NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for adjuvant treatment of resected stage III and IV melanoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for adjuvant treatment of resected stage III and IV melanoma.

Background

Cutaneous melanoma is a cancer of the skin. In its early stages, melanoma is normally asymptomatic and can often be cured by surgery (resection). However, it can spread or metastasise to nearby lymph nodes or to other parts of the body. Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, intermittent sun exposure and sunburn.

There were 12,993 new diagnoses of melanoma in 2014 and 2,080 deaths registered in England[1]. In the UK in 2012-2014, on average half of cases were diagnosed in people aged 65 and over[1].

The stage of melanoma describes how deeply it has grown into the skin, and whether it has spread. At stage I and II, there is no evidence that the tumour has spread anywhere else in the body, although there is a possibility of microscopic spread. Stage III melanoma means that the melanoma cells have spread into skin, lymph vessels, or lymph glands close to the melanoma. Stage III melanomas are considered intermediate to high risk as they are more likely to spread to other distant parts of the body (stage IV melanoma) than in earlier melanoma stages. In 2012, the proportion of people in the UK diagnosed with melanoma at stage III disease was 3%[2]. Advanced melanoma (stage IV) means the cancer has spread from where it started to another part of the body. Five-year survival rates are approximately 50-55% for stage III disease and 20-30% for stage IV disease[3].

Surgery (tumour removal and wide local excision) is the main treatment for early (stage I) and medium stage (stage II and III) melanoma. Only a small proportion of advanced (stage IV) melanoma can be completely removed by surgery[4]. Surgical removal of the nearly lymph nodes is also considered if there is evidence of microscopic spread. Early recognition of melanoma and accurate diagnosis present the best opportunities for cure. Adjuvant chemotherapy and immunotherapy following tumour removal are not widely used in UK practice.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Nivolumab does not currently have a marketing authorisation in the UK for treating people with resected melanoma. It is being studied in a clinical trial compared with ipilimumab in people with completely resected stage IIIb/C or Stage IV melanoma. Nivolumab has a marketing authorisation in the UK for treating adults with unresectable or metastatic melanoma, alone or in combination with ipilimumab.

Intervention	Nivolumab
Population	People with completely resected stage III or IV melanoma
Comparators	• Routine surveillance
Outcomes	The outcome measures to be considered include: • Overall survival • Recurrence-free survival • Distant metastases free survival • Duration of response • 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	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: None Related Technology Appraisals in development (including suspended appraisals) 'Ipilimumab for the adjuvant treatment of completely resected high risk stage III or IV melanoma' NICE technology appraisals guidance [ID721]. Publication date to be confirmed. 'Dabrafenib with trametinib for adjuvant treatment of resected BRAF V600 positive malignant melanoma' NICE technology appraisals guidance [ID1226]. Expected publication date December 2018. 'Vemurafenib for the adjuvant treatment of resected BRAF V600 mutation-positive melanoma with high risk of recurrence' NICE technology appraisals guidance [ID1250]. Suspended October 2017 'Pembrolizumab for adjuvant treatment of melanoma with high risk of recurrence' NICE technology appraisals guidance [ID1266]. Publication date to be confirmed Related Guidelines: 'Melanoma: assessment and management of melanoma'. (2015) NICE guidelines NG14. Related Quality Standards: http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp 'Skin cancer' (2016) NICE quality standard QS130 Related NICE Pathways: Melanoma (2017) NICE pathway NICE pathway http://pathways.nice.org.uk/
Related National Policy	Department of Health (2016) NHS outcomes framework 2016 to 2017 Department of Health (2014) The national cancer

	strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy NHS England (2013/14) NHS standard contract for cancer: skin (adult) A12/S/b NHS England (2013/14) NHS standard contract for cancer: chemotherapy (children, teenagers and young adults). B12/S/b NHS England Manual for Prescribed Specialised Services 2016/17. Chapter 105. Specialist cancer services (adults) https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1–5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Are there any adjuvant treatments considered to be established clinical practice in the NHS for adjuvant treatment following complete resection of stage III or stage IV melanoma?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom nivolumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider nivolumab will fit into the existing NICE pathway, Melanoma?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which nivolumab will license;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider nivolumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of nivolumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Cancer Research UK (2014) Skin cancer statistics. Accessed November 2017 http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/skin-cancer

2. National Cancer Intelligence Network and Cancer Research UK (2015) Routes to diagnosis by stage 2012-2013 workbook. Accessed November 2017 http://www.ncin.org.uk/publications/routes_to_diagnosis

3. Cancer Research UK (2014) Skin cancer survival statistics. Accessed November 2017 http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/skin-cancer/survival#heading-Three

4. Cancer Research UK (2014) Skin cancer survival statistics. Accessed November 2017 http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/skin-cancer/survival#heading-Three

5. Stage IV melanoma: completely resectable patients are scarce. Wevers and Hoekstra. Ann Surg Oncol. 2013 Jul;20(7):2352-6