NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
March 2026

Datopotamab deruxtecan with or without osimertinib for treating locally advanced or metastatic EGFR-mutated non-small cell lung cancer after one therapy

Company/Developer	Daiichi Sankyo UK Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 40216	NICE ID: Not Available	UKPS ID: 675228

Licensing and Market Availability Plans

Currently in phase III clinical development

Summary

Datopotamab deruxtecan, with or without osimertinib, is currently in development for the treatment of EGFR-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) in patients whose disease has progressed on prior osimertinib treatment. NSCLC is the most common type of lung cancer in the UK. Locally advanced lung cancer means the cancer has spread into tissues around the lungs and may have spread into nearby small structures called lymph nodes. Metastatic lung cancer has spread around the body from where it started in the lung. Epidermal growth factor receptor (EGFR) is a naturally occurring protein on cells that helps them grow. Certain changes (mutations) in the EGFR protein can cause the cells to grow too much, which can cause cancer. EGFR mutation is one of the most common mutations in NSCLC and is most commonly associated with nonsmokers and those of Asian ethnicity. Disease progression after current treatments is common, and treatment options after progression are limited.

Datopotamab deruxtecan is a medicine that consists of a monoclonal antibody (a type of protein, datopotamab) and an anticancer drug (deruxtecan) linked together. Datopotamab deruxtecan is designed to attach to cancer cells that express a protein called TROP-2, killing them when they divide and grow. Osimertinib is a cancer medicine that blocks the activity of EGFR helping to reduce the growth and spread of cancer. Using osimertinib together with datopotamab deruxtecan may help stop cancer from becoming resistant to treatment and slow down tumour growth. Datopotamab deruxtecan is injected into a vein (intravenous). Osimertinib is administered orally. If approved (licensed), datopotamab deruxtecan with or without osimertinib would provide an additional treatment option for patients with EGFR-mutated locally advanced or metastatic 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 available to comment.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Proposed Indication

Treatment of epidermal growth factor receptor (EGFR)-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) in patients whose disease has progressed on prior osimertinib monotherapy treatment.[1]

Technology

Description

Datopotamab deruxtecan (Dato-DXd, DS-1062a) is made up of two components that are linked together. Datopotamab is a monoclonal antibody that has been designed to attach to Trophoblast cell surface antigen 2 (TROP-2) which is present at high levels on the surface of NSCLC cells. Deruxtecan is a toxic substance that kills cells when they divide and grow. It becomes active once datopotamab has attached to TROP-2 and enters the cancer cell. Deruxtecan blocks an enzyme called topoisomerase I which is involved in copying the cell DNA needed to make new cells. When topoisomerase I is blocked, cancer cells cannot multiply and eventually die.[2]

Datopotamab deruxtecan with or without osimertinib is currently in clinical development for the treatment of EGFR-mutated locally advanced or metastatic NSCLC when disease has progressed on prior osimertinib treatment. In the phase III clinical trial (TROPION-Lung15, NCT06417814), participants are administered 6 mg/kg of datopotamab deruxtecan via intravenous (IV) infusion every three weeks on day 1 of every 21-day cycle, with or without 80 mg of osimertinib administered orally once daily.[1]

Key Innovation

Lung cancer is the leading cause of cancer-related deaths worldwide, accounting for more deaths worldwide than colon cancer, breast cancer and prostate cancer combined.[3,4] EGFR mutations are the most common oncogenic drivers in NSCLC.[5] Osimertinib is the preferred treatment for patients with EGFR-mutated NSCLC in several settings.[6] An advantage of osimertinib is its increased selectivity for exon 19, L858R, and T790M mutations over wild-type EGFR, thereby improving the off-target toxicity profile.[5] However, disease progression after osimertinib is common, and treatment options after progression are limited.[6] Combining osimertinib and datopotamab deruxtecan may overcome heterogeneous osimertinib resistance mechanisms and limit tumour progression. Datopotamab deruxtecan has demonstrated efficacy in advanced NSCLC, including previously treated EGFR-mutated advanced NSCLC.[6]

If licensed, datopotamab deruxtecan, with or without osimertinib, would provide an additional treatment option for patients with EGFR-mutated locally advanced or metastatic NSCLC whose disease has progressed on prior osimertinib treatment.

Regulatory & Development Status

Datopotamab deruxtecan currently has Marketing Authorisation in the EU for the treatment of unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer in adult patients who have received endocrine therapy and at least one line of chemotherapy in the advanced setting.[7]

Osimertinib currently has Marketing Authorisation in the EU/UK for the following indications:[8]

- adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

- treatment of adult patients with locally advanced, unresectable (stage III) NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and whose disease has not progressed during or following platinum-based chemoradiation therapy.
- first-line treatment of adult patients with locally advanced or metastatic NSCLC with activating EGFR mutations.
- treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC.
- in combination with pemetrexed and platinum-based chemotherapy for the first-line treatment of adult patients with advanced NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.

Datopotamab deruxtecan is also in phase II and III clinical development for the following indications:[9]

- urothelial cancer
- bladder cancer
- endometrial cancer
- gastric cancer
- ovarian cancer
- colorectal cancer
- biliary tract cancer
- breast cancer

Patient Group

Disease Area and Clinical Need

NSCLC is the most common form of lung cancer, accounting for around 80 to 85 out of 100 cases.[4] EGFR mutations are the most common oncogenic drivers in NSCLC.[5] Locally advanced lung cancer is cancer that has spread into tissues around the lungs and might have spread into nearby lymph nodes. Metastatic lung cancer means that the cancer has spread from where it started in the lung.[10] The most common symptoms of lung cancer include: a cough that does not go away after three weeks, recurrent chest infections, coughing up blood, aches or pains when breathing or coughing, breathlessness, tiredness, loss of appetite, and unexplained weight loss.[11] EGFR-mutated lung cancer occurs in 15–20% of patients with adenocarcinoma and is most commonly associated with nonsmokers and those of Asian ethnicity.[5]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2017-19).[12] In England (2024-25), there were 128,356 finished consultant episodes (FCEs) and 108,616 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34), which resulted in 83,351 day cases and 220,624 FCE bed days.[13] In 2023, there were 26,041 deaths where malignant neoplasm of bronchus and lung (ICD-10 code C34) was the underlying cause.[14] Between 2013 and 2017, the one-year and five-year survival rates for lung cancer were 40.6% and 16.2%, respectively.[15]

Recommended Treatment Options

There is no treatment option recommended by National Institute for the Health and Care Excellence (NICE) for EGFR-mutated locally advanced or metastatic NSCLC in patients whose disease has progressed on prior osimertinib monotherapy treatment. However, the following treatment options are recommended for EGFR-positive NSCLC:[16-18]

- osimertinib for adjuvant treatment of EGFR mutation-positive NSCLC after complete tumour resection
- osimertinib for treating EGFR T790M mutation-positive advanced NSCLC

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

- amivantamab for treating EGFR exon 20 insertion mutation-positive advanced NSCLC after platinum-based chemotherapy

Clinical Trial Information

Trial	**TROPION-Lung15;** NCT06417814; A Phase III, Open-label, Sponsor-blind, Randomised Study of Dato-DXd With or Without Osimertinib Versus Platinum-based Doublet Chemotherapy for Participants With EGFR-mutated Locally Advanced or Metastatic NSCLC Whose Disease Has Progressed on Prior Osimertinib Treatment **Phase III** – Recruiting **Locations:** Ten EU countries, UK, USA, Canada and other countries **Primary Completion Date (estimated):** September 2026
Trial Design	Randomised, parallel assignment, open label
Population	N = 744 (estimated); adults with non-squamous EGFR-mutated NSCLC who have received less than or equal to two prior lines of EGFR tyrosine kinase inhibitor (TKI) treatments, where osimertinib is the only permitted prior third-generation TKI
Intervention(s)	• Group 1: Datopotamab deruxtecan 6 mg/kg (IV) every three weeks (Q3W) on day 1 of every 21-day cycle + osimertinib 80 mg (oral) once daily • Group 2: Datopotamab deruxtecan 6 mg/kg (IV) Q3W on day 1 of every 21-day cycle • Group 3: Platinum-based doublet chemotherapy [pemetrexed 500mg/m^2 + carboplatin (AUC5) or cisplatin 75 mg/m^2 (IV) Q3W for four cycles, followed by pemetrexed maintenance 500 mg/m^2 (IV) Q3W]
Comparator(s)	None
Outcome(s)	Primary outcome measure: Progression free survival [Time frame: up to 2.5 years] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of datopotamab deruxtecan is not yet known.

Osimertinib is already marketed in the UK; a pack of 30 x 80 mg or 30 x 40mg tablets costs £5,770.[19]

Relevant Guidance

NICE Guidance

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

- NICE technology appraisal in development. Cimavax for treating wild-type EGFR-positive non-small-cell lung cancer (GID-10225). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Lazertinib with amivantamab and platinum-based chemotherapy for EGFR mutation-positive metastatic non-small-cell lung cancer after a tyrosine kinase inhibitor (GID-11229). Expected date of issue to be confirmed.
- NICE technology appraisal. Osimertinib for treating EGFR T790M mutation-positive advanced non-small-cell lung cancer (TA653). October 2020.
- NICE quality standard. Lung cancer in adults (QS17). March 2012. Updated 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
- NHS England. Clinical Commissioning Policy: Proton Beam Therapy for Lung Cancer (Adults). 201201P. February 2021.
- NHS England. Clinical Commissioning Policy: Robotic assisted lung resection for primary lung cancer. 16024/P. July 2016.
- NHS Commissioning Board. Clinical Commissioning Policy: Stereotactic ablative body radiotherapy for non-small-cell lung cancer (Adult). NHSCB/B01/P/a. April 2013.

Other Guidance

- European Society for Medical Oncology (ESMO). Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2018.[20]
- European Society for Medical Oncology (ESMO). Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2017.[21]
- London Cancer Alliance. LCA Lung Cancer Clinical Guidelines. 2016.[22]
- Scottish Intercollegiate Guideline Network (SIGN). Management of lung cancer. 2014.[23]

References

1 ClinicalTrials.gov. *A Phase III, Open-label, Sponsor-blind, Randomized Study of Dato-DXd With or Without Osimertinib Versus Platinum-based Doublet Chemotherapy for Participants With EGFR-mutated Locally Advanced or Metastatic Non-small Cell Lung Cancer Whose Disease Has Progressed on Prior Osimertinib Treatment (TROPION-Lung15)*. 2024. Available from: https://clinicaltrials.gov/study/NCT06417814 [Accessed 03 Feb 2026].

2 European Medicines Agency. *Datopotamab deruxtecan Daiichi Sankyo*. 2025. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/datopotamab-deruxtecan-daiichi-sankyo [Accessed 03 Feb 2026].

3 Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*. 2021;71(3):209-49. Available from: https://doi.org/10.3322/caac.21660.

4 National Health Service UK. *Lung cancer overview*. 2022. Available from: https://www.nhs.uk/conditions/lung-cancer/ [Accessed 03 Feb 2026].

5 O'Leary C, Gasper H, Sahin KB, Tang M, Kulasinghe A, Adams MN, et al. Epidermal Growth Factor Receptor (EGFR)-Mutated Non-Small-Cell Lung Cancer (NSCLC). *Pharmaceuticals (Basel)*. 2020;13(10). Available from: https://doi.org/10.3390/ph13100273.

6 Tan DS-W, Nadal E, Cheema P, Wu Y-L, Ahn M-J, Tanizaki J, et al. TROPION-Lung15: a randomized phase III study of osimertinib combined with datopotamab deruxtecan (Dato-DXd) or Dato-DXd alone versus platinum-doublet chemotherapy in patients with EGFR-

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

mutated advanced non-small cell lung cancer and whose disease has progressed on prior osimertinib. *Therapeutic Advances in Medical Oncology*. 2025;17:17588359251385410. Available from: https://doi.org/10.1177/17588359251385410.

7 European Medicines Agency. *Datroway*. 2025. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/datroway [Accessed 03 Feb 2026].

8 European Medicines Compendium (EMC). *TAGRISSO 40 mg film-coated tablets*. 2025. Available from: https://www.medicines.org.uk/emc/product/1985/smpc [Accessed 17 Feb 2026].

9 ClinicalTrials.gov. *Search for: Datopotamab deruxtecan | Not yet recruiting, Recruiting, Active, not recruiting, Completed studies | Phase: 2, 3 | Sponsor/Collaborator: Daiichi Sankyo*. 2026. Available from: https://clinicaltrials.gov/search?intr=Datopotamab%20deruxtecan%20&aggFilters=phase:2%203,status:not%20rec%20act&spons=Daiichi%20Sankyo [Accessed 03 Feb 2026].

10 Cancer Research UK. *What is metastatic lung cancer?* 2023. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/metastatic/what-is [Accessed 03 Feb 2026].

11 National Health Service UK. *Lung cancer symptoms*. 2022. Available from: https://www.nhs.uk/conditions/lung-cancer/symptoms/ [Accessed 03 Feb 2026].

12 Cancer Research UK. *Lung cancer incidence statistics*. 2024. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer/incidence#heading-Zero [Accessed 03 Feb 2026].

13 National Health Service Digital. *Hospital Admitted Patient Care Activity, Diagnosis 2024-25*. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2024-25 [Accessed 03 Feb 2026].

14 National Health Service National Disease Registration Service (NDRS). *Cancer Incidence and Mortality*. 2025. Available from: https://nhsd-ndrs.shinyapps.io/incidence_and_mortality/ [Accessed 06 Nov 2025].

15 Office for National Statistics. *Cancer survival in England - adults diagnosed*. 2019. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed.

16 National Instituite for Health and Care Excellence (NICE). *Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (TA1043)*. Last Update Date: 2025. Available from: https://www.nice.org.uk/guidance/ta1043 [Accessed 03 Feb 2026].

17 National Instituite for Health and Care Excellence (NICE). *Osimertinib for treating EGFR T790M mutation-positive advanced non-small-cell lung cancer (TA653)*. Last Update Date: 2020. Available from: https://www.nice.org.uk/guidance/ta653 [Accessed 03 Feb 2026].

18 National Instituite for Health and Care Excellence (NICE). *Amivantamab for treating EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer after platinum-based chemotherapy (TA850)*. Last Update Date: 2022. Available from: https://www.nice.org.uk/guidance/ta850 [Accessed 03 Feb 2026].

19 British National Formulary (BNF). *Osimertinib Medicinal Forms*. 2026. Available from: https://bnf.nice.org.uk/drugs/osimertinib-specialist-drug/medicinal-forms/ [Accessed 04 Feb 2026].

20 European Society for Medical Oncology. *Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up*. Last Update Date: 2018. Available from: https://www.annalsofoncology.org/article/S0923-7534(19)31710-7/fulltext [Accessed 03 Feb 2026].

21 European Society for Medical Oncology. *Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up*.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Last Update Date: 2017. Available from: https://www.annalsofoncology.org/article/S0923-7534(19)42150-9/fulltext [Accessed 04 Feb 2026].

22 London Cancer Alliance. *LCA Lung Cancer Clinical Guidelines*. Last Update Date: 2016. Available from: https://rmpartners.nhs.uk/wp-content/uploads/2017/03/lca-revised-lung-cancer-clinical-guidelines-december-2013-updated-march-2016-.pdf [Accessed 03 Feb 2026].

23 Scottish Intercollegiate Guideline Network (SIGN). *Management of lung cancer* (*SIGN 137)*. Last Update Date: 2014. Available from: https://www.sign.ac.uk/our-guidelines/management-of-lung-cancer/ [Accessed 03 Feb 2026].

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

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.