CORRESPONDENCE

Current Standards in the Treatment of Chronic Hepatitis C

by PD Dr. med. Wolf-Peter Hofmann, Prof. Dr. med. Christoph Sarrazin, Prof. Dr. med. Stefan Zeuzem in volume 19/2012

Early Assessment of Benefits

In their review article the authors present the results from the licensing studies for two recently approved hepatitis C virus (HCV) protease inhibitors (boceprevir, telaprevir). Both substances were evaluated by Germany's Institute for Quality and Efficiency in Health Care (IQWiG), which was commissioned by the Federal Joint Committee Gemeinsamer Bundesausschuss, G-BA (early benefit assessment). The evaluation was discussed in expert circles with great excitement and sometimes in an unobjective manner. We therefore expressly welcome the matter-of-fact presentation of the authors.

The authors' assessment is largely consistent with that of IQWiG. With regard to the end point "sustained virologic response (SVR)," IQWiG has also concluded on the basis of the available literature that it is a sufficiently valid surrogate for the subsequent complication "hepatocellular carcinoma" (HCC). We therefore noted an additional benefit for boceprevir and telaprevir in most patients. In the early assessment of benefits, however, the extent of the additional benefit also needs to be determined. This means putting a number to the risk reduction for the development of HCC. This is not possible on the basis of existing studies. The mention of a possible "cure" does not solve this problem, because the disease may progress even in patients with SVR, and HCC may develop.

Our evaluation differs in one crucial point from the authors' conclusions. From the authors' point of view, all patients benefit from treatment with boceprevir and telaprevir. However, some patient groups merely develop more adverse effects when taking boceprevir and telaprevir, without any improvement to the virological response (1, 2). This information should be made available to doctors and patients in an unredacted form, so that they may take this into account when deciding on treatment.

All documents regarding the early assessment of benefits are accessible to the public at the G-BA website (www.g-ba.de).

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Conflict of interest statement

The authors work for IQWiG. They declare that no other conflict of interest exists.

In Reply:

We thank your correspondents for their letter and welcome the IQWiG's willingness to enter into an objective dialogue with experts. We wish to point out that the discussions about the benefits assessments of boceprevir and telaprevir that were held by the medical specialty societies (DGVS [Deutsche Gesellschaft für Verdauungs- und Stoffwechselkrankheiten e.V., German Society for Digestive and Metabolic Diseases], DGIM [Deutsche Gesellschaft für Innere Medizin, German Society of Internal Medicine] and others) were extremely objective and constructive (1, 2).

While the IQWiG regards "sustained virologic response" (SVR) in the treatment of patients with chronic hepatitis C as merely a sufficiently valid surrogate for the subsequent complication "hepatocellular carcinoma" (HCC), the international consensus is that virus eradication leads to a reduction in inflammatory activity in the liver and regression of fibrosis and even cirrhosis. Furthermore, there is no doubt that the regression of fibrosis in turn reduces the risks of other complications of cirrhosis (among others, portal hypertension, ascites). In line with the medical specialty societies, the authors also regard the benefit of SVR in patients with chronic hepatitis as fundamentally (semi-)quantifiable (3).

Indeed there are small groups of patients whose SVR rate cannot be raised by adding an HCV protease inhibitor to treatment with peginterferon-alfa/ribavirin. The IQWiG does not take into account in its analysis, however, that by giving triple, rather than dual, therapy to these patients, the overall duration of treatment can be shortened, in some cases substantially, and that this is clinically of major importance on the background of the side effects of peginterferon-alfa/ribavirin.

With regard to information for doctors and patients, the authors think it's more important to document the dynamics of the clinical development of other, directly

antivirally effective, medications for the treatment of chronic hepatitis C. On the basis of current studies, effective interferon-free therapeutic options with fewer side effects may be available in just a few years' time.

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Conflict of interest statement

Dr Hofmann has received participation fees for continuing medical educational events from Bristol-Myers Squibb, Gilead Sciences, MSD, and Roche. Furthermore he has received honoraria for preparing scientific continuing educational events from Bristol-Myers Squibb, Gilead Sciences, MSD, Janssen-Cilag, and Roche. For conducting clinical studies and a study project he initiated he has received funding from Roche.

Professor Sarrazin co-holds a patent regarding the resistances of HCV-NS3-protease inhibitors. He is on the advisory boards of the following companies: Abbott, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead Sciences, Janssen-Cilag, MSD, Novartis, Pharmasset, and Roche. He has received honoraria for preparing scientific continuing educational events from Abbott, Bristol-Myers Squibb, Boehringer Ingelheim, Falk Pharma, Gilead Sciences, MSD, Novartis, and Roche. He has received funding for conducting clinical studies from Abbott, Gilead Sciences, Merck, MSD, Roche, and Vertex Pharmaceuticals.

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