Thirty-Second Board Meeting

Global Fund and Hepatitis C Treatment

The Global Fund

The Global Fund Thirty-Second Board Meeting

GF/B32/22

Board Decision

GLOBAL FUND SUPPORT FOR HEPATITIS C TREATMENT

Purpose:

Seeking a Board decision on an interim measure regarding Hepatitis C treatment within existing grants until the Board has a broader discussion on the Global Fund's role in funding treatment of co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria.

EXECUTIVE SUMMARY

1. The Global Fund has received a number of requests from countries for financing of Hepatitis C treatment in the past. With the preparation and submission of concept notes following the full launch of the funding model, rapidly changing Hepatitis C treatment landscape, and the potential resource and mandate questions that arise from funding Hepatitis C treatment, the Strategy, Investment and Impact Committee (SIIC) examined this issue at its 13th meeting in October. The Global Fund has provided limited support for Hepatitis C treatment under TRP guidance in the past, but the Board has not specifically considered the question of funding for Hepatitis C nor the broader question of financing for other co-infections and co-morbidities of the three diseases. This paper summarizes the epidemiology of Hepatitis C, reviews Global Fund support for Hepatitis C to date, and recommends an interim decision on the specific question of funding for Hepatitis C treatment while undertaking a broader analysis with respect to the Global Fund's role in financing co-infections and co-morbidities of the three diseases for future Board consideration.

INTRODUCTION and BACKGROUND

2. Hepatitis C infection is a blood-borne viral infection. Globally, there are an estimated 170 million people chronically infected with the Hepatitis C virus (HCV). Every year 3 to 4 million people are newly infected and 350,000 people die[1]. There is poor data quality on HIV/HCV co-infection but estimates suggest that approximately 5 million people worldwide are living with both viruses.[2]

3. Regions with highest HCV prevalence (>3.5 percent) include Central and East Asia and in North Africa/Middle East, moderate prevalence (1.5 to 3.5 percent) is found in South and Southeast Asia, sub-Saharan Africa, Latin America and the Caribbean, Australia, Oceania, and Europe, and low prevalence in Asia Pacific and North America (< 1.5 percent)[1]. In sub-Saharan Africa, prevalence's between 5 to 8 percent have been reported[1]. In low and some middle-income countries, HCV infection is due largely to health-care associated transmission while in middle and high-income countries transmission is most frequently associated with injection drug use[3]. Globally, people who inject drugs (PWID) are disproportionately affected by HCV. A 2011 study showed that approximately 67 percent of PWID are infected with HCV; representing 10 million people across 148 countries[4].

4. HCV causes both acute and chronic infection. Acute HCV infection is usually asymptomatic, and is only very rarely associated with life-threatening disease. About 15 to 45 percent of infected persons spontaneously clear the virus within 6 months of infection without any treatment. The remaining 55 to 85 percent of persons will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis of the

[1] Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology. 2013; 57(4): 1333-42.
[2] Alter M. Epidemology of viral hepatitis and HIV co-infection. J Hepatol 2006; 44 (1 Suppl): S6-9. http://www.sciencedirect.com/science/article/pii/S0168827805007269 and http://www.hopkinsmedicine.org/news/media/releases/hepatitis_cured_in_co_infected_hiv_patients
[3] World Health Organization. Guidelines for the screening, care and treatment of persons with Hepatitis C infection. Geneva, April 2014. Available at: http://www.who.int/hiv/pub/hepatitis/hepatitis-c-guidelines/en/
[4] Nelson PK et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet. 2011; 378(9791): 571-83.

liver is 15 to 30 percent within 20 years, and 5 to 7 percent will develop liver failure or liver cancer[3].

5. HIV and Hepatitis C may interact as co-infections. HIV negatively impacts the natural disease progression of Hepatitis C at every stage of the disease; people living with HIV (PLHIV) are less likely to spontaneously clear the HCV following infection, have higher HCV viral loads, progress faster to HCV-related liver disease, and are twice as likely to develop cirrhosis and six times as likely to develop end-stage liver disease. Evidence has shown that chronic HCV infection is independently associated with a 50 percent increase in mortality among patients with a diagnosis of AIDS. Antiretroviral therapy (ART) for HIV improves outcomes for persons with dual infection, increases rates of HCV remission, but higher progression rates may still be evident[5]. As ART for HIV has become more widely available, end-stage liver disease has become a leading cause of morbidity and mortality in some settings[6].

6. In April 2014, WHO issued its first guidance for the treatment of Hepatitis C[3]. The new guidelines make nine key recommendations. These include approaches to increase the number of people screened for Hepatitis C infection, advice as to how to mitigate liver damage for those who are infected and how to select and provide appropriate treatments for chronic Hepatitis C infection.

7. In 2013, Gilead Sciences Inc. launched its Hepatitis C drug Sovaldi (Sofosbuvir), which clinical studies show achieves high cure rates when used in combination with other agents over a 12 week course of treatment, including among patients co-infected with HIV[7]. Sovaldi currently costs US$ 84,000 for a 12-week course of treatment, although costs are expected to decrease in the coming years. On September 15, 2014, Gilead licensed Sofosbuvir to seven India-based drug makers that will sell less expensive versions of the medicine in 91 developing nations. The 91 countries covered by the deal have an average per capita income of US$ 1,900 and account for about 54 percent of those living with Hepatitis C[8]. A number of additional new treatments for Hepatitis C are expected to come to the market in the next several years.

Global Fund support for Hepatitis C

8. Recognizing the shared transmission route of HIV and HCV, key harm reduction stakeholders recommended in 2011 that the comprehensive harm reduction package for PWIDs include interventions aimed at preventing, detecting, and treating hepatitis. The Global Fund supports harm reduction programmes for PWID, is the largest external donor in this field globally, and is the only donor to support harm reduction in some country contexts.

9. The TRP report from Round 10 (December 2010 and predating the launch of new treatments)[9] stated the following regarding provision of Hepatitis C treatment:

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[5] Thein HH et al. Natural history of hepatitis C virus infection in HIV-infected individuals and the impact of HIV in the era of highly active antiretroviral therapy: a meta-analysis. AIDS. 2008; 22(15): 1979-91.
[6] Bica I et al. Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. Clin Infect Dis. 2001; 32(3): 492-7.
[7] Sulkowski M et al. Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. JAMA. 2014; 312(4): 353-361.
[8] Information available at: http://in.reuters.com/article/2014/09/15/gilead-sciences-india-idINKBN0HA0TI20140915

[9] GF/B22/13

a. The TRP reviewed several proposals that included funds for the treatment of Hepatitis C and recommended one proposal for funding subject to clarifications. The TRP is concerned that currently available therapy for the treatment of Hepatitis C (Interferon and Ribavirin) is generally not accessible to the estimated 170 million people living with chronic Hepatitis C. Furthermore, evidence suggesting effectiveness of the combined treatment is limited; the treatment is often poorly tolerated in combination with ARV, needs to be closely supervised and presents operational challenges with treatment access and adherence. More effective and better tolerated regimes are expected to come on the market within a short period of time. Applications for funding of treatment using the present regime will only be recommended by the TRP after close scrutiny of the country context, including well-documented evidence that Hepatitis C treatment and funding is available to the general population and that funding from the Global Fund is to fill-in the gap for HIV infected individuals. Applicants should be required to supply this information in their proposal.

b. The TRP therefore recommends that Global Fund resources be used at this time to increase the evidence base for the need of Hepatitis C treatment (e.g. prevalence surveys), create awareness and increase prevention efforts (e.g. through supporting methadone substitution and needle exchange program, as well as focusing on infection control in health care setting and blood transfusion safety, which would also benefit prevention of other blood-borne diseases) and support advocacy for access and affordability of new Hepatitis C treatments as they become available. Clearer guidance to applicants in this regard is recommended. The TRP urges partners (UNITAID and Clinton Foundation) to explore possibilities with pharmaceutical industry to see how treatments can be made more affordable.

10. Under previous funding rounds, the Global Fund has funded HCV screening and testing in Myanmar, Nepal and Timor Leste, and limited cohorts with Hepatitis C were treated in Belarus, Georgia, FYR Macedonia, Thailand and Ukraine. The Global Fund has received requests to provide Hepatitis C treatment from Georgia, Ukraine, FYR Macedonia and Vietnam.

DISCUSSION

11. The introduction and quest to scale up access to new curative Hepatitis C treatments, including but not limited to Sofosbuvir, recalls the efforts of the late 1990s and early 2000s to provide global access to ART. As with HIV/AIDS, lifesaving medicines are available in wealthy countries but their deployment to poorer countries and key populations is in question. However, current HIV treatment regimens are well established, while the Hepatitis C treatment landscape is rapidly evolving with new products expected to come to the market in the near term and considerable global variability in pricing and domestic programs that address Hepatitis C.

12. The Global Fund supports comprehensive harm reduction packages, as outlined by the WHO in 2014[10] and supports efforts to expand access to prevention, testing and treatment for Hepatitis C. Irrespective of this decision, the Secretariat will continue to actively use its considerable influence and leverage to work alongside partners to support increased and more equitable access to effective and affordable HCV treatment.

[10] World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva, July 2014. Available at: http://www.who.int/hiv/pub/guidelines/keypopulations/en/

13. The launch of new and effective treatment regimens for Hepatitis C and the requests from countries to procure new HCV treatments raises the question of the appropriate role of Global Fund financing for Hepatitis C treatment. The Secretariat considers the financing of Hepatitis C treatment to general populations with Global Fund grants to be outside of our mandate to fight the three diseases. Recognizing scenarios where Hepatitis C treatment may relate to the Global Fund's mission and gains against the three diseases, the SIIC considered both the benefits and risks inherent in using Global Fund resources to fund the treatment of Hepatitis C.

14. The SIIC considered the option to continue to fund Hepatitis C treatment for HIV/HCV co-infected persons within country requests, which would allow the Global Fund to finance treatment for Hepatitis C in PLHIV who would likely not otherwise receive treatment and to fund a full package of harm reduction services for PWID. This approach would rely on countries to consider and balance the relative priorities of Hepatitis C treatment with interventions directly addressing HIV, TB and malaria in their concept notes, and could help build demand for HCV treatment and therefore help catalyze negotiations for lower prices.

15. Resource needs were considered as HCV treatment regimens are rapidly evolving and currently expensive. The global population of people living with HIV/HCV co-infection is estimated to be 5 million and the number of persons living with HIV/HCV co-infection in countries with programs financed by the Global Fund is currently unknown. While pricing of Sofosbuvir and other new HCV treatments will vary by country and will likely come down sharply in the coming years, the costs of procuring HCV treatment at discounted prices for a sub-set of HIV/HCV co-infected persons in need can be significant.

16. Furthermore, moving forward with expanded HCV treatment could create the perception that the Global Fund will finance diseases such as Hepatitis C before a broader discussion occurs on the Global Fund's role with respect to financing of other co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria. While a decision is needed to respond to country requests for HCV treatment, the issue of funding for other co-infections and co-morbidities is significantly broader and has not yet been considered by the Board. For example, the Global Fund does not currently support efforts to address the Human papillomavirus (HPV) despite HPV also being a co-infection of HIV where HPV infection facilitates HIV acquisition and HIV accelerates the health impact of HPV infection. [11] Similarly, Soil-transmitted helminths (STH) including roundworm, whipworm and the hookworms, are co-infections of both HIV and malaria, with an estimated 22m people living with HIV and an STH infection in sub-Saharan Africa. [12] The WHO identifies and highlights a number of important co-infections and co-morbidities which require consideration for a comprehensive HIV programmatic response in the era of successful anti- retroviral therapy.[13] In the course of the SIIC's examination of the options around HCV, and their implications, it became clear that a threshold discussion on the broader question on co-infections and co-morbidities had to first take place.

17. The SIIC therefore recommends that the Secretariat undertake, with partners, an analysis of the Global Fund's role in funding treatment of co-infections and co-

[11] Konopnicki D., De Wit S., Clumeck N. HPV and HIV Coinfection. Future Virology. 2013; 8(9): 903-915.
[12] Pullan RL, Smith JL, Jasrasaria R, Brooker SJ. Global numbers of infection and disease burden of soil transmitted helminth infections in 2010. Parasit Vectors. 2014 Jan 21;7:37. doi: 10.1186/1756-3305-7-37. Parasit Vectors. 2014 Jan 21;7:37. doi: 10.1186/1756-3305-7-37.
[13] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. http://www.who.int/hiv/pub/guidelines/arv2013/download/en/

morbidities of HIV/AIDS, tuberculosis and malaria, and to provide recommendations for future Board consideration.

18. Considering the Global Fund's support for comprehensive harm reductions programs, the need to continue support for existing treatment provision for HIV/HCV co-infected persons, and the rapidly changing HCV treatment landscape, the SIIC recommends that the Board undertake an interim decision that continues funding HCV treatment, up to the currently approved funding amount, where the Global Fund is already financing HCV treatment, but does not increase funding for HCV treatment until the broader review of financing for co-infections and co-morbidities is complete. This interim measure, if adopted by the Board at its Thirty-Second Meeting in November 2014, permits continued funding for HCV treatment within Global Fund grants that have already financed HCV treatment, up to approved budgets for HCV treatment within such grants. The SIIC will re-evaluate the question of financing for HCV treatment pending the review of financing for all the co-infections and co-morbidities of the three diseases.

19. Finally, the SIIC recommends that the Global Fund work with partners, including UNITAID, to shape the market for HCV treatment and encourage partners to finance HCV treatment needs, including those identified within Global Fund grant programs. Accordingly, the Secretariat will seek to accelerate partnerships, advocacy and research efforts with UNITAID and other stakeholders to increase access to and funding for HCV treatment.

DECISION

Decision Point: GF/B32/DP07

1. ***The Board acknowledges the Strategy, Investment and Impact Committee's (the "SIIC") plan to develop recommendations for Board consideration at its March 2015 meeting on the Global Fund's role in funding treatment of co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria, and directs the Secretariat to engage and collaborate with partners to support the SIIC's development of such recommendations.***

2. ***As an interim measure until there is an outcome to those deliberations, where there is a currently approved budget for Hepatitis C virus ("HCV") treatment within an existing Global Fund grant, the Global Fund may continue to fund such treatment up to the approved budget amount, as set forth in GF/B32/22, and may otherwise permit continuation of Global Fund funded HCV treatment programs during this interim period with new grants in these countries up to previously approved budgeted levels.***

3. ***The Board encourages partners to finance broader and additional HCV treatment needs, including those identified within Global Fund grant programs.***

4. ***The Board acknowledges the close working relationship and collaboration among the Global Fund, UNITAID and other partners on market-shaping activities, including the expansion of access to HCV treatments.***