Health Technology Briefing
October 2025

Sacituzumab tirumotecan for treating advanced or metastatic gastroesophageal adenocarcinoma after 2 or more previous treatments

Company/Developer	Merck Sharp & Dohme Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 38898	NICE ID: Not Available	UKPS ID: 675069

Licensing and Market Availability Plans

Currently in phase III clinical development.[1]

Summary

Sacituzumab tirumotecan is in development for the treatment of adults with advanced or metastatic gastroesophageal adenocarcinoma who have had three or more previous treatments. Gastroesophageal adenocarcinoma is a type of cancer in either the stomach, oesophagus, or where the oesophagus joins the stomach. Most cancers in these areas are adenocarcinomas, which form from a specific cell type. Symptoms may include difficulty swallowing, persistent indigestion, stomach pain, or feeling full quickly after meals. In more advanced cases, patients may also experience blood in the stool or loss of appetite. These cancers can spread to nearby lymph nodes (making the disease advanced) and other parts of the body (metastatic). Survival rates are low, and treatment options for patients who have already tried several lines of therapy are limited.

Sacituzumab tirumotecan is given intravenously (into a vein) and consists of two parts an antibody (a type of protein used in the immune system) and a drug. The antibody targets a molecule on cancer cells called TROP2. Once attached, it delivers a cancer destroying drug into the cancer cells. This blocks cell growth and leads to cancer cell death. If licensed, sacituzumab tirumotecan could provide an additional treatment option for adults with advanced gastroesophageal adenocarcinoma who have already received three prior therapies.

Proposed Indication

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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Treatment of patients who have received, and progressed on, at least 2 prior chemotherapy and/or immunotherapy regimens for advanced/metastatic gastroesophageal adenocarcinoma (gastric adenocarcinoma, gastroesophageal junction adenocarcinoma, and oesophageal adenocarcinoma) in adults.[1]

Technology

Description

Sacituzumab tirumotecan (MK-2870) is an antibody-drug conjugate (ADC) composed of an anti-TROP2 monoclonal antibody coupled to a cytotoxic belotecan-derived topoisomerase I inhibitor (KL610023) via a novel linker.[1,2] The anti-TROP2 antibody targets and binds to TROP2 expressed on tumour cells.[3] Sacituzumab tirumotecan has a novel methyl sulfonyl pyrimidine linker that conjugates the payload, a belotecan-derivative topisomerase I inhibitor. Extracellular pH-sensitive cleavage and intracellular enzymatic cleavage in tumor cells affect the linker, which then releases the payload in the tumour cells and the tumour microenvironment.[4] KL610023 is a topoisomerase I inhibitor belotecan derivative with a bystander effect, and can arrest cell cycle at the G2/S stage after its internalisation, leading to cell death.[5]

Sacituzumab tirumotecan is currently in clinical development for the treatment of patients for who have received, and progressed on, at least 2 prior chemotherapy and/or immunotherapy regimens for advanced/metastatic gastroesophageal adenocarcinoma. In the phase III clinical trial (NCT06356311) participants receive sacituzumab tirumotecan as 4mg/kg intravenous (IV) infusion on days 1, 15, and 29 of every 42-day cycle.[1]

Key Innovation

Cancers of the upper gastrointestinal tract are difficult to treat. Even with aggressive management, the survival rates are low, and the recurrence rates are high. Immunotherapy and targeted therapies have shown some promise, but they have not yet been proven to improve overall survival.[6] Furthermore, third-line treatment options or beyond for gastroesophageal cancers are especially limited.[7] TROP2 is reputed as a prognostic factor linked to tumour growth and enhanced proliferation, which has been reported to be overexpressed in gastric and oesophagus cancers.[8] ADCs such as sacituzumab tirumotecan directly targets TROP2 expressing tumour cells and also uses a novel linker that is sensitive to the pH levels found within cancer cells and the surrounding tumour environment allowing for targeted release of the cytotoxic payload directly into the tumour cell and microenvironment.[3,4,9]

If licensed, sacituzumab tirumotecan will offer an additional treatment option for those who have received, and progressed on, at least 2 prior chemotherapy and/or immunotherapy regimens for advanced/metastatic gastroesophageal adenocarcinoma.

Regulatory & Development Status

Sacituzumab tirumotecan does not currently have marketing authorisation in the EU/UK for any indication.

Sacituzumab tirumotecan is currently in phase II/III clinical development for, but not limited to, the following:[10]

- Non-small cell lung cancer
- Recurrent/metastatic head and neck squamous cell carcinoma
- Triple-negative breast cancer
- Locally advanced and metastatic urothelial carcinoma

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- Cholangiocarcinoma

Patient Group

Disease Area and Clinical Need

Adenocarcinomas can form in the oesophagus, gastro oesophageal junction and stomach from adenomatous cells.[11-13] The majority of gastric cancers (approximately 90–95%) and oesophageal cancers (approximately 80%) are adenocarcinomas.[12,14] This includes cancers that develop in the gastro-oesophageal junction, where the oesophagus joins the stomach.[15] The symptoms of gastro oesophageal junction cancers are very similar to oesophageal cancer and include difficulty swallowing, unexplained weight loss and indigestion/heartburn that doesn't go away.[13] Similarly, symptoms of gastric cancers can include stomach pain, indigestion/heartburn and feeling very full after meals. More advanced symptoms of oesophageal and gastric cancer can include blood in the stool and loss of appetite.[16] Risk factors of these cancer types include being male, being over the age of 50, being obese and smoking.[17] Being diagnosed with Barrat's oesophagus can also increase the risk of oesophageal and gastro oesophageal cancers.[13,17] Adenocarcinomas can spread to nearby lymph nodes in advanced stages and metastasise to other areas of the body.[14]

The 5-year survival for oesophageal cancer is approximately 15% and 20% and for stomach cancer.[18] Over 8,000 new oesophageal cancers and 7,000 new stomach cancers are diagnosed each year in the UK.[19] In England, 2024-25, there were 30,297 and 48,162 finished consultant episodes (FCEs), 25,200 and 39,623 finished admission episodes (FAEs), 54,979 and 81,596 FCE bed days and 20,493 and 32,391 day cases for the ICD-10 codes for malignant neoplasm of the stomach (C16) and malignant neoplasm of the oesophagus (C15), respectively.[20]

Recommended Treatment Options

NICE currently recommend the following treatment for metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after 2 or more treatments:[21]

- Trifluridine–tipiracil

Clinical Trial Information

Trial	NCT06356311; A Phase 3, Multicenter, Open-label, Randomized Study to Compare the Efficacy and Safety of MK-2870 Versus Treatment of Physician's Choice in 3L+ Advanced/Metastatic Gastroesophageal Adenocarcinoma (Gastric Adenocarcinoma, Gastroesophageal Junction Adenocarcinoma, and Esophageal Adenocarcinoma) **Phase III –** Recruiting **Location(s):** USA, UK, Canada, seven EU countries and other countries **Primary completion date:** 04 January 2027
Trial Design	Randomised, parallel assignment
Population	N=450 (estimated); participants with third line or later (3L+) advanced/metastatic gastroesophageal adenocarcinoma (gastric adenocarcinoma, gastroesophageal junction adenocarcinoma, and oesophageal adenocarcinoma); aged 18 years and older.

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Intervention(s)	Sacituzumab tirumotecan as 4mg/kg IV infusion.
Comparator(s)	Treatment of physician's choice, either trifluridine-tipiracil, irinotecan, paclitaxel or docetaxel.
Outcome(s)	Primary outcome: overall survival (defined as the time from randomisation to death due to any cause). See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of sacituzumab tirumotecan is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Trifluridine–tipiracil for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after 2 or more treatments (TA852). December 2022.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Oesophageal and Gastric (Adult). B11/S/a.
- 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: Robotic assisted surgery for oesophagogastric cancers. 16006/P. July 2016.

Other Guidance

- European Society of Medical Oncology (ESMO). Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. 2022. eUpdate 2025.[22,23]
- Upper GI Oncology Summit. Clinical practice guidelines for esophagogastric junction cancer: Upper GI Oncology Summit 2023. 2024.[24]
- National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers, Version 2.2023, NCCN Clinical Practice Guidelines in Oncology. April 2023.[25]
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