

**PARTNERSHIP MODEL BETWEEN GOVERNMENT OF UKRAINE AND GILEAD**  
**CONCEPT PAPER FOR DISCUSSION DURING THE MEETING ON JULY, 15 2016**

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## **1. Introduction**

Chronic hepatitis C virus (HCV) infection is a disease with a global prevalence of approximately 180 million, and every year three to four million people are newly infected. The impact of HCV on human health is evident, as 80% of acute hepatitis C cases transform into a chronic form and 10-20% of these cases progress to liver cancer<sup>1</sup>.

Ukraine has one of the highest burdens of HCV in Europe. National HCV prevalence in Ukraine is estimated by World Health Organization (WHO) to be approximately 3%, corresponding to 1,200,000 patients<sup>2</sup>. However experts consider this to be underestimated. The prevalence in high risk groups such as people who inject drugs or sex workers is much higher, with high rates of HIV/HCV co-infection. Also, there is important variability in the HCV prevalence across regions.

The impact on health outcomes and costs is uncertain driven by high level of under-diagnosis and variable definition of HCV cases by the different epidemiological surveillance bodies.

What is clear is that the burden is mainly related to liver complications, namely cirrhosis, liver cancer and also extrahepatic complications<sup>3,4</sup>. The costs related to the management of these consequences are very high and unsustainable for the health care system. The number of deaths per year due to HCV complications is estimated to be approx. 4,700.<sup>5</sup>

HCV has different genotypes. In Ukraine there seems to be a higher prevalence of genotypes 1, 3 and 4. However, the majority of HCV cases have an unknown genotype.

Genotyping costs can be substantial and often this test is not being performed. Therefore, the benefits for a treatment effective across all genotypes (pan-genotypic) would simplify treatment and reduce costs.

80,000 patients are on the regional HCV registries. Historically about 1,500 patients have been treated with old treatments (interferon) which have low cure rates, severe side effects and are no longer recommended by WHO. Sofosbuvir was the first new direct-acting antiviral (DAA) introduced in Ukraine by end of 2015. In combination with other drugs it delivers cure rates above 90% and with a good safety profile. This treatment represents a paradigm shift in the management of HCV and a great opportunity for Ukraine to appropriately control HCV. Current WHO guidelines only recommend treatment with DAAs and sofosbuvir is recommended as the backbone of HCV treatment, i.e. the treatment should be based on combinations that always contain sofosbuvir. Since 2015 Gilead has been highly committed to make sofosbuvir available to Ukrainian patients. Gilead has a donation program in place since 2015 with Alliance Ukraine which is allowing 1,250 people to be treated (the cure rates so far have been 90%). Also recently, Gilead has provided an affordable price for sofosbuvir in a tender performed by UNDP and established an agreement that will allow treating additional 1,500 patients. This agreement is an important first step in delivering access but this number is still very low considering the high prevalence and the high number of patients diagnosed and waiting for treatment. According to the experts in Ukraine the capacity to treat HCV is currently between 10,000 to 20,000 patients a year, which represents a 3 to 6 times increase in current treatment rates.

In order to control the HCV infection in Ukraine it is crucial to increase the number of patients on treatment, the treatment capacity, the diagnosis and the linkage to care. WHO recommends all countries to implement plans to eliminate the HCV as a major public health threat. In addition to sofosbuvir, Gilead has now also approved Harvoni in Ukraine. Harvoni is a combination of sofosbuvir and ledipasvir, in a single tablet regimen, for GT1, 4, 5 and 6. Since this treatment is more simple it will facilitate the increase in the treatment capacity. Besides, Epclusa, a combination of sofosbuvir and velpatasvir, has recently been approved by the FDA and the European CHMP has adopted a positive opinion for its use on adults with any genotype of chronic hepatitis C. A pan-genotypic regimen such as this could spare the need of genotyping patients and, therefore, reduce costs of HCV management.

## 2. Objective

Given the high burden of HCV and the possibility that countries now have to cure this disease, WHO recommends and urges countries to implement health plans to eliminate HCV as a public health threat by 2030.

The strategy recommended by WHO considers 5 directions: 1 – Information for focused action: developing a strong strategic information system to understand viral hepatitis epidemics and focus the response; 2 - Interventions for impact: defining essential, high-impact interventions on the continuum of hepatitis services that should be included in health benefit packages; 3 – Delivering for equity: strengthening health and community systems to deliver high-quality services to achieve equitable coverage and maximum impact; 4 - Financing for sustainability: proposing strategies to reduce costs, improve efficiencies and minimize the risk of financial hardship for those requiring the services; 5 – Innovation for acceleration: promoting and embracing innovation to drive rapid progress.

In addition to implementing this strategy, WHO established 5 components: leadership, partnerships, accountability, monitoring and evaluation.

Within this framework Gilead would like to propose to the Ukrainian government a partnership model to accelerate access to the new treatments and increase the treatment capacity to control HCV.

## 3. Partnership model

We propose to discuss this model during the meeting. Based on previous and current partnerships with other countries, we propose a non-comprehensive list of options below in order to progress towards WHO strategic objectives.

### Strategic direction 1: Information for focused action (know the epidemic and response)

- Baseline serosurvey to inform the national surveillance system.
- Improve the national routine surveillance for viral hepatitis by including information about diagnosis, genotype, patients in care, patients on treatment, patients cured, cirrhosis, hepatocellular carcinoma,

transplant and deaths. Some countries have developed a patient registry to collect and analyze these data on a regular basis in order to evaluate health outcomes and economic impact.

Strategic direction 2: Interventions for impact (supporting the range of services needed).

- Providing quality screening, care and treatment for persons with HCV infection requires involvement of appropriately trained individuals as well as facilities suitable for the regular monitoring of patients, especially those on therapy. For the education of healthcare providers we propose the following program, which could be run in 3 phases, depending on the specific needs:

Phase 1 - A conference run over a few days covering an overview of HCV and its treatment provided to the population of gastroenterologists/infectious diseases specialists who form the main group of providers for HCV treatment.

Phase 2 - Short term preceptorship attended by the core of the aforementioned providers in one center of excellence in Europe.

Phase 3- This third phase would aim ensuring that a broader base of healthcare providers are well versed in the screening and management of HCV patients, given that this is crucial to achieve broad coverage, particularly critical in a country of the size of Ukraine. A well tested approach is Project ECHO (Extension for Community Healthcare Outcomes), which is a telemedicine and distance-learning program designed to improve access to quality health care. It was firstly implemented for New Mexicans with HCV in the US and has been extended to other American states characterized by having a high proportion of medically underserved rural areas with highly dispersed population and shortage of HCV specialists. It is also involved in the Georgian HCV elimination program. ECHO connects primary care doctors in local communities with specialists, establishing a working network of healthcare professionals that can collaborate and exchange information such as patient lab results and treatment plans. Through a video conferencing platform, the teams are given an opportunity to inform each other of their own personal experiences and challenges to share applied learning opportunities. These sessions, called Knowledge Networks, allow PCPs to acquire the critical skills necessary in treating geographically isolated HCV <sup>6, 7, 8, 9, 10</sup>.

- Due to the high prevalence on PWIDs reinforce and extend existing harm reduction initiatives in Ukraine.
- Evaluate access to point of care (POC) HCV tests to broader population to improve speed and access to diagnosis <sup>11</sup>.
- Analyze and understand lessons learnt from the program run by Alliance Ukraine to scale up their efforts in a stepwise approach to broader population.
- Disease awareness campaign amongst high risk groups focused on the prevention and transmission of HCV. This could be developed in partnership with Alliance Ukraine and Patients of Ukraine. As treatment rates increase education and awareness could be extended to target the general population to improve understanding of HCV, reduce stigma around the condition and drive people to be screened for HCV. Partnerships with commercial organizations and employers could help drive uptake.

Strategic direction 3: Delivering for equity (supporting the populations in need of services).

- Establish clinical guidelines for the management of viral hepatitis to contribute to a unified treatment and diagnostic algorithms focused on enhancing efficiency.
- Broad access to diagnostic methods (Ab and RNA, POC tests) which need to be under quality management systems for the provision of consistently high quality testing results.
- Prison program aimed at identifying and treating patients during their incarceration in order to prevent reinfection by reducing the community HCV viral load.

Strategic direction 4: Financing for sustainability (covering the financial costs of services).

- Discuss a staged treatment approach that will help manage the immediate impact on the healthcare system, allow predictable year-on-year budget spend and support the elimination of HCV:
  - Treat patients currently diagnosed and under treater care, followed by those at highest risk of onward transmission;
  - Develop targeted screening programs to identify undiagnosed HCV-infected individuals and link them to care;
  - Raise awareness of HCV and educate people on how to prevent the spread of the disease.
- Explore models to ensure funding to increase treatment rates at an affordable way, taking into account the country's burden of disease, economic means and commitment to scale up treatment. This approach has worked successfully in several countries and has enabled to increase treatment rates by 6 times in some cases.

We also suggest exploring the creation of a Bilateral Working group between Ukraine and Georgia, with the collaboration of international institutions, to share best practices and discuss the implementation of some of the options mentioned above.

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<sup>1</sup> Mandrik, O. et al, Cost comparison of treating chronic hepatitis C genotype one with pegylated interferons in Ukraine, Central European Journal of Medicine, Volume 10, Issue 1, Jan 2015

<sup>2</sup> Report "Hepatitis C in Eastern Europe and Central Asia: Epidemic and Response", available at <http://www.aidsalliance.org.ua/cgi-bin/index.cgi?url=/en/coop/hepc/index.htm> , accessed on the 29th June 2016.

<sup>3</sup> Negro F et al. Extrahepatic morbidity and mortality of chronic hepatitis C. Gastroenterology 2015, 149 (6): 1345-60

<sup>4</sup> Lee MH et al for the R.E.V.E.A.L.-HCV Study Group. Chronic Hepatitis C Virus Infection Increases Mortality From Hepatic and Extrahepatic Diseases: A Community-Based Long-Term Prospective Study. J Infect Dis. first published online July 17, 2012 doi:10.1093/infdis/jis385

<sup>5</sup> Mühlberger N et al. HCV-related burden of disease in Europe: a systematic assessment of incidence, prevalence, morbidity, and mortality, BMC Public Health 2009, 9:34

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<sup>6</sup> Arora S et al. Project ECHO: linking university specialists with rural and prison-based clinicians to improve care for people with chronic hepatitis C in New Mexico. *Public Health Rep* 2007; 122: 74–77

<sup>7</sup> Arora S et al. Expanding access to hepatitis C virus treatment--Extension for Community Healthcare Outcomes (ECHO) project: disruptive innovation in specialty care. *Hepatology* 2010 Sep; 52: 1124–1133

<sup>8</sup> Mitruka K et al. Expanding primary care capacity to treat hepatitis C virus infection through an evidence-based care model--Arizona and Utah, 2012-2014. *MMWR Morb Mortal Wkly Rep* 2014;63:393-8

<sup>9</sup> Arora S et al. Outcomes of treatment for hepatitis C virus infection by primary care providers. *N Engl J Med* 2011;364:2199-207

<sup>10</sup> Tahan V et al. Extension for Community Health Outcomes-hepatitis C: Small steps carve big footprints in the allocation of scarce resources for hepatitis C virus treatment to remote developing areas. *World J Hepatol.* 2016; 8: 509–512

<sup>11</sup> <http://www.poc-hcv.eu/> Accessed on the 29th of June 2016.