NIHR | Innovation Observatory

Newcastle University

# Health Technology Briefing
# September 2023

# Sacituzumab govitecan for previously treated advanced non-small cell lung cancer

| Company/Developer | Gilead Sciences |
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☐ New Active Substance ☒ Significant Licence Extension (SLE)

| NIHRIO ID: 34026 | NICE ID: N/A | UKPS ID: 652738 |
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## Licensing and Market Availability Plans

Currently in phase III clinical trials.

## Summary

Sacituzumab govitecan is in development for advanced or metastatic non-small cell lung cancer (NSCLC), that has progressed on or after previous therapies with platinum-based chemotherapy and immunotherapy. NSCLC is the most common type of lung cancer accounting for 80-85% of lung cancers. Most common symptoms include a cough, recurrent chest infections, coughing up blood, tiredness or lack of energy, and loss of appetite. Advanced or metastatic cancer is incurable and has spread from its original area in the lung to other parts of the body. Although outcomes for patients with NSCLC have been improved over the last decade, the probability of a cure in the advanced setting is rare. Therefore, there is a great unmet need to provide more effective therapeutic strategies to further improve outcome in patients with advanced NSCLC.

Sacituzumab is given by intravenous (into the vein) infusion on days 1 and 8 of a 21-day cycle. Sacituzumab govitecan has two active components: a monoclonal antibody (a type of protein) that has been linked to a small molecule called SN-38. The monoclonal antibody attaches to a specific area on the cancer cell then releases SN-38 into it. SN-38 blocks an enzyme in the cancer cell called topoisomerase I. Topoisomerase I is responsible for copying DNA and is needed for the cancer cells to multiply. By blocking topoisomerase I, sacituzumab govitecan prevents cancer from multiplying and they eventually die. If licenced sacituzumab would offer an additional treatment option for people with NSCLC that has progressed after platinum-based chemotherapy and immunotherapy.

## Proposed Indication

For the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy and anti-programmed death protein 1 (PD-1)/programmed death ligand 1 (PD-L1) immunotherapy.[1]

# Technology

## Description

Sacituzumab govitecan (Trodelvy; SG; GS-0132; IMMU-132) is an antibody-drug conjugate that has two active components: a monoclonal antibody and a small molecule called SN-38. The monoclonal antibody has been designed to recognise and attach to trophoblast cell-surface antigen 2 (TROP-2). Once attached, the medicine is taken up by the cell and SN-38 becomes active. SN-38 is a topoisomerase inhibitor that blocks an enzyme called topoisomerase I. Topoisomerase I is involved in copying cell DNA and is needed to make new cells. By blocking this enzyme, cancer cells are prevented from multiplying and eventually die (through apoptosis).[1-3]

Sacituzumab govitecan is in phase III clinical development (EVOKE-01, NCT05089734) for the treatment of advanced or metastatic NSCLC for patients who have had progression on or after platinum-based chemotherapy and PD-1/PD-L1 immunotherapy. Sacituzumab govitecan is administered by intravenous (IV) infusion 10 mg/kg on days 1 and 8 of a 21-day cycle.[1]

## Key Innovation

The emergence of targeted therapy and immunotherapy has changed the treatment paradigm of advanced NSCLC. However, for those who are not eligible for current therapy, or have no available standard treatment options, have a need for new precision treatments. TROP-2 is highly expressed on several epithelial cancers including NSCLC and is recognised as a promising molecular target for therapies in TROP-2 expressing malignancies. (48).[4,5] Some research indicates higher TROP-2 expression by NSCLC tumour cells significantly lowers progression free survival and overall survival compared to lower TROP-2 expression and worsens outcomes independent of PD-1 expression.[6]
Sacituzumab govitecan has been shown to be effective against various cancers without severe side effects, including NSCLC resistant to anti-PD-1/PD-L1 therapy.[4,6] In the phase I/II clinical trial (NCT01631552) almost one in five patients with metastatic NSCLC had objective responses, and 30% (14/47) of the assessable patients had one or more immune checkpoint inhibitors (CPIs) as their most recent therapy. 36% (5/14) of patients who received CPIs showed tumour shrinkage, including two (14%) with partial response. Serious adverse events (grade ≥3) that occurred in ≥5% of patients were neutropenia (28%), leukopenia (9%), pneumonia (9%), diarrhoea (7%), nausea (7%), and fatigue (6%).[7,8] If licenced sacituzumab govitecan would offer a treatment option for patients with advanced or metastatic NSCLC who have received platinum-based chemotherapy and anti-PD-1/PD-L1 immunotherapy, but whose disease had progressed.

## Regulatory & Development Status

Sacituzumab govitecan currently has marketing authorisation in the UK for treatment of unresectable or metastatic triple negative breast cancer .[2,9]

Sacituzumab govitecan is in phase II/III clinical development for:[10]

- Solid tumours
- Genitourinary cancers
- Gastric adenocarcinoma
- Oesophageal cancer

- Salivary gland cancers

## Patient Group

### Disease Area and Clinical Need

NSCLC is one of two types of lung cancer and makes up approximately 80-85% of lung cancers in the UK. NSCLC is categorised by three main types: adenocarcinoma, squamous cell cancer, and large cell carcinoma.[11] Advanced lung cancer means that the cancer has spread from its original site in the lung to other areas of the body such as lymph nodes, bones and other organs and cannot usually be cured; advanced is used interchangeably with metastatic.[12] Main symptoms of lung cancer include a cough, recurrent chest infections, coughing up blood, tiredness or lack of energy, and loss of appetite.[13,14] Other symptoms vary depending on where the cancer has spread e.g., memory problems if it has spread to the brain, or stomach pain and feeling sick if it has spread to the liver.[14] The leading cause of lung cancer is smoking (>70%) although some people who have never smoked can also develop the condition from exposure to pollution, chemicals and substances that increase risk of developing lung cancer.[15]

In England, 2013-17, 10% of people with lung cancer survive for 10 or more years.[16] Age-standardised mortality rates per 100,000 for lung cancers in males and females, in England (2017) were; 65.8, and 46.1, while the incidence rates were 86.9 and 67.0 respectively.[17] In England, 2021-22, there were 119,396 finished consultant episodes (FCE) of malignant neoplasm of bronchus and lung (ICD-10 code C34), resulting in 75,969 day cases and 206,640 FCE bed days.[18] In England (2017), there were 38,888 patients diagnosed with malignant neoplasm of bronchus and lung and 28,170 deaths registered had malignant neoplasm of bronchus and lung as the underlying cause.[19]

### Recommended Treatment Options

Treatment for NSCLC depends on the type of cancer (e.g., squamous) and what mutations the cancer has (e.g., anaplastic kinase positive). The National Institute for Health and Care Excellence (NICE) currently recommends the following pharmacological treatment options for patients with advanced/metastatic NSCLC who have received a previous treatment:[20]

- Docetaxel
- Docetaxel with nintedanib
- Atezolizumab
- Nivolumab
- Ceritinib
- Lorlatinib
- Pemetrexed
- Osimertinib
- Pembrolizumab
- Mobocertinib
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Mobocertinib is recommended for treating locally advanced or metastatic NSCLC after platinum-based chemotherapy in adults, whose tumours have epidermal growth factor receptor (EGFR) exon 20 insertion mutations.[21]

## Clinical Trial Information

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| Trial | **EVOKE-01; NCT05089734; EudraCT 2021-003578-30;** Open-Label, Global, Multicentre, Randomized, Phase 3 Study of Sacituzumab Govitecan Versus Docetaxel in Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) With Progression on or After Platinum-Based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy<br>**Phase III –** Active, not recruiting.<br>**Location(s):** 10 EU countries, UK, USA, Canada and other countries<br>**Primary completion date:** May 2024 |
| Trial Design | Randomised, open label, parallel assignment. |
| Population | N=580 (estimated); all sexes; aged 18 years and older; stage IV NSCLC; epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and programmed death protein (PD-1)/programmed death ligand 1 (PD-L1) results; cancer progression after platinum-based chemotherapy in combination with anti-PD-1/PD-L1 antibody OR platinum-based chemotherapy and anti-PD-1/PD-L1 antibody (in either order) sequentially. |
| Intervention(s) | Participants will receive sacituzumab govitecan (SG) 10 mg/kg on days 1 and 8 of a 21-day cycle (i.e., 2 weekly doses plus 1 week without treatment) until progressive disease (PD), death, unacceptable toxicity, or another treatment discontinuation criterion is met. |
| Comparator(s) | Participants will receive docetaxel 75 mg/m$^2$ on day 1 of a 21-day cycle (i.e., once every 3 weeks) until PD, death, unacceptable toxicity, or another treatment discontinuation criterion is met. |
| Outcome(s) | **Primary outcome measure:**<br>Overall Survival [Time frame: up to 30 months]<br><br>See trial record for full list of other outcomes. |
| Results (efficacy) | - |
| Results (safety) | - |

## Estimated Cost

Sacituzumab govitecan is already marketed in the UK for the treatment of breast cancer; a single 180mg vial costs £793.[22]

## Relevant Guidance

### NICE Guidance

- NICE technology appraisal guidance. Mobocertinib for treating EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer after platinum-based chemotherapy (TA855). January 2023.

- NICE technology appraisal guidance. Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy. (TA713). July 2021
- NICE technology appraisal guidance. Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy. (TA655). October 2020
- NICE technology appraisal guidance. Osimertinib for treating EGFR T790M mutation-positive advanced non-small-cell lung cancer. (TA653). October 2020
- NICE technology appraisal guidance. Lorlatinib for previously treated ALK-positive advanced non-small-cell lung cancer. (TA628). May 2020
- NICE technology appraisal guidance. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer. (TA584). June 2019
- NICE technology appraisal guidance. Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy. (TA428). September 2017
- NICE technology appraisal guidance. Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin. (TA402). August 2016
- NICE technology appraisal guidance. Ceritinib for previously treated anaplastic lymphoma kinase positive non-small-cell lung cancer. (TA395). June 2016
- NICE technology appraisal guidance. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. (TA347). July 2015
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2023.

### 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). Non-Small Cell Lung Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. 2022.[23]
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2020 update.[24]
- Scottish Intercollegiate Guidelines Network. Management of lung cancer (SIGN 137). 2014.[25]

## Additional Information

## References

1 Clinicaltrials.gov. *Study of Sacituzumab Govitecan (SG) Versus Docetaxel in Participants With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) (EVOKE-01). Trial ID: NCT05089734*. Status: Active, not recruiting. Available from: https://classic.clinicaltrials.gov/ct2/show/NCT05089734 [Accessed 18 Jul 2023].

2 European Medicines Compendium (emc). *Trodelvy 180 mg powder for concentrate for solution for infusion*. 2023. Available from: https://www.medicines.org.uk/emc/product/12880/smpc [Accessed 19 Jul 2023].

3 European Medicines Agency (EMA). *Trodelvy (sacituzumab govitecan)*. 2022. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/trodelvy [Accessed 19 Jul 2023].

4 Ahmed Y, Berenguer-Pina JJ, Mahgoub T. The Rise of the TROP2-Targeting Agents in NSCLC: New Options on the Horizon. *Oncology*. 2021;99(10):673-80. Available from: https://doi.org/10.1159/000517438.

5 Kuo P, Elboudwarej E, Diehl L, Patel J, Mekan S, Jürgensmeier JM. Abstract 4396: TROP2 expression in non-small cell lung cancer. *Cancer Research*. 2023;83(7_Supplement):4396-. Available from: https://doi.org/10.1158/1538-7445.Am2023-4396.

6 Italiano A, Leroy L, Guegan J-P, Cousin S, Peyraud F, Cabart M, et al. TROP2 expression and response to immune checkpoint inhibition in patients with advanced non-small cell lung cancer. *Journal of Clinical Oncology*. 2023;41(16_suppl):9040-. Available from: https://doi.org/10.1200/JCO.2023.41.16_suppl.9040.

7 Heist RS, Guarino MJ, Masters G, Purcell WT, Starodub AN, Horn L, et al. Therapy of Advanced Non–Small-Cell Lung Cancer With an SN-38-Anti-Trop-2 Drug Conjugate, Sacituzumab Govitecan. *Journal of Clinical Oncology*. 2017;35(24):2790-7. Available from: https://doi.org/10.1200/jco.2016.72.1894.

8 Clinicaltrials.gov. *Study of Sacituzumab Govitecan-hziy (IMMU-132) in Adults With Epithelial Cancer*. 2012. Available from: https://classic.clinicaltrials.gov/ct2/show/NCT01631552 [Accessed 19 September 2023].

9 British National Formulary (BNF). *Sacituzumab govitecan [Specialist drug]*. Available from: https://bnf.nice.org.uk/drugs/sacituzumab-govitecan-specialist-drug/#indications-and-dose [Accessed 18 Jul 2023].

10 ClinicalTrials.gov. *Gilead phase II/III clinical development for sacituzumab govitecan* Available from: https://classic.clinicaltrials.gov/ct2/results?cond=&term=Sacituzumab+govitecan%2C+Gilead&cntry=&state=&city=&dist=&Search=Search&phase=1&phase=2 [Accessed 18 Jul 2023].

11 Cancer Research UK. *Types of lung cancer*. 2022. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/types [Accessed 25 Jul 2023].

12 Cancer Research UK. *What is metastatic lung cancer?* 2023. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/metastatic/what-is [Accessed 25 Jul 2023].

13 NHS. *Lung cancer - Symptoms*. 2022. Available from: https://www.nhs.uk/conditions/lung-cancer/symptoms/ [Accessed 25 Jul 2023].

14 Cancer Research UK. *Symptoms of metastatic lung cancer*. 2023. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/metastatic/symptoms [Accessed 25 Jul 2023].

15 NHS. *Lung cancer - Causes*. 2022. Available from: https://www.nhs.uk/conditions/lung-cancer/causes/ [Accessed 25 Jul 2023].

16 Cancer Research UK. *Lung cancer statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer [Accessed 25 Jul 2023].

17 Cancer Research UK. *Lung cancer statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer [Accessed 20 September 2023].

18 NHS Digital. *Hospital Admitted Patient Care Activity, 2021-22*. 2022. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2021-22 [Accessed 25 Jul 2023].

19 Office for National Statistics. *Cancer registration statistics, England*. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland [Accessed 20 September 2023].

20 National Institute for Health and Care Excellence. *Systemic anti-cancer therapy (SACT) for advanced non-small-cell lung cancer*. Available from: https://www.nice.org.uk/guidance/ng122/chapter/Treatment#systemic-anti-cancer-therapy-sact-for-advanced-non-small-cell-lung-cancer [Accessed 20 September 2023].

21 National Institute for Health and Care Excellence (NICE). *Mobocertinib for treating EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer after platinum-based chemotherapy* (*TA855)*. Last Update Date: January 2023. Available from: https://www.nice.org.uk/guidance/ta855/chapter/1-Recommendations [Accessed 25 Jul 2023].

22 British National Formulary (BNF). *Trodelvy 180mg powder for concentrate for solution for infusion vials*. Available from: https://bnf.nice.org.uk/drugs/sacituzumab-govitecan-specialist-drug/medicinal-forms/ [Accessed 18 Jul 2023].

23 Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman JR, Bharat A, et al. Non-Small Cell Lung Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2022;20(5):497-530. Available from: https://doi.org/10.6004/jnccn.2022.0025.

24 Planchard D, Popat S, Kerr K, Novello S, Smit EF, Faivre-Finn C, et al. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29(Suppl 4):iv192-iv237. Available from: https://doi.org/10.1093/annonc/mdy275.

25 Scottish Intercollegiate Guidelines Network (SIGN). *Management of lung cancer* (*SIGN 137)*. Last Update Date: Feb 2014. Available from: https://www.sign.ac.uk/media/1075/sign137.pdf [Accessed 25 Jul 2023].

***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.***