

# Cure of Hepatitis C

## Cura da Hepatite C



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Since the discovery of the hepatitis C virus in 1989, many epidemiological data have been acquired, especially in Europe. Treatments have showed substantial improvement over the past 25 years and have taken a great leap forward with the development of the direct antiviral agents (DAAs). However, the burden of hepatitis C remains important in Europe with more than 5 million individuals living with HCV in the European Union. The peak of highest incidence occurred between 1970 and 1990 in most countries through transfusion, unsafe care and development of intravenous drug use. Transmission among intra-venous drug users is still an issue in most European countries, providing the majority of the new cases of HCV infection. Due to the chronic state of the viral infection and the usual slow progression of the liver disease, the peak of prevalence occurred around 2010, but the peak of complications, such as decompensated cirrhosis and hepatocellular carcinoma is still to come in most of the European countries.<sup>1</sup> The risk of cirrhosis is usually estimated at 10 to 20% in 20 to 30 years of HCV infection evolution,<sup>2</sup> higher in men than in women, but this risk increases in case of comorbidities such as excessive alcohol consumption, diabetes, obesity, HBV or HIV coinfection. The risk of decompensated cirrhosis can be estimated at 2 to 3% per year and that of hepatocellular carcinoma at 1 to 4% per year, also depending on the presence of comorbidities. In the next future, the challenge will be to identify infected people and treat with new effective treatments all patients at risk of developing complications, with the objective of decreasing the disease burden.

Large discrepancies exist in Europe between countries in terms of knowledge of the disease burden, rate of infected people screened and access to treatment. All these factors play a major role on the expected evolution of the HCV epidemics. In countries where drug use has been the major risk factor of transmission, where screening and access to treatment are at a low level (e.g. England), the risk of decompensated cirrhosis, HCC and liver transplant will still increase in the coming years. By contrast, in countries where transfusions have played a large role in the diffusion of the epidemics, where screening and access to treatment

are rather high (e.g. France), the peak of complications is nearly behind us.<sup>1,3,4</sup>

As recently stated by WHO, developing and implementing national hepatitis plans is the keystone in the way to prevent, diagnose and treat hepatitis C. Only few countries have already developed a comprehensive approach for hepatitis C management. From my point of view the most crucial step is to be able to identify infected people and bring them to care. However, screening strategies should be adapted to the own epidemiology of a given country. For example, the USA have adopted the 'birth cohort screening strategy' since epidemiological data showed that three quarters of the infected individuals were born between 1945 and 1965.<sup>5</sup> Such a strategy would not be valid for a country like Portugal where the peak of prevalence seems to be in a younger age bracket.<sup>6</sup> A large identification of the infected population would afford the possibility a) to reduce transmission, b) to treat eligible patients, and c) to avoid most complications in patients reaching a sustained virological response (SVR). Indeed, it has been shown, on large series of patients with advanced fibrosis, that the 5-year risk of HCC was reduced by four in patients with SVR compared to patients without SVR. It has also been shown that patients who have cured from HCV infection have roughly recovered the same risk of liver related mortality as the general population. By contrast, patients who have not been cured have a 26 % probability of liver related mortality at 10 years.<sup>7</sup> Such observations speak in favor of a wide use of anti-viral treatment.

HCV treatment is going through a true revolution. After more than twenty years of indirect therapy aiming at enhancing immunological response of the host with a weak antiviral effect, we are now entering a new era with the direct antiviral agents (DAAs). They have a potent antiviral effect, and the association of two or three drugs acting on different targets (NS3/4A protease, NS5A, NS5B polymerase) for a short time (mainly 12 weeks) leads to the disappearance of the virus in more than 90% of cases. Moreover, they are very well tolerated, compared to Peginterferon, ribavirin and particularly the first generation of anti-proteases, boceprevir and telaprevir, the use of which is made limited by the

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frequency of unpleasant or severe adverse events. Very few patients have contra-indication to the new drugs, thus allowing treatment for a majority of patients who could not receive interferon-based regimens. However, the greatest flaw of the DAAs is their cost, especially in developed countries such as European countries. Cost-effectiveness studies<sup>8</sup> have proved that the use of sofosbuvir associated with Peginterferon and ribavirin was efficient compared to classical treatments, especially in advanced fibrosis stages.<sup>9</sup> Yet regarding the cost-effectiveness of interferon free regimens, it is highly dependent on the cost of the DAAs.<sup>9</sup> New efficiency studies of interferon free regimens are needed with the final costs of the drugs and various comparators.

Nevertheless, considering the high innovative nature of the DAAs and the potential benefit for the patients, The French Parliament recently resolved that the Social Security Financing Act would allow an amount of 750 million

euros per year over the next two years for the treatment of around 15000 patients per year with advanced HCV liver disease or with severe extra-hepatic manifestations. Rather than a selective use of the DAAs, these indications can be considered as a prioritization of severe patients to avoid any loss of chance. In a second step, when all patients with severe fibrosis will have been offered a treatment with DAAs, indications could be opened to less severe stages of fibrosis, thus leading towards HCV eradication, or at least a dramatic reduction of the disease burden.

#### CONFLICTS OF INTEREST

The author has acted as speaker for Roche, BMS, Gilead, and Abbvie.

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