Regorafenib: Hint of minor added benefit

January 10 2014

Regorafenib (trade name: Stivarga) has been approved in Germany since August 2013 for adults with metastatic colorectal cancer in whom previous treatments are no longer effective or for whom these alternatives are not an option. In an early benefit assessment pursuant to the Act on the Reform of the Market for Medicinal Products (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) examined whether this new drug offers an added benefit over the appropriate comparator therapy specified by the Federal Joint Committee (G-BA).

According to the findings, there is a hint of a minor added benefit of regorafenib. Patients have a survival advantage, but certain severe side effects occur more frequently.

"Best supportive care" was appropriate comparator therapy

The G-BA specified "best supportive care" (BSC) as appropriate comparator therapy. 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 manufacturer presented data from the approval study (CORRECT) in its dossier. One study group was treated with regorafenib plus BSC, and the control group received a placebo plus BSC. However, it was not allowed to use other systemic anticancer treatments as part of the BSC.

Reduced reliability of the conclusions: not more than a hint can be derived

There are several reasons why the reliability of the conclusions of the results from CORRECT is limited: On the one hand, it remained unclear whether the excluded anticancer treatments would have been able to relieve the symptoms and thus should have been part of the – palliative – BSC. In the follow-up phase, i.e. after the end of the study treatment, 25 to 30 per cent of the patients received this kind of further systemic anticancer treatment.

On the other hand, only patients with a certain status of the disease (ECOG-PS 0 or 1) could participate in the study, although regorafenib is also approved for patients with poorer general condition (ECOG-PS > 1).

For these reasons, not more than a hint of an added benefit can be derived from the data presented in the dossier.

Advantage in overall survival

The analysis of the data showed a statistically significant difference between the two study arms in favour of regorafenib for the outcome "overall survival". Half of the patients who received regorafenib had died after 6.5 months. In the control group, this was already the case after about 5 months. IQWiG therefore considers there to be a hint of a considerable added benefit.

Data on morbidity and quality of life were not evaluable

Data on symptoms and complaints (morbidity) and on health-related quality of life were recorded with questionnaires, but were not evaluable for the benefit assessment. The main reason was that this information

was only actually available for some of the participants at the end of the treatment (

Severe side effects more frequent under regorafenib

There were no statistically significant differences between the two treatment arms with regards to serious adverse events and treatment discontinuation due to adverse events. The situation was different with regards to severe side effects (CTCAE Grade 3): They were more frequent in the regorafenib group than in the placebo group. The biggest differences (? 5%) occurred in fatigue, diarrhoea, hand-foot syndrome and certain types of skin rash (exanthemas).

Regarding side effects, IQWiG therefore derives a hint of greater harm with the extent "major". However, this greater harm does not completely outweigh the survival advantage, so that, overall, IQWiG considers there to be a hint of a minor added benefit.

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.

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 regorafenib.

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 regorafenib.

Provided by Institute for Quality and Efficiency in Health Care