Trastuzumab emtansine: Indication of major added benefit in one subpopulation

April 7 2014

The antibody-drug conjugate trastuzumab emtansine (trade name: Kadcyla) has been approved since November 2013 for the treatment of patients with unresectable, locally advanced or metastatic breast cancer that is HER2-positive, i.e. that overexpresses the human epidermal growth factor receptor 2. Patients must have already received trastuzumab or a taxane – alone or in combination. They should also have already received treatment for the locally advanced or metastatic disease or have developed disease recurrence during or within six months of completing adjuvant therapy.

The Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the added benefit of the conjugate in these patients. It distinguished between four subpopulations and appropriate comparator therapies. IQWiG found an indication of a major added benefit for patients who have received previous treatment with trastuzumab and taxanes and with anthracyclines. For the remaining three subpopulations, an added benefit is not proven.

Antibody combined with mitotic inhibitor

If the cancer cells in locally advanced breast cancer or breast cancer that has already formed metastases produce excessive quantities of the growth factor receptor HER2, the disease progresses particularly aggressively because the cells multiply rapidly and hardly respond to conventional chemotherapy. In this HER2-positive breast cancer, the

patient can be treated with the antibody drug trastuzumab, which blocks the receptor.

However, this is often not sufficient to stop the carcinoma from spreading. The drug manufacturer now combined trastuzumab with a strong cell division inhibitor: Whereas the antibody aims to block the receptor from outside the cell, the inhibitor is designed to destroy the tumour cells from within. IQWiG was commissioned to find out in an early benefit assessment whether, and if so, which patients benefit from this new treatment.

Different comparator therapy depending on stage and pretreatment

Depending on the stage of the breast cancer and the previous treatments received, the G-BA distinguished between four subpopulations, each with its own appropriate comparator therapy. In locally advanced, unresectable breast cancer without metastases, the new conjugate was to be compared with radiotherapy. In metastatic breast cancer that has already been treated with anthracyclines, taxanes and trastuzumab, chemotherapy with lapatinib and capecitabine was the appropriate comparator therapy.

In metastatic breast cancer that has already been treated with taxanes and trastuzumab, but not with anthracyclines, the G-BA specified an anthracycline as comparator therapy – unless this treatment was not an option for the patients. Then the conjugate was to be compared with a treatment tailored to the individual patient under consideration of the approval of the drugs used.

Added benefit could only be derived for one subpopulation

The manufacturer presented no relevant data for three of the four subpopulations: In locally advanced unresectable breast cancer, it envisaged lapatinib and capecitabine as comparator therapy instead of radiotherapy. It also considered this combination to be suitable for patients who have not yet received anthracyclines. However, this contradicts the approval of lapatinib, according to which treatment with lapatinib and capecitabine always has to be preceded by a treatment including anthracyclines. These deviations from the appropriate comparator therapies were not sufficiently justified so that an added benefit of trastuzumab emtansine in these cases is not proven.

For patients with metastatic breast cancer who have already received anthracyclines, the manufacturer cited results from the EMILIA study. Patients who have been pretreated with anthracyclines and now received either the conjugate or lapatinib and capecitabine also participated in this open-label, randomized controlled trial.

Positive effects predominate

This study showed both positive and negative effects of trastuzumab emtansine. The positive effects regarding the outcome categories "mortality", "health-related quality of life" and "serious or severe side effects" together provide an indication of a major added benefit. One out of two women who received trastuzumab emtansine was still alive after 31 months – compared with 24 months under lapatinib and capecitabine. Severe hand-foot syndrome, which can be caused by chemotherapy, was also considerably less common than in the comparator group.

This was offset by a hint of greater harm in non-serious and non-severe side effects. This harm was far from outweighing the benefit because these were mainly mild cases of nose bleed.

Overall, there was an indication of a major added benefit of trastuzumab emtansine – but only for patients with metastatic HER2-positive breast cancer who have already been treated with anthracyclines, taxanes and trastuzumab.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments supervised by the G-BA. After publication of the manufacturer's dossier and IQWiG's assessment, the G-BA conducts a commenting procedure, which may provide further information and 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: An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the website " www.gesundheitsinformation.de, published by IQWiG, provides easily understandable and brief German-language information on trastuzumab emtansine.

The G-BA website contains both general English-language information on benefit assessment pursuant to §35a Social Code Book (SGB) V and specific German-language information on the assessment of trastuzumab emtansine. More English-language information will be available soon (Sections 2.1 to 2.6 of the dossier assessment as well as subsequently published health information on www.informedhealthonline.org).

Provided by Institute for Quality and Efficiency in Health Care

Citation: Trastuzumab emtansine: Indication of major added benefit in one subpopulation (2014,

April 7) retrieved 19 July 2023 from https://medicalxpress.com/news/2014-04-trastuzumab-emtansine-indication-major-added.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.