Added benefit of idelalisib is not proven

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Idelalisib (trade name Zydelig) has been available since September 2014 for patients with follicular lymphoma or chronic lymphocytic leukaemia (CLL). The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether this drug offers an added benefit over the appropriate comparator therapy. According to the findings, such an added benefit is not proven for any of the two therapeutic indications because the drug manufacturer presented no suitable data.

Drug can be used as first- and second-line treatment

Idelalisib can be prescribed to patients with follicular lymphoma that has not responded to two prior lines of treatment and is therefore considered to be refractory.

For patients with CLL, idelalisib is an option if at least one prior treatment had been unsuccessful (refractory CLL) or if the disease has recurred after initially successful treatment (relapsed CLL). Idelalisib can also be used as first-line treatment if chemo-immunotherapy is unsuitable because of certain genetic characteristics (17p deletion or TP53 mutation).

G-BA specifies appropriate comparator therapy

The Federal Joint Committee (G-BA) specified "best supportive care" (BSC) as appropriate comparator therapy for the assessment of idelalisib in patients with refractory follicular lymphoma. BSC means a therapy

that provides the patient with the best possible, individually optimized, supportive treatment to alleviate symptoms and improve quality of life.

The G-BA distinguishes between five treatment situations in CLL

The G-BA distinguished between a total of five treatment situations in CLL: For treatment-naive patients, for whom idelalisib is an option as first-line treatment, the comparison was to be conducted versus BSC.

The G-BA made the same specification for relapsed and refractory CLL if another chemotherapy or other tumour-targeted treatments (antineoplastic treatments) are not an option for the patients.

In relapsed CLL in which further chemotherapy is possible, the comparison was to be conducted versus chemotherapy in combination with rituximab. In refractory CLL in which antineoplastic treatments are an option, the comparison was to be conducted versus an individually optimized treatment specified by the physician.

Data from one-arm studies allow no comparison

However, the dossier contained no suitable data for any of the therapeutic indications and treatment situations. One of the reasons is that the manufacturer - contrary to the G-BA's specification - combined the patients with relapsed and refractory CLL, which also resulted in deviations regarding the appropriate comparator therapy.

For patients with refractory follicular lymphoma and for two treatment situations of CLL, the manufacturer only used results from one-arm studies and did not conduct an adequate comparison of these results with the appropriate comparator therapy.

Appropriate comparator therapy not adequately implemented

For two further treatment situations of CLL, the manufacturer presented the results of an approval study, in which idelalisib plus rituximab was compared with rituximab plus placebo (relapsed CLL, chemotherapy no longer indicated, and refractory CLL, antineoplastic treatment is an option).

However, the respective appropriate comparator therapy specified by the G-BA was not adequately implemented in the study: It was not clear that the study participants received individually optimized treatment. Moreover, rituximab was used as monotherapy in the comparator arm, for which the drug is not approved.

Hence an added benefit of idelalisib is not proven for any of the therapeutic indications or for any of the treatment situations distinguished by the G-BA.

More information: www.iqwig.de/download/A14-35_I … ertung-35a-SGB-V.pdf

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