Engagement report

Topic details

Title of policy or policy statement:	Neoadjuvant followed by adjuvant pembrolizumab for stage III macroscopic resectable melanoma (> 12 years)
Programme of Care:	Cancer
Clinical Reference Group:	Chemotherapy (and other anti-systemic cancer treatment)
URN:	2426

1. Summary

This report summarises the feedback NHS England received from engagement during the development of this policy proposition, and how this feedback has been considered.

2. Background

Melanoma is a cancer of melanocytes, the pigment (melanin) producing cells of the body. Most melanoma originates from the skin. Melanoma is more common in older populations, with more than a quarter of melanoma cases being in patients aged 75 years and older. However, there are a significant number of younger patients. Other risk factors include exposure to ultraviolet radiation (e.g. sun, tanning beds) and gene mutations (e.g. BRAF mutation). It is estimated that 86% of melanoma cases in the UK are preventable (Cancer Research UK, n.d.).

Stage III melanoma, where the cancer cells have spread to regional lymph nodes has a 5-year survival of 75% however stage IV melanoma has a 5-year survival of approximately 20% (Cancer Research UK, n.d.). It is therefore important to minimise the likelihood of patients with stage III disease progressing to stage IV disease.

This clinical commissioning policy proposition recommends that the 54 weeks of pembrolizumab treatment is started 9 weeks before surgery (neoadjuvant). Patients will then have surgery to remove the melanoma and lymph node disease and then complete the remaining pembrolizumab as adjuvant therapy. Neoadjuvant therapy generates more anti-tumour T cells (cancer fighting cells) and has been shown to improve clinical outcomes, not only for pembrolizumab but for the wider class of immune checkpoint inhibitors as well (Blank et al 2024; Patel et al, 2023). Under this new regime, patients would continue to complete the same number of total cycles of pembrolizumab equating to 54 weeks treatment and would continue to have the same number of scans and appointments.

Currently, pembrolizumab is licensed in melanoma for patients aged 12 years and older with advanced (unresectable or metastatic) melanoma or for adjuvant treatment for stage IIB, IIC or III melanoma who have undergone complete resection (EMC, 2024). The licensing recommends up to one year's treatment with adjuvant pembrolizumab for advanced melanoma. The use of pembrolizumab as neoadjuvant followed by adjuvant therapy for macroscopic, resectable stage IIIB-D melanoma as outlined by this policy proposition is therefore off-label. Neoadjuvant pembrolizumab is now a standard of care in several other countries including Australia, Ireland, Canada, Italy and Sweden.

3. Engagement

Following stakeholder testing feedback, the Programme of Care (PoC) has considered that the proposition offers a clear and positive impact on patient treatment, by potentially making a new treatment available which widens the range of treatment options without disrupting current care or limiting patient choice, and therefore further public consultation was not required. This decision has been assured by the Patient Public Voice Advisory Group.

NHS England has a duty under Section 13Q of the NHS Act 2006 (as amended) to 'make arrangements' to involve the public in commissioning. Full guidance is available in the Statement of Arrangements and Guidance on Patient and Public Participation in Commissioning. In addition, NHS England has a legal duty to promote equality under the Equality Act (2010) and reduce health inequalities under the Health and Social Care Act (2012).

The policy proposition underwent a four-week stakeholder testing between the 12th August 2025 and closed on 3rd September 2025 with registered stakeholders from the following Clinical Reference Group:

- Chemotherapy (and other anti-systemic cancer treatment)

Respondents were asked the following consultation questions:

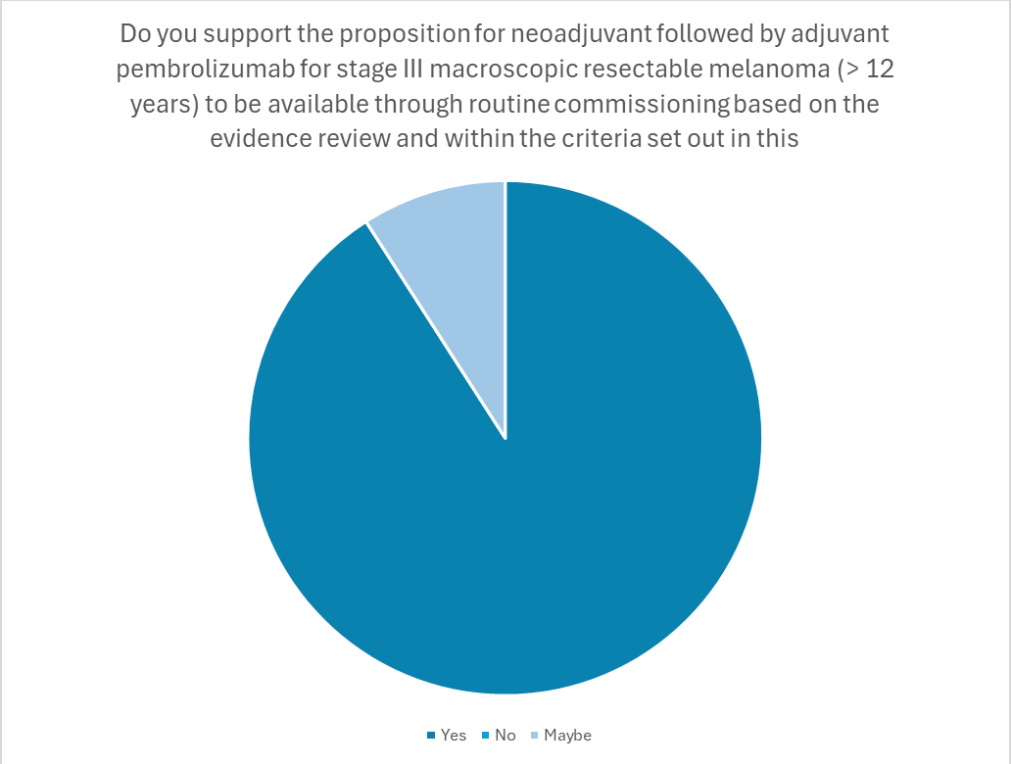
- RC: Do you support the proposition for neoadjuvant followed by adjuvant pembrolizumab for stage III macroscopic resectable melanoma (> 12 years) to be available through routine commissioning based on the evidence review and within the criteria set out in this document?
- NRC: Do you support the proposition that neoadjuvant followed by adjuvant pembrolizumab for stage III macroscopic resectable melanoma (> 12 years) will not be routinely commissioned based on the evidence review and the criteria set out in this document?
- Do you believe that there are any potential positive and/or negative impacts on patient care as a result of making this treatment option available?
- Do you believe that there is any additional information that we should have considered in the evidence review?
- Do you support the Equality and Health Inequalities Impact Assessment (EHIA)?
- Does the Patient Impact Assessment (PIA) present a true reflection of the patient and carers lived experience of this condition?
- Do you have any further comments on the policy proposal?
- Do you have any potential conflict of interest relating to this document or service area?

4. Engagement Results

Number stakeholders responded: 11

- 6 clinicians
- 3 pharmacists
- 2 patients

All bar one respondent were supportive of the policy proposition.



5. How has feedback been considered?

Responses to engagement have been reviewed by the Policy Working Group (PWG) and the Cancer PoC. The following themes were raised during engagement:

Key themes in feedback	NHS England Response
Policy Proposition	
The majority supported the policy proposition with one stating 'Maybe' citing several studies noting discrepancies in lymph node removal.	Some of the referenced papers were out of scope due to differing interventions to the present policy proposal. SWOG 1801 is a post-hoc analysis and is not used to guide treatment decisions. A full nodal resection was performed with neo-adjuvant pembrolizumab and is consistent with the policy proposition.

One respondent stated that the policy proposition would be cost neutral.	As part of the policy development process, cost effectiveness is explored in the single paper summary however, none of the papers shared any evidence. Further, the policy proposition is currently in the process of financial modelling which aids in rationalising the cost of treatment.
One respondent requested consideration of six-weekly dosing.	Six-weekly pembrolizumab is a standard alternative to three-weekly pembrolizumab in adjuvant and metastatic settings. However, the PWG recommended the three-weekly schedule pre-operatively as it is helpful to identify and manage early onset emergent toxicity, rapid progression of macroscopic disease and reduce the risk that toxicities preclude surgery as per the trial data.
One respondent shared concerns on the legibility of the 'Dosing' section with the use of 'x' as a multiplier.	All Specialised Commissioning publications should be accessible for all individuals, including those who may not be familiar with the content. The 'Dosing' section of the Policy Proposition has been updated to improve accessibility.
Additional information	
One individual requested consideration of expanding the interventions to include ipilimumab and nivolumab through the Nadina trial; noting discrepancies between current commissioning stances between Scotland and England.	Health is a devolved administration responsibility and there are many differences of commissioning between the different countries. The single paper summary and subsequent policy proposition include pembrolizumab only. Ipilimumab and nivolumab is therefore out of scope and a separate Preliminary Policy Proposal would be required.
Equality and Health Inequalities Impact Assessment	
All individuals supported the EHIA with one recommending an update to the 'Age' section, requesting it be changed to 'surveillance' from 'best supportive care'.	The EHIA was updated accordingly.

The responses should answer all the themes reported in section 4 and cover the outcome of reviews of any additional evidence highlighted during engagement

6. Has anything been changed in the policy proposition as a result of the stakeholder testing and consultation?

The following change(s) based on the engagement responses has (have) been made to the policy proposition:

Section	Actions taken
Dosing	The section now reads (with the changes underlined): "**Adults:** The recommended dose of pembrolizumab is 200mg as an intravenous infusion over 30 minutes every 3 weeks or 400mg every 6 weeks. The total treatment time with pembrolizumab is 54 weeks. Neoadjuvant pembrolizumab is where the first **3 treatments (or cycles) are given every 3 weeks** before surgery. Patients should then have surgery (resection of melanoma and lymph node disease) within 3 weeks of the last dose of neoadjuvant pembrolizumab. Adjuvant therapy should be resumed as soon as safely possible after surgery, however this should not exceed 3 months. Following this, patients would continue with adjuvant pembrolizumab **usually given every 6 weeks for 7 treatments OR every 3 weeks for 15 treatments**. **Children (12 years and older):** The recommended dose in children aged 12 years and over is 2mg/kg (up to a maximum of 200mg). The total treatment time with pembrolizumab is 54 weeks (1 year). Neoadjuvant pembrolizumab is where the **first 3 treatments (or cycles) are given every 3 weeks before surgery.** Patients should then have surgery (resection of melanoma and lymph node disease) within 3 weeks of the last dose of neoadjuvant pembrolizumab. Adjuvant therapy should be resumed as soon as safely possible after surgery, however this should not exceed 3 months. Following this, children should complete their adjuvant treatment with 1 year of treatment."
Inclusion Criteria	An error was noted in the inclusion criteria where the inclusion criteria references "a sentinel lymph node biopsy" as a key determinate of proceeding with the intervention. However, sentinel lymph node biopsy is a staging procedure to determine eligibility for adjuvant therapy. Therefore, the policy proposition and supplementary documents have been updated to state, "Complete surgical resection of the tumour and therapeutic lymph node dissection..."

7. Are there any remaining concerns outstanding following the consultation that have not been resolved in the final policy proposition?

Nil