



EASL Policy Statement on Hepatitis C Elimination

Executive Summary

Treatment of hepatitis C virus (HCV) infection with direct acting antiviral (DAA) therapy is one of the major clinical advances in recent times. In many countries, however, treatment has been restricted to a minority of the infected population, in large part due to the initial very high cost of DAA therapy and, to a lesser extent, to capacity issues related to the large number of known, untreated patients. Further, many HCV infected individuals have not yet been diagnosed or are diagnosed, but not linked to treatment and care.

Given the ability to easily cure HCV infection, in 2014 the World Health Assembly adopted Resolution 67.6, calling on all countries to develop a comprehensive viral hepatitis national strategy. Two years later, in 2016, the World Health Organization (WHO) adopted its first *Global Health Sector Strategy on Viral Hepatitis*, with the overall goal of eliminating viral hepatitis as a public health threat by 2030, measured principally by two targets: reduction of new infections by 80% and mortality by 65%.

The aim of this policy statement from the European Association for the Study of the Liver (EASL) is to inform policy-makers, health care professionals, affected communities and patients that hepatitis C can- and should- be eliminated as a public health threat by 2030, or even earlier as could be the case in many central and western European countries. We believe that medical associations and clinicians, in collaboration with other key stakeholders, such as patients and affected communities, play a critical role in eliminating HCV as a public health threat and we commit to working with the HCV community to do so.

Key messages

EASL recommends that:

- All European countries develop a comprehensive hepatitis C national strategy or action plan to: increase awareness throughout the population and to ensure appropriate preventive measures; offer testing; provide linkage to care, treatment and follow-up of patients in line with the *WHO Global Health Sector Strategy on Viral Hepatitis* and the WHO Action Plan for the health sector response to viral hepatitis in the WHO European Region (2017);
- All European countries adopt EASL recommendations on the management of hepatitis C, where it is stated that every hepatitis C patient should be considered for treatment, and that treatment should be initiated with DAAs;

- DAAs be globally available at reasonable prices, to avoid any further reimbursement restrictions, and to allow governments to implement a comprehensive elimination strategy.

What is Hepatitis C and its elimination?

Hepatitis is an inflammatory condition of the liver that may be caused by a virus (viral hepatitis). When persisting for years, it may progress to lethal conditions, such as cirrhosis and hepatocellular carcinoma (HCC). Hepatitis C is also a systemic disease affecting the whole body causing a multitude of extrahepatic manifestations. Viral hepatitis is the seventh most frequent cause of death in the world, surpassing HIV (1). Among the five viral agents capable of causing hepatitis, hepatitis C virus (HCV) is one of the most deadly, causing some 400,000 deaths annually (2). Globally, there are an estimated 71 million people actively infected with HCV, and 11-14 million of them reside in Europe (3).

HCV infection may persist in the host without causing any symptoms, therefore remaining unnoticed for many years, even decades. Many symptoms of hepatitis C like fatigue, joint pain and neurocognitive impairment, are not specific and affected persons do not necessarily associate them with hepatitis C virus infection. For this reason, case finding is inefficient, late diagnosis is common, and effective testing strategies difficult to implement (4). During this time, not only onward transmission can occur, but also the persisting inflammation may lead to cirrhosis, where liver tissue is transformed into scar tissue, ultimately resulting in liver failure, and HCC. These complications of HCV are a major cause of early mortality. Because many infections occurred decades ago, the relentless progression of liver disease has resulted in a constant increase in late-stage complications and deaths in many countries. It is also estimated that, in the absence of increased diagnosis rates and appropriate linking to effective treatment, these figures will continue to increase for many years to come (3).

Although preventive measures in the field of blood banks and invasive medical procedures have greatly reduced the risk of healthcare acquired transmission of HCV, several populations remain at high risk of infection, including people who inject drugs. Other groups that are at increased risk of HCV infection are men who have sex with men that engage in high-risk sexual practices, prisoners, sex workers, migrants from high endemicity areas and patients undergoing hemodialysis.

There is no available vaccine to prevent HCV infection. However, years of collaboration between the pharmaceutical industry, clinical investigators and patients have resulted in the development of novel medicines directly interfering with the HCV lifecycle: direct acting antivirals (DAAs). Since 2014, very effective, well-tolerated, all-oral DAA-based combination therapies have been available. They now consist of the daily administration of 1-4 tablets, for only 8-16 weeks, and can clear the virus in $\geq 95\%$ of cases (5). Treatment-induced viral clearance is associated with a dramatic improvement in clinical outcomes, by reducing the risk of long-term complications such as decompensated liver disease and HCC, as well as extra-hepatic manifestations and both liver- and non-liver-related mortality.

The advent of DAAs has ushered in a true medical revolution in the field. In principle, all patients with HCV can now be treated and cured, but in reality, this is still not the case (6). Many barriers hamper universal access to therapy. Due to the high prices of DAAs in some settings, only patients with advanced disease can be treated; in others, only liver specialists can prescribe DAAs, which limits

access and the development of novel models of care. Further, in some countries, DAAs are only prescribed if a patient is abstinent from active drug or alcohol consumption (7).

In 2016, the World Health Organization adopted its first *Global Health Sector Strategy on Viral Hepatitis*, calling for its elimination as a public health threat. There were two main targets: reducing new HCV infections by 80% and mortality by 65% by 2030 (8) and a series of service coverage targets with an interim 2020 date. It presented five strategic directions (strategic information, interventions for impact, equity, financing for sustainability and innovation for acceleration) encompassing specific measures aimed at reducing new infections and saving lives between 2015 and 2030. All WHO Member States approved this strategy in 2016 and EASL strongly recommends that they implement it.

Recommendations

EASL supports World Health Assembly resolution 67.6 (8) calling on all countries to develop viral hepatitis strategies and recommends that such strategies should now have the goal of eliminating hepatitis C as a public health threat by the year 2030. National action plans should specifically mention this goal and should be costed and comprehensive, i.e. covering all steps of the continuum of hepatitis C care, including prevention measures, testing, linkage to care, treatment and follow-up after cure has been achieved. Plans should follow a public health approach within a health systems framework, aiming to provide the best available treatment while at the same time affording the widest benefit at the population level (9, 10).

The inclusion of patients and those most at risk of infection at all stages of the elimination effort is crucial. We encourage all stakeholders to collaborate to achieve this important goal. EASL wishes to further draw all relevant stakeholders' attention to the ethical considerations regarding withholding a curative, simple and safe therapy from patients who can develop life-threatening complications, such as those due to hepatitis C.

All the measures suggested in the following recommendations will require increased efforts to raise the overall awareness for viral hepatitis at all levels, including health professionals, patients, policy-makers, the media, and the public.

Robust data on the number of newly, as well as chronically HCV infected patients, and on how many persons are screened, diagnosed, linked to care and treated in all sub-groups, should be provided at the national, and where relevant, regional level, so that progress towards the WHO targets can be consistently monitored and efforts refined accordingly.

Prevention

EASL supports the United Nations General Assembly resolution (11) on harm reduction in all settings to prevent HCV transmission. Both healthcare personnel and the general population should be made aware of the different transmission modalities, and of the most effective preventive measures. As there is no prophylactic vaccine, the implementation of harm reduction strategies (e.g. access to opioid substitution therapy and safe injecting equipment for people who inject drugs, safe sex, and increased awareness among all high-risk populations, including prisons) should be increased, while at the same time combating the stigma and discrimination that is associated with HCV infection. Preventive measures should also be encouraged in those cured, as a successful treatment does not protect from reinfection.

Testing for hepatitis C

EASL advocates the use of rapid point-of-care tests, including for viremia. These assays should be implemented in all relevant settings. Screening should include testing for HIV and the hepatitis B virus, as these two pathogens are often transmitted together with HCV, and priority should be given to persons engaging in high-risk practices. General practitioners and drug and alcohol specialists should be informed about the importance of testing members of these groups. Screening strategies other than risk-based (such as those targeting birth cohorts or even the general population) should be evaluated in regard to their cost-effectiveness and feasibility, depending on the local epidemiology. Countries should take actions to avoid late presentation and diagnosis (4) by increasing testing in non-hospital settings, such as addiction and harm reduction services and prisons.

Linkage to care

Linkage to care should be facilitated by increasing the number of authorized prescribers if needed, by promoting telemedicine-based clinical case discussion and decisions, and by an increased involvement of peers and mid-level providers in the continuum of care, during and after treatment.

Treatment

Countries should focus on removing any existing reimbursement restrictions, as they impede access to DAAs, in line with EASL recommendations on the treatment of hepatitis C (5). Payers and providers must recognize the advantage of treating HCV infection early, to prevent later disease development and onward transmission. Treating hepatitis C patients early will reduce costs related to monitoring disease progression and improve the quality of life for patients as well as reduce loss of work productivity. On the other hand, treating at advanced disease stages will require continued care, even after achievement of cure, to monitor for the development of liver cancer. Treatment should be expanded to shared care between specialists and addiction centers, prisons and other relevant settings. The positive effect of DAA therapy on morbidity and mortality should be described at the national level, to support policy-makers in increasing access to DAA therapy. Special attention should be devoted to retreat those patients who get re-infected after achieving SVR, since they are likely to be engaging in high-risk practices and therefore contributing to onward transmission. Payers and the pharmaceutical industry should agree on price reductions, as has been the case in numerous European countries.

EASL believes that medical associations and clinicians, in collaboration with other key stakeholders, play a critical role in eliminating HCV and we will continue to work on the implementation of the WHO viral hepatitis strategy and our guidelines to ensure that hepatitis C virus elimination in Europe by 2030 will become a reality.

References

1. Stanaway JD, *et al.* The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *Lancet* 2016;388(10049):1081-8.
2. World Health Organization. Global Hepatitis Report 2017. <http://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf?sequence=1> (accessed May 26, 2018)

3. Razavi H, *et al.* Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study. European Union HCV Collaborators. *Lancet Gastroenterol Hepatol* 2017;2(5):325-36
4. Mauss S, *et al.* Late presentation of chronic viral hepatitis for medical care: a consensus definition. *BMC Med* 2017;15(1):92.
5. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C 2018. *J Hepatol* 2018 Apr 9 [Epub ahead of print]
6. Cooke *et al.* Lancet Gastroenterology & Hepatology Commission: Accelerating the Elimination of Viral Hepatitis, 2019; 4: 135–84.
7. Marshal AD, *et al.* Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe *Lancet Gastroenterol Hepatol* 2018;3(2):125-133
8. World Health Organization. Global Health Sector Strategy on Viral Hepatitis 2016–2021. Towards ending viral hepatitis. <http://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf;jsessionid=19275FA9575F8F110A73E0E94130C338?sequence=1> (accessed May 26, 2018)
9. Papatheodoridis GV, *et al.* Hepatitis C: The beginning of the end-key elements for successful European and national strategies to eliminate HCV in Europe. *J Viral Hepat* 2018;25(Suppl 1):6-17
10. Heffernan A, *et al.* Aiming at the global elimination of viral hepatitis: challenges along the care continuum. *Open Forum Infect Dis* 2017;5(1)
11. United Nations General Assembly resolution of April 14, 2016. Available at <http://undocs.org/A/S-30/L.1> (accessed May 26, 2018)

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