

**NIHR Innovation Observatory
Evidence Briefing: April 2017****BV-NSCLC- 002 (Cimavax) for non-small-cell lung
cancer wild type EGF receptor positive patients**

NIHRIO (HSRIC) ID: 7145

NICE ID: 8823

LAY SUMMARY

Lung cancer is the third most common type of cancer. As it is often diagnosed at a late or advanced stage, the survival rate decreases. Of those who have the disease, the majority have non-small cell lung cancer.

BV-NSCLC-002 is a new vaccine being developed to treat patients with advanced non-small cell lung cancer where the cells have a specific mutation (referred to as EGFR positive). The treatment is given as an injection at four sites after first-line chemotherapy then a reduced dose is given at two sites during the pre-progression phase.

A study is currently determining how safe and efficacious BV-NSCLC-002 is in inoperable, late stage non-small cell lung cancer patients. If licensed it will offer an additional and more specific treatment option for patients with advanced EGFR positive non-small cell lung cancer and may improve survival.

This briefing is based on information available at the time of research 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.

This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

TARGET GROUP

- Non-small-cell lung cancer (NSCLC): late stage/inoperable – in adults who are positive in the selective EGF biomarker and wild type EGF-Receptor

TECHNOLOGY

DESCRIPTION

BV-NSCLC-002 (rEGF-P64K/Montanide ISA 51 vaccine; SAI-EGF; CimaVax EGF; EGF-P64K) is a humanised recombinant antigen and an adjuvant that targets the epidermal growth factor receptor (EGFR) signalling pathway to prevent the activation and production of tumour cells. BV-NSCLC-002 is intended to treat late stage non-small-cell lung cancer in adults who are positive in the selective EGF biomarker and wild type EGFR.

A conjugate-adjuvant injection mix is administered subcutaneously at a dose of 1.2 ml at four sites during the post first-line chemotherapy. During pre-progression phase, the dose will be reduced at two sites.¹

BV-NSCLC-002 does not currently have Marketing Authorisation in the EU for any indication.

INNOVATION and/or ADVANTAGES

As EGF concentration has potential importance in the proliferation of tumours and disease, if licensed, BV-NSCLC-002 may provide an alternative and more specific treatment to those NSCLC patients who are positive in the selective EGF biomarker and wild type EGF-Receptor.

DEVELOPER

Bioven International Ltd.

AVAILABILITY, LAUNCH or MARKETING

Currently in phase III clinical trials.

PATIENT GROUP

BACKGROUND

In the UK lung cancer is the third most common type of cancer.² Approximately 80 to 85% of those sufferers have non-small cell lung cancer (NSCLC), which grows and spreads more rapidly than small cell lung cancer.³ The three subtypes include adenocarcinoma, squamous cell carcinoma and large cell carcinoma, which are derived from the different type of lung cell affected.⁴ Lung cancer diagnosis's each year are typically linked to major lifestyle and other risk factors, with smoking identified as the primary cause in an estimated 86% of cases.² Consequently evidence suggests that smoking has a significant influence on the symptoms of lung cancer actually predicting the disease incidence.⁵

Genetic mutations in tumour cells cause several unique metabolic phenotypes that are critical for cancer cell proliferation.¹³ Tumours harbouring EGFR-activating mutations constitute a unique

subset of biologically distinct diseases in which EGFR activation is a driving molecular event.¹⁴ In EGFR-mutated lung adenocarcinoma cells, EGFR signalling regulates the global metabolic pathway.¹³

CLINICAL NEED and BURDEN OF DISEASE

Lung cancer is the second most common cancer in men and women. In 2014 a total of 46,403 people were diagnosed with the condition in the UK². The majority of those with lung cancer, are diagnosed at a late stage (72-76% are diagnosed at stage III or IV).² According to the prognosis for lung cancer, only 1 in 10 people are living for more than 5 years after diagnosis. This is mainly due to a consequence of a late stage diagnosis, which limits the use of curative treatment.⁹ However, encouragingly a cohort of patients (44,116) from the UK in 2015 had increasingly greater one year survival rates than in previous years (38% to 31% from 2010).¹¹

Of lung cancer patients with NSCLC, 20% are diagnosed with early-stage disease, which is associated with the best chance of cure.¹⁰ The most common type of NSCLC is adenocarcinoma, accounting for 40% of lung cancer patients.⁷ For survival rates in those with NSCLC, as the stage progresses from IIa to stage IV, the five year survival rate decreases from 30% to approximately 1%.¹² Whilst 50%-60% of patients diagnosed with late stage NSCLC have an over-expression of EGF, approximately 15% are evaluated as EGFR positive.^{7,15}

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE Technology Appraisal in development. Lung cancer (non-small-cell, EGFR T790M-positive, metastatic, treated) – rociletinib (ID883). Expected date of issue to be confirmed.
- NICE Technology Appraisal. Osimertinib for treating locally advanced or metastatic EGFR T790M mutation-positive non-small-cell lung cancer (TA416). Oct 2016
- NICE Technology Appraisal. Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer (TA258). Jun 2012
- NICE guidelines. Lung cancer: diagnosis and management (CG121). April 2011
- Quality Standard. Lung cancer in adults. March 2012.
- Diagnostics guidance. EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer. August 2013.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013 Clinical Commissioning Policy: Stereotactic Ablative Body Radiotherapy for Non-Small Cell Lung Cancer (Adult). B01/P/a
- NHS England. 2016 Clinical Commissioning Policy: Robotic assisted lung resection for primary lung cancer. 16024/P
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a

OTHER GUIDANCE

- European Society for Medical Oncology. Metastatic non-small cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2014. ¹⁶
- Scottish Intercollegiate Guidelines Network. Management of lung cancer (137). 2014. ¹⁷
- National Comprehensive Cancer Network. The NCCN clinical practice guidelines in oncology. Non-small cell lung cancer. 2013. ¹⁶
- American College of Chest Physicians. Treatment of stage IV non-small cell lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. 2013. ¹⁸

CURRENT TREATMENT OPTIONS

The goal of treating NSCLC is to prolong survival and control disease-related symptoms. Factors influencing treatment selection include comorbidity, performance status (PS), histology, and molecular genetic features of the cancer, therefore treatment should consider these important factors.⁷ Due to the detrimental effect of smoking on lung cancer, it is recommended that this should be ceased.⁵ Emerging evidence suggests that oncologic and palliative care should be concurrent at the initial diagnosis of advanced NSCLC to alleviate depression and improve quality of life in patients.⁸

Current NICE guidance indicates that chemotherapy should be offered to patients with stage III or IV NSCLC and good performance status (WHO 0, 1 or a Karnofsky score of 80–100), to improve survival, disease control and quality of life. Chemotherapy for advanced NSCLC should be a combination of a single third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine) plus a platinum drug. Either carboplatin or cisplatin may be administered, taking account of their toxicities, efficacy and convenience. Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy with a third-generation drug. Afatinib is recommended as an option treating adults with locally advanced or metastatic non-small-cell lung cancer only if the tumour tests positive for the EGFR-TK mutation and the person has not previously had an EGFR-TK inhibitor. Pemetrexed is also recommended for the first-line treatment of non-small-cell lung cancer.⁶

EFFICACY and SAFETY

Trial	CimaVax EGF, NCT02187367, adults aged ≥18 years; BV-NSCLC-001 vs standard treatment and supportive care; phase III	
Sponsor	Bioven	
Status	Ongoing	
Source of Information	Trialtrove	
Location	Malaysia, Philippines, Thailand and United Kingdom	
Design	Randomised intervention	
Participants	N=418 (planned); aged ≥18 years; non-small-cell lung cancer, stage IV biomarker positive wild type EGF-R.	
Schedule	In the experimental arm EGF vaccine patients will receive a low dose of cyclophosphamide and the recombinant human rEGF-P64K/Montanide	

	ISA 51. 1.2 mL of conjugate-adjuvant mix, injected at four sites during the Post First-Line chemotherapy. Reduced dose of injection at two sites during the Pre-Progression Phase. Best supportive care patients will receive best supportive care.	
Follow-up	Each patient will be followed till objective tumour progression or death (whichever occurs first) within time frame of study of 3 years.	
Primary Outcomes	Overall survival	
Secondary Outcomes	<ul style="list-style-type: none"> • Safety of EGF cancer vaccine as assessed by adverse events. • Progression-Free Survival. • Survival Rate. • Time to Progression. • Response Rate. • Safety of EGF Cancer Vaccine by Laboratory Assessment. • Safety of EGF Cancer Vaccine assessed by Vital Signs. • Safety of EGF Cancer Vaccine as assessed by Physical Examination. • Quality of Life. 	
Key Results	-	
Adverse effects (AEs)	-	
Expected reporting date	March 2020	

ESTIMATED COST and IMPACT

COST

The cost of BV-NSCLC- 002 is not yet known.

IMPACT – SPECULATIVE

IMPACT ON PATIENTS and CARERS

- Reduced mortality/increased length of survival Reduced symptoms or disability
 Other No impact identified

IMPACT ON HEALTH and SOCIAL CARE SERVICES

- Increased use of existing services Decreased use of existing services

- | | |
|---|---|
| <input type="checkbox"/> Re-organisation of existing services | <input type="checkbox"/> Need for new services |
| <input type="checkbox"/> Other | <input checked="" type="checkbox"/> None identified |

IMPACT ON COSTS and OTHER RESOURCE USE

- | | |
|---|---|
| <input type="checkbox"/> Increased drug treatment costs | <input type="checkbox"/> Reduced drug treatment costs |
| <input type="checkbox"/> Other increase in costs | <input type="checkbox"/> Other reduction in costs |
| <input type="checkbox"/> Other | <input checked="" type="checkbox"/> None identified |

OTHER ISSUES

- | | |
|--|---|
| <input type="checkbox"/> Clinical uncertainty or other research question identified: | <input checked="" type="checkbox"/> None identified |
|--|---|

REFERENCES

- 1 Bioven. Safety & Efficacy Study of EGF Cancer Vaccine to Treat Stage IV Biomarker Positive, Wild Type EGF-R NSCLC Patients (EGF). (2017). Available from <https://clinicaltrials.gov/ct2/show/NCT02187367>
- 2 Cancer Research UK. Lung cancer statistics. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer> [Accessed 21st April 2017]
- 3 Lung Cancer Alliance. Types of lung cancer. Available from: <http://www.lungcanceralliance.org/get-information/types-of-lung-cancer.html> [Accessed 21st April 2017]
- 4 American Cancer Society. What Is Non-Small Cell Lung Cancer? Available from: <https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html> [Accessed 21st April 2017]
- 5 National Institute for Health and Care Excellence. Suspected cancer: recognition and referral. Available from: <https://www.nice.org.uk/guidance/ng12/chapter/Introduction> [Accessed 21st April 2017]
- 6 National Institute for Health and Care Excellence. Treating non-small-cell lung cancer. Available from: <https://pathways.nice.org.uk/pathways/lung-cancer/treating-non-small-cell-lung-cancer> [Accessed 21st April 2017]
- 7 National Cancer Institute. Non-Small Cell Lung Cancer Treatment. Available from: <https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq> [Accessed 21st April 2017]
- 8 Greer J.A., Jackson V.A., Meier D.E, Temel J.S. Early integration of palliative care services with standard oncology care for patients with advanced cancer. CA: a cancer journal for clinicians. 2013; 63(5): 349-63.
- 9 National Institute for Health and Care Excellence. Lung cancer in adults. Available from: <https://www.nice.org.uk/guidance/qs17> [Accessed 21st April]
- 10 NHS England. Clinical Commissioning Policy: Stereotactic Ablative Body Radiotherapy for Non-Small-Cell Lung Cancer (Adult). Available from: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2013/08/b01-p-a.pdf> [Accessed 21st April]
- 11 Royal College of Physicians. NLCA annual report 2016. Available from: <https://www.rcplondon.ac.uk/projects/outputs/nlca-annual-report-2016> [Accessed 21st April]
- 12 American Cancer Society. Non-Small Cell Lung Cancer Survival Rates, by Stage. Available from: <https://www.cancer.org/cancer/non-small-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html> [Accessed 21st April 2017]

- 13 Makinoshima H, Takita M, Matsumoto S, Yagishita A, Owada S, Esumi H, et al. Epidermal growth factor receptor (EGFR) signaling regulates global metabolic pathways in EGFR-mutated lung adenocarcinoma. *Journal of Biological Chemistry*. 2014; 289(30): 20813-23.
- 14 Dziadziuszko R, Jassem J. Epidermal growth factor receptor (EGFR) inhibitors and derived treatments. *Annals of Oncology*. 2012; 23(suppl 10): x193-x6.
- 15 Bioven. PHASE III TRIAL - BVNSCLC 002. Available from: http://www.bioven.com/product-egf_pti.php [Accessed on 21st April]
- 16 National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 1. 2015. Available from http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf [Accessed 20th April 2017]
- 17 Scottish Intercollegiate Guidelines Network. Management of Lung cancer (SIGN 137). Available from <http://www.sign.ac.uk/pdf/SIGN137.pdf> [Accessed 20th April 2017]
- 18 Socinski MA, Evans T, Gettinger S et al. Treatment of stage IV non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143 suppl5:e341S-e368S. Available from <https://www.guideline.gov/summaries/summary/46174/treatment-of-stage-iv-nonsmall-cell-lung-cancer-diagnosis-and-management-of-lung-cancer-3rd-ed-american-college-of-chest-physicians-evidencebased-clinical-practice-guidelines> [Accessed 20th April 2017]