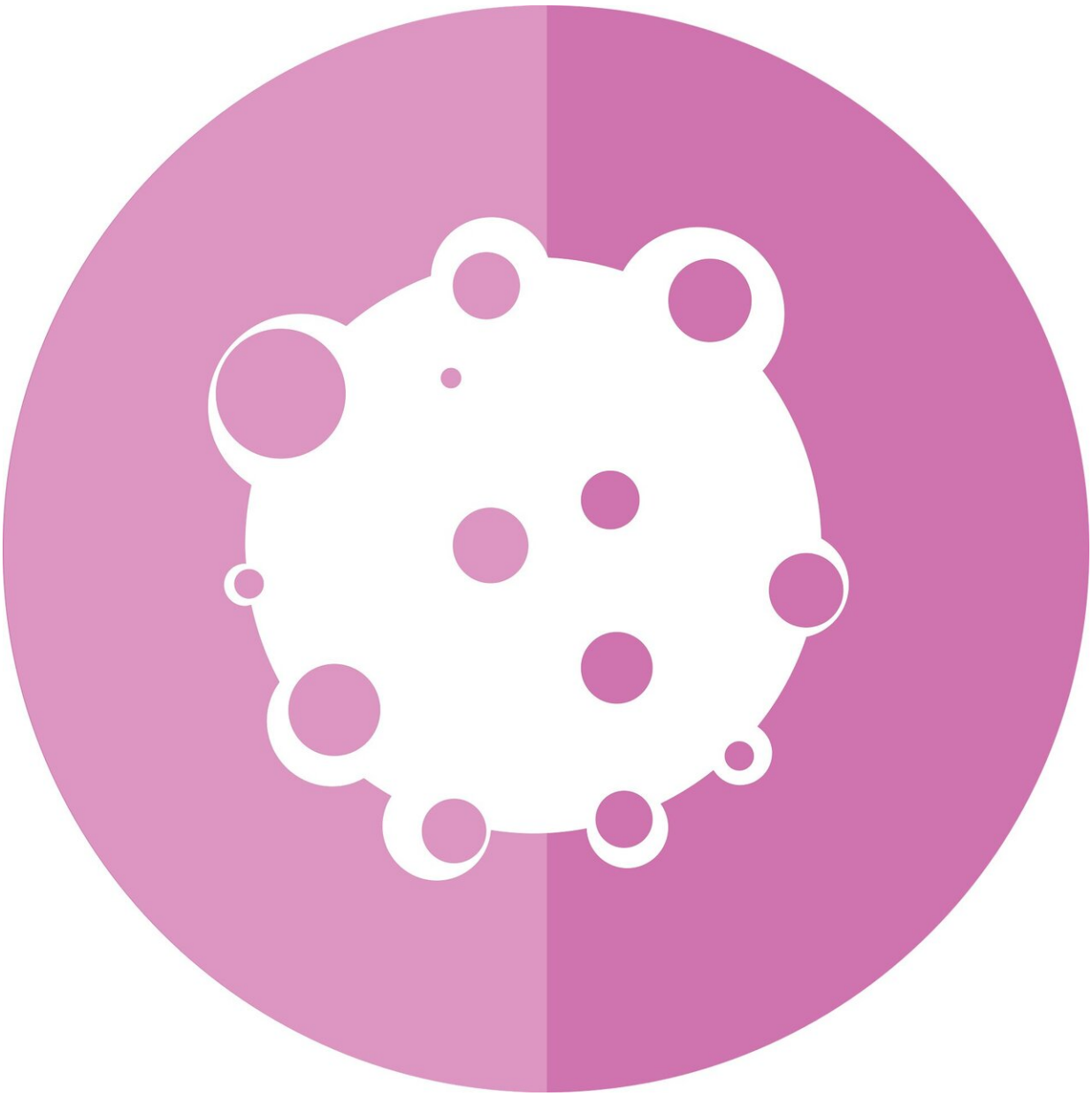
Nivolumab + ipilimumab: Added benefit in pleural mesothelioma with non-epithelioid tumour histology

October 4 2021



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The monoclonal antibodies nivolumab and ipilimumab have already undergone several early benefit assessments in various oncological indications. Since April 2021, the drug combination has also been approved for first-line treatment of unresectable malignant pleural mesothelioma in adults. Therefore, the German Institute for Quality and Efficiency in Health Care (IQWiG) has now investigated whether it offers an added benefit to the patients.

The effect depends on a subgroup characteristic, i.e. "tumor histology": For patients with non-epithelioid mesothelioma, there is an indication of considerable added benefit compared to platinum-based chemotherapy consisting of pemetrexed and cisplatin or carboplatin. An added benefit versus the same appropriate comparator therapy is not proven for patients with epithelioid mesothelioma. An added benefit of the new combination compared to the triple combination of bevacizumab, cisplatin and pemetrexed is also not proven—regardless of tumor histology.

First antibody combination for first-line treatment

Malignant pleural mesothelioma is an aggressive tumor of the pleura that grows around the lungs and can invade surrounding tissues and organs such as the pericardium and the lungs. It often also forms metastases in the local lymph nodes. It is usually triggered by exposure to asbestos, which may date back decades. The prognosis is better for women than for the more frequently affected men, and it also depends on the tumor histology: On average, patients with epithelioid mesothelioma survive

longer than those with non-epithelioid mesothelioma, which involves other cell types.

As long as only one side is affected, this side of the lung including the pleura can be removed. However, the pleural mesothelioma is often diagnosed too late for a successful resection. To date, radiotherapy or a combination of pemetrexed and platinum-containing chemotherapy has often been used for treatment in such cases.

For some years now, studies have suggested that certain monoclonal antibodies also prolong the survival period, even if they cannot halt tumor growth permanently. Now, the drug combination of nivolumab plus ipilimumab is the first one from the substance class of immunotherapeutics to be approved for first-line treatment of unresectable malignant pleural mesothelioma.

Approval study does not cover all treatment options

The Federal Joint Committee (G-BA) specified a therapy of physician's choice as appropriate comparator therapy. According to the guidelines, options to be considered include the dual combinations pemetrexed + cisplatin and pemetrexed + carboplatin as well as the triple combination bevacizumab + cisplatin + pemetrexed.

In its dossier, the manufacturer presents data from a randomized controlled approval study, in the comparator arm of which only the two dual combinations were used. Therefore, conclusions about the advantages and disadvantages of nivolumab + ipilimumab cannot be made for patients who could also have been treated with bevacizumab + cisplatin + pemetrexed; an added benefit compared to this triple combination is thus not proven.

The tumor histology influences the effects

78 percent of the patients who took part in the approval study had epithelioid and 22 percent had non-epithelioid pleural mesothelioma. Overall, the median survival time of participants was about four months longer with the new drug combination than with pemetrexed and platinum-containing chemotherapy. However, as in some other outcomes, there is a strong effect modification by tumor histology: While median overall survival for the epithelioid subtype was just under 19 months in the intervention arm and a good 16 months in the comparator arm, the difference for the non-epithelioid subtype was statistically significant and clinically relevant at just under 17 versus just under 9 months: For the prognostically disadvantageous subtype, the achieved median survival periods were of the same order of magnitude as the ones previously only achieved for the prognostically advantageous subtype.

In the category of side effects, there are also effect modifications due to tumor histology: In the case of epithelioid mesothelioma, more serious adverse events and more diseases of the kidneys and urinary tract occurred under the new drug combination than under the appropriate comparator therapy, while no statistically significant differences were observed in the case of the non-epithelioid subtype. Some other side effects occurred more frequently or less frequently in the intervention arm than in the comparator arm, irrespective of the tumor histology.

The result of the assessment is likewise twofold: For patients with non-epithelioid tumor histology, there is an indication of considerable added benefit. An added benefit of nivolumab plus ipilimumab compared to a combination of pemetrexed and platinum-containing chemotherapy is not proven for patients with epithelioid tumor histology.

More information: Assessment (in German): www.g-