Nivolumab 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		Nivolumab 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 tumour is PD-L1 positive (TPS ≥ 1%) and whose tumour does not have EGFR or ALK positive mutations. Patients should be in good general condition (ECOG 0-1), have no serious immunity-weakening diseases or medication, 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 treatment of non-small-cell lung cancer. The PD-1 inhibitor pembrolizumab, which affects the T-cell-mediated immune response, as well as the PD-L1 inhibitor atezolizumab are also treatment options.
	Effectiveness	In the second-line (and later) treatment of non-small-cell lung cancer, nivolumab has been shown to prolong the median overall survival by about three months compared to docetaxel. In the treatment of non-squamous lung cancer, the effects of nivolumab on survival were favourable only when the level of PD-L1 expression of the tumours was at least 1%.
	Safety	Considerably fewer serious adverse effects occurred among patients who received nivolumab than among patients who received docetaxel. Of the severe adverse effects, in particular, neutropenias were less common in the nivolumab group than in the docetaxel group. Discontinuation of treatment due to adverse effects was also less common in the nivolumab group. 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 nivolumab per patient is estimated at EUR 121,000. If 60 patients were treated for 12 months, the total cost would be a little over EUR 7 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 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. 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, the duration of treatment and outcomes, as well as data on other cancer treatment 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)