Eribuli: Positive effects predominate in certain patients, negative effects in others

November 7 2014

Eribulin (trade name: Halaven) is approved for women with locally advanced or metastatic breast cancer in whom the disease has progressed despite prior drug therapy. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether the drug offers an added benefit over the appropriate comparator therapy in these patient groups.

According to the findings, there are both positive and negative effects. There is proof of minor added benefit for one group of patients. For other groups, there are hints or indications of lesser benefit.

Second assessment of eribulin

IQWiG already presented a dossier assessment of eribulin in February 2012. The subsequent decision on the added benefit made by the Federal Joint Committee (G-BA) was limited until April 2014. In addition, the drug manufacturer meanwhile obtained approval for an expanded therapeutic indication: In March 2011 eribulin was only available for patients who have progressed further after at least two chemotherapeutic regimens. Since June 2014, however, the drug can already be used after one unsuccessful treatment attempt. Hence there were two reasons — independent from each other — for the reassessment of eribulin.

G-BA specified appropriate comparator therapies

When the G-BA specified the appropriate comparator therapy, it distinguished between several treatment situations: The first one refers to patients who are not eligible for further chemotherapy with a taxane or an anthracycline. In this situation, eribulin was to be compared with individual chemotherapy containing the drugs capecitabine or vinorelbine.

In patients for whom taxanes or anthracyclines are principally still an option, eribulin was to be compared with an individual chemotherapy containing a taxane or an anthracycline.

The decision for the adequate treatment should take into account whether the patients' cancer cells have highly increased levels of certain human epidermal growth factor receptors (HER) ("HER2/neu status positive"). If treatments targeting these growth receptors (anti-HER2/neu treatments) are an option for these patients, eribulin was to be compared with an anti-HER2/neu treatment. If this was not the case, the comparator therapies mentioned above applied to these patients.

Only data for patients with negative HER2/neu status evaluable

Two studies were available for the assessment, study 301 and EMBRACE. EMBRACE was already the basis of the first dossier assessment of eribulin. Both studies were open-label, randomized, controlled, multinational approval studies.

However, IQWiG could only include the data of the participants with HER2/neu status negative in the dossier assessment because it was unclear whether it was assessed if the patients with positive status were suitable for anti-HER2/neu treatment. And it was unknown how many of the patients with an unclear status were to be rated as positive and how

many as negative. It has been the standard approach in Germany for several years, however, to determine the HER2/neu status of the primary tumour as a basis for decision for further treatment.

Advantage in survival, but disadvantage in severe side effects

Overall, IQWiG sees proof of an added benefit of eribulin with an extent that is to be rated as minor for patients who can no longer be treated with taxanes or anthracyclines and whose HER2/neu status is negative. These patients survived longer under eribulin treatment. But at the same time, severe side effects (CTCAE grade 3 and 4) were more common under eribulin.

Number of affected organs influences the result

There were both positive and negative effects of eribulin in patients who can still be treated with a taxane or an anthracycline and whose HER2/neu status is negative. However, the treatment result also depended on the number of organs where the tumour had already formed metastases.

Study discontinuation less common, severe side effects more common

On the one hand, patients in the eribulin group discontinued treatment less frequently due to adverse events, which resulted in a hint of lesser harm. On the other hand, severe adverse events (CTCAE grade 3 and 4) were more common, i.e. eribulin caused greater harm.

The dossier contained no data on the outcomes of symptoms (morbidity) and quality of life for women who can still be treated with a taxane or an

anthracycline and whose HER2/neu status is negative.

Overall, IQWiG considers there to be a hint or an indication of lesser benefit in these patients.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments according to the Act on the Reform of the Market for Medicinal Products (AMNOG) 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.

An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the Website gesundheitsinformation.de, published by IQWiG, provides easily understandable and brief German-language information on eribulin.

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 eribulin.

More information:
www.iqwig.de/download/IQWiG_informationflyer.pdf

Provided by Institute for Quality and Efficiency in Health Care