Ribociclib in advanced breast cancer: Survival advantages, but also severe side effects

April 17 2019

In 2017, the German Institute for Quality and Efficiency in Health Care (IQWiG) already examined the advantages and disadvantages of ribociclib in combination with an aromatase inhibitor versus the appropriate comparator therapy in patients with HR-positive, HER2-negative, locally advanced or metastatic breast cancer. At that time, the examination concentrated on the application as initial endocrine-based therapy in postmenopausal women. The study data expressed no statistically significant advantage, but strong side effects of the new combination, resulting in the following conclusion: Ribociclib in combination with an aromatase inhibitor provides lesser benefit than the appropriate comparator therapy.

Meanwhile, the therapeutic indication of ribociclib was extended to pre-menopausal or menopausal women. Combination of the drug is not restricted to an aromatase inhibitor, it can also be combined with fulvestrant. Besides initial treatment, the substance can also be applied as subsequent therapy. Therefore, the Federal Joint Committee (G-BA) commissioned IQWiG with a new dossier assessment, which was to be based on data from the studies MONALEESA-3 and MONALEESA-7.

Advantages, but also clear disadvantages

For certain patients, there is an advantage in overall survival on this basis, which results in a hint of a minor added benefit in the outcome

category "mortality". "This survival advantage is statistically insignificant when the data are analysed for only one of the research questions", says the Institute's Deputy Director Stefan Lange. "However, we found it adequate to subject the data of the two relevant patient groups participating in the MONALEESA-3 study to joint consideration. Therewith, the significance threshold has been reached."

However, this advantage is accompanied by clear disadvantages, namely indications of major harm in the outcome category "adverse events", commonly referred to as side effects: Women who had been treated with ribociclib developed severe diseases of the blood and the lymphatic system much more frequently than the study participants in the comparator arm did.

The affected women developed so-called neutropenias, i.e. a lack of neutrophilic granulocytes—immune cells essential for the defence against infections. Eventually, these disadvantages are grave enough to outweigh the hint of a survival advantage. Overall, the Institute arrived at the following conclusion: An added benefit for postmenopausal women is not proven for any of the research questions. For pre-menopausal and menopausal women, however, the manufacturer presented relevant data only for a subgroup of pretreated women. For these women, lesser benefit in comparison with the appropriate comparator therapy must still be assumed.

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 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 English-language information will be available soon (Sections 2.1 to 2.8 of the dossier assessment 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/projects-resul … de-book-v.11476.html

Provided by Institute for Quality and Efficiency in Health Care