NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 21 May 2025

Intervention: Pembrolizumab in combination with dabrafenib and trametinib

Indication: BRAF mutated anaplastic thyroid cancer (adults)

URN: 2418

Gateway: 2, Round 1

Programme: Cancer

CRG: Chemotherapy

Information provided to the Panel

Policy Proposition

Change of Policy Title report

Evidence Reviews completed by Solutions for Public Health

Clinical Priorities Advisory Group (CPAG) Summary Report

Evidence to Decision (EtD) Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq® Form – initiation for adults and initiation form for post-pubescent children (in line with NHS England Commissioning Medicines for Children policy)

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the use of pembrolizumab in combination with dabrafenib and trametinib for inoperable, anaplastic thyroid cancer (ATC) with a BRAF mutation (adults). The proposition recommends that all three drugs can be started together, or dabrafenib and trametinib be started first and pembrolizumab added later. ATC is a rare and aggressive form of thyroid cancer and usually presents at an advanced stage or as an emergency with symptoms such as a neck mass, difficulty swallowing and difficulty breathing. ATC has a poor prognosis, with median survival being only 3.16 months.

For ATCs that carry a BRAF mutation, targeted dual therapy such as dabrafenib and trametinib has significantly improved prognosis, however eventually patients develop resistance to this treatment combination and their disease progresses. Hence adding pembrolizumab as a monoclonal antibody to deactivate ATCs ability to evade the host's immune system and slow tumour growth.

Pembrolizumab works by stopping cancer cells being able to evade the host's immune system and this slows down tumour growth. The proposition recommends that all three drugs can be started together, or dabrafenib and trametinib be started first and pembrolizumab added later. The use of pembrolizumab, dabrafenib and trametinib for this indication would be off-label.

An evidence review was completed which included two papers: one retrospective cohort study and one subgroup of patients from a retrospective case series, both carried out in the US in single centres. No cost-effectiveness studies were identified for inclusion. Limitations of the studies were highlighted including the small sample size. The main limitations relating to the retrospective case series are the lack of a comparator group and the very limited results reported with no summary statistics for the in scope patients.

The retrospective cohort study reported a statistically significant increase in progression free survival in patients with inoperable BRAF-mutated ATC when adding pembrolizumab to dabrafenib and trametinib compared to standard treatment. Progression free survival increased to 11 months for the patients that received pembrolizumab, compared to 4 months for patients that received only dabrafenib and trametinib.

Outcomes that were considered critical and important to decision making were presented to Panel members. No evidence was identified for quality of life, activities of daily living, or symptom control. The evidence was graded very low certainty.

The proposition and the supporting documentation were presented to Clinical Panel members. The Panel members were informed that this proposition is an end-of-life treatment, which provides patients with inoperable BRAF-mutated ATC some extra months of life. Dabrafenib and trametinib treatment has been available for patients since 2022, and approximately 2 patients a month in England access this combination treatment for this indication. Not all of these patients would have sufficient fitness to tolerate the additional pembrolizumab, therefore the number of patients who would be able to benefit from this treatment is small.

EHIA – no amendments requested.
PIA – no amendments requested.

Recommendation

Clinical Panel recommends that this proposition progresses as a routine commissioning policy proposition.

Why the panel made these recommendations

Panel members agreed that the evidence base, although of very low certainty, supported the proposition, and improvements that were reported across the studies.

There was an extended and challenging discussion on the quality of evidence for this proposition and the nature of the condition. Although the proposition is progressing as a routine commissioning policy, there was a strong opinion from Panel members that further research in this area would be beneficial.

Documentation amendments required Policy Proposition:

- Amend minor typo on commissioning in the “Summary” section of the document.
- Consider amending the wording in the sentence “*Emerging evidence shows that pembrolizumab, in combination with dabrafenib and trametinib, improves patient outcomes”* to “*Emerging evidence shows that pembrolizumab, in combination with dabrafenib and trametinib, improves short term survival”.*

Declarations of Interest of Panel Members: None received

Panel Chair: Anthony Kessel, Deputy National Medical Director (Specialised Services)

2423: Pembrolizumab in combination with dabrafenib and trametinib for patients with BRAF mutated anaplastic thyroid cancer (adults) [2418]: List of May Clinical Panel Requested Amendments and Policy Working Group (PWG) responses

Policy proposition		
Panel comment	**Amendment**	**Page number (if applicable)**
Amend minor typo on commissioning in the "Summary" section of the document	'Routinely commissioning' was changed to 'routinely commissioned.'	**Page 2: Summary**
Consider amending the wording in the sentence "*Emerging evidence shows that pembrolizumab, in combination with dabrafenib and trametinib, improves patient outcomes"* to "*Emerging evidence shows that pembrolizumab, in combination with dabrafenib and trametinib, improves short term survival".*	The sentence was amended as suggested.	**Page 4: About Pembrolizumab**