# Health Technology Briefing
# December 2023

# Cobolimab with dostarlimab and docetaxel for advanced non-small-cell lung cancer after anti-PD-L1 therapy and chemotherapy

| Company/Developer | GlaxoSmithKline UK Ltd |
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☒ New Active Substance ☐ Significant Licence Extension (SLE)

| NIHRIO ID: 30985 | NICE ID: Not available | UKPS ID: 667618 |
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## Licensing and Market Availability Plans

Currently in phase II/III clinical trials

## Summary

Cobolimab in combination with dostarlimab and docetaxel is in clinical development for the treatment of advanced non-small cell lung cancer (NSCLC) in patients who have progressed on prior treatment with anti-PD-L1 therapy and chemotherapy. NSCLC is the most common type of lung cancer. Symptoms include a cough, repeated chest infections, breathlessness, unexplained pain, weight loss or tiredness. Cobolimab and dostarlimab combined has the potential to improve anti-tumour immunity.

Cobolimab is a monoclonal antibody, a type of immunotherapy, that is delivered intravenously. It works by blocking mucin domain-containing protein 3 (TIM-3) which is a protein found on multiple immune cells that causes suppression of antitumour response. Blocking TIM-3 enhances antitumour activity and reduces tumour growth. Dostarlimab is another monoclonal antibody immunotherapy that is administered intravenously. It works by blocking a protein called programmed death receptor-1 (PD-1) on certain cells of the immune system thereby increasing the immune system's ability to kill the cancer cells. It has been found that targeting TIM-3 and PD-1 together is more effective in reducing tumour growth than targeting either of them alone. Docetaxel is a chemotherapy that is used to treat different types of cancers. It is administered intravenously, and it works by preventing cancer cells from growing by preventing cell division. If licensed, cobolimab in combination with dostarlimab and docetaxel may provide an additional treatment option for patients with NSCLC who have progressed on prior treatment with anti-PD-L1 therapy and chemotherapy.

## Proposed Indication

Treatment of advanced NSCLC in patients who have progressed on prior treatment with anti-PD-(L)1 therapy and chemotherapy.[1]

## Technology

### Description

Cobolimab is a monoclonal antibody against the inhibitory T-cell receptor, T-cell immunoglobulin and mucin domain-containing protein 3 (TIM-3), with potential immune checkpoint inhibitory and antineoplastic activities.[2]

Dostarlimab (Jemperli) is a monoclonal antibody, a protein that has been designed to block programmed death receptor-1 (PD-1) on certain cells of the immune system. Some cancers can make PD-1 ligands (PD-L1 and PD-L2), proteins that combine with PD-1 to switch off the activity of the immune cells, preventing them from attacking the cancer. By blocking PD-1, dostarlimab stops the cancer switching off these immune cells, thereby increasing the immune system's ability to kill the cancer cells.[3]

Docetaxel is a standard of care that belongs to the group of cancer medicines known as taxanes. It is commonly used to treat several types of cancers. Docetaxel blocks the ability of cells to break down the internal 'skeleton' that allows them to divide. With the skeleton still in place, the cells cannot divide, and they eventually die. Because docetaxel works on dividing cells, it also affects non-cancer cells such as blood cells, which can cause side effects.[4]

The COSTAR Lung clinical trial (NCT04655976) evaluates the efficacy and safety of cobolimab (300 mg IV) plus dostarlimab (500 mg IV) and docetaxel (75 mg/m$^2$ IV) every 3 weeks (Arm A) to dostarlimab plus docetaxel (Arm B) to docetaxel alone (Arm C), in adult patients who have received ≤2 prior lines of therapy that include an anti-PD-1/PD-L1 therapy plus platinum-based chemotherapy only. Cobolimab and dostarlimab treatment will continue until disease progression, unacceptable toxicity, patient withdrawal, investigator's decision, or death. Docetaxel treatment will continue for ≥4 cycles or until unacceptable toxicity or disease progression.[1,5]

### Key Innovation

Immunotherapy is one of the leading treatments in NSCLC patients, but it is not effective in a proportion of patients due to primary or secondary resistance mechanisms which are difficult to predict. One scientific concept is to avoid resistance or to provide salvage second-line treatments in the form of dual immunologic checkpoint blockade so immunotherapy not only blocks a single molecule with specific antibodies but acts on two different immune checkpoint targets.[6] TIM-3 has been implicated in resistance to immunotherapy and inhibition of TIM-3 using novel checkpoint inhibitors including anti-TIM-3 monoclonal antibodies such as cobolimab have shown a safe toxicity profile and may alleviate treatment resistance potentially leading to better outcomes.[7] If licenced, cobolimab in combination with dostarlimab and docetaxel will offer an additional treatment option of NSCLC patients whose cancer has progressed following anti-PD-(L)1 therapy and chemotherapy.

### Regulatory & Development Status

Cobolimab does not currently have marketing authorisation in the UK for any indication.

Dostarlimab currently has Marketing Authorisation in the UK as a:[8]

- Combination treatment with platinum-containing chemotherapy for adults with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy.
- Monotherapy for adults with dMMR/ MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen.

Dostarlimab is currently in phase II/III clinical development for the treatment of:[9]

- Rectal cancer
- Colon cancer
- Endometrial cancer
- Ovarian cancer
- Melanoma
- Head and neck cancer
- Penile carcinoma
- Breast cancer

## Patient Group

### Disease Area and Clinical Need

NSCLC is the most common form of lung cancer in the UK with subtypes that can be defined as adenocarcinoma (non-squamous), squamous cell carcinoma and large cell carcinoma.[10] Metastatic NSCLC (stage 4) is when the cancer spreads to other parts of the body such as the bones, lungs, brain, liver or adrenal glands.[11,12] Locally advanced NSCLC (Stage 3) is cancer that has spread into tissues around the lungs.[13] The most common symptoms of lung cancer include cough, breathlessness, coughing up phlegm with blood, pain in the chest or shoulder, recurrent chest infections, loss of appetite, weight loss and fatigue.[14]

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (2016-18).[15] In England (2022-23), there were 122,866 finished consultant episodes (FCEs) and 104,232 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34), which resulted in 80,131 day cases and 217,569 FCE bed days.[16] There were 38,888 patients diagnosed with malignant neoplasm of bronchus and lung, 28,170 deaths registered with malignant neoplasm of bronchus and lung being the underlying cause in England (2017).[17] In 2013-2017 in England, the 1 year survival rate for all stages of lung cancer was 40.6%, with 19.3% for stage 4. The 5 year survival rate for all stages of lung cancer was 16.2%, and for stage 4 was 2.9%.[18]

### Recommended Treatment Options

NICE recommended treatments for advanced NSCLC following treatment with anti-PD1 therapy with no targetable mutations include:[19]

- Docetaxel as a monotherapy for patients with squamous NSCLC and PD-L1 <50%.
- Docetaxel as a monotherapy for patients with squamous NSCLC and PD-L1 ≥50%.
- Docetaxel as a monotherapy for patients with non-squamous NSCLC and PD-L1 <50%.
- Docetaxel as a monotherapy for patients with non-squamous NSCLC and PD-L1 ≥50%.
- Docetaxel in combination with nintedanib for patients with non-squamous NSCLC and PD-L1 <50%.
- Docetaxel in combination with nintedanib for patients with non-squamous NSCLC and PD-L1 ≥50%.

## Clinical Trial Information

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| Trial | **COSTAR Lung, NCT04655976, 2020-003433-37;** A Randomized, Open Label Phase 2/3 Study Comparing Cobolimab + Dostarlimab + Docetaxel To Dostarlimab + Docetaxel To Docetaxel Alone In Participants With Advanced Non-Small Cell Lung Cancer Who Have Progressed On Prior Anti-PD-(L)1 Therapy And Chemotherapy (COSTAR Lung)<br>**Phase II/III** – Active, not recruiting<br>**Location(s) –** 8 EU countries and UK, USA, Canada and other countries<br>**Primary completion date:** October 2024 |
| Trial Design | Randomised, parallel assignment (2:2:1), open label |
| Population | N=758 (actual); Participants with advanced non-small cell lung cancer (NSCLC) who have progressed on prior anti-PD-L1 therapy and chemotherapy; aged 18 years and over |
| Intervention(s) | Arm A: Cobolimab plus dostarlimab plus docetaxel<br><br>Arm B: Dostarlimab plus docetaxel |
| Comparator(s) | Arm C: Docetaxel |
| Outcome(s) | Primary outcomes:<br>- Overall survival in participants receiving cobolimab + dostarlimab + docetaxel relative to participants receiving docetaxel alone [Time frame: up to 44 months]<br>- Overall survival in participants receiving dostarlimab + docetaxel relative to participants receiving docetaxel alone [Time frame: up to 44 months]<br><br>See trial record for full list of other outcomes |
| Results (efficacy) | - |
| Results (safety) | - |

## Estimated Cost

The cost of cobolimab is not yet known.
The NHS indicative cost of one vial of dostarlimab (50mg/1ml) is £5,887.33.[20]

## Relevant Guidance

### NICE Guidance

- NICE technology appraisal awaiting development. Tarlatamab for treating advanced small-cell lung cancer after 2 or more treatments [ID11925]. Expected date of issue to be confirmed.
- NICE technology appraisal awaiting development. Plinabulin with docetaxel for previously treated advanced non-small-cell lung cancer [ID3895]. Expected date of issue to be confirmed.
- NICE technology appraisal awaiting development. Datopotamab deruxtecan for treating advanced non-small-cell lung cancer after platinum-based chemotherapy [TS ID 11840]. Expected date of issue to be confirmed.

- NICE technology appraisal awaiting development. Sacituzumab govitecan for treating advanced non-small-cell lung cancer after platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor [TS ID 11931]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Lurbinectedin for treating advanced small-cell lung cancer on or after platinum-based chemotherapy [ID3872]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Pembrolizumab with ipilimumab for treating PD-L1-positive advanced non-small-cell lung cancer [ID3861]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Lung cancer (non-small-cell, advanced or metastatic second line) - erlotinib (in combination with bevacizumab) [ID43]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tislelizumab for treating advanced non-small-cell lung cancer after platinum-based chemotherapy [ID6161]. Expected date of issue to be confirmed.
- NICE technology appraisal. Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy [TA713]. July 2021.
- NICE technology appraisal. Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy [TA655]. October 2020.
- NICE technology appraisal. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer [TA403]. August 2016.
- NICE technology appraisal. Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy [TA374]. December 2015.
- NICE technology appraisal. Pemetrexed for the treatment of non-small-cell lung cancer [TA124]. August 2007.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2023.
- NICE quality standard. Lung cancer in adults (QS17). December 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

- National Comprehensive Cancer Network (NCCN) Guidelines Insights: Non–Small Cell Lung Cancer, Version 2. 2023.[21]
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up 2018.[22]
- Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer (SIGN 137). 2014.[23]

## Additional Information

## References

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*Therapy and Chemotherapy (COSTAR Lung)*. *Trial ID: NCT04655976*. Status: ongoing. Available from: https://clinicaltrials.gov/study/NCT04655976 [Accessed 30 October 2023].

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