Neoadjuvant use of pertuzumab in HER2-positive breast cancer: Hint of lesser benefit

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Pertuzumab (trade name: Perjeta) is approved for two therapeutic indications. Its use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer was already investigated by the German Institute for Quality and Efficiency in Health Care (IQWiG) in a dossier assessment in 2013. This assessment resulted in a survival advantage for certain patients and hence for a hint of a major added benefit.

In a further dossier assessment, the Institute now examined the benefit of the drug in its second therapeutic indication, i.e. in preoperative use. In this so-called neoadjuvant treatment, pertuzumab is used in HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence, also in combination with trastuzumab and chemotherapy. The study data presented resulted in a hint that pertuzumab is of lesser benefit than the appropriate comparator therapy.

Trastuzumab and docetaxel as comparator therapy

The Federal Joint Committee (G-BA) specified trastuzumab, a taxane (paclitaxel or docetaxel) and, if applicable, an anthracycline as appropriate comparator therapy in its commission to assess the drug. In a combination of trastuzumab and anthracycline, the cardiac function was to be closely monitored because of the cardiovascular risks involved. The drug manufacturer decided to use trastuzumab and docetaxel.

Transferability to the German health care system is limited

One relevant study (NeoSphere) was available for the benefit assessment. The study consisted of three phases: neoadjuvant treatment (before the operation), adjuvant treatment (after the operation) and a follow-up observation phase. In the neoadjuvant phase, patients in the relevant study arms received pertuzumab plus trastuzumab plus docetaxel or trastuzumab plus docetaxel. In the adjuvant phase, patients in both study arms received trastuzumab, partly parallel to the so-called FEC regimen (5-fluorouracil, the anthracycline epirubicin and cyclophosphamide).

This parallel use of an anthracycline is not recommended in the Summary of Product Characteristics of trastuzumab. Furthermore, the guidelines advise against dividing chemotherapy as the one used in the study in a neoadjuvant and an adjuvant phase. Hence conclusions on the added benefit can only be derived for the investigated treatment regimens; the transferability of the study results to the German health care context is limited.

Outcome treatment discontinuation: hint of negative effect

There were no statistically significant differences between the study arms compared here regarding the following outcomes: all-cause mortality, recurrence, breast-conserving surgery, and overall rate of serious and severe side effects. The outcome "quality of life" was not investigated in the study. Statistically significant differences in the results in both study arms were only shown for the outcome "discontinuation due to side effects": More patients discontinued treatment in the group receiving pertuzumab. Four of six recorded side

effects leading to treatment discontinuation were cardiac disorders (functional impairment of the left ventricle).

Overall, there was therefore a hint of greater harm in comparison with the comparator therapy, i.e. lesser benefit of pertuzumab in neoadjuvant treatment of HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.

G-BA decides on the extent of added benefit

This 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 information: www.iqwig.de/download/A15-34_P … ertung-35a-SGB-V.pdf

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