

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Nivolumab-relatlimab for untreated unresectable or metastatic melanoma

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of nivolumab-relatlimab within its marketing authorisation for untreated unresectable or metastatic 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 (metastasise) to nearby skin and/or lymph nodes (stage 3) or other parts of the body (stage 4). 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.¹

In England in 2017, there were 13,740 registrations of newly diagnosed cases of malignant melanoma of the skin.² In the same year, England and Wales recorded 2,106 deaths with malignant melanoma of the skin as the underlying cause.³ Approximately 50% of melanomas harbour activating BRAF mutations.⁴

NICE technology appraisal 319 recommends ipilimumab as an option for previously untreated unresectable or metastatic melanoma. In addition, NICE technology appraisals 366, 384 and 400 recommend pembrolizumab (for melanoma that has not previously been treated with ipilimumab), nivolumab, and nivolumab with ipilimumab as treatment options, respectively. NICE guideline 14 recommends immunotherapy with nivolumab plus ipilimumab. Pembrolizumab or nivolumab are suitable only when nivolumab plus ipilimumab is unsuitable or unacceptable, for example due to potential toxicity. For people with BRAF mutation positive melanoma, targeted therapies are recommended when immunotherapy is contraindicated or unsuitable. Single agents dabrafenib or vemurafenib are suitable only when combination therapy with binimetinib and trametinib is contraindicated. When targeted therapies and immunotherapy treatment are contraindicated, dacarbazine chemotherapy or best supportive care is recommended.

The technology

Nivolumab-relatlimab (Opdualag, Bristol-Myers Squibb) does not have a UK marketing authorisation for untreated unresectable or metastatic melanoma.

It has been studied in a randomised clinical trial compared with nivolumab monotherapy in adults and adolescents 12 years of age and older with previously untreated unresectable or metastatic melanoma.

Intervention(s)	Nivolumab-relatlimab
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Population(s)	People aged 12 years and older with previously untreated unresectable or metastatic melanoma
Subgroups	<p>If the evidence allows the following subgroups will be considered:</p> <ul style="list-style-type: none"> • programmed death ligand 1 (PD-L1) expression status; • BRAF V600 mutation status
Comparators	<ul style="list-style-type: none"> • Nivolumab • Nivolumab with ipilimumab • Pembrolizumab
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression-free survival • overall survival • response rate • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.</p> <p>The economic modelling should include the costs associated with diagnostic testing for PD-L1 expression in people with melanoma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).</p>
<p>Other considerations</p>	<p>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.</p>
<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>Encorafenib with binimetinib for unresectable or metastatic BRAF V600 mutation-positive melanoma (2019) NICE Technology Appraisal 562. Review date 2022</p> <p>Cobimetinib in combination with vemurafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2016) NICE Technology Appraisal 414. Review date to be confirmed.</p> <p>Nivolumab in combination with ipilimumab for treating advanced melanoma (2016) NICE Technology Appraisal 400. Review date to be confirmed.</p> <p>Trametinib in combination with dabrafenib for treating unresectable or metastatic melanoma (2016) NICE</p>

	<p>Technology Appraisal 396. Review date to be confirmed.</p> <p>Nivolumab for treating advanced (unresectable or metastatic) melanoma (2016) NICE Technology Appraisal 384. Review date to be confirmed.</p> <p>Pembrolizumab for advanced melanoma not previously treated with ipilimumab (2015; updated 2017) NICE Technology Appraisal 366. Review date to be confirmed.</p> <p>Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2014) NICE Technology Appraisal 321. Review date to be confirmed.</p> <p>Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma (2014) NICE Technology Appraisal 319. Review date to be confirmed.</p> <p>Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma (2012; updated 2015) NICE Technology Appraisal 269. Review date to be confirmed.</p> <p>Related Guidelines:</p> <p>Melanoma: assessment and management (2015; updated 2022) NICE guideline NG14.</p> <p>Improving outcomes for people with skin tumours including melanoma (2006, updated 2010) NICE guideline CSG8</p> <p>Related Interventional Procedures:</p> <p>Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma (2013). NICE interventional procedures guidance 446.</p> <p>Related Quality Standards:</p> <p>Skin cancer (2016; updated 2022). NICE quality standard 130</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p> <p>NHS Standard Contract for Cancer: Skin (Adult) Section B Part 1 – Service Specifications (2013).</p>

References

1. Cancer Research UK (2020) [Risks and causes of melanoma](#). Accessed July 2021
2. Office for National Statistics (2019). [Cancer registration statistics, England 2017 dataset](#). Accessed July 2021

3. Office for National Statistics (2018). [Death registrations summary tables - England and Wales 2017 dataset](#). Accessed July 2021
4. Ascierto, Paolo A et al. "The role of BRAF V600 mutation in melanoma." *Journal of translational medicine* vol. 10 85 (2012).
5. NHS (2020) [Skin cancer \(melanoma\) – overview](#). Accessed July 2021