Nivolumab in NSCLC: Indication of major added benefit for under 75-year-olds

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Nivolumab is an anti-tumour drug from the group of monoclonal antibodies. It has been available since June 2015 under the trade name Opdivo for adults with advanced melanoma, and since July 2015 under the trade name Nivolumab BMS also for adults with metastatic squamous non-small cell lung cancer (NSCLC) after prior chemotherapy.

The German Institute for Quality and Efficiency in Health Care (IQWiG), which in October 2015 had already found an added benefit of the drug for patients with advanced melanoma, now examined in another dossier assessment whether nivolumab also offers an added benefit over the appropriate comparator therapy in the treatment of NSCLC.

According to the findings, there is an indication of major added benefit of nivolumab over the appropriate comparator therapy docetaxel for under-75-year-olds in relatively good general condition, and a hint of a non-quantifiable added benefit for over-75-year-olds in relatively good general condition. For patients in worse general condition, an added benefit is not proven due to a lack of study data.

Comparator therapy depends on general condition

The Federal Joint Committee (G-BA) distinguished between two treatment situations in its commission: In patients with Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0, 1, and

possibly 2, the benefit or harm of nivolumab was to be compared with docetaxel as appropriate comparator therapy.

For patients for whom docetaxel is not indicated due to their worse general condition (ECOG PS 4, 3, and possibly 2), the appropriate comparator therapy was to be the so-called best supportive care, i.e. treatment tailored to the individual patient's needs, which aims to alleviate symptoms such as pain and improve quality of life.

Informative data on the outcome 'overall survival'

Since the manufacturer presented no data on the second research question in its dossier, an added benefit of nivolumab is not proven for patients with a higher ECOG PS in comparison with the appropriate comparator therapy best supportive care.

For the first research question, data from the study CA209-017 were available, a randomized, open-label, active-controlled approval study on the comparison of nivolumab with docetaxel in patients who had already had platinum-based chemotherapy and whose general condition corresponded to ECOG PS 0 or 1.

The risk of bias was low both at study level and for the outcome 'overall survival'. In other outcomes such as severe adverse events or treatment discontinuation due to adverse events, the risk of bias was high, however. No evaluable data were available on further benefit outcomes such as health-related quality of life.

Gained life expectancy depends on age

The results for the outcome 'overall survival' depended on age. Patients under the age of 75 years had a statistically significant advantage of

nivolumab. Their median survival time was 9.5 months, which is 3.5 months longer than in the docetaxel arm of the study (6 months): an indication of major added benefit. Over-75-year-olds, in contrast, had no advantage, and shorter overall survival cannot be excluded. Hence in older patients, there is no hint of an added benefit of nivolumab for this outcome.

No suitable data were available for the outcome categories 'morbidity (symptoms and health status)' and 'health-related quality of life'; an added benefit is therefore not proven.

Advantages in side effects

In the outcome category 'side effects', there was a hint of lesser harm from nivolumab in each case for treatment discontinuations due to adverse events and for severe adverse events. Greater or lesser harm was not proven for serious adverse events (SAEs).

Only qualitative interpretation was possible of the data on specific side effects because of the different observation durations in the study arms: There was a hint of lesser harm from nivolumab in each of the non-severe specific adverse events 'myalgia', 'peripheral neuropathy' and 'alopecia', and an indication of lesser harm in blood and lymphatic system disorders.

Under-75-year-olds: indication of major added benefit

Overall, there is an indication of major added benefit of nivolumab in comparison with the appropriate comparator therapy for patients with ECOG PS 0 or 1 in whom docetaxel treatment is indicated and who are younger than 75 years.

For patients who are older than 75 years, an added benefit is not proven for the outcome 'overall survival'. Overall, the marked positive effects of nivolumab in the outcomes 'treatment discontinuation' and 'severe side effects' and in the specific adverse events resulted in a positive conclusion also here: In patients with ECOG PS 0 or 1 who are 75 years of age or older, a hint of a non-quantifiable added benefit of nivolumab versus the appropriate comparator therapy docetaxel remains.

G-BA decides on the extent of added benefit

This dossier assessment is part of the early benefit assessment according to the Act on the Reform of the Market for Medicinal Products (AMNOG) supervised by the G-BA. After publication of the dossier assessment, the G-BA conducts a commenting procedure and makes a final decision on the extent of the added benefit.

More information: www.iqwig.de/download/A15-32_N … ertung-35a-SGB-V.pdf

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