Medical Xpress

Daclatasvir for hepatitis C: Added benefit not proven

December 10 2014

The drug daclatasvir (trade name Daklinza) has been available since August 2014 for the treatment of adults with chronic hepatitis C (CHC) infection. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether this new drug offers an added benefit over the appropriate comparator therapy.

The drug manufacturer presented data for patients without cirrhosis of the liver who are infected with hepatitis C virus (HCV) genotype 1, and for patients with HCV genotype 4. However, these data are unsuitable in various aspects to prove an added benefit.

The manufacturer dossier contained no data at all for three further patient groups with HCV genotype 1 infection (pretreated patients, untreated patients with cirrhosis of the liver, and patients with HIV coinfection) as well as for patients with HCV genotype 3 (with compensated cirrhosis and/or treatment-experienced).

Different virus types cause inflammation

Hepatitis C viruses can trigger inflammation in the liver. If this becomes chronic, cirrhosis can develop and organ function progressively deteriorates. Moreover, the risk of liver cancer (hepatocellular carcinoma, HCC) increases. Daclatasvir aims to inhibit the reproduction of HCV by interfering with viral DNA replication. Experts assume that if no viruses are detectable in the blood over a sustained period after

treatment (sustained virologic response, SVR), the risk of secondary disease is reduced.

There are six different main types (genotypes) of the hepatitis C virus, which are subdivided into more than 60 subtypes. The effectiveness of different drugs is not the same against all viruses.

Comparison with dual therapy or triple therapy

Depending on the type of virus, the clinical picture and the course of the disease, daclatasvir is used in dual therapy together with the virostatic drug sofosbuvir, in triple therapy with the virostatic drugs sofosbuvir and ribavirin, or in triple therapy with peginterferon alfa to enhance the immune system and ribavirin. According to the approval, treatment duration differs for certain patient groups (12 to 48 weeks).

Depending on patient characteristics, the options for the comparator therapy are dual therapy with peginterferon alfa and ribavirin, or triple therapy consisting of peginterferon alfa and ribavirin plus a protease Inhibitor (boceprevir or telaprevir). The Federal Joint Committee (G-BA) specified a different appropriate comparator therapy for each of six different subindications:

For treatment-naive adults with chronic HCV genotype 1 infection without cirrhosis, and for treatment-experienced patients with HCV genotype 1, the G-BA specified both dual therapy and triple therapy as appropriate comparator therapy.

In four further subindications, daclatasvir was to be compared only with dual therapy: 1) in treatment-naive HCV patients with genotype 1 and cirrhosis, 2) in patients with HCV genotype 1 and additional HIV infection, 3) in patients with HCV genotype 3 infection with compensated cirrhosis and/or treatment-experienced, and 4) in patients

with HCV genotype 4 infection.

However, the manufacturer only presented data for treatment-naive adults with chronic HCV genotype 1 infection without cirrhosis and for patients with HCV genotype 4 infection.

Incomplete study pool for HCV genotype 1

Since studies for the direct comparison were lacking, the manufacturer presented an indirect comparison for HCV genotype 1 patients without cirrhosis in its dossier. Using a "historical" comparison of individual arms of different studies, it aimed to derive conclusions on the superiority of daclatasvir versus the triple therapy. The manufacturer did not meet the requirements for the dossier, however: A search in trial registries was not conducted. In addition, the inclusion and exclusion criteria for the choice of studies were unsuitable. At least one relevant study was lacking in the study pool because of this.

The Bayesian Benchmarking Analysis (BBA) additionally cited was used to determine the minimum threshold a study would have to reach in order to show a statistically significant superiority of daclatasvir. The manufacturer did not meet the requirements for the dossier in this analysis either: The search was limited to a period of time up to 2012 and there was no search in trial registries. In addition, the analysis was restricted to the outcome "SVR" without addressing side effects of Treatment.

Genotype 4: unsuitable data due to lacking values

The manufacturer only evaluated one study of the two studies it presented for the direct comparison of daclatasvir in combination with dual therapy versus dual therapy alone in treatment-naive HCV genotype

4 patients. Due to treatment futility, there were treatment discontinuations in both study arms, and hence missing values in the outcome "SVR", the proportions of which differed greatly between the study arms. The imputation strategy for the values was unsuitable because its results were not robust and biased to the disadvantage of the appropriate comparator therapy.

The criteria for discontinuation in the appropriate comparator therapy did not comply with the Summary of Product Characteristics and were also not reasonable because they considerably shorten the treatment duration in a large proportion of patients thus causing a disadvantage for the comparator therapy with regard to the outcome "SVR". In summary, no suitable data were available for treatment-naive HCV genotype 4 patients either.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments according to the Act on the Reform of the Market for Medicinal Products (AMNOG) 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.

Provided by Institute for Quality and Efficiency in Health Care

Citation: Daclatasvir for hepatitis C: Added benefit not proven (2014, December 10) retrieved 5 May 2024 from https://medicalxpress.com/news/2014-12-daclatasvir-hepatitis-added-benefit-proven.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.