Bronchial carcinoma: Added benefit of crizotinib for first-line treatment not proven

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The drug crizotinib (trade name: Xalkori) has been available since 2012 for patients with advanced non-small cell lung cancer (bronchial carcinoma) who have a high activity of the enzyme anaplastic lymphoma kinase (ALK) and have already received another treatment. In November 2015, the approval was extended to first-line treatment.

After its assessment in 2013, the German Institute for Quality and Efficiency in Health Care (IQWiG) therefore now reassessed the added benefit of the drug in comparison with the appropriate comparator therapy - and found out: An added benefit of crizotinib for the first-line treatment of advanced bronchial carcinoma is not proven.

Carboplatin only in advanced risk of cisplatin side effects

Advanced bronchial carcinoma can only be treated palliatively. The Federal Joint Committee (G-BA) specified several appropriate comparator therapies for this. Either cisplatin in combination with a third-generation cytostatic agent was to be used in the control arm, or - in case of an increased risk of cisplatin side effects - carboplatin with a third-generation cytostatic agent. Monotherapy with gemcitabine or vinorelbine was an alternative option for patients with already severe limitations.

Use of carboplatin attached to condition

The drug manufacturer did not use the latter option and only submitted data from a randomized study in which crizotinib was directly compared with cisplatin or carboplatin, each in combination with the cytostatic agent pemetrexed. Carboplatin is not approved for the treatment of advanced non-small cell lung cancer, but can be prescribed in so-called off-label use. This is only the case for patients with an advanced risk of cisplatin side effects, e.g. in neuropathy, hearing impairment or susceptibility to nausea, renal insufficiency or cardiac failure.

The only submitted study did not fulfil the condition

Almost half of the participants received carboplatin in the control arm of the PROFILE 1014 study; the criteria for this individual medical decision were not comprehensible. A large proportion of the patients in the control arm did not correspond to the criteria of the Pharmaceutical Directive for the off-label use of carboplatin. Patients with neuropathy, renal insufficiency or cardiac failure were excluded from participation in the study and only about two and six per cent of the participants had notable hearing impairment or nausea as accompanying disease.

Hence the control group of the study did not adequately represent the appropriate comparator therapy. The data submitted were therefore unsuitable for the derivation of an added benefit of crizotinib in comparison with this comparator therapy.

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/A15-59_C … ertung-35a-SGB-V.pdf