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Health Technology Briefing
January 2026

Olomorasib with pembrolizumab for previously untreated, locally advanced or metastatic non-small cell lung cancer with KRAS G12C mutation and PD-L1 ≥ 50%

Company/Developer	Eli Lilly and Company Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 38253	NICE ID: Not applicable	UKPS ID: 674948

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Olomorasib in combination with pembrolizumab is currently in development for previously untreated, locally advanced or metastatic non-small-cell lung cancer (NSCLC) with a KRAS G12C mutation and PD-L1 expression. NSCLC is the most common type of lung cancer in the UK. Locally advanced cancer means the cancer has spread into tissues around the lungs and might have spread into nearby small structures called lymph nodes. When a cancer has a gene mutation called KRAS G12C, it can lead to cell growth and drive cancer progression. This mutation in the genes happens in around 13% of NSCLC cases. First line treatments for NSCLC with a KRAS mutation are currently limited. Therefore, there is a need to develop new treatment options.

Olomorasib is a medication that can be taken by the mouth. It is designed to stop mutations in the KRAS gene, which then helps prevent the growth of tumours. It was developed so that it stays in the body long enough and at the right levels to strongly block this target. If approved, olomorasib, in combination with pembrolizumab, could provide an additional treatment option for patients with previously untreated, locally advanced or metastatic NSCLC with a KRAS G12C mutation and PD-L1 expression ≥ 50%.

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

First-line treatment of patients with KRAS G12C-mutant, locally advanced or metastatic non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50%.[1]

Technology

Description

Olomorasib (LY3537982) is an investigational, oral, potent, and highly selective second-generation inhibitor of the KRAS G12C protein. KRAS is the most common oncogene across all tumour types, and KRAS G12C mutations occur in 13% of patients with NSCLC.[2] Mutation of glycine 12 (G12) causes RAS activation by interfering with GTPase-Activating Protein (GAP) binding and GAP-stimulated guanosine triphosphate (GTP) hydrolysis. In addition to genetic alterations associated spontaneous tumour development, it has been increasingly appreciated that KRAS mutation also exhibits a broad impact on tumour microenvironment, which contributes to the promotion and maintenance of cancer malignancy.[3] Olomorasib binds to GDP-bound KRAS G12C to prevent the activation of the inactive KRAS G12C.[4]

Olomorasib, in combination with pembrolizumab, is currently in clinical development for locally advanced or metastatic NSCLC with a KRAS G12C mutation and PD-L1 expression. In the phase III clinical trial (SUNRAY-01, NCT06119581) participants are given olomorasib orally twice a day and pembrolizumab intravenously (IV) every three weeks.[1]

Key Innovation

First line treatments for NSCLC with PD-L1 expression and KRAS mutation are currently limited.[5] While immunotherapy is established as the cornerstone of first-line treatment for KRAS-mutant NSCLC, outcomes remain suboptimal. Further progress may be achieved with the addition of targeted therapy to immunotherapy, an established first-line paradigm in some other cancer types but historically challenging in NSCLC.[6] Olomorasib was specifically designed to target KRAS G12C mutations and has pharmacokinetic properties which allow for high predicted target occupancy and high potency when used as a monotherapy or in combination.[2] A phase I study in people with various solid tumours, including NSCLC, suggested preliminary efficacy and a favourable safety profile for olomorasib monotherapy.[7] Additionally, olomorasib in combination with pembrolizumab demonstrated favourable safety and antitumour activity in patients with KRAS G12C-mutant advanced NSCLC.[6] If licensed, olomorasib in combination with pembrolizumab will provide an additional treatment option for patients with advanced or metastatic NSCLC with a KRAS G12C mutation and PD-L1 expression.

Regulatory & Development Status

Olomorasib does not currently have Marketing Authorisation in the EU/UK for any indication.

Olomorasib in combination is also in phase III clinical development for patients with previously treated, unresectable or resected NSCLC.[8]

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. It can be one of three types: squamous cell carcinoma, adenocarcinoma, or large-cell carcinoma.[9] The KRAS G12C

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mutation is the most common KRAS variant, occurring in approximately 13% of NSCLC cases overall.[10] Locally advanced 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. It is also called advanced lung cancer.[11] 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.[12] In the UK, lung cancer is more common in people of European family origin than in people of African or Asian family origin. It is strongly linked to socioeconomic deprivation. There are many risk factors for lung cancer, including age, genetics, lifestyle (especially smoking) and occupation.[13]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2017-19).[14] 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.[15] In 2020, there were 26,922 deaths where malignant neoplasm of bronchus and lung (ICD-10 code C34) was the underlying cause.[16] Between 2013 and 2017, the one-year and five-year survival rates for stage 3 lung cancer were 48.7% and 12.6%, respectively. For stage 4 lung cancer, the one-year and five-year survival rates were 19.3% and 2.9%, respectively.[17]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following therapies for previously untreated, metastatic squamous NSCLC that is KRAS G12C positive and with PD-L1 of 50% or more.[5]

- Pembrolizumab with carboplatin and paclitaxel (only if urgent clinical intervention is needed).
- Pembrolizumab.
- Atezolizumab.

NICE currently recommends the following therapies for previously untreated, metastatic non-squamous NSCLC that is KRAS G12C positive and with PD-L1 of 50% or more.[5]

- Pembrolizumab with pemetrexed and platinum chemotherapy.
- Pembrolizumab.
- Atezolizumab.

Clinical Trial Information

Trial	**SUNRAY-01, NCT06119581;** SUNRAY-01, A Global Pivotal Study in Participants With KRAS G12C-Mutant, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Comparing First-Line Treatment of LY3537982 and Pembrolizumab vs Placebo and Pembrolizumab in Those With PD-L1 Expression ≥ 50% or LY3537982 and Pembrolizumab, Pemetrexed, Platinum vs Placebo and Pembrolizumab, Pemetrexed, Platinum Regardless of PD-L1 Expression **Phase III** – Recruiting **Locations:** 15 EU countries, UK, USA, Canada, Australia, and other countries **Primary completion date (estimated):** October 2026
Trial Design	Randomised, parallel assignment, placebo controlled, double blind
Population	N=1016 (estimated); adults aged 18 years and older with histologically or cytologically confirmed Stage 3B-3C or Stage 4 NSCLC with KRAS G12C mutation

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	PD-L1 expression and is not suitable for curative intent radical surgery or radiation therapy.
Intervention(s)	Part A: oral administration of olomorasib combined with IV pembrolizumab in 21-day cycles
Comparator(s)	Part A: oral placebo and IV pembrolizumab administered in 21-day cycles.
Outcome(s)	Part A primary outcome: • Progression-Free Survival (PFS) [Time frame: Randomisation to first documented progression of disease or death from any cause. (estimated as approximately 1 year)] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of olomorasib is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal awaiting development. Tiragolumab–atezolizumab for PD-L1-positive recurrent or advanced non-small-cell lung cancer untreated with checkpoint inhibitors (GID-TA11594). Expected publication date TBC.
- NICE technology appraisal awaiting development. Tiragolumab with atezolizumab for untreated PD-L1-positive advanced non-small-cell lung cancer (GID-TA11021). Expected publication date TBC.
- NICE technology appraisal in development. Avelumab for untreated PD-L1 positive recurrent or metastatic non-small-cell lung cancer (GID-TA10250). Expected publication date TBC.
- NICE technology appraisal awaiting development. Retifanlimab with chemotherapy for previously untreated metastatic non-small-cell lung cancer (GID-TA11532). Expected publication date TBC.
- NICE technology appraisal. Cemiplimab with platinum-based chemotherapy for untreated advanced non-small-cell lung cancer (TA1108). November 2025.
- NICE technology appraisal. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (TA770). February 2022.
- NICE technology appraisal. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (TA705). June 2021.
- NICE technology appraisal. Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (TA683). March 2021.
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- NICE technology appraisal. Pemetrexed for the first-line treatment of non-small-cell lung cancer (TA181) September 2009.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2024.
- NICE quality standard. Lung cancer in adults (QS17). December 2019.

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NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
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Other Guidance

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