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Health Technology Briefing
July 2025

Datopotamab deruxtecan with durvalumab adjuvant therapy for treating triple-negative breast cancer

Company/Developer	Daiichi Sankyo Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 36262	NICE ID: Not available	UKPS ID: 675159

Licensing and Market Availability Plans

Currently in phase III clinical development

Summary

Datopotamab deruxtecan in combination with durvalumab is in clinical development for the treatment of non-metastatic triple-negative breast cancer (TNBC), following neo-adjuvant therapy. Breast cancer is the growth of abnormal cells in the breast that divide uncontrollably to eventually form a tumour. Non-metastatic refers to cancer that has not spread beyond the primary site of origin, nor invaded distant organs or tissues. TNBC is a subtype of breast cancer that lacks hormone receptor expression. The risk factors for TNBC include a history of breast disease and radiation therapy, family history of TNBC, alcohol intake, smoking, exposure to carcinogenic chemicals, and the intake of processed food. Chemotherapy is the main form of treatment for patients with TNBC; however, the effectiveness of chemotherapy for TNBC remains limited.

Datopotamab is a monoclonal antibody that attaches to a protein called trophoblast cell-surface antigen 2 (TROP2) on cancer cells. It then releases deruxtecan into the cancer cell. Deruxtecan kills or damages the cancer cells. Datopotamab deruxtecan is administered intravenously (through the vein). If licensed, datopotamab deruxtecan with durvalumab may provide a new treatment option for patients with non-metastatic TNBC, following neoadjuvant therapy.

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.

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Proposed Indication

Treatment of adults with stage I-III triple-negative breast cancer without pathological complete response following neoadjuvant therapy. [1]

Technology

Description

Datopotamab deruxtecan (Datroway, Dato-DXd, DS-1062a)[2] is a trophoblast cell surface antigen 2 (TROP2)-directed antibody-drug conjugate (ADC).[3] The antibody is a humanised anti-TROP2 IgG1 attached to deruxtecan, a topoisomerase I inhibitor bound by a tetrapeptide-based cleavable linker. The antibody-drug conjugate is stable in plasma. The antibody binds to TROP2 expressed on the surface of certain tumour cells. After binding, datopotamab deruxtecan undergoes internalisation into the tumour cells. Subsequently, the release of deruxtecan (DXd) leads to DNA damage and apoptotic cell death by inhibiting topoisomerase I. Datopotamab deruxtecan may also exhibit indirect cytotoxicity, as shown *in vitro*, through mechanisms such as antibody-dependent cellular cytotoxicity, antibody-dependent cellular phagocytosis, and bystander cytotoxicity of DXd against TROP2-expressing tumour cells and neighbouring cells.[2]

Datopotamab deruxtecan in combination with durvalumab is in clinical development for the treatment of non-metastatic TNBC patients who have residual disease following systemic neoadjuvant therapy. In the phase III clinical trial (TROPION-Breast03, NCT05629585), patients received 6 mg/kg of datopotamab deruxtecan intravenously (IV) every three weeks (8 cycles) in combination with 1,120 mg durvalumab IV every three weeks (9 cycles).[1]

Key Innovation

TNBC is a subtype of breast cancer that is aggressive,[4] especially when there is residual invasive disease in the breast and/or axillary lymph nodes at surgical resection, following systemic neo-adjuvant therapy; these patients are prone to recurrence and metastasis.[5,6] Chemotherapy is the primary form of treatment for patients with TNBC, however, its effectiveness for TNBC remains limited.[4] There is a need for more novel treatment options.

Preclinical evidence suggests that topoisomerase I inhibitors like DXd can enhance antitumour immunity by recruiting immune cells. Given that many solid tumours, including TNBC, are known to evade the immune system, combination therapy with both Dato-DXd and an immune cell-activating agent such as durvalumab may be more effective than either therapeutic agent alone. Therefore, the combination of Dato-DXd and durvalumab may lead to improved clinical responses through complementary pharmacodynamic effects- Dato-DXd increases the recruitment of immune cells to tumour sites, and durvalumab enhances the activation of immune cells.[7]

If licensed, datopotamab deruxtecan with durvulumab may provide an additional treatment option for patients with non-metastatic TNBC who have residual invasive disease in the breast and/or axillary lymph nodes at surgical resection following neoadjuvant systemic therapy.

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Regulatory & Development Status

Durvalumab currently has Marketing Authorisation in the UK as a combination or monotherapy for the following:[8]

- non-small cell lung cancer
- small cell lung cancer
- biliary tract cancer
- hepatocellular carcinoma
- endometrial cancer

Datopotamab deruxtecan is marketed in the EU as a monotherapy for hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), unresectable or metastatic breast cancer.[2]

Datopotamab deruxtecan as a combination is currently in phase II or III clinical development for the following indications:[9]

- non-small cell lung cancer
- HER2-negative metastatic breast cancer
- endometrial cancer
- gastric cancer
- metastatic castration-resistant prostate cancer
- brain metastases

Patient Group

Disease Area and Clinical Need

Breast cancer occurs when abnormal cells in the breast begin to grow and divide in an uncontrolled way, forming a tumour.[10] It commonly starts in the cells that line the ducts of the breast. Breast cancer can be grouped according to types, stages, and grades. Stage I/II is early breast cancer, which means that the cancer is small and only in the breast tissue or in lymph nodes close to the breast, or both. Stage III is called locally advanced breast cancer, because the cancer has spread from the breast to the lymph nodes, or skin, or the chest wall, close to the breast.[11] TNBC is a specific subtype of breast cancer, representing approximately 15-20% of breast cancer cases. It is a highly aggressive subtype, characterised by the lack of expression of the oestrogen receptor, progesterone receptor, and HER2 receptor on the cell surface.[4,12,13] Residual disease after neoadjuvant chemotherapy is a poor prognostic sign in early-stage TNBC and is often associated with early recurrence or metastasis.[5,6] TNBC signs and symptoms include a lump or thickening in the breast or armpit, changes in the position of the nipple, such as an inverted nipple, and changes in the skin of the breast, such as redness, rash, puckering, or dimpling of the skin.[13] The risk factors for TNBC include, history of breast disease and radiation therapy, family history of TNBC, alcohol intake, smoking, exposure to carcinogenic chemicals, and the intake of processed food.[14]

Breast cancer is the most common cancer in the UK, accounting for 15% of all new cancer cases -about 56,800 new breast cancer cases in the UK annually (2017-2019).[15] The age-standardised incidence rate of breast cancer in England is 1.2 and 169.9 per 100,000 amongst males and females, respectively (2017-2019).[16] In England (2023-24), there were 265,571 finished consultant episodes (FCEs) and 261,890 admissions for malignant neoplasm of the breast (ICD-10 code C50), which resulted in 240,356 day cases and 64,821 FCE bed days.[17]

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Recommended Treatment Options
The National Institute for Health and Care Excellence (NICE) currently recommends pembrolizumab for neoadjuvant and adjuvant treatment of triple-negative early or locally advanced breast cancer.[18]

Clinical Trial Information

Trial	**TROPION-Breast03;** NCT05629585; 2022-002680-30; A phase 3 open-label, randomised study of datopotamab deruxtecan (DatoDXd) with or without durvalumab versus investigator's choice of therapy in patients with Stage I-III triple-negative breast cancer who have residual invasive disease in the breast and/or axillary lymph nodes at surgical resection following neoadjuvant systemic therapy **Phase III:** Active, not recruiting **Location(s):** 8 EU countries, UK, USA, Canada, and other countries **Primary completion date:** September 2027
Trial Design	Randomised, parallel assignment, open label
Population	N= 1174 (actual); aged 18 years and older; all sexes; subjects with invasive, non-metastatic TNBC with residual invasive disease after completing at least six cycles of neoadjuvant therapy; with no adjuvant systemic therapy
Intervention(s)	Datopotamab deruxtecan 6mg/kg every 3 weeks with/without durvalumab 1120mg every 3 weeks, both administered IV
Comparator(s)	Capecitabine (oral), pembrolizumab (IV), capecitabine + pembrolizumab
Outcome(s)	Primary outcome measure: Invasive disease-free survival for Dato-DXd + durvalumab versus active comparators See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of datopotamab deruxtecan is currently unknown.

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Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Pembrolizumab for adjuvant treatment of triple-negative breast cancer after neoadjuvant chemotherapy (GID-TA11724). Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Pembrolizumab for neoadjuvant and adjuvant treatment of triple-negative early or locally advanced breast cancer (TA851). Published: December 2022.
- NICE clinical guideline. Early and locally advanced breast cancer: diagnosis and management (NG101). July 2018.
- NICE quality standard. Breast cancer (QS12). June 2016.

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

- NHS England – West Midlands Expert Advisory Group for Breast Cancer. Clinical guidelines for the management of breast cancer 2016.[19]
- European Society of Medical Oncology. Clinical Practice Guidelines: Early Breast Cancer 2024.[20]
- American Society of Clinical Oncology. Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Clinical Practice Guideline Focused Update. August 2018.[21]

Additional Information

A UK Pharmascan record was opened for the technology on 22 April 2025.

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