Indication of considerable added benefit of vemurafenib in advanced melanoma

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Vemurafenib has been approved since February 2012 for the treatment of certain groups of adults with advanced melanoma. The drug offers major advantages in terms of survival, but also causes major side effects. Overall, there is an indication of a considerable added benefit. This is the conclusion of a dossier assessment by the IQWiG, Cologne, which was published in June 2012 and for which an English-language extract is now available.

The drug vemurafenib (trade name Zelboraf) has been approved since February 2012 for the treatment of advanced melanoma (cancer of the skin cells that produce the dark pigment, melanin). It can be an option for adults whose melanoma cannot be removed by surgery or has formed secondaries (metastases) and in whose cancer a change (mutation) has occurred in a certain gene (BRAF-V600). The German Institute for Quality and Efficiency in Health Care (IQWiG) has examined the added benefit of the drug pursuant to the Act on the Reform of the Market for Medicinal Products (AMNOG). According to the findings, major advantages in terms of overall survival are accompanied by major potential harm in the form of side effects. Overall, there is an indication that vemurafenib offers considerable added benefit.

Vemurafenib in comparison with dacarbazine

The Federal Joint Committee (G-BA) has specified the drug dacarbazine as the appropriate comparator therapy. One study that compared

vemurafenib directly with dacarbazine was available for the benefit assessment. This is a randomized and open-label study, i.e. patients were randomly assigned to one of the two treatment groups and both they and their doctors knew which of the two drugs was used in each case.

Longer survival means major added benefit

IQWiG always assesses a drug with a view to patient-relevant outcomes such as survival (mortality), symptoms and complications (morbidity) as well as quality of life. The study provides an indication that vemurafenib can prolong life. While half of the patients who received dacarbazine died after less than 10 months, in the vemurafenib group this was the case only after more than 13 months. The differing course of the two survival curves provides an indication of a major added benefit of vemurafenib.

Pain was the only outcome recorded in the study in relation to morbidity. There were, however, no statistically significant differences between the treatment groups - and hence also no indication of an added benefit of vemurafenib. As regards the quality of life (including physical and emotional well-being), there were no differences, so here, too, an added benefit is not proven.

Major potential harm in the form of side effects

Overall, the side effect profile of vemurafenib is less favourable than that of dacarbazine, because severe adverse events (according to the Common Terminology Criteria for Adverse Events (CTCAE) Grade ≥ 3) and serious adverse events were more frequent in patients who received vemurafenib. The proportion of those who discontinued the treatment due to side effects was comparable in the treatment groups. All in all, IQWiG sees an indication of greater harm from vemurafenib

and rates its extent as "major".

Potential for harm reduces the extent of the added benefit

In order to derive proof of benefit from a single study, it must meet special requirements. This particular study does not fulfil them. Therefore no conclusions with the highest probability (proof) are possible - for example, on added benefit; at most indications can be derived from the study.

In summary, there are positive and negative results of the same degree of certainty (indications). On the positive side, the greatest extent - namely "major" - is attained for overall survival. On the negative side, due to side effects, there is an indication of greater harm, and this is also of major extent. For this reason, the Institute downgrades the overall added benefit of vemurafenib relative to the appropriate comparator therapy with dacarbazine from "major" to "considerable".

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessment conducted by the G-BA. After publication of the manufacturer's dossier and its assessment by IQWiG, the G-BA initiates a formal commenting procedure, which provides further information and can result in a change to the benefit assessment. The G-BA then decides on the extent of the added benefit, thus completing the early benefit assessment.

More information: www.gesundheitsinformation.de/