NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Lifileucel for previously treated unresectable or metastatic melanoma ID3863

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of lifileucel within its marketing authorisation for previously treated unresectable or metastatic melanoma.

Background

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 (stage III) or to other parts of the body (stage IV). Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, sun exposure and sunburn.

BRAF mutation is found in 40–50% of patients with metastatic disease and 70% to 90% of BRAF mutations involve a mutation at position 600 (BRAF V600).[1] Treatment for unresectable or metastatic melanoma is based upon the person's BRAF mutation status and their previous treatment history. A BRAF inhibitor with or without an MEK inhibitor and immunotherapy are both options for treating BRAF mutation-positive advanced melanoma.

In England in 2020, there were 12,477 registrations of newly diagnosed cases of malignant melanoma of the skin.[2] In the same year, 2,010 deaths with malignant melanoma of the skin as the underlying cause were recorded in England.[3]

For BRAF V600 mutation-positive unresectable or metastatic melanoma, NICE technology appraisal (TA) guidance recommends the BRAF inhibitor, dabrafenib alone (TA321) or with the MEK inhibitor, trametinib (TA396) and the BRAF inhibitor, vemurafenib alone (TA269). BRAF inhibitor encorafenib with MEK inhibitor binimetinib (TA562) alongside dabrafenib with trametenib are considered standard options in clinical practice, replacing the use of targeted BRAF inhibitor monotherapy. NICE technology appraisal guidance 414 does not recommend the use of vemurafenib with the MEK inhibitor, cobimetinib, for treating BRAF V600 mutation-positive advanced melanoma.

Treatment of advanced melanoma with immunotherapies is effective regardless of BRAF mutation status. NICE TA guidance recommends nivolumab alone (TA384) and in combination with ipilimumab (TA400) for treating advanced melanoma. Ipilimumab monotherapy is recommended for previously treated (TA268) unresectable or metastatic melanoma. For people not previously treated with ipilimumab, pembrolizumab alone (TA366) is recommended for treating advanced melanoma. Pembrolizumab is also recommended after disease progression with ipilimumab (TA357) for treating advanced melanoma.

In addition, intralesional therapy talimogene laherparepvec is recommended for treating unresectable, regionally or distantly metastatic melanoma that has not spread to bone, brain, lung or other internal organs (TA410).

The technology

Lifileucel (AMTAGVI, Iovance Biotherapeutics) does not currently have a marketing authorisation in the UK. It has been studied in an open label clinical trial in adults with previously treated unresectable or metastatic melanoma. Patients must have progressed following at least one prior systemic therapy:

- including a programmed death ligand 1 (PD-L1) blocking antibody (such as nivolumab or pembrolizumab);
- and a BRAF inhibitor in combination with mitogen-activated extracellular signal-regulated kinase for BRAF V600 mutation-positive melanoma.

Intervention(s)	Lifileucel
Population(s)	Adults with previously treated unresectable or metastatic melanoma
Subgroups	If the evidence allows the following subgroups will be considered: • programmed death ligand 1 (PD-L1) expression status • BRAF V600 mutation status
Comparators	• Nivolumab with ipilimumab • Nivolumab monotherapy • Ipilimumab monotherapy • Pembrolizumab monotherapy • Pembrolizumab with ipilimumab • Talimogene laherparepvec Targeted therapies for BRAF V600 mutation-positive unresectable or metastatic melanoma: • Encorafenib with binimetinib • Trametinib with dabrafenib • Dabrafenib monotherapy • Vemurafenib monotherapy
Outcomes	The outcome measures to be considered include: • progression free survival • overall 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 commercial arrangements for the intervention, comparator and subsequent treatment 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	**Related technology appraisals:** Encorafenib with binimetinib for unresectable or metastatic BRAF V600 mutation-positive melanoma (2019). NICE technology appraisal guidance 562. Cobimetinib in combination with vemurafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2016). NICE technology appraisal guidance 414. Talimogene laherparepvec for treating unresectable metastatic melanoma (2016) NICE technology appraisal guidance 410. Nivolumab in combination with ipilimumab for treating advanced melanoma (2016) NICE technology appraisal guidance 400. Trametinib in combination with dabrafenib for treating unresectable or metastatic melanoma (2016). NICE technology appraisal guidance 396. Nivolumab for treating advanced (unresectable or metastatic) melanoma (2016) NICE technology appraisal guidance 384. Pembrolizumab for advanced melanoma not previously treated with ipilimumab (2015) NICE technology appraisal guidance 366. Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab (2015) NICE technology appraisal guidance 357.

	Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2014). NICE technology appraisal guidance 321. Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma (2012). NICE technology appraisal guidance 269. Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma (2012). NICE technology appraisal guidance 268. **Related NICE Guidelines:** Melanoma: assessment and management (2015) NICE guideline NG14. Under review - update due in May 2022. Improving outcomes for people with skin tumours including melanoma (2010) NICE Cancer Service guideline CSG8. Under review. **Related Quality Standards:** Skin cancer (2016) NICE quality standard 130.
Related National Policy	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)

Questions for consultation

Have all relevant comparators for lifileucel been included in the scope? Which treatments are considered to be established clinical practice in the NHS for unresectable or metastatic melanoma that has progressed following at least one prior systemic therapy:

- including a programmed death ligand 1 (PD-L1) blocking antibody;
- and a BRAF inhibitor in combination with mitogen-activated extracellular signal-regulated kinase for BRAF V600 mutation-positive melanoma?

Are the proposed subgroups appropriate?

Where do you consider lifileucel will fit into the existing care pathway for previously treated unresectable or metastatic melanoma?

Please select from the following, will lifileucel be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would lifileucel be a candidate for managed access?

Do you consider that the use of lifileucel can result in any potential 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 committee to take account of these benefits.

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 lifileucel will be licensed;
- 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Kong BY CM, Menzies AM (2016) Biology and treatment of BRAF mutant metastatic melanoma. *Melanoma management:* 3(1):33-45
2. NHS Digital (2022). Cancer registration statistics, England, 2020. Accessed March 2024
3. NHS Digital (2022). Cancer registration statistics: cancer mortality in England, 2020. Accessed March 2024