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HEALTH ACCESS
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01 November, 2016

Dear HCV advocates and organizations in Asia:

Thank you for your letter raising issues regarding our HCV Quick-Start program. We very much respect the work that you do and we take your concerns very seriously. We would like to engage with you to address your concerns and to work together to accomplish as much as is possible in HCV diagnosis and treatment.

CHAI believes that the global health community has not taken the problem of hepatitis C seriously enough and we are committed to working hard to address the plight of the millions of people suffering from this terrible disease around the world.

We agree with many of the points you raise, having encountered similar challenges in HIV treatment many years ago. In this letter we provide some initial responses to your questions and concerns.

CHAI believes that there must be a robust response to the HCV epidemic that enables patients of all income categories access to diagnosis, treatment and cure. Similar to what happened with HIV treatment, we recognize that getting started, even with imperfect programs or access agreements, is critical so as not to delay the beginning of program scale up while in parallel facilitating better programs and more inclusive access agreements. We agree that the Quick-Start program is just a starting point from which to create broader programs and we hope to collaborate with you all so we can concurrently treat as many patients as we can immediately, while continuing to facilitate programs to expand access to diagnosis and treatment.

We very much appreciate and agree with your comments about not designing a program based on available, limited donations. CHAI has always pressed for access to the BEST products, not the least expensive or easiest to get in our HIV and other program areas. Quick-Start was designed to allow treatment to start immediately while we try to accelerate the availability of SRA approved generic versions of the best products. In situations like this there is always a tension between wanting to wait for the best possible treatment regimens and programs while also wanting to alleviate the suffering of people today. With the Quick-start, we want to try to minimize the suffering of as many people as possible immediately at the same time that we try to develop optimal sustainable programs for the future.

Need for patients to pay out of pocket for care

We agree with you that it would be best to have a system where patients that cannot afford out of pocket payments receive HCV diagnosis and treatment without having to pay. However, we did not want to hold up all treatment until this could be achieved.

With major bilateral/multilateral donors and governments unlikely to provide free HCV diagnosis and treatment in the near future, Quick-Start in collaboration with Ministry of Health partners has focused on facilitating care for patients who require immediate treatment (HIV/HCV co-infected patients as well as F3 and F4) while simultaneously working to bridge the major financing gaps

that restrict universal access. CHAI has taken a three-pronged approach to accelerating the availability and affordability of care:

1. *Simplification of the diagnostic algorithm.* Together with experts from Duke University, and after consultations with the WHO and various other partners, CHAI has developed a simplified algorithm for diagnosing and monitoring patients on DAA therapy while maintaining high quality of care. Facilitated by the use of safe and highly effective pan-genotypic DAAs, the algorithm removes costly genotyping and eliminates unnecessary on-treatment viral load monitoring. CHAI is working with Ministries to adopt this algorithm reducing the cost of diagnosis and monitoring and making treatment more accessible than before.

2. *Commodity price negotiation.* CHAI has negotiated with drug and diagnostic suppliers to lower the cost of commodities essential to DAA therapy. To enable the use of the simplified Duke algorithm, Quick-Start countries have prioritized the use of SOF+DCV for all patients. Several generic suppliers have agreed to register and sell SOF into Quick-Start markets at a reduced price. Generic DCV development has lagged behind SOF, prompting CHAI to request a BMS donation to bridge the gap until a quality approved generic equivalent becomes available. CHAI has also entered into a pricing agreement with Roche to lower the cost of viral load assays for the Quick-Start program. Discussions with other viral load suppliers are in the early development stages. CHAI is also working with Ministries of Health on procurement practices to try and limit any mark-ups included by importers and distributors within country.

3. *Alternative financing mechanisms.* In recognition that resources currently aren't available for free HCV diagnosis and treatment programs, CHAI is working with Ministries of Health to launch sustainable programs that offer patients access to care as widely as possible. Part of that work includes advocating for and supporting Ministries to develop budget lines for HCV, leverage social health insurance, explore donor resources, and establishing mechanisms for patients to pay for treatment if needed. CHAI is also actively exploring alternative financing options (i.e. insurance programs, micro-financing) that could potentially ease the financial burden on patients.

While progress has been made on pricing, significant implementation and financing challenges remain. We welcome the opportunity to further discuss how we can work together with you and with Ministries of Health to strengthen diagnostic and treatment systems and explore options for reducing the financial burden on patients.

Recommendation of SOF+DCV for genotype 6 patients

CHAI and its Ministry of Health partners have taken the following into account when recommending SOF+DCV be used by all patients, despite a lack of clinical performance data in genotypes 5&6:

1. EASL guideline recommendation of SOF+DCV as a pan-genotypic regimen
2. Strong in-vitro performance data for DCV in GT 5 & 6[1,2,3]

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[1] Wang et al. Comparison of Daclatasvir Resistance Barriers on NS5A from Hepatitis C Virus Genotypes 1 to 6: Implications for Cross-Genotype Activity. *Antimicrobial Agents and Chemotherapy.* September 2014 Volume 58 Number 9

[2] Chayama K, Takahashi S, Toyota J, Karino Y, Ikeda K, Ishikawa H, Watanabe H, McPhee F, Hughes E, Kumada H. 2012. Dual therapy with the nonstructural protein 5A inhibitor, daclatasvir, and the nonstructural protein 3 protease inhibitor, asunaprevir, in hepatitis C virus genotype 1b-infected null responders. Hepatology 55:742–748.

3. Duke University expert opinion that SOF/DCV should be used for all patients. Dr. Andrew Muir (Chief of Gastroenterology) and Dr. Susanna Naggie (Associate Professor of Medicine Infectious Disease Department) are some of the world's leading experts on HCV treatment with DAAs and recommend using it across all patient populations. In their opinion, there are no safety or efficacy concerns with prescribing SOF/DCV to genotype 5 or 6 patients with the current evidence base.

Ministries of Health have been very comfortable with this approach and finding ways to make these products available to patients. Myanmar and Vietnam have included the SOF+DCV combination as an option for all patients in their national guidelines as have Ethiopia, Nigeria and Rwanda. Indonesia's guidelines are currently under revision.

Patient enrollment criteria and retreatment of failures

While specific enrollment criteria for the Quick-Start program are determined by each Ministry of Health and thus may slightly vary by country, patients with advanced disease or HIV/HCV co-infection will likely be prioritized for treatment. Patients who complete treatment but fail to achieve SVR are to be referred to a specialist to determine a course of action for retreatment. Unfortunately in the short-term there won't be many alternative DAA options for patients who require retreatment. Patients who fail on SOF+DCV will likely only have the option of taking SOF+LDV (if they are GT1, 4, 5 or 6) and vice versa until Gilead's sofosbuvir + velpatasvir combination reaches access markets or until DNDI finishes its development work. We look forward to the SRA approved generic arrival of sofosbuvir + velpatasvir but understand that this is likely more than a year away. There is a potential to engage innovators such and AbbVie and Merck to discuss options for making their product available to treatment failures but these products have limited genotype use and these conversations are in their infancy. If there are other drugs under development or other promising combinations that you think we should monitor or investigate further, we welcome your suggestions.

Thanks again for writing. I would like the opportunity to meet with you on my next trip to the region which will likely be in January or February. Meanwhile, I suggest that we organize a call with CHAI staff leading this program to further respond to any questions or concerns you may have and to understand how we can best work together towards the common goal of universal access to HCV treatment.

Please suggest some dates and times for a possible call.

Sincerely,

Ira C. Magaziner
Chief Executive Officer
Clinton Health Access Initiative

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[3] Sulkowski MS, Gardiner DF, Rodriguez-Torres M, Reddy KR, Hassanein T, Jacobson I, Lawitz E, Lok AS, Hinestrosa F, Thuluvath PJ, Schwartz H, Nelson DR, Everson GT, Eley T, Wind-Rotolo M, Huang S-P, Gao M, Hernandez D, McPhee F, Sherman D, Hindes R, Symonds W, Pasquinelli C, Grasela DM. 2014. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. N. Engl. J. Med. 370:211–221.