Trifluridine/tipiracil in colorectal cancer: Added benefit only for some patients

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The fixed combination of trifluridine/tipiracil (trade name: Lonsurf) has been approved since April 2016 for the treatment of metastatic colorectal cancer. The drugs are an option for adult patients with metastatic colorectal cancer whose disease has progressed despite treatment or who cannot be given other treatments.

In an early benefit assessment, the German Institute for Quality and Efficiency in Health Care (IQWiG) has now examined whether the combination has an added benefit for the patients. According to the findings, there are positive and negative effects of equal certainty of results (hints). The extent of the survival advantage differs between the two tumour types, however:

For patients with non-mutant tumour (KRAS wild type), the balancing of advantages in survival and disadvantages due to serious side effects resulted in a hint of a minor added benefit of trifluridine/tipiracil. In tumours with KRAS mutation, an added benefit of the drug combination was not proven: Here the survival advantage was less pronounced and was outweighed by at least considerable harm due to serious side effects.

Another relevant factor for the balancing was the fact that health-related quality of life was not investigated in the study presented. This outcome is of major importance particularly in palliative care, however.

Comparison with best supportive care

The new drug combination is used to prevent cells from dividing and multiplying to inhibit tumour growth and disease progression. Trifluridine/tipiracil is to be used in patients with metastatic colorectal cancer in whom other chemotherapeutic regimens with the drugs fluoropyrimidine, oxaliplatin, and irinotecan, and treatments against vascular endothelial growth factors (VEGF) or epidermal growth factor receptors (EGFR) have not been effective or are not an option.

The comparator therapy specified by the Federal Joint Committee (G-BA) was best supportive care (BSC), which, based on the individual needs of a patient, aims to alleviate symptoms such as pain and improve quality of life.

Longer survival, but at least considerable side effects

Patients with a non-mutant tumour (KRAS wild type) survived considerably longer, which corresponds to a major added benefit. However, this advantage was accompanied by greater harm of at least considerable extent from severe side effects. Since data were lacking, disadvantages regarding health-related quality of life could also not be excluded. In summary, a hint of a minor added benefit of trifluridine/tipiracil can be derived from advantages and disadvantages.

An added benefit of the drug combination was not proven in tumour with KRAS mutation, however, because the survival advantage was less pronounced and only reached a minor extent. In the overall consideration, this advantage was outweighed by the disadvantages, i.e. at least considerable harm due to serious side effects and the fact that impairment in quality of life could not be excluded.

Data on health-related quality of life not recorded

Only patients who had no or only minor limitations on physical exertion due to their disease were investigated in the study presented. The drug manufacturer presented no data for patients who were no longer able to work or already in need of care.

Another relevant factor for the balancing on the added benefit was the fact that health-related quality of life was not investigated at all in the study presented. This outcome is of outstanding importance particularly in palliative care, however. Patients, physicians and researchers as well as representatives of the industry all stress this point.

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.

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