Telaprevir: Added benefit in certain patients with hepatitis C

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The drug telaprevir (trade name: Incivo) has been available for treatment of chronic hepatitis C infection of genotype 1 since autumn 2011. 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 telaprevir offers an added benefit compared with the present standard therapy.

According to the findings of the assessment, the new drug telaprevir offers advantages in various groups of patients with chronic hepatitis C infection of genotype 1. The available studies provide proof, indications or "hints" of an added benefit. However, not only the probability but also the extent of added benefit varies.

An addition to previous standard drug therapy

Hepatitis C viruses attack the liver and can trigger inflammation there. If this becomes chronic, cirrhosis can develop and liver function progressively deteriorates. Moreover, the risk of liver cancer (hepatocellular carcinoma, HCC) increases. The virostatic drug telaprevir inhibits the reproduction of hepatitis C viruses. Experts assume that if no viruses are detectable in the blood over a sustained period after treatment (sustained virological response, SVR), the risk of secondary disease is reduced.

Telaprevir is administered in addition to peginterferon alfa (immune-system enhancing drug) and ribavirin (virostatic drug), which are already on the market. In accordance with the approval status, different patient groups are treated for different periods, which was allowed for in the assessment. The dual combination of peginterferon alfa and ribavirin is the present standard therapy, and this was compared with the triple combination of these two standard drugs and telaprevir.

Studies largely only provide data on morbidity and adverse effects

Overall 3 relevant studies were identified. The outcomes considered were "mortality", "secondary complications of treatment (morbidity)", measured in the studies by means of the surrogate outcome "SVR", as well as "health-related quality of life" and "adverse effects".

The quality-of-life results for treatment-naïve (i.e. previously untreated) patients without cirrhosis were not statistically significant. No evaluable data on this outcome were available for other patient groups. Due to the too short study duration, the event rates for mortality were too low in all patient groups to be able to draw robust conclusions.

Extent of added benefit cannot be classified on the basis of the surrogate outcome for morbidity

The extent of added benefit cannot be classified on the basis of the surrogate outcome "SVR". This parameter is not a patient-relevant outcome in itself and there are no studies in which SVR is validated as a surrogate outcome in accordance with the usual criteria employed by IQWiG. Nevertheless, the Institute accepts SVR in the context of this assessment as a surrogate for the reduced incidence of liver cancer. This is because it is currently accepted that patients with no detectable

hepatitis C virus in the blood are at lower risk of liver cancer. However, it is not known how many cases of liver cancer can in fact be prevented by telaprevir and it is therefore unclear whether the added benefit can be classified as "minor" "considerable" or "major".According to the corresponding legal ordinance, the added benefit is thus "unquantifiable".

Under consideration of the beneficial and harmful effects of telaprevir, overall IQWiG reaches different conclusions for different patient groups.

Advantages for treatment-naïve patients without cirrhosis who have a high viral load

Different results for morbidity were shown for treatment-naïve patients without cirrhosis, depending on the viral load in the blood at the start of treatment. Proof of an added benefit of telaprevir was only determined for patients with a high viral load. However, the extent of the added benefit is unquantifiable as it refers to the surrogate outcome "SVR".

For treatment-naïve patients without cirrhosis, the data also provide proof and an indication of greater harm due to the adverse effects "anaemia" and "rash" respectively, the extent being classified as "considerable" in the former and "minor" in the latter case. In the consideration of the beneficial and harmful effects of telaprevir, this did not lead to a restriction in the overall conclusion for patients with a high viral load, as these side effects were nearly exclusively classified as "not serious".

In contrast, for treatment-naïve patients without cirrhosis who have a low viral load at baseline, the data provide an indication of lesser benefit of telaprevir versus the comparator therapy. This is due to the fact that an

added benefit regarding SVR is not proven, so that only the harmful effects are taken into account.

An added benefit of telaprevir is not proven for treatment-naïve patients with cirrhosis, as the manufacturer dossier did not contain any evaluable data.

Indication of an advantage also in patients with unsuccessful pre-treatment

Depending on the cirrhosis status, different results were shown for patients in whom treatment had so far been unsuccessful (non-responders). Regarding morbidity, the data provide an indication of an added benefit of telaprevir in patients without cirrhosis. The data only provide a "hint" of an added benefit in non-responders with cirrhosis. In this context, "indication" and "hint" refer to the surrogate outcome "SVR". Therefore the extent of added benefit is unquantifiable.

As in the case of treatment-naïve patients without cirrhosis, indications of greater harm due to the side effects "anaemia" and "rash" did not lead to a restriction in the overall conclusion.

No additional benefit for relapsed patients

In patients without cirrhosis who relapsed after standard therapy, the treatment regimen deviated from the approval status. Consequently, the added benefit cannot be assessed on the basis of the available data so that an added benefit is not proven.

In patients with cirrhosis who relapsed, the data provide an indication of an added benefit regarding SVR. However, at the same time they also provide an indication of greater harm (extent: considerable) regarding

serious adverse events. Under consideration of the beneficial and harmful effects of telaprevir, IQWiG concluded that overall an added benefit is not proven for this patient group.

G-BA decides on the extent of added benefit

The procedure for inferring the overall conclusion on the extent of added benefit is a proposal from IQWiG. The G-BA, which has opened a formal commenting procedure, decides on the extent of added benefit.

Provided by Institute for Quality and Efficiency in Health Care