Pembrolizumab monotherapy in second-line (or later) treatment of non-small-cell lung cancer

Approved at the meeting of the Council for Choices in Health Care in Finland (COHERE) on 13 March 2019

Recommendation by COHERE		Pembrolizumab is included in the range of services as monotherapy in the treatment of locally advanced or metastatic non-small-cell lung cancer among adult patients who have previously been treated with a cytostatic agent, whose tumours express PD-L1 ligand (TPS ≥ 1%) and whose tumours do not have EGFR or ALK positive mutations. Patients should be in good general condition (ECOG 0-1), have no serious immunity-weakening diseases or medications, and should not have been treated previously with PD-1/PD-L1 inhibitors. The effectiveness of treatment in relation to the adverse effects should be assessed closely and the treatment stopped when the cancer progresses. A precondition for this recommendation is that the pharmaceutical company and the purchaser of the drug agree on a price lower than the drug's wholesale price.
Grounds	Severity and prevalence of the health issue	Lung cancer causes the most mortality of all cancer in Finland. The majority of lung cancers are non-small-cell cancers and are only detected in the metastatic stage, when the goal of treatments is generally to slow disease progression and prolong life. The age-adjusted relative survival rate of non-small-cell lung cancer 5 years after diagnosis is 11% for men and 16% for women. Fimea estimates that each year there are about 60 patients in Finland with lung cancer suitable for treatment in accordance with this recommendation.
	Treatment options	Treatments with cytostatic agents, such as docetaxel, are usually used in second-line (and later) treatment of non-small-cell lung cancer. The PD-1 inhibitor nivolumab and PD-L1 inhibitor atezolizumab, which affect the T-cell-mediated immune response, are also treatment options.
	Effectiveness	In the second-line (and later) treatment of non-small-cell lung cancer, pembrolizumab has been shown to prolong the median overall survival by about two months compared to docetaxel. No significant difference between treatments was found in the effect on survival before disease progression.
	Safety	Pembrolizumab is linked with fewer serious adverse effects than treatment with docetaxel. Discontinuation of treatment owing to an adverse effect was also less frequent among patients receiving pembrolizumab. Among some patients, the use of PD-1/PD-L1 inhibitors has been found to be associated with clinically significant adverse effects on the immune system. Adverse effects may occur only months after the end of treatment.
	Costs and impact on the budget	The cost of one year of treatment with pembrolizumab per patient is estimated at EUR 162,000. Treatment for an estimated 60 patients would cost nearly EUR 10 million annually. In practice, the budgetary impact is lower depending on the duration of the treatments given and how patients are distributed between different treatment options. For a considerable share of patients, the duration of treatment will probably be less than one year.
	Ethical and financial aspects as a whole	The likelihood of benefit from treatments with PD-1/PD-L1 inhibitors increases with the tumour's PD-L1 expression. The optimal administration frequency or duration of treatments is not known. From the perspective of the financial resources available to the healthcare system, it is justified to target the use of PD-1/PD-L1 inhibitors at patients who, with adequate certainty, will benefit from the treatment. Second-line (and later) treatments should use the PD-1/PD-L1 inhibitor with the lowest procurement and administration costs.
Collection of further evidence		It is recommended that data on the number of patients treated, characteristics, the duration of treatment and outcomes, as well as data on other cancer treatments given, be collected and reported routinely.
Diagnosis (ICD-10) codes		C34 Lung cancer
Background information and references		COHERE memorandum (in Finnish), Assessment report by Fimea (In Finnish with English Summary)