell Lung Cancer Treatment (PDQ®)–Health Professional Version*. 2021. Available from: <https://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq> [Accessed 10 December 2021].
- 7 American Cancer Society. *Small Cell Lung Cancer Stages*. 2019. Available from: <https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/staging-sclc.html> [Accessed 10 December 2021].
- 8 Macmillan Cancer Support. *Small cell lung cancer (SCLC)*. 2021. Available from: <https://www.macmillan.org.uk/cancer-information-and-support/lung-cancer/small-cell-lung-cancer> [Accessed 14 December 2021].
- 9 Cancer Research UK. *Lung cancer statistics*. 2021. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer> [Accessed 14 December 2021].
- 10 Digital N. *Hospital Admitted Patient Care Activity 2020-21*. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21> [Downloaded 13 October 2021].
- 11 Dingemans AMC, Früh M, Ardizzone A, Besse B, Faivre-Finn C, Hendriks LE, et al. Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2021;32(7):839-53. Available from: <https://doi.org/10.1016/j.annonc.2021.03.207>.
- 12 National Institute for Health and Care Excellence. *NICE pathways: Treating small-cell lung cancer: Subsequent treatment*. 2021. Available from: <https://pathways.nice.org.uk/pathways/lung-cancer/lung-cancer-overview#content=view-node%3Anodes-subsequent-treatment&path=view%3A/pathways/lung-cancer/treating-small-cell-lung-cancer.xml> [Accessed 14 December 2021].
- 13 National Institute for Health and Care Excellence. *BNF: Medicinal forms: Durvalumab*. 2021. Available from: <https://bnf.nice.org.uk/medicinal-forms/durvalumab.html> [Accessed 14 December 2021].
- 14 Ganti AKP, Loo BW, Bassetti M, Blakely C, Chiang A, D'Amico TA, et al. Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*. 2021 01 Dec. 2021;19(12):1441-64. Available from: <https://doi.org/10.6004/jnccn.2021.0058>.
- 15 Simone CB, II, Bogart JA, Cabrera AR, Daly ME, DeNunzio NJ, Detterbeck F, et al. Radiation Therapy for Small Cell Lung Cancer: An ASTRO Clinical Practice Guideline. *Practical Radiation Oncology*. 2020;10(3):158-73. Available from: <https://doi.org/10.1016/j.prr.2020.02.009>.
- 16 Scottish Intercollegiate Guidelines Network. *SIGN 137 - Management of lung cancer*. 2014. Available from: <https://www.sign.ac.uk/media/1075/sign137.pdf> [Accessed 14 December 2021].

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