DEFUSE HEPATITIS C, THE VIRAL TIME BOMB!
TEST AND TREAT HEPATITIS C

Position Paper for the 67th World Health Assembly May 19-24, 2014

The World Health Organization (WHO) has referred to hepatitis C as a "viral time bomb". The Global Commission on Drug Policy recommends that "[…] to respond effectively and urgently to the global human, social and economic costs that the [HCV] epidemic threatens to inflict, governments need to scale-up both prevention and treatment, especially for people who use drugs".[1]

In 2010, the 63rd World Health Assembly (WHA) adopted the first resolution on viral hepatitis (WHA63.18). A new resolution will be presented at the 67th WHA.

Globally, an estimated 185 million people have been infected with hepatitis C virus (HCV). Since 2010, more than a million people have died from HCV, **although it is treatable and curable**. Nine to twelve million people have been infected since 2010, a**lthough HCV is preventable**. Most new infections occur among people who inject drugs (PWID), yet access to HCV prevention tools (such as sterile injection equipment) is woefully inadequate, reaching a tiny percentage of those who need it. This shocking public health failure allows the epidemic to continue spreading.

Only a tiny fraction of people who have been infected with HCV are aware of their status. Most live in low and middle-income countries (LMICs) and have no access to diagnostics, care, or treatment. Pegylated interferon (peginterferon, or PEG-IFN), the backbone of the current standard of care for HCV, is priced cruelly out of reach. Even in places where HCV treatment is available, injecting drug use is often used as a criteria for denying access: only 2-4 percent of people who inject drugs are currently receiving treatment.

We, people living with HCV, HIV/AIDS, people who use drugs and our advocates, urge United Nations (UN) Member States to act strongly in order to tackle the hepatitis C epidemic; it is feasible!

Asia Pacific Network of People Living with HIV/AIDS (APN+) is the network of PLHIV living in the Asia Pacific region. It was established in 1994 at a meeting in Kuala Lumpur by 42 PLHIV from eight countries. It was established in response to the need for a collective voice for PLWHA in the region, to better link regional PLHIV with the Global Network of PLHIV (GNP+) and positive networks throughout the world, and to support regional responses to widespread stigma and discrimination and better access to treatment and care.

International Network of People who Use Drugs (INPUD) is a global peer-based organisation that seeks to promote the health and defend the rights of people who use drugs. We will expose and challenge stigma, discrimination and the criminalisation of people who use drugs and its impact on our community's health and rights. We will achieve this through processes of empowerment and international advocacy.

Médecins du Monde (MdM) is an international aid organization working in more than 60 countries caring for the most vulnerable populations, for victims of armed conflicts and natural disasters and for those who are gradually being forgotten about. As an independent civil society organization, its actions go beyond medical care. It openly condemns violations of human rights and fights to improve the situation of these populations.

Treatment Action Group (TAG) is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS. TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end AIDS.

Act Up-Basel is an activist coalition based in Basel, Switzerland, the home of the pharmaceutical companies Roche and Novartis. Act up Basel advocates for the access to treatments and the right to health for all, and focuses on intellectual property barriers to access.

International Treatment Preparedness Coalition (ITPC) is the world's leading community-based movement of people living with HIV and their supporters who are united in promoting access to treatment. The coalition members include community organisations, local NGOs, researchers, and activists with strong expertise in HIV treatment, HIV co-infections, health systems and related issues. For nearly a decade, ITPC has been engaged in treatment advocacy and literacy, ensuring that PLHIVs are at the forefront of actively shaping their own futures and leading productive lives.

1.Report of the global commission on drug policy, The negative impact of the war on drugs on public health: the hidden hepatitis C epidemic, 2013.

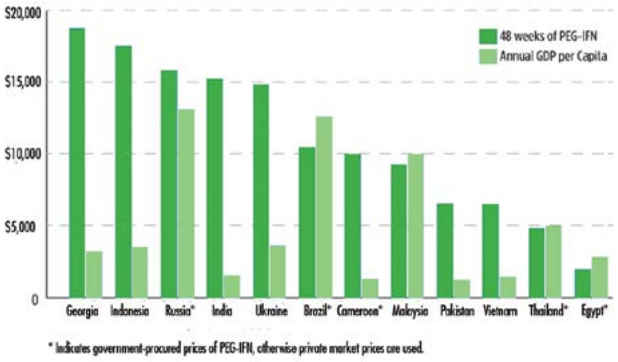
1. Reducing the cost of existing and future hepatitis treatments should be an urgent priority for governments and the World Health Organization

HCV treatment: unaffordable for governments and people living with hepatitis C

Due to exorbitant prices, access to HCV treatment is severely limited for most people living with hepatitis C. Two pharmaceutical companies—Roche and Merck— own the patents on Peg-IFN and share the global market. This duopoly allows them to fix prices. In LMICs, where the vast majority of people in need of treatment live, the cost of pegylated interferon can be as high as USD$ 18,000. In LMICs, one 48-week course of PEG-IFN can cost 10 times the average annual per capita income.

As numerous supply sources are needed to lead to a decrease in drug prices, access to more alternative Peg-IFN suppliers is critical to bringing down prices and expanding access.

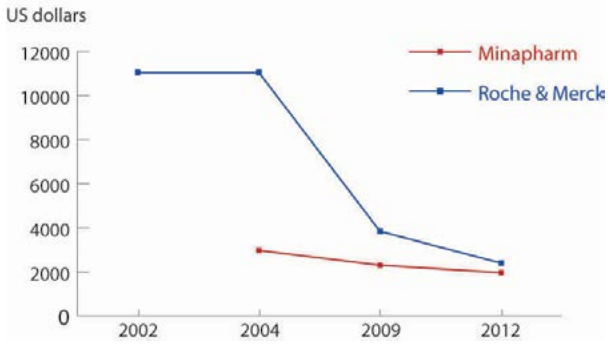
Cost of a 48-week Course of Brand-Name PEG-IFN Treatment vs. Gross Domestic Product (GDP) per Capita



Drastic price reduction for Peg-IFN is possible

Several alternative sources of pegylated interferon have recently been developed, which have helped to drive down the cost of treatment. In Egypt, for example, a locally-manufactured alternative pegylated interferon, Reiferon Retard, has been produced and marketed since 2004. Market competition has supported a six-fold reduction in the price of both originator and alternative products: a 48-week treatment course of pegylated interferon and ribavirin (RBV) currently costs less than USD $2,000 in Egypt. This is the lowest available price worldwide, demonstrating that substantial price reductions are possible, where there is competition.

48 weeks PEG-IFN prices in Egypt: Role of Reiferon Retard®



Where there is generic/biosimilar competition, prices can be driven down dramatically

Compulsory license

One of the key lessons from the global AIDS treatment access movement is that countries may utilize legal flexibilities such as compulsory licensing to ensure access to essential medications. Issuing a **compulsory license (CL) makes treatment affordable by ensuring access to generic or biosimilar versions of drugs and biologics, thereby increasing coverage** for people in need of treatment. For example, in 2000, a first-line triple-therapy antiretroviral (ARV) medication originator price was USD$ 10,430; when several generic versions entered the market, the cost for the same HIV combination therapy was driven down to USD $ 62.[2]

The use of compulsory licensing is recommended in WHA's 2010 resolution on viral hepatitis: *"to consider, as necessary, national legislative mechanisms for the use of the flexibilities contained in the Agreement on Trade-Related Aspects of Intellectual Property Rights in order to promote access to specific pharmaceutical products."* LMIC governments who elect to issue CLs must not be threatened or punished with sanctions or otherwise, by upper-income governments. WHO must reaffirm and vocally support governments' right to issue them.

Patent Opposition

National legislative mechanisms also allow most countries to revoke patents when it is proven that the 'new' medicine does not match all patentability criterias. Roche's patent on Pegasys has thus been opposed and revoked in India in November 2012[3].As a consequence, any Indian producer can now produce a biosimilar of peginterferon alfa-2b and export it to any country where no patent has been granted.

2. Médecins Sans Frontières, Untangling the web of antiretroviral price reduction 14th Edition July 2011, utw.msfaccess.org
3. PharmaTimes – 'India revokes Roche's patent on Pegasys': http://www.pharmatimes.com/article/12-11-05/India_revokes_Roche_s_patent_on_Pegasys.aspx

Chart sources: Cost of PEG-IFN from Momenghalibaf A. Global snapshot: HCV epidemiology and response (Draft). Open Society Foundations Access to Essential Medicines Initiative and International Harm Reduction Development Program. Forthcoming 2013. GDP per capita data from http://data.worldbank.org/indicator/NY.GDP.PCAP.CD. (Accessed 2013 May 31). Kaplan K. Low- and Middle-Income Countries Defuse Hepatitis C, the "Viral Time Bomb", TAG/i-Base 2013 Pipeline Report; 2013. From: http://www.pipelinereport.org/2013/hcv-global-access (Accessed 2013 November 13).

Challenges to increase competition & access

However, issuing a CL or revoking patents would require concerned countries to dispose of alternative supply sources – which is the case in only a very limited number of countries, such as Egypt and India. Indeed, while Peg-IFN could theorically simply be 'copied' and sold as a biosimilar in LMICs by alternative producers --as is the case for many HIV/AIDS medicines --patent protections discourage potential biosimilar producers. In some cases, pharmaceutical companies may challenge country actions to produce biosimilars by filing patent lawsuits against them.[4]

The lack of a regulatory system at the global level also complicates the attempts of biosimilar producers to export their products on a global scale. Moreover, international treatment funders (such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and UNITAID) have to 'respect' the rule to fund only WHO-prequalified medicines. This excludes *de facto* any biosimilar of Peg-IFN, thus strengthening Roche and Merck's duopoly.

Because of this rule and of the lack of global regulation system on biosimilars, countries are reluctant to replace branded Peg-IFN by cheaper, imported biosimilars.

In the context of monopoly or duopoly, neither tiered pricing nor voluntary licensing strategies have been as effective at reducing drug prices as generic competition, due to the lack of an incentive for patent owners to cut the price of their drugs ; on the contrary, these modalities have severely delayed or impaired governments' use of legal flexibilities in their intellectual property laws to access essential medications.

New treatment in the pipeline: DAAs

"If the prices [of new HCV treatments] were to be unaffordable once more in history, it would be one more scandal around inequity of access to health care."

Michel Kazatchkine, the United Nations Secretary General's Special Envoy on HIV/AIDS in Eastern Europe and Central Asia

In the coming years, peginterferon-free HCV treatment will be on the market, revolutionizing the current course of care of hepatitis C. Oral direct-acting antivirals (DAAs) (some of which still must be used with PEG-IFN and/or RBV), are dramatically increasing cure rates; in clinical trials DAA combinations lead to cure rates of up to 100%, regardless of HCV treatment history, cirrhosis, or host genotype. DAAs have the potential to eradicate hepatitis C virus from the planet, if -and *only if* - they are affordable for the vast majority who need them. According to a recent study[5], "within the next 15 years, large-scale manufacture of ribavirin plus two generic HCV DAAs is feasible, with target prices of $100-$200 per 12 weeks treatment course," if the drugs can be produced generically.

Focus on Gilead's sofosbuvir

Gilead's sofosbuvir should receive U.S. Food and Drug Administration (FDA) approval in December 2013, and in the EU shortly thereafter.

Gilead is expected to charge US $80,000 to $90,000 per 12-week course of sofosbuvir. Yet DAAs (including sofosbuvir and many others in late-stage development) can be produced generically for a tiny fraction of that price, just like ARVs for HIV. For example, if a generic version of sofosbuvir were produced, a twelve-week course could cost as little as USD $130-US $270[5].

Financing Hepatitis C treament

Another key lesson from the global AIDS treatment access movement is that **bulk-buying prequalified generics** of ARV **allows additional, substantial price reductions**. Currently, neither governments, nor international agencies on the hepatitis C frontline, have allocated adequate resources for tackling this global epidemic. Only a few LMICs (i.e., Georgia, Ukraine or Macedonia) have HCV treatment programs for people with HIV/HCV coinfection, funded by the GFATM.

There is an urgent need for adequate resources in order to effectively tackle hepatitis C.

4. In December 2010, Roche filed a complaint in Vietnam for violation of its patent on Peg-IFN Alpha 2.b 'Pegasys'. A Vietnamese company, Nanogen, had indeed started to produce a biosimilar of the drug. http://www.firstwordpharma.com/node/817015?tsid=17#axzz2iuPPtCFm.

5. Hill A, Khoo S, Ford N. What is the minimum cost per person to cure HCV? 7th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Kuala Lumpur, Malaysia, July 2013 [TULBPE16].

2. The World Health Organization must act!

WHO must urgently prequalify biosimilars and DAAs

The WHO's prequalification program was launched in 2001 and aims to "make quality priority medicines available for the benefit of those in need". The program assesses the safety and efficacy of medicines for HIV/AIDS, malaria and tuberculosis, and runs inspection activities in order to guarantee compliance of manufacturing sites with WHO Good Manufacturing Practices (GMP).
Since 2001, this program has played a key role for a better access to cheap and high-quality medicines, in particular for ARVs. Nearly 75 percent (or, 265) of prequalified medicines are ARV: 53 from originator companies and 212 from generic companies.[7]

It's time for WHO to open its program to HCV and prequalify biosimilar peginterferon and generic DAAs.
Similarly, quality assurance for pegylated interferon and HCV DAA will give confidence to donors, people living with HCV, and implementing organizations. It will allow developing countries to fast-track registration of generics and biosimilars to treat HCV.[8]

WHO's Essential Medicines List (EML)

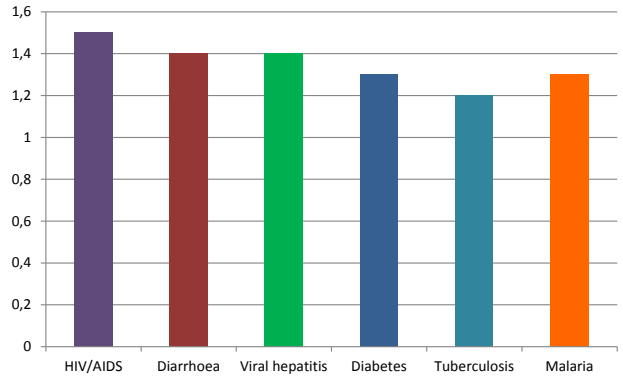
The WHO EML is a powerful tool. Considered a model for countries, many governments refer to WHO recommendations when making decisions on health spending. A drug included in the WHO EML is more likely to appear on a country's national EML and is given priority for coverage under a national health care scheme.

Until 2013, hepatitis C treatment was not included in the WHO's EML. In July 2013, following a strong civil society advocacy campaign, PEG-IFN was included on the "complementary list" (rather than the main list) to the EML because of "consistent higher costs". It is a first step.
What is at stake now is inclusion of DAAs on the EML. New DAAs—especially generic versions-- must rapidly be prequalified. Including DAAs on the EML is critical, both symbolically and practically, for procurement of affordable HCV treatment in LMICs.

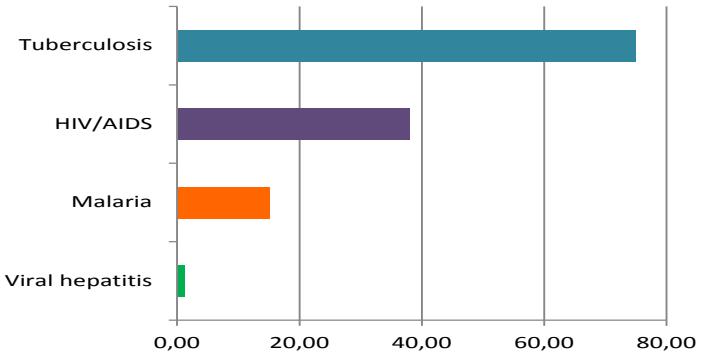
WHO must prioritize viral hepatitis at the height of its burden

Both financial and human resources are vastly insufficient for an adequate response to this global epidemic.
Although viral hepatitis is one of the 4 main communicable diseases, the WHO assigns only three staff persons to work on it, compared to 98 people for TB, 75 for Malaria and 59 for HIV/AIDS.

Number of deaths (million) per diseases and per year 2010[9]



WHO 2012 - Budget allocation compared to number of deaths[9]



7. La « Préqualification » OMS. Origines, Déploiement et Impacts sur la disponibilité des ARV dans les Pays du Sud, Christopher Lantenois (ANRS/CEPN) Benjamin Coriat (CEPN) N° 2011-22.
8. Nathan Ford et al, Expanding Access to Treatment for Hepatitis C in Resource-Limited Settings: Lessons From HIV/AIDS in Clinical Infectious Diseases Advance Access published March 19, 2012.
9. Lozano et al, Global Burden of Disease Study 2010 Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010, Lancet 2012.

3. Identifying and prioritizing people with urgent need for treatment

PWID are disproportionately affected by hepatitis C

- An estimated 10 million PWID were HCV antibody positive in 2010, with a global HCV prevalence of 67% among PWID.
- About 80% of HIV-positive PWID are coinfected with hepatitis C.
- 90% of new infections result from unsterile injecting equipment.
- HCV incidence is high among PWID: 5%-25% per year.

Harm reduction services are too scarce

- Globally, an average of 2 needle–syringes are distributed per PWID per month.[10]
- Of 100 PWID, only 8 (range, 6–12) receive opioid substitution therapy (OST).
- Only 4 HIV-positive PWID (range 2–18) of 100 receive ART.

Promotion of evidence-based harm reduction services can impact HCV transmission.

HCV prevalence among PWID in selected countries

Country or territory	Adult HCV prevalence among people who inject drugs
Brazil	39.5–69.6%
Estonia	90%
Georgia	92,1%*
Germany	75%
India	92%
Indonesia	60–98%
Kazakhstan	65.7%
Mauritius	95%
New Zealand	70%
Pakistan	89%
Sweden	83.8%
Tanzania	28%**
Thailand	90%
Ukraine	70–90%
United States	50–80%

To be effective, HCV prevention requires an approach that combines prevention (high coverage NSP, OST, and peer education) with HCV treatment programs

Implementation and scale-up of evidence-based harm reduction programs, particularly needle and syringe programs (NSP) and OST have successfully contained and reversed HIV infection rates among people who inject drugs[11]. Similar actions should be taken to control HCV, which is 10 times more infectious than HIV. According to recent studies, "each intervention alone will achieve modest reductions in HCV transmission, and prevention of HCV transmission necessitates high-coverage and combined approaches." [12] A meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs found a "substantial and statistically significant reduction in HCV incidence in PWID - of approximately 75 percent - when combination prevention strategies were applied". [13]

A standard package for HCV control in PWID, as recommended by WHO,[14] must consist of:

- High coverage needle and syringe programs (HCNSP) defined as obtaining 1 or more sterile needle and syringe from an NSP for each injection
- Opioid substitution treatment (OST)
- Peer education programs
- Treatment programs

People who inject drugs have largely been excluded from HCV care; fewer than 1% having access to HCV treatment in LMICs. When included in treatment programs, however, cure rates among **people who inject drugs are similar to those of the general population**. PWID "...demonstrate high adherence, low discontinuation of therapy, and a low rate of reinfection (1%–5% per year)."[15] In accordance with human rights norms "decisions about treatment should be made independently of an individual's injection drug use status."[16]

10. For instance, just an estimated 10% of PWID in Eastern Europe, and 36% in Central Asia, access NSPs Stuikyte R, Votyagov S & Pinkham S (2012) *Quitting While Not Ahead. The Global Fund's retrenchment and the looming crisis for harm reduction in Eastern Europe & Central Asia*. Vilnius: Eurasian Harm Reduction Network.
11. UNAIDS Report on the Global AIDS Epidemic, 2010.
12. Louisa Degenhardt, Bradley Mathers, Peter Vickerman, Tim Rhodes, Carl Latkin, Matt Hickman. HIV in people who use drug, Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are Needed. Lancet 2010; 376: 285–301.
13.Hagan H, Pouget ER, Des Jarlais DC. A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs. J Infect Dis 2011; 204:74–83.
14. Guidance on Prevention of hepatitis B and C among people who use drugs, July 2012.
15. Grady B, Schinkel J, Thomas XV, Dalgard O. Hepatitis C virus reinfection following treatment among people who use drugs. Clin Infect Dis 2013; 57(Suppl 2):S105–10.
16. Aspinall E, Corson S, Doyle J, et al. In Treatment of Hepatitis C Virus Infection Among People Who Are Actively Injecting Drugs: A Systematic Review and Meta-analysis. Clin Infect Dis 2013; 57(Suppl 2):S80–9.

Table Sources: Cook, C. & Kanaef, N. (2008) Global State of Harm Reduction: Mapping the response to drug-related HIV and hepatitis C epidemics. International Harm Reduction Association (www.ihra.net/files/2010/06/16/GSHRFullReport1.pdf). *High prevalence of hepatitis C infection and important treatment needs among people who inject drugs in Tbilisi, Georgia Results of a respondent driven sampling survey by Médecins du Monde, June 201.**Assessment of risk practices and infectious disease among drug users in Temeke District, Dar es Salaam, Tanzania Burnett Institute and MDM, 2011.

A large proportion of people who inject drugs are coinfected with HIV and HCV

An estimated 80% of people with HIV who inject drugs also have hepatitis C virus (HCV) [17]. In Asia and Eastern Europe, HIV/HCV coinfection rates among PWID range from 70 % to 95 %.

In fact, the vast majority of people living with HIV/HCV coinfection have acquired both viruses from lack of access to sterile injecting equipment.

Now that antiretroviral therapy has extended the life expectancy of people with HIV/AIDS, liver disease from HCV has become a leading cause of non-AIDS-related deaths in this population.

Worldwide, an estimated 4—5 million people are HCV/HIV co-infected[18]. HIV accelerates HCV disease progression, and more than triples the risk for liver disease, liver failure, and liver-related death from HCV.

People who are HCV/HIV co-infected can be cured of HCV regardless of their HIV status. Treatment for HCV/HIV co-infected people is recommended, because curative hepatitis C treatment reduces the risk for liver-related disease and death, and also reduces all-cause and AIDS-related death rates[19].

People who inject drugs and/or are HIV coinfected must be screened and treated as a priority.

Recommendations to effectively address the global hepatitis C virus epidemic:

To UN Member States:

- *Give hepatitis C global priority on par with HIV/AIDS, TB and malaria in the post-2015 health agenda and provide adequate resources for a continuum of hepatitis C prevention, treatment, care and support programs for all who need these services—especially people who inject drugs--- through national, regional and international mechanisms;*
- *Ensure access to safe, effective, and affordable standard of care HCV treatment to the 99% who can't currently access any treatment, by importing cheaper biosimilars/generics, and by using the flexibilities of the TRIPs agreement in every country where intellectual property rights (IPR) are a significant obstacle to access*
- *Massively increase provision of evidence-based harm reduction services, in particular, NSP and OST, using a combination approach that includes HCV care and treatment, to effectively tackle hepatitis C transmission and ensure that people who use drugs are not excluded from these life-saving services;*
- *Meaningfully involve civil society-- specifically people who use and inject drugs—in the creation of tailored hepatitis C control plans. PWID and their organizations should be involved in the design, implementation, and monitoring of these programs;*
- *Decriminalize drug use and remove legal, structural and institutional barriers to healthcare and HCV services for PWID, as well as those legal and structural factors that actively drive the epidemic amongst the injecting community. Immediately put an end to human rights abuses and discrimination in the health care setting.*

To Dr. Margaret Chan, WHO Director-General:

- *Include hepatitis C products in the WHO prequalification program: both biosimilar pegylated interferon and, once approved, generic direct-acting antivirals*
- *Prioritize the inclusion of key DAAs on WHO's Essential Medicines List in an ongoing and timely manner;*
- *Produce regulatory guidance on biosimilars;*
- *Vocally and unequivocally support governments' right to utilize TRIPS flexibilities to ensure access to lifesaving tests, diagnostics and treatment;*
- *Allocate adequate resources, both human and financial, to its Viral Hepatitis Program, to help effectively address the global HCV epidemic.*

17. CDC Fact sheet HIV and Viral Hepatitis, May 2013.
18. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol* 2006; 44 (suppl 1): S6-S9.
19. Berenguer J, Rodríguez E, Miralles P, et al; GESIDA HIV/HCV Cohort Study Group. Sustained virological response to interferon plus ribavirin reduces non-liver-related mortality in patients coinfected with HIV and Hepatitis C virus. Clin Infect Dis. 2012 Sep;55(5):728-36.