Ibrutinib with rituximab in previously untreated CLL: Indication of added benefit over FCR

January 5 2021

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The combination of ibrutinib plus rituximab is approved for the treatment of adults with previously untreated chronic lymphocytic leukemia (CLL). In an early benefit assessment, the German Institute for

Quality and Efficiency in Health Care (IQWiG) now examined which advantages and disadvantages this drug combination has for the patients. For patients who could also be treated with the chemo-immunotherapy FCR, the assessment found an indication of a major added benefit in comparison with this appropriate comparator therapy. No study data are available for patients for whom FCR or other chemo-immunotherapy is not an option due to their poorer general health. An added benefit is therefore not proven.

Study data on only one of three research questions

The Federal Joint Committee (G-BA) distinguished three groups of patients. For the first group, which was also the largest, the appropriate comparator therapy was fludarabine + cyclophosphamide + rituximab (FCR). This chemo-immunotherapy is usually only given if the patient is in good general health. For the second group, FCR is not an option, but another chemo-immunotherapy is. In the third group, chemo-immunotherapies are generally not indicated, for example because of the mutation status of the patients. Here, the appropriate comparator therapy is ibrutinib alone.

In its dossier, the drug manufacturer only presented data on the question of whether ibrutinib plus rituximab offers an added benefit in comparison with FCR for the patients in the first group. These data are from the ongoing ECOG-E1912 study, which is not conducted by the manufacturer, but which it also used already in its application for approval. Data from about 40 per cent of the study participants are relevant for the present assessment.

Prolonged overall survival

There was an indication of a major added benefit for overall survival in

patients for whom FCR therapy is an option. In the outcome category of side effects, there was a hint of lesser harm for the overall rate of severe side effects and for discontinuations due to side effects, which were of minor and of considerable extent respectively. Predominantly positive effects were shown in severe and non-serious/non-severe side effects. No results were available on health-related quality of life.

Overall, there is an indication of a major added benefit of ibrutinib plus rituximab in comparison with FCR for patients with previously untreated CLL for whom FCR therapy is an option. Since no data were available for the other patients, an added benefit in comparison with the respective appropriate comparator therapy is not proven for them.

Promising therapeutic option

"This means that a relatively large group of people with chronic lymphocytic leukemia now have a chemotherapy-free treatment alternative that has a clear survival advantage," says Volker Vervölgyi from IQWiG's Drug Assessment Department. "This is good news, as we have not seen an added benefit in comparison with FCR in the previous early benefit assessments for untreated CLL."

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.

Provided by Institute for Quality and Efficiency in Health Care