BV-NSCLC- 002 (Cimavax) for non-small-cell lung cancer wild type EGF receptor positive patients

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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 develop 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.

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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. In EGFR-mutated lung adenocarcinoma cells, EGFR signalling regulates the global metabolic pathway.

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 UK. The majority of those with lung cancer, are diagnosed at a late stage (72-76% are diagnosed at stage III or IV). 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. 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).

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

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 guidelines. Lung cancer: diagnosis and management (CG121). April 2011

NHS ENGLAND and POLICY GUIDANCE

• NHS England. 2016 Clinical Commissioning Policy: Robotic assisted lung resection for primary lung cancer. 16024/P
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

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

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

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<th>Primary Outcomes</th>
<th>Overall survival</th>
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| **Secondary Outcomes** | • 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
− Re-organisation of existing services

− Need for new services

− Other

☐ None identified

**IMPACT ON COSTS and OTHER RESOURCE USE**

− Increased drug treatment costs

− Reduced drug treatment costs

− Other increase in costs

− Other reduction in costs

− Other

☐ None identified

**OTHER ISSUES**

− Clinical uncertainty or other research question identified:

☐ None identified

**REFERENCES**


