NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Encorafenib with binimetinib for treating BRAF V600E mutation-positive advanced non-small-cell lung cancer [ID6177]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of encorafenib with binimetinib within its marketing authorisation for treating BRAF V600E mutation-positive advanced non-small-cell lung cancer (NSCLC).

Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 10% of all new cancer cases and 20% of all cancer deaths in 2020.[1] There were around 37,000 new lung cancer cases and 27,000 deaths from lung cancer in England in 2020.[1] Most lung cancers are diagnosed at an advanced stage, when the cancer has spread to lymph nodes and other organs in the chest (locally advanced disease; stage 3) or to other parts of the body (metastatic disease; stage 4).[2] In 2021, 91% (around 31,000) of people diagnosed with lung cancer in England had NSCLC.[2]

BRAF is a protein which is part of a signalling pathway which helps to regulate cell proliferation, differentiation and death. Between 1-5% of people with NSCLC are estimated to have a mutation in the BRAF gene. A third to half of mutations in the BRAF gene are called BRAF V600 mutations with the majority of these being specifically BRAF V600E. [3,4]

Current clinical management for advanced or metastatic (stage 3 or 4) NSCLC typically aims to control the cancer for as long as possible and help with symptoms. The treatment pathway for NSCLC can be divided into interconnected decision points based on the number staging system and line of therapy. Treatment choices are influenced by the presence of biological markers (including programmed cell death 1 ligand PD-L1 status), oncogenic driver genetic alterations, histology (squamous or non-squamous) and previous treatment.

For untreated advanced NSCLC with a BRAF V600 mutation, NICE guidance recommends dabrafenib with trametinib as a first-line treatment (TA898). For previously treated NSCLC NICE guidance recommends nivolumab (TA655 and TA713), atezolizumab (TA520) and pembrolizumab (TA428) monotherapies as well as docetaxel with nintedanib (TA347). Docetaxel alone and platinum doublet chemotherapy may also be offered.

The technology

Encorafenib (Braftovi, Pierre-Fabre) with binimetinib (Mektovi, Pierre-Fabre) does not currently have a marketing authorisation in the UK for BRAF V600E positive NSCLC. It is being studied in single arm trials in adults with BRAF V600 mutation positive non-small cell lung cancer.

Encorafenib with binimetinib has a marketing authorisation for treatment of unresectable or metastatic melanoma with a BRAF V600 mutation.

Intervention(s)	Encorafenib with binimetinib
Population(s)	People with advanced NSCLC that is positive for a BRAF V600E mutation
Subgroups	If the evidence allows the following subgroups will be considered: • line of therapy (treated or untreated) • histology (squamous or non-squamous) • PD-L1 expression
Comparators	For people with untreated advanced NSCLC • Dabrafenib with trametinib • Pembrolizumab with platinum doublet chemotherapy (cisplatin or carboplatin with either gemcitabine, vinorelbine, docetaxel or pemetrexed) • Pembrolizumab monotherapy • Atezolizumab as monotherapy or in combination with bevacizumab and chemotherapy • Platinum doublet chemotherapy For people with previously treated advanced NSCLC • Atezolizumab monotherapy • Pembrolizumab monotherapy • Nivolumab monotherapy • Docetaxel with nintedanib • Docetaxel • Platinum doublet chemotherapy • Best-supportive care

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • time to treatment discontinuation • time to subsequent therapy • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Dabrafenib plus trametinib for treating BRAF V600 mutation-positive advanced non-small-cell lung cancer (2023) NICE technology appraisal guidance 898 Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy (2020) NICE technology appraisal guidance 655 Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy (2021) NICE technology appraisal guidance 713 Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 520

	Pembrolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 428 **Related NICE guidelines:** Lung cancer: diagnosis and management (2019; updated 2023) NICE guideline 122 **Related interventional procedures:** Microwave ablation for primary or metastatic cancer in the lung (2022) Interventional procedures guidance 716. Irreversible electroporation for treating primary lung cancer and metastases in the lung (2013) Interventional procedures guidance 441. Percutaneous radiofrequency ablation for primary or secondary lung cancers (2010) NICE interventional procedures guidance 372. **Related quality standards:** Lung cancer in adults (2012; updated 2019) NICE quality standard 17
Related National Policy	Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017 The NHS Long Term Plan (2019) NHS Long Term Plan The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 105: Specialist cancer services (adults).

References

1. NHS England. Cancer Registration Statistics, England 2020. Accessed March 2024
2. Royal College of Surgeons of England (2023). National Lung Cancer Audit: State of the Nation Report 2023. Accessed March 2024
3. O'Leary, CG., Andelkovic, V., Ladwa. R, et al Targeting BRAF mutations in non-small cell lung cancer. Translational Lung Cancer Research. Vol 8, No 6. Accessed March 2024
4. Owsley, J., Stein, MK., Porter. J, et al. Prevalence of class I-III BRAF mutations among 114,662 cancer patients in a large genomic database. Exp Biol Med (Maywood). 2021 Jan;246(1):31-39. Accessed March 2024