

Health Technology Briefing March 2022

Canakinumab adjuvant therapy for treating completely resected non-small-cell lung cancer

Company/Developer

Novartis Pharmaceuticals UK Ltd.

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 24065

NICE ID: 10646

UKPS ID: 651873

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Canakinumab is in clinical development as an adjuvant therapy for stage II-III non-small cell lung cancer (NSCLC) that has been surgically completely removed. NSCLC accounts for most lung cancers that are diagnosed and can originate anywhere in the lungs but may spread to surrounding tissues as the disease progresses. Adjuvant therapy is a treatment given after the primary treatment, which in II-III stage NSCLC is often the complete surgical removal of the cancer. The risk of recurrence/relapse without additional adjuvant therapy remains high, as some cancer cells may have been left behind.

Canakinumab is a first-in-class, subcutaneously administered, inhibitor treatment that blocks the pro-tumour inflammatory pathway, enhancing the immune response against cancer cells and limiting how much they can grow and spread. If licensed, canakinumab will offer a new adjuvant treatment option for patients who have had or are candidates for complete surgical resection.

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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Adjuvant therapy for adult subjects with stage IIA-IIIB non-small cell lung cancer (NSCLC) that has been completely resected or are candidates for complete resection.¹

Technology

Description

Canakinumab (Ilaris, ACZ-885) is a recombinant human monoclonal antibody that selectively inhibits interleukin-1 beta (IL-1 β) receptor binding.² Overexpression of IL-1 β is seen in many solid tumours, including those in NSCLC, and can promote angiogenesis, tumour invasiveness, and induce tumour-associated immunosuppression. Data has shown that IL-1 β inhibition stably reduces tumour growth, by limiting inflammation and inducing the maturation myeloid-derived suppressor cells into M1 macrophages.³

Canakinumab is in clinical development as an adjuvant therapy for NSCLC patients who have had or are candidates for complete resection.¹ In the phase III clinical trial (NCT03447769), canakinumab will be administered over 18 cycles over approximately 54 weeks, receiving 200mg via subcutaneous injection every three weeks.^{1,4}

Key Innovation

Canakinumab is a potential first-in-class IL-1 β inhibitor of the pro-tumour inflammation pathway (PTI), with high specificity and affinity for receptors, enhancing the immune response and reducing tumour cell proliferation. PTI, which enables tumour development by driving cancer-causing processes and suppressing anti-tumour immune responses, is one of the potential hallmarks of cancer and targets in NSCLC.⁵ If licensed, canakinumab will offer a new adjuvant treatment option for patients with completely resected stage II-IIIB NSCLC, who have completed standard-of-care adjuvant therapies such as cisplatin-based chemotherapy and mediastinal radiotherapy if applicable.³

Regulatory & Development Status

Canakinumab has marketing authorisation in the UK for the following indications:²

- Gouty arthritis
- Cryopyrin-associated periodic syndromes
- Tumour necrosis factor receptor associated periodic syndrome
- Hyperimmunoglobulin D syndrome
- Familial Mediterranean fever
- Still's disease

Canakinumab is currently in phase II/ III clinical development for:⁶

- Anaemia
- Myelodysplastic syndromes
- Auto-inflammatory syndromes
- Pulmonary sarcoidosis
- Dry eye
- Melanoma
- COVID-19
- Arthritis
- Cardiovascular diseases
- Diabetes Mellitus

- Alzheimer's Disease

Patient Group

Disease Area and Clinical Need

Lung cancers can be broadly grouped into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), with NSCLC accounting for 80-85% of lung cancer diagnoses in the UK. NSCLC can then be further categorised into adenocarcinoma, squamous cell carcinoma and large cell carcinoma- these are often grouped together as they all respond to treatments in a similar way.⁷ 79% of lung cancers diagnosed in 2015 were deemed preventable, with lifestyle factors such as smoking and occupational hazards (inhalation of chemicals such as asbestos) being the leading causes (70% and 13% respectively). Age, gender, and genetics also show influence on prevalence with most cases diagnosed in those aged 80-85, males, and those with a family history. Medical conditions such as chronic obstructive pulmonary disease (COPD) and pneumonia also increase the likelihood of development.⁸ In the earlier stages of the disease there are often no signs or symptoms, but as the disease progresses symptoms can include a persistent cough, recurrent chest infections, breathlessness, chest and shoulder pain, and fatigue.⁹

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (28,549) and 21% of cancer deaths (35,137) (2016-18). The one-year survival rate in England is 40.6%, dropping to 16.2% over five years, and 9.5% over ten years (2013-17).⁸ In England (2020-21), there were 103,856 finished consultant episodes (FCE) for malignant neoplasm of the bronchus and lung (ICD-10 code: C34), with 86,043 hospital admissions that resulted in 62,688 days cases and 170,030 FCE bed days.¹⁰ In England between 2013 and 2017, the age-standardised net lung cancer survival for stage II was 73% at one year and 34.1% at five years, and for stage III was 48.7% at one year and 12.6% at five years.¹¹ In 2020, there were 28,730 registrations of deaths in England and Wales for malignant neoplasms of the trachea, bronchus and lung in England (ICD-10 code C34).¹²

Recommended Treatment Options

Patients diagnosed with lung cancer are all first advised to stop smoking as this can cause pulmonary complications. Surgery is the main treatment option with curative intent for patients with stage II-IIIa lung cancer, with options ranging from a lobectomy to more extensive surgery's such as a pneumonectomy, lymph node sampling, or a chest wall resection.¹³ Chemotherapy or chemoradiotherapy can be delivered before or after surgery to shrink the tumour and/or lower the chances of recurrence, with adjuvant cisplatin-based chemotherapy being the standard of care after complete resection of stage II-IIIa NSCLC.^{14,15}

Clinical Trial Information

Trial

CANOPY-A; [NCT03447769](#), [2017-004011-39](#); A Phase III, Multicenter, Randomized, Double Blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Canakinumab Versus Placebo as Adjuvant Therapy in Adult Subjects With Stages AJCC/UICC v. 8 II -IIIA and IIIB (T>5cm N2) Completely Resected (R0) Non-small Cell Lung Cancer (NSCLC)

Phase III - Active, not recruiting

Location(s): 17 EU countries, UK, USA, Canada and other countries

	Primary completion date: August 2023
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N= 1500 (planned); Subjects with stage IIA-IIIB NSCLC who have had a full resection or are candidates for full resection; aged 18 years and older.
Intervention(s)	Canakinumab subcutaneous injection (200mg/ml) ⁴
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Disease Free Survival (DFS) by local investigator [Time Frame: up to 5 years]
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Canakinumab is already marketed in the UK; a vial (150mg/ml) costs £9927.80.¹⁶

Relevant Guidance

NICE Guidance

- NICE interventional procedure guidance. Percutaneous radiofrequency ablation for primary or secondary lung cancers (IPG372). December 2010.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 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.

Other Guidance

- European Society for Medical Oncology. Early and locally advanced non-small-cell lung cancer: an update of the ESMO Clinical Practice Guidelines focusing on diagnosis, staging and systemic and local therapy. 2021¹⁷
- European Respiratory Journal. International guidelines on stage III N2 non-small cell lung cancer: surgery or radiation. 2020.¹⁸
- Healthcare Improvement Scotland. Management of lung cancer (SIGN 137). 2014.¹⁹
- British Thoracic Society and the Society for Cardiothoracic Surgery. Guidelines on the radical management of patients with lung cancer. 2010.²⁰

Additional Information

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