Dabrafenib / trametinib: Considerable added benefit for men with advanced melanoma

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Dabrafenib (trade name: Tafinlar) has been approved since 2013 for the treatment of adults with advanced, i.e. metastatic or unresectable, melanoma with a BRAF V600 mutation. Since September 2015, dabrafenib has been approved for this therapeutic indication also in combination with trametinib (trade name: Mekinist). In the end of 2015, the German Institute for Quality and Efficiency in Health Care (IQWiG) determined in two dossier assessments: There is an indication of a major added benefit for women and of a non-quantifiable added benefit for men for this combination therapy.

To quantify this added benefit also for men, the drug manufacturer subsequently submitted study data in the commenting procedure, which the Institute investigated in an addendum. According to the findings, there is now an indication of a considerable added benefit for men. For women, there is still an indication of a larger, i.e. major added benefit.

Prolongation of life in men not proven

The manufacturer again submitted data from the COMBI-v study, in which dabrafenib/trametinib was directly compared with vemurafenib, in the commenting procedure on the dossier assessments from December 2015. Primary outcome of the study was overall survival, which was significantly longer in the dabrafenib/trametinib arm - with an effect modification by sex, however: There was an indication of an added benefit for women, whereas an added benefit in overall survival for men

was not proven.

No effect modification by sex for other outcomes

The assessment of the dossiers from 2015 resulted in an indication of lesser harm in comparison with the comparator therapy for men regarding serious side effects, i.e. of an advantage of the combination therapy. However, it could not be inferred from the data whether the effects in other patient-relevant outcomes also differed according to sex. It was therefore not possible to quantify the overall added benefit for men.

The subgroup analyses subsequently submitted now showed no proof of an effect modification by sex for the following outcomes: symptoms, health-related quality of life, health status, severe and serious adverse events and discontinuations due to such events. Hence the advantage men have from the combination therapy regarding serious side effects does not have to be adjusted.

Health status: hint of added benefit

A sensitivity analysis of data on morbidity recorded with the measurement instrument EQ-5D that had not been evaluable before was also subsequently submitted and resulted in a hint of considerable added benefit of dabrafenib/trametinib in comparison with vemurafenib.

Overall, there is now an indication of considerable added benefit in comparison with the appropriate comparator therapy for men with advanced melanoma with a BRAF V600 mutation. For women with advanced melanoma with a BRAF V600 mutation, there is still an indication of a major added benefit.

G-BA decides on the extent of added benefit

The 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 Federal Joint Committee (G-BA). After publication of the manufacturer's dossier and the IQWiG dossier assessment, the manufacturer submitted additional information in the commenting procedure. The G-BA subsequently commissioned IQWiG to assess the data subsequently submitted. IQWiG now presents this assessment in the form of an addendum. The G-BA makes a final decision on the extent of added benefit.

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