Ribociclib in breast cancer: Added benefit for certain women after menopause

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In 2017 and 2019, the German Institute for Quality and Efficiency in Health Care (IQWiG) had already examined the advantages and disadvantages of ribociclib in combination with an aromatase inhibitor or fulvestrant in comparison with the appropriate comparator therapy in patients after menopause, with hormone receptor-positive,

HER2-negative, locally advanced or metastatic breast cancer. Since the assessments were based on ongoing studies, the Federal Joint Committee (G-BA) had limited its corresponding decisions.

After expiry of the decisions, IQWiG now reassessed the combinations on the basis of further data from the same studies. According to the findings, an added benefit is not proven for initial endocrine therapy with ribociclib in combination with the aromatase inhibitor letrozole and for subsequent endocrine therapy with ribociclib plus fulvestrant. For initial endocrine therapy with ribociclib plus fulvestrant, in contrast, there is now an indication of a minor added benefit.

Newer data confirm survival advantages, but also severe side effects

In the first assessment conducted in 2017, on the basis of the data from the ongoing MONALEESA-2 study available at that time, the Institute found the drug in combination with an aromatase inhibitor to have lesser benefit than the comparator therapy due to partly very severe side effects. In 2019, the survival advantage for the combination with fulvestrant shown in the also still ongoing MONALEESA-3 was outweighed by the severe side effects; the resulting conclusion was therefore: An added benefit is not proven.

The new data cut-offs from both studies now confirmed the survival advantages for the combination with fulvestrant, and for the first time showed survival advantages for the combination with an aromatase inhibitor, but also confirmed the major disadvantages: Women treated with ribociclib developed severe side effects much more frequently than study participants in the comparator arms of the studies, particularly severe neutropenia. This means that the number of neutrophil granulocytes—immune cells which are essential for fighting

infection—in their blood was too low.

In initial endocrine therapy for the advanced stage, these negative effects did not completely call into question the survival advantage of ribociclib plus fulvestrant versus placebo plus fulvestrant, but they resulted in a downgrading of the extent of the added benefit. An indication of a minor added benefit remained.

An added benefit is not proven for two of three research questions

In women who have already received endocrine therapy for the advanced stage, there was no statistically significant advantage in overall survival under ribociclib plus fulvestrant; this was only shown if results of the total study—including patients without pretreatment—were additionally taken into account. This and the major positive effect for emotional functioning in the outcome category "health-related quality of life" (but only for patients aged 65 years and older) did not have greater weight in the assessment than the mostly severe side effects of considerable or major extent, so that an added benefit is not proven for these patients.

Both positive and negative effects were also shown for the combination of ribociclib and the aromatase inhibitor letrozole in comparison with placebo and letrozole. The advantages in overall survival and future perspective (another aspect of the outcome category "health-related quality of life") and the disadvantages in severe side effects (besides the already mentioned neutropenia, also gastrointestinal disorders, infections and infestations) balanced each other out; an added benefit is not proven also in this case.

G-BA decides on the extent of added benefit

The dossier assessments are 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 assessments, the G-BA conducts commenting procedures and makes decisions on the extent of the added benefit.

More English-language information will be available soon (extracts of the dossier assessments as well as easily understandable information on informedhealth.org). If you would like to be informed when these documents are available, please send an e-mail to info@iqwig.de.

More information: www.iqwig.de/en/press/press-re … menopause.13059.html

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