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

Final scope

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

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 (Opdivo, Bristol-Myers Squibb) 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 currently has a marketing authorisation in the UK for locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults. 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
Comparators	**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 (for people who have not previously had an EGFR-TKI) or erlotinib (if no previous EGFR-TKI therapy received due to delayed confirmation of mutation status) • After two prior therapies (an EGFR-TKI and one other therapy): – Docetaxel monotherapy – Erlotinib (if not received previously) – Nintedanib in combination with docetaxel – Best supportive care **Non-squamous EGFR-TK mutation negative or unknown tumours:** • After one prior therapy: – Docetaxel monotherapy

	– Erlotinib (only for unknown EGFR-TK mutation status) – Nintedanib in combination with docetaxel – Crizotinib (only for patients with ALK positive mutation status) – Ceritinib (only for patients with ALK positive mutation status) – Best supportive care • After two prior therapies: – Docetaxel monotherapy – Erlotinib (if not received previously) – Best supportive care
Outcomes	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	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 patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	If the evidence allows, consideration will be given to subgroups based on biological markers. If appropriate, the appraisal should include consideration 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	Related Technology Appraisals: Technology Appraisal 484, Nov 2017, 'Nivolumab for previously treated non-squamous non-small-cell lung cancer'. This is being reviewed in this scope's appraisal (ID1572), ongoing. Technology Appraisal 483, Nov 2017, 'Nivolumab for previously treated squamous non-small-cell lung cancer'. Review technology appraisal in preparation (ID1559), ongoing. Technology Appraisal 310, Mar 2014, 'Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer'. Reviewed Jun 2018. Technology Appraisal 422, Dec 2016, Crizotinib for previously treated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer'. Review Proposal Date 2019. Technology Appraisal 175, Jul 2009, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small-cell lung cancer (terminated appraisal)'. Replaced by Technology Appraisal 374. Technology Appraisal 162, Nov 2008, 'Erlotinib for the treatment of non-small-cell lung cancer'. Replaced by Technology Appraisal 374. Technology Appraisal 374, Dec 2015, 'Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy'. Reviewed Dec 2018. Technology Appraisal 124, Aug 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Static list. Technology Appraisal 347, July 2015, 'Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer'. Review Proposal Date 2018. Technology Appraisal 395, Jun 2016, 'Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer'. Review Proposal Date TBC. Related Guidelines:

	NICE Guideline 122, Mar 2019, 'Lung cancer: diagnosis and management'. Review date TBC. Related Quality Standards: Quality Standard 17, Mar 2012, 'Lung cancer in adults'. Updated Mar 2019. https://www.nice.org.uk/guidance/qs17 Related NICE Pathways: NICE Pathway: Lung cancer. Pathway created: Mar 2012. Updated Jun 2019. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	Department of Health, The national cancer strategy: 4th annual report, Dec 2014. https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England, Manual for prescribed specialised services, service 105: specialist cancer services (adults), Jan 2014. https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual.pdf Department of Health, NHS Outcomes Framework 2016-2017, Apr 2016. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf Department of Health, Cancer commissioning guidance, Dec 2009. https://webarchive.nationalarchives.gov.uk/20130123201014tf_/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.