Nivolumab in melanoma: Added benefit in certain patients

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Nivolumab (trade name: Opdivo) has been approved since June 2015 for adults with advanced melanoma. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether this drug offers an added benefit over the appropriate comparator therapy.

According to the findings, treatment-naive patients with BRAF V600 mutation-negative tumour have an advantage in overall survival. This advantage varies by sex, however. Overall, IQWiG sees an indication of considerable added benefit in men, and a hint with the extent "minor" in women.

The dossier contained no evaluable data for further patient Groups.

G-BA defined three research questions

The Federal Joint Committee (G-BA) distinguished between three treatment situations in its commission: In treatment-naive patients whose tumour is BRAF V600-positive (BRAF V600 mut tumour), nivolumab was to be compared with vemurafenib. In treatment-naive patients whose tumour is BRAF V600-negative (BRAF V600 wt tumour), the G-BA specified dacarbazine or ipilimumab as appropriate comparator therapy. In pretreated patients, the added benefit was to be assessed in comparison with treatment adapted to the individual patient at the physician's discretion.

Survival advantage varies by sex

The dossier contained suitable data from one randomized controlled trial (RCT), which compared nivolumab with dacarbazine, only for treatment-naive patients with BRAF V600 wt tumour. This study was stopped prematurely after an unplanned interim analysis because patients in the nivolumab arm survived longer.

Correspondingly, the dossier assessment resulted in a prolongation of overall survival. This effect varies by sex: An indication of major added benefit can be derived from the data for men; and a hint of a minor added benefit for women.

Data on adverse events not interpretable

The data on symptoms and late complications (morbidity) and on health-related quality of life as well as the data on side effects and treatment discontinuation due to side effects were not evaluable. Adverse events were also recorded that may be caused by progression of the disease. Hence no conclusive interpretation of these results is possible.

No hint of added benefit in two patient groups

For further patient groups, suitable data were lacking in the dossier: The drug manufacturer presented only an adjusted indirect comparison with vemurafenib for treatment-naive patients with BRAF V600 mut tumour. This comparison was not evaluable, however, because the included studies were not sufficiently similar. There was one RCT for pretreated patients. However, the manufacturer analysed them in such a way that the results were not evaluable for the assessment of the added benefit of nivolumab. As a result, for both groups no hint of an added benefit can be derived from the dossier.

Positive effect predominates

Overall, there is an added benefit of nivolumab only in treatment-naive patients with BRAF V600 wt tumour. The results on side effects are uncertain, and it is therefore not possible to balance benefit and harm. But there is no sign that a negative effect in side effects could completely outweigh the positive effect in overall survival. IQWiG therefore sees an indication of considerable added benefit of nivolumab in comparison with dacarbazine in men, and a hint of a minor added benefit in women.

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/A15-27_N … ertung-35a-SGB-V.pdf

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