NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for previously treated locally advanced or metastatic non-squamous non-small-cell lung cancer (CDF review of TA484)

Final scope – re-issued May 2021

Remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for previously treated locally advanced or metastatic non-small cell lung cancer.

Background (not updated when scope re-issued)

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers[1,2]. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma; about 25–30% of lung cancers are squamous cell carcinomas[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 III) or to other parts of the body (metastatic disease; stage IV). In 2013, approximately 26,800 people were diagnosed with NSCLC in England, of whom 3551 (13.2%) had stage IIIA, 2527 (9.4%) had stage IIIB and 12,229 (45.6%) had stage IV disease[2].

Lung cancer caused 28,000 deaths in England in 2012[3]. The median survival with lung cancer (all stages) is approximately 6 months; 35% of people with lung cancer, and 14% of people with stage IV disease, survive for more than 1 year[2,3].

The aims of therapy are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as activating mutations in the epidermal growth factor receptor [EGFR]), histology (squamous or non-squamous) and previous treatment experience. For people with locally advanced or metastatic NSCLC whose disease has progressed after previous treatment with chemotherapy, NICE recommends docetaxel monotherapy, erlotinib, afatinib and nintedanib as options in certain circumstances (CG121, technology appraisal 162 [subject to ongoing NICE appraisal], technology appraisal 310 and technology appraisal 347 respectively). Crizotinib is not recommended by NICE (technology appraisal 296), however it is available via the Cancer Drugs Fund. Best supportive care may be considered for some people for whom chemotherapy is unsuitable or may not be tolerated.

The technology

Nivolumab (Nivolumab BMS, Bristol-Myers Squibb UK) is a monoclonal antibody that targets a receptor on the surface of lymphocytes known as PD-1. This receptor is part of the immune checkpoint pathway, and blocking its activity may promote an anti-tumour immune response. Nivolumab is administered by IV infusion.

Nivolumab has a marketing authorisation in the UK for previously treated locally advanced or metastatic non-squamous non-small cell lung cancer. It has been studied in one randomised, open-label clinical trial compared with docetaxel, in adults with non-squamous non-small-cell lung cancer, which has progressed after platinum-based chemotherapy.

Intervention(s)	Nivolumab
Population(s)	People with previously treated locally advanced or metastatic non-squamous non-small cell lung cancer whose tumours are PD-L1 positive (that is with a tumour proportion score ≥ 1%).
Comparators (not updated when scope re-issued)	**Non-squamous EGFR-TK mutation positive tumours:** • After one prior therapy: – Platinum therapy (in combination with gemcitabine, vinorelbine, pemetrexed or a taxane) – Single agent gemcitabine and vinorelbine (for people for whom platinum therapy is not appropriate) – Afatinib, erlotinib or gefitinib (if no previous EGFR-TKI therapy received due to delayed confirmation of mutation status; erlotinib and gefitinib subject to ongoing NICE appraisal) • After two prior therapies (an EGFR-TKI and one other therapy): – Docetaxel monotherapy – Erlotinib – Nintedanib in combination with docetaxel – Best supportive care **Non-squamous EGFR-TK mutation negative or unknown tumours:** • After one prior therapy:

	– Docetaxel monotherapy – Erlotinib (subject to ongoing NICE appraisal) – Nintedanib in combination with docetaxel – Crizotinib (only for patients with ALK positive mutation status) – Ceritinib (only for patients with ALK positive mutation status; subject to ongoing NICE appraisal) – Best supportive care • After two prior therapies: – Docetaxel monotherapy – Erlotinib (if not received previously; subject to ongoing NICE appraisal) – Best supportive care
Outcomes (not updated when scope re-issued)	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis (not updated when scope re-issued)	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 or subsequent treatment technologies will be taken into account.
Other considerations (not updated when	If the evidence allows, consideration will be given to subgroups based on biological markers. If appropriate, the appraisal should include consideration

scope re-issued)	of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices. 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 and NICE Pathways (not updated when scope re-issued)	Related Technology Appraisals: Technology Appraisal No. 310, Mar 2014, 'Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer'. Review Proposal Date Apr 2017. Technology Appraisal No. 296, September 2013, 'Crizotinib for previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene'. Review Proposal Date May 2016. Technology Appraisal No. 175, Jul 2009, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small-cell lung cancer (terminated appraisal)'. Review in progress. Technology Appraisal No. 162, Nov 2008, 'Erlotinib for the treatment of non-small-cell lung cancer'. Review in progress. Technology Appraisal No. 124, Nov 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Static list. Technology Appraisal No. 347, July 2015, 'Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer'. Technology Appraisal in preparation, 'Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175)' [ID620]. Expected date of publication TBC. Technology Appraisal in preparation, 'Nivolumab for previously treated locally advanced or metastatic squamous non-small-cell lung cancer'. Expected date of publication May 2016. Technology Appraisal in preparation, 'Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer' [ID729]. Expected date of

	publication January 2016. Related Guidelines: Clinical Guideline No. 121, Apr 2011, 'The diagnosis and treatment of lung cancer'. Review date March 2016 Related Quality Standards: Quality Standard No. 17, Mar 2012, 'Quality standard for lung cancer'. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy (not updated when scope re-issued)	Department of Health, Improving Outcomes: A Strategy for Cancer, third annual report, Dec 2013 https://www.gov.uk/government/publications/the-national-cancer-strategy-3rd-annual-report--2 NHS England, Manual for prescribed specialised services, service 105: specialist cancer services (adults), Jan 2014. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2013-2014, Nov 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health, Cancer commissioning guidance, Dec 2009. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_110115

References

1. American Cancer Society (2015) Learn about cancer: What is non-small-cell lung cancer? Accessed June 2015.
2. Health and Social Care Information Centre (2014) National Lung Cancer Audit: 2013 patient cohort. Accessed June 2015.
3. Cancer Research UK (2014) Lung cancer statistics. Accessed June 2015.