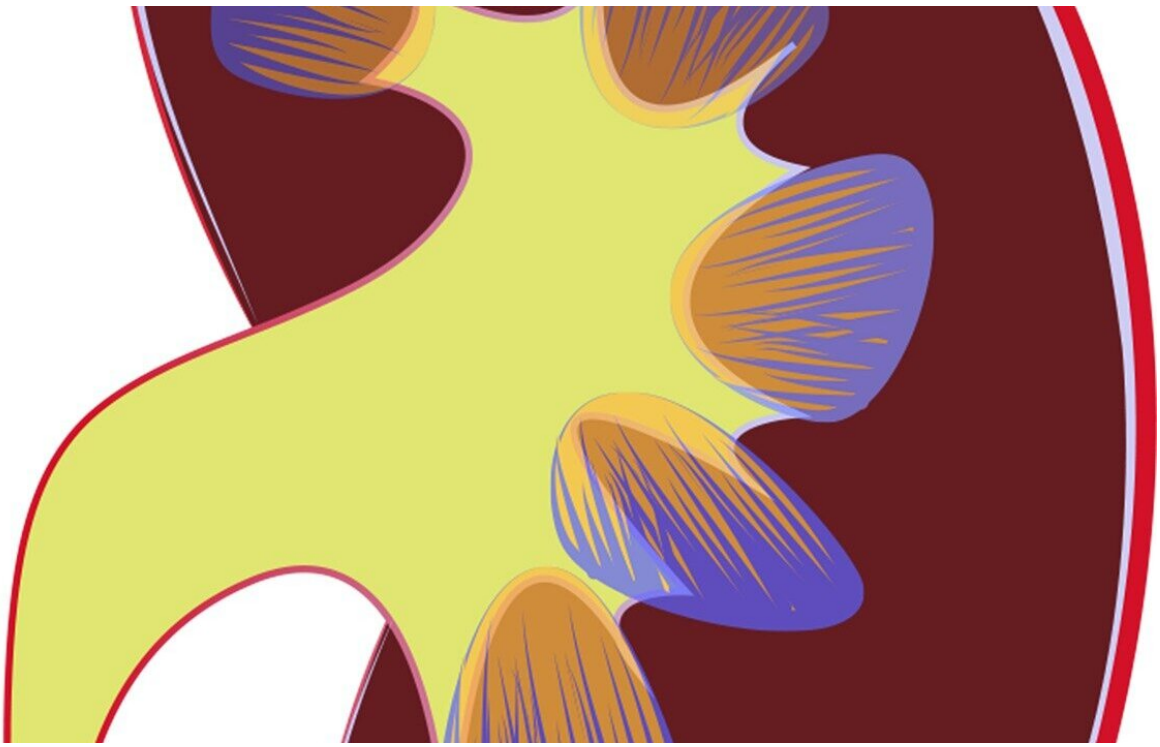
Nivolumab with ipilimumab: Combination has added benefit in advanced renal cell carcinoma

May 17 2019



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Renal cell carcinoma is one of the cancers for which the range of promising treatment options has become considerably wider in recent years. In several early benefit assessments since 2013, the German

Institute for Quality and Efficiency in Health Care (IQWiG) has already been able to determine an added benefit of a new drug in comparison with the respective appropriate comparator therapy (ACT).

The Institute has also come to a positive conclusion in its current assessment of nivolumab with ipilimumab: The drug combination has considerable added benefit in comparison with the ACT (sunitinib) for patients with advanced renal cell carcinoma and an intermediate risk score, and even major added benefit for patients with at least three risk factors and a corresponding unfavourable prognosis.

Antibodies as multipurpose weapons

In recent years, both monoclonal antibodies have already been subject of several early benefit assessments because, alone or in combination, they are also used against other types of cancer, e.g. melanoma, squamous cell carcinoma of the lung and non-small cell lung cancer. As so-called checkpoint inhibitors, they block different molecules on the outside of immune cells.

Nivolumab binds to the PD-1 receptors on T lymphocytes and thus prevents their defence-inhibiting effect. Ipilimumab, in contrast, weakens the inhibitory effect of the CTLA-4 molecules on the T lymphocytes. Both increase proliferation and activity of the immune cells, so that they can fight the tumour cells more vigorously.

Premature end of study after interim analysis

The data for both corresponding dossier assessments—in each case of one of the drugs in combination with the other—are from the randomized controlled trial CheckMate 214. The study was ended prematurely after the first interim analysis because the results on overall

survival were clearly in favour of the combination.

For patients with an intermediate risk score, the study data showed statistically significant and clinically relevant advantages in overall survival, symptoms and health-related quality of life. With both positive and negative effects of approximately the same magnitude regarding side effects, the conclusion for this outcome category was: Greater or lesser harm is not proven. Overall, there was an indication of a considerable added benefit.

The survival advantage was even more pronounced in patients with higher risk scores. In addition, there were hints of lesser harm of different extent for a number of side effects. This was offset by hints of greater harm in three side effects. However, these did not outweigh the advantages, so that the Institute sees an overall indication of a major added benefit.

G-BA decides on the extent of added benefit

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

More information: More English-language information will be available soon (extracts of the dossier assessments as well as easily understandable information on informedhealth.org). The website http://www.gesundheitsinformation.de, published by IQWiG, provides easily understandable German-language information.