Dabrafenib: Also no added benefit over vemurafenib

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Dabrafenib (trade name: Tafinlar) has been approved since August 2013 for the treatment of advanced melanoma. In January 2014, in an early benefit assessment pursuant to the "Act on the Reform of the Market for Medicinal Products" (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) had determined that dabrafenib has no added benefit in comparison with dacarbazine. IQWiG now assessed dabrafenib in comparison with vemurafenib. The report presented in the form of an addendum came to the same conclusion because the results from the indirect comparison presented by the drug manufacturer did not allow any reliable conclusions.

G-BA specified appropriate comparator therapy

Dabrafenib is an option for adult patients with melanoma that has a certain abnormal protein (BRAF V600 mutation) and that is unresectable or has already formed metastases.

In the first dossier assessment, the Federal Joint Committee (G-BA) had specified the drug dacarbazine as the appropriate comparator therapy. Hence IQWiG did not assess data on an indirect comparison with vemurafenib, which the manufacturer had also presented in the dossier. However, the G-BA subsequently commissioned IQWiG to consider these data and to assess the added benefit of dabrafenib versus vemurafenib because the G-BA specified vemurafenib as appropriate comparator therapy during the hearing procedure. It considered its

current decision on vemurafenib and the evidence on dacarbazine in this specification.

Manufacturer used two approval studies

The manufacturer used data from the respective approval study on dabrafenib (BREAK-3) and on vemurafenib (BRIM-3) for the indirect comparison. The drugs were tested directly against dacarbazine in both studies. Dacarbazine could therefore be used as a so-called common comparator. Results on the outcomes "overall survival" and "adverse events (side effects)" were available from both studies.

Indirect comparison must fulfil certain requirements

It depends on various factors whether or not the results of such an indirect comparison are informative: On the one hand, the method must be suitable; on the other hand, the data used in the comparison have to fulfil certain minimum requirements regarding their risk of bias and their structural quality. With regard to the latter, it is decisive, among other things, whether the patients investigated in the studies are sufficiently similar.

Results on overall survival highly biased

The researchers found out that these requirements were not sufficiently fulfilled. It was unclear whether the patients investigated in the two studies were sufficiently similar in the prognosis of their disease.

The results on overall survival were highly biased: This was due to the fact that it was possible in one of the studies (BREAK-3) to switch to dabrafenib treatment (crossover) at an early stage. This already played an important role in the first dossier assessment of dabrafenib.

Regarding the outcome "side effects", the informative value of the indirect comparison was limited because patients within the studies, i.e. in the two study arms, were observed for different lengths of time.

An added benefit of dabrafenib compared with vemurafenib is therefore not proven.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments supervised by the G-BA. After publication of the manufacturer's dossier and the IQWiG dossier assessment, the G-BA conducted a commenting procedure. If, in the course of the discussions on a commission of the G-BA, a need for further revision arises, IQWiG presents its report in the form of an addendum. The Institute sent the addendum on dabrafenib to the commissioning agency on 14 March 2014. The G-BA decided on the extent of the added benefit of dabrafenib on 3 April 2014, thus completing the early benefit assessment.

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