Sacubitril/valsartan in chronic heart failure: Indication of considerable added benefit

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The fixed-dose combination of sacubitril and valsartan (trade name: Entresto) has been approved since November 2015 for adults with symptomatic chronic heart failure with reduced pump function (ejection fraction). The German Institute for Quality and Efficiency in Health Care (IQWiG) now examined in an early benefit assessment whether this drug combination offers an added benefit for patients in comparison with the appropriate comparator therapy.

According to the findings, the positive effects regarding mortality, necessity of heart failure hospitalizations, and quality of life predominate. These were not put into question by a negative effect in non-severe side effects; hence overall an indication of considerable added benefit can be derived from the data.

Approval study terminated prematurely

In its dossier, the drug manufacturer used data from a randomized controlled trial, which compared sacubitril/valsartan directly with enalapril, each in combination with a beta-blocker. Since a planned interim analysis was able to show after 51 months already that fewer cardiovascular deaths occurred under sacubitril/valsartan, the study was terminated prematurely.

Fewer deaths due to cardiovascular failure

The data from the dossier showed that all-cause mortality was lower under sacubitril/valsartan than under enalapril, which was mainly caused by fewer cardiovascular deaths.

The results regarding the frequency of hospitalizations due to heart failure were also in favour of the new fixed-dose combination; however, these were limited to patients with a lower severity grade (NYHA class I and II). Finally, the data on health-related quality of life also showed an advantage of sacubitril/valsartan.

Hypotension more common

The only outcome for which the results were less favourable for the new fixed-dose combination than for enalapril was low blood pressure (hypotension), which belongs to non-severe side effects.

The data could not be finally interpreted for further important aspects of side effects, i.e. severe adverse events and treatment discontinuation due to adverse events, because late complications or symptoms of the disease were also recorded here. However, there was no sign that sacubitril/valsartan could cause greater harm here.

The data for further patient-relevant outcomes such as myocardial infarction, stroke or renal failure showed no relevant differences between the study arms.

Positive effects predominate

There was an indication of considerable added benefit in all-cause mortality and heart failure hospitalizations, and a hint of a minor added benefit in health-related quality of life. The data on hypotension showed a hint of greater harm, the extent of which cannot be quantified however. Overall, IQWiG therefore sees an indication of considerable added benefit of sacubitril/valsartan in comparison with enalapril (each in combination with a beta-blocker).

Conclusive studies feasible also in chronic diseases

The Act on the Reform of the Market for Medicinal Products (AMNOG) has been criticized, especially in recent times, to favour drugs for severe diseases with a short life expectancy such as cancer in the advanced stage. It has been claimed that only these settings allow to provide robust study data in a reasonable period of time to prove an added benefit. "The approval study on sacubitril/valsartan

shows once again that large and conclusive studies can be conducted also for chronic diseases", commented Thomas Kaiser, Head of the IQWiG Drug Assessment Department. "The manufacturers only need the will", Kaiser added.

More information:
www.iqwig.de/download/A15-60_S … ertung-35a-SGB-V.pdf

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