

A PUBLIC HEALTH APPROACH TO THE HEPATITIS C EPIDEMIC



Extending access to the HCV treatment
revolution to neglected patients

DNDi
Drugs for Neglected Diseases *initiative*



The World Health Organization (WHO)'s Global Strategy on Viral Hepatitis aims for 90% of people with hepatitis C virus (HCV) to be diagnosed, and 80% of those eligible to be treated by 2030.

There are many different challenges to realising this ambitious public health goal. One, and not the least, will be securing a wide access to DAA treatments, so that their potential impact to reverse the epidemic can be seized.

Cure rates of 90% and above in new, safe, short-course, oral treatments have opened the possibility of rolling back the disease.

In recent years, the treatment of hepatitis C has evolved considerably. With cure rates of 90% and above, safe, short-course oral treatments known

as direct-acting antivirals (DAAs) have opened up the possibility of rolling back the disease: because hepatitis C is curable, if people are diagnosed and treated sufficiently early enough, they could avoid infecting others.

One, and not the least, will be securing a wide access to DAA treatments, so that their potential impact to reverse the epidemic can be seized.

But today a vicious circle exists, and the epidemic continues to grow: with treatments largely unaffordable, the national HCV programmes to increase awareness about the disease and to scale up diagnosis and treatment are stalled. Exorbitant drug prices in many countries keep treatment out of reach

for the most vulnerable, leaving them at risk of liver failure and cancer.

To enable a public health approach to the disease, treatment will need to fulfil three principal conditions:

- it needs to be pan-genotypic, in that it works for all six strains of HCV;
- it needs to be simple, so that it minimises any burden on health systems and patients alike, and can enable massive treatment scale-up;
- and it needs to be affordable enough for affected individuals to seek care without difficulty, and for countries to launch and scale up ambitious treatment programmes.

HCV IN FACTS

- HCV is a blood-borne virus which if left untreated can lead to chronic and debilitating liver disease, including cirrhosis, fibrosis and cancer, as well as other health problems
- It's a silent epidemic, as the huge majority of those infected are not aware of their status and are asymptomatic
- HIV/HCV co-infection is an urgent public health issue that could jeopardise the progress made in addressing the HIV epidemic
- Injecting drug users are particularly at risk of both HCV and HIV infection, are often difficult to reach and therefore diagnose, and can find treatment compliance a challenge
- There are six different HCV genotypes (GT), or strains, and each region has its own distribution of genotypes, with GT1 common in the US, GT4 in Egypt and GT6 in South-East Asia, for example. The appropriate HCV medicines for treatment can differ according to the genotype.

HCV IN NUMBERS^{1,2}

About 71 million people live with hepatitis C in the world (2015)

Only 13% of them have so far had access to treatment (2016)

75% live in low- and middle-income countries (2016)

Over 1.75 million people are newly infected every year (2015)

Only 1.76 million people, were put on treatment (2016)

400,000 people die every year from hepatitis C (2015)

Photo: Suriyan Tanasri/DNDi



1 WHO Factsheet on Hepatitis C, October 2017. <http://www.who.int/news-room/fact-sheets/detail/hepatitis-c>

2 WHO Progress report on access to hepatitis C treatment: focus on overcoming barriers in low- and middle-income countries, March 2018. <http://www.who.int/hepatitis/publications/hep-c-access-report-2018/en/>

The search for a pan-genotypic, simple, and affordable regimen

The DNDi strategy

DNDi's HCV programme has three main pillars.

- 1 R&D:** DNDi partners with access-oriented pharmaceutical companies to develop promising drug candidates in the R&D pipeline and ultimately deliver a pan-genotypic, simple and affordable treatment;
- 2 ACCESS:** DNDi seeks to support policy change and political will to increase affordable access to affordable pan-genotypic DAAs, notably by overcoming intellectual property and regulatory barriers;
- 3 MODELS OF CARE:** DNDi works with health providers to develop simpler and innovative models of care, needed to support scale up of treatment to the millions still waiting.

The first step of DNDi's HCV programme was to conduct a pipeline analysis to assess promising compounds in late-stage clinical development that could be suitable tools for a public health approach to HCV, in that they are pan-genotypic, simple, and affordable.

The analysis identified ravidasvir (RDV), an NS5A inhibitor drug candidate developed by California biopharmaceutical company Presidio Pharmaceuticals (Presidio). Data published in December 2015 from Phase III clinical trials in Egypt by the generic manufacturer Pharco Pharmaceuticals (Pharco) showed a 100% cure rate for the ravidasvir/sofosbuvir (RDV/SOF) combination in 170 GT4 patients, and a 94% cure rate in 130 GT4 cirrhotic patients.³

In March 2016, DNDi concluded a licence agreement with Presidio for low- and middle-income countries (LMICs), and an agreement with Pharco to secure

clinical supplies of RDV and generic SOF, with a view to accelerating the development of RDV as part of a pan-genotypic, simple-to-use and affordable regimen.⁴ An R&D programme known under the acronym STORM-C (Strategic Transformation of the Market of Hepatitis C Treatments) was launched to assess the efficacy, safety, tolerance, and pharmacokinetics of RDV/SOF. The first clinical trial, STORM-C-1, began in Malaysia in 2016 co-sponsored by the Malaysian Ministry of Health, and in Thailand in 2017 in partnership with the government.

DNDi's pipeline analysis identified ravidasvir, an NS5A inhibitor drug candidate.

The two countries were selected as ideal partners given their high prevalence of HCV, established HCV control programmes, and capacity to scale up screening. Just as, if not more important, was their exclusion (at the time) from voluntary licence agreements for recently approved DAAs and the very high prices charged by originator companies. In addition, both countries demonstrate strong political commitment to support public health programmes that make treatments available and affordable for their populations, and a commitment to scaling up.

In the first stage of the STORM-C-1 trial, 301 patients were recruited, with various levels of liver fibrosis, various genotypes, both with and without HIV co-infection. Patients without cirrhosis of the liver were treated with the RDV/SOF combination for 12 weeks, and those with compensated cirrhosis for 24 weeks. Most people enrolled had genotype 1 (42% of participants) or genotype 3 (53%).

³ Effectiveness of ravidasvir plus sofosbuvir in interferon-naïve and treated patients with chronic hepatitis C genotype-4. Esmat G, et al J Hepatol, September 2017. <https://www.ncbi.nlm.nih.gov/pubmed/28935432>

⁴ DNDi and Pharco Pharmaceuticals to test affordable hepatitis C regimen with support of Malaysian and Thai governments, April 2016. <https://www.dndi.org/2016/media-centre/press-releases/dndi-pharco-hepc-malaysia-thailand/>



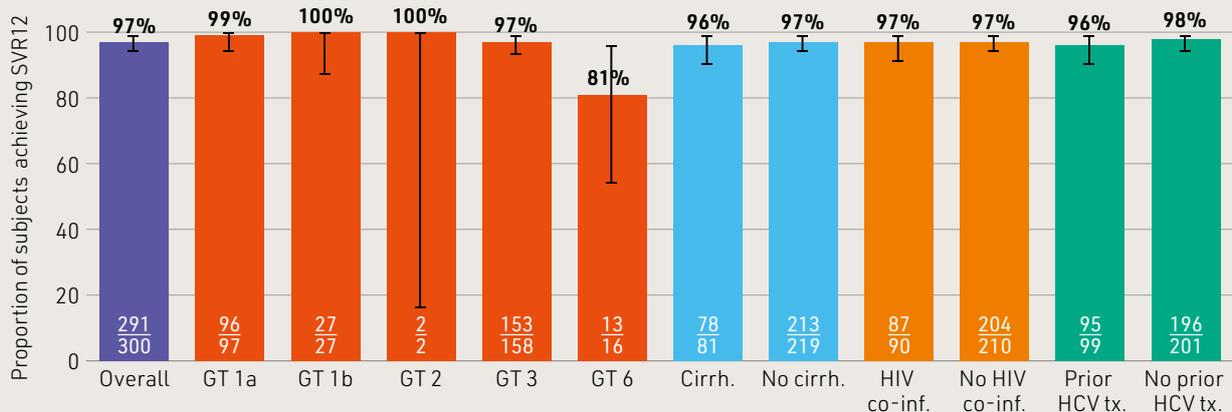
**A COMBINATION
COMPARABLE
TO THE VERY BEST
EXISTING TREATMENTS,
BUT AT A FRACTION
OF THE COST**

Initial results from the STORM-C-1 clinical trial were presented in April 2018 at the AFRAVIH conference⁵ and the EASL International Liver Congress.⁶ In accordance with international standards defining cure for HCV treatments, 12 weeks after treatment completion, 97% of those enrolled were cured (95% CI: 94.4-98.6). No unexpected safety signals were detected. The results indicate that the RDV/SOF combination is comparable to the very best hepatitis C therapies available today.

As such, the results show the potential impact for RDV to fulfil the three conditions required to enable a public health approach: a regimen that is pan-genotypic, simple and affordable.

STORM-C-1 TRIAL: SUSTAINED VIRAL RESPONSE FOLLOWING 12 WEEKS OF TREATMENT (SVR12)

Outcomes in intent-to-treat analysis with full analysis set



⁵ Tolérance et efficacité du ravidasvir- sofosbuvir chez les patients coinfectés VIH-HCV avec génotypes 1, 2, 3 ou 6 dans l'essai STORM-C-1, Andrieux-Meyer et al.

⁶ Safety and efficacy of ravidasvir plus sofosbuvir 12 weeks in non-cirrhotic and 24 weeks in cirrhotic patients with hepatitis C virus genotypes 1, 2, 3 and 6: the STORM-C-1 phase II/III trial. Andrieux-Meyer et al. https://www.dndi.org/wp-content/uploads/2018/03/Andrieux-Meyer_STORM-C-1_phase_II_III_trial_EASL_ILC_2018.pdf

PAN-GENOTYPIC

Pan-genotypic regimens, so-called because they are proven to be effective across all six HCV genotypes, are an essential component of a public health strategy to address HCV. They eliminate the need and considerable expense of pre-treatment genotype testing, as well as simplifying the procurement and delivery of treatment, and facilitating “test-and-treat” programmes and scale-up.

The promising results for the hardest-to-treat cases are all the more important for enabling a public health approach.

There are now at least 11 different DAA regimens that have been approved by at least one stringent regulatory authority since 2013⁷. Only three of these are currently approved as pan-genotypic regimens, and each of the three comes with limitations in terms of access in LMICs. The first, sofosbuvir/velpatasvir (SOF/VEL, manufactured by Gilead) is registered for use in only a handful of countries in the developing world, with registration at present underway in only around 20 countries in total.⁸ Sofosbuvir/velpatasvir/voxilaprevir (Gilead) is not a first-line treatment, as it is registered for use only for people with HCV who have previously failed a DAA regimen.⁹ The manufacturer of the third, glecaprevir/pibrentasvir (AbbVie) is yet to announce an access programme for LMICs.

At the time of going to print, as a result of a lack of data supporting the efficacy and safety of sofosbuvir/daclatasvir (SOF/DCV) in genotypes 5 and 6, the latest EASL¹⁰ and AASLD guidelines do not classify the combination as pan-genotypic. Unitaid’s assessment of the HCV drug pipeline considers SOF/DCV as “potentially pan-genotypic,”¹¹ and an update to WHO guidelines is pending. Confirmation of SOF/DCV’s pan-genotypic profile¹² would be welcome, given that it is

the most commonly used treatment in LMICs and could play a fundamental role in enabling a public health approach to the epidemic.

Potential impact of RDV/SOF

The STORM-C-1 trials on RDV/SOF give *in vitro* data on all genotypes, and *in vivo* data predominantly on genotypes 1, 3, 4 and 6.

Significantly, the cure rates for genotype 3 (GT3), a geographically widely spread genotype considered to be the hardest to treat, were as good as the very best of existing DAAs. 97% of patients enrolled with GT3 were cured; 96% of those with both GT3 and advanced liver disease (cirrhosis) were cured.



Photo: Suriyan Tanasri/DNDi

The promising results for the hardest-to-treat cases are all the more important in enabling a public health approach. As many DAAs are from the same drug class, treatment failure from any one drug could induce resistance to all drugs within the same class. In that sense, treatment with RDV poses a lesser risk of inducing resistance to all NS5A drugs as the cure rates are high. Multiple therapeutic options are needed in the HCV treatment toolbox, not least because the lifespan of the effectiveness of certain DAAs could be cut if resistant strains of the disease begin to spread.

7 WHO Progress report on access to hepatitis C treatment: focus on overcoming barriers in low- and middle-income countries, March 2018. <http://www.who.int/hepatitis/publications/hep-c-access-report-2018/en/>

8 Epclusa registration in the developing world. Gilead. December 2017. http://www.gilead.com/-/media/files/pdfs/other/2017%20aoem%20registration%20pdfs/epclusa_december%202017%20final.pdf

9 https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209195Orig1s000lbl.pdf

10 European Association for the Study of the Liver Recommendations on Treatment of Hepatitis C, 2018 <http://www.easl.eu/research/our-contributions/clinical-practice-guidelines/detail/easl-recommendations-on-treatment-of-hepatitis-c-2018>

11 Unitaid Technology and Market Landscape Hepatitis C Medicines, August 2017. https://unitaid.eu/assets/HCV-Medicines-Landscape_Aug-2017.pdf

12 Real-world effectiveness and safety of daclatasvir/sofosbuvir with or without Ribavirin among genotype 5 and 6 Hepatitis C Virus patients, AASLD LiverLearning, Sann K, October 2017. <http://liverlearning.aasld.org/aasld/2017/thelivermeeting/201650/kimchamroeun.sann.real-world.effectiveness.and.safety.of.daclatasvir.html>

SIMPLE

In addition to having a pan-genotypic regimen, a public health strategy relies on having a regimen that is effective for *all* people infected with HCV, including the hardest-to-treat patients. This includes people with GT3 and/or with advanced liver disease and cirrhosis, active injecting drug users and people on opioid substitution therapy, and people who have previously failed HCV treatment. A simple regimen would also be one that is safe and easy-to-use for patients with other conditions, notably people co-infected with both HIV and HCV.



Photo: Suriyan Tanasri/DNDi

A simple regimen is also needed to enable treatment providers to apply the lessons learnt from the successful scaling up of HIV treatment to millions of people in resource-poor settings. This includes strategies such as shifting of tasks and follow up of non-complicated cases from doctors to nurses, the simplification of the diagnostic algorithms, and other tools to reduce patient loss to follow-up in what is known as the “treatment cascade”, by enabling for example decentralization of diagnostics and treatment to all levels of the health system.

—

The need for simple regimens is already apparent from the difficulties faced by treatment providers today.

—

The need for simple regimens is already apparent from the difficulties faced by treatment providers today. In 2016, Médecins Sans Frontières / Doctors Without Borders (MSF) opened an HCV treatment programme in a 250-bed hospital in Phnom Penh, Cambodia. Within months, the clinic was overwhelmed by patient demand. MSF identified the need for complex laboratory tests and the sheer number of follow-up visits required as major obstacles to efforts to reach a greater number of patients.¹³

Potential impact of RDV/SOF

According to the data generated by the STORM-C-1 trial, the good tolerability and the absence of safety signals, even for patients with multiple co-morbidities, suggests that the safety profile of RDV/SOF supports simplification and task-shifting in the model of care for HCV.

Very high cure rates (97%) were observed among HIV/HCV co-infected patients. The favourable pharmacological profile of RDV was further confirmed by the absence of clinically significant drug interactions between ravidasvir and the most common antiretroviral drugs used to treat HIV. There were no meaningful modifications in the drug levels for tenofovir, efavirenz, nevirapine, and emtricitabine, nor in the RDV levels.¹⁴ There was no need to adapt the doses of antiretroviral therapy for people living with HIV during their HCV treatment, and HIV viral loads were kept under very good control.

Other clinical significant results include the high efficacy in patients with advanced liver disease and cirrhotics (96% cured); in people who had been exposed to previous HCV treatments (96%); and importantly, patients combining *several* of these risk factors were also cured.

¹³ From a complex to a simplified approach in a HCV project – Experience from Médecins Sans Frontières pilot HCV program in Phnom Penh, Cambodia, April 2018.

¹⁴ Cressey TR et al (2018). Ravidasvir Pharmacokinetics and ARV Drugs Interactions in HCV+/- HIV Infected Adults. Poster, CROI, March 2018. Available at: https://www.dndi.org/wp-content/uploads/2018/01/Cressey_Ravidasvir_Pharmacokinetics_ARV_Interactions_HCVHIV_Adults_CROI_2018.pdf

AFFORDABLE

Affordability is still a challenge in most countries. When it was launched at USD 1,000 per single pill in the US, SOF became the poster child for exorbitant pricing upheld by patent monopolies that prevent access to more affordable generic medicines. (The price represented USD 84,000 for the full treatment course, to which the cost of other drugs still needed to be added). With similar pricing for other DAAs and in other countries, the new generation of HCV treatments were, in the first years after their arrival on the market, rationed to the very sickest.

For some countries, prices have now fallen considerably since then. The lowest generic prices reported to WHO in 2017 include USD 375 for a three-month course of SOF/VEL. An MSF tender in 2017 resulted in USD 120 for a three-month course of SOF/DCV, which provides a useful benchmark for countries seeking to attain lower prices, in places where generic competition is possible.¹⁵

DNDi has been able to secure an entirely new chemical entity from an originator and ensure affordable pricing from the outset.

But the affordability crisis is far from over. Prices have not fallen enough for countries to implement strategies that seek to identify asymptomatic people living with HCV, nor “test-and-treat” strategies that could lead towards elimination. Indeed, the majority of people living with HCV worldwide are still not diagnosed and have no access to HCV treatment.

Costs remain too high particularly in countries where patents on DAAs have been filed or granted and that have been excluded from licence agreements. Middle-income countries are notably often excluded, and are thus said to be “stuck in the middle” – neither poor enough to be eligible for generic pricing, nor

rich enough to be able to afford the prices charged by originators. This includes, for example, Brazil, China, Colombia, Kazakhstan, Mexico and Turkey, which together are home to about 14 million people living with HCV infection. WHO estimates 38% of people living with HCV globally are excluded from affordable access.¹⁶

Potential impact of RDV/SOF

Thanks to commitments from Pharco and our other industrial partners, DNDi has been able to promote an alternative approach, securing an entirely new chemical entity from an originator, but at the same time, through our collaboration and sub-licence agreements, ensuring affordable pricing from the outset. This is in stark contrast to the traditional drug development model, particularly for HCV, which has centred first and foremost on maximising revenue generation, at the expense of access.

In Malaysia, Pharco has committed to making the RDV/SOF combination available, once approved, at a price of USD 300 or less per treatment course for the national treatment programme¹⁷. Such a price represents more than a 100-fold drop compared to the cost of the existing originator DAA regimen in Malaysia, at over USD 75,000 for SOF/DCV¹⁸, or USD 33,000 for SOF alone.¹⁹

In Latin America, DNDi has partnered with Argentinian companies Insud Pharma and Laboratorio Elea Phoenix to work towards registering RDV and manufacturing and distributing RDV and generic SOF across the region.²⁰ The agreement envisions that the combination will be available at an affordable price of less than USD 500. Once RDV is registered and launched in multiple countries, it is expected that increased sales volumes will bring prices down further, towards a target price of USD 300. At the time of going to print the best price in the region for a pan-genotypic regimen stands at USD 4,500 through the Pan-American Health Organization.²¹

15 MSF secures lower price for generic hepatitis C treatment, October 2017. <https://www.msf.org/msf-secures-lower-price-generic-hepatitis-c-treatment>

16 WHO Progress report on access to hepatitis C treatment: focus on overcoming barriers in low- and middle-income countries, March 2018. <http://www.who.int/hepatitis/publications/hep-c-access-report-2018/en/>

17 DNDi and Pharco Pharmaceuticals to test affordable hepatitis C regimen with support of Malaysian and Thai governments, April 2016. Available at: <https://www.dndi.org/2016/media-centre/press-releases/dndi-pharco-hepc-malaysia-thailand/>

18 Hope for hepatitis C patients, The Star Online, March 2018. <https://www.thestar.com.my/news/nation/2018/03/02/hope-for-hepatitis-c-patients-18-state-hospitals-offering-treatment-through-affordable-medicine/>

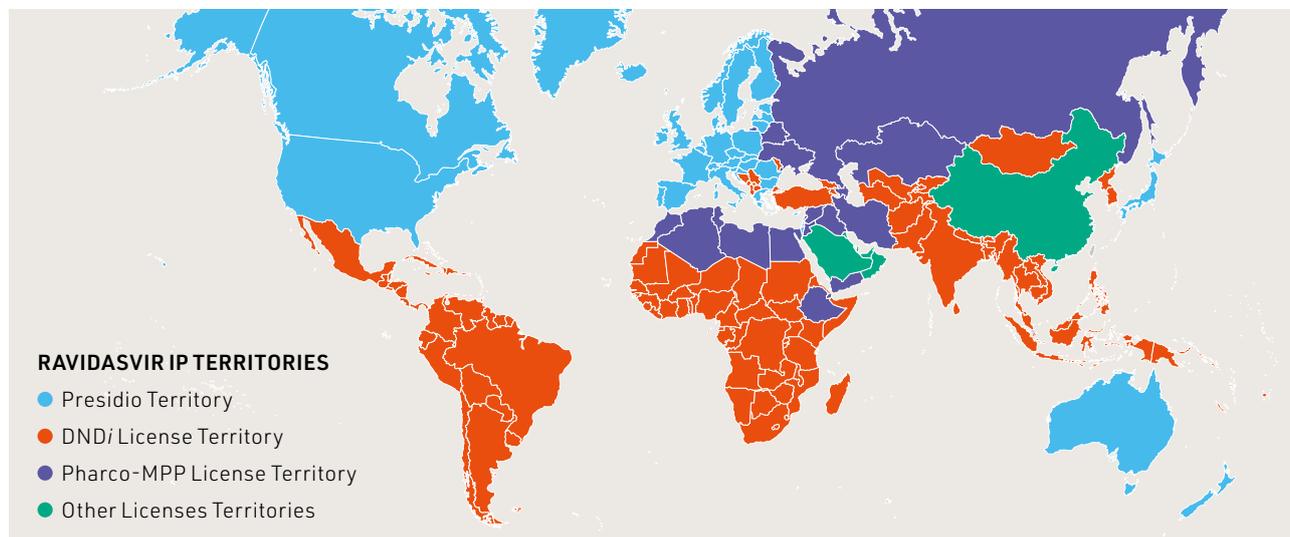
19 *Op. cit.* 16.

20 Pharmaceutical companies and non-profits team up to provide affordable hepatitis C treatment in Latin America, March 2018. <https://www.dndi.org/2018/media-centre/press-releases/pharmaceutical-companies-non-profits-team-up-affordable-hepc-treatment-latin-america/>

21 The Grounds for Opposing Patent Applications on Velpatasvir, MSF Access Campaign, July 2018. <https://msfaccess.org/grounds-opposing-patent-applications-velpatasvir>

WHERE AND WHEN WILL THE NEW COMBINATION BE AVAILABLE?

DNDi and its industrial partners will pursue registration of RDV in Malaysia, Argentina and in other middle-income countries willing to implement a public health approach for HCV, with a target date of mid-2019 for first submissions.



RDV: licences and territories

Patents on RDV are owned by Presidio, from whom DNDi secured non-exclusive licence rights for LMICs. DNDi also has an option to negotiate the licence rights for high-income countries.

Separately, Pharco sub-licensed RDV rights to the Medicines Patent Pool (MPP), opening up the possibility of generic competition in several countries that were not included in the DNDi licence, including high-prevalence LMICs such as Russia, Ukraine, Egypt and Iran.²² According to the MPP, “combined, the MPP and DNDi agreements could potentially benefit countries where 85.3% of people live with hepatitis C in the 139 economies classified by the World Bank as low- and middle-income.”

The rights to RDV for China, Hong Kong and Taiwan are held by the Chinese biopharmaceutical

company Ascleptis, which concluded an exclusive licence agreement with Presidio in 2014.²³

Overcoming access barriers

Securing access to SOF, the current backbone of DAA treatments, needs to be considered, particularly for countries excluded from pharmaceutical company voluntary licence schemes in addition to other patented DAAs, such as DCV, for which access is extremely limited in upper-middle and high-income countries due to the exclusion from Bristol Myers Squibb’s preferential pricing structure.

In countries where because of patenting and high pricing, affordability is the most limiting factor to access and scale-up of DAAs, governments will need to take active steps. This includes making use of TRIPS flexibilities allowed under international trade rules, such as opposing patent applications, or issuing

government user compulsory licences, to overcome the barriers posed by granted patents.

DNDi’s HCV programme aims to deliver affordable combinations of DAAs that will be optimal for public health use. This project will be synergistic with other efforts aimed at increasing access to treatment for patients and improving HCV education, surveillance, screening, testing, and linkage to care and prevention. DNDi’s efforts at supporting affordable access seek to complement the work of others. Coordination with governments, industry, and other key stakeholders, notably the powerful global HCV treatment access movement that has emerged over the past several years, is necessary to procure pan-genotypic DAAs at prices that will allow governments to afford and sustain dramatic scale-up of treatment for people with HCV.

²² MMP (2017). The Medicines Patent Pool and Pharco Pharmaceuticals Sign Licence for Promising Hepatitis C Drug Candidate Ravidasvir. Press release. 21 April 2017. Available at: <https://medicinespatentpool.org/mpp-media-post/the-medicines-patent-pool-and-pharco-pharmaceuticals-sign-licence-for-promising-hepatitis-c-drug-candidate-ravidasvir/>

²³ Chinese biotech firm Ascleptis first to apply for Hong Kong IPO under new rules. South China Morning Post. International edition. 8 May 2018. Available at: <https://www.scmp.com/business/companies/article/2145082/chinese-biotech-firm-ascleptis-first-apply-hong-kong-ipo-under-new>

Malaysia

Leading by example in access and innovation

Over 500,000 Malaysians, about one out of every fifty people in the country, are infected with hepatitis C.²⁴ Like many other middle-income countries, Malaysia had been excluded by Gilead from its “Access Program” of voluntary licences, so it could not access affordable generic versions of Gilead’s HCV treatments. This meant that Malaysians with HCV had to pay around USD 75,000 for treatment.

In 2016, DNDi and the Malaysia Ministry of Health began collaborating with a view to usher in public health approach to HCV, within framework of the country’s National Strategic Plan on viral hepatitis.

Malaysia took a leading role in the STORM-C-1 clinical trials that followed, investing considerable strategic efforts and co-sponsoring the studies to assess the safety, effectiveness of RDV/SOF. To enable patient scale-up of treatment with DAAs, DNDi, Pharco and Pharmaniaga, a Malaysian generic manufacturer, concluded a collaboration agreement for the registration of RDV and manufacture and distribution of RDV and generic SOF on an affordable basis in Malaysia, and potentially other countries in South-East Asia.²⁵ The agreement also covers the transfer of the RDV manufacturing technology from Pharco to Pharmaniaga to enable local production.

In September 2017, Malaysia issued a “government use” licence to source generic SOF, a move which has allowed it to accelerate access to affordable hepatitis C treatment in its public hospitals. Through the government use licence, Malaysia has implemented a unique patient-centric access strategy. Free HCV care is now provided in around 20 government hospitals using SOF/DCV, which the government purchases at USD 300 from Pharmaniaga.²⁶

The pressure thus exerted by the government led to the subsequent inclusion of the country in Gilead’s voluntary licence scheme, which will foster a more competitive environment as additional generic players seek to enter the market. The registration of generic pan-genotypic regimens under the Gilead voluntary licence scheme should soon be underway in Malaysia.

—
**Malaysia has implemented
 a unique patient-centric
 access strategy.**
 —

This access strategy, when combined with Malaysia’s collaboration with DNDi in R&D efforts to develop an additional pan-genotypic option, will enable the country to access multiple pan-genotypic treatments at an affordable price and thereby facilitate a public health strategy for the disease.

The next steps of this strategy were announced in July 2018, with a collaboration between the Foundation for Innovative New Diagnostics (FIND) and the Ministry of Health, and supported by DNDi. FIND will demonstrate the feasibility of using rapid diagnostic tests in decentralized local health facilities, and all people diagnosed with HCV will be given treatment via the national HCV programme or the ongoing DNDi clinical trial. The evidence generated will be used to update national guidelines that will cover HCV screening, diagnosis, treatment and monitoring, for an effective HCV public health approach in Malaysia.²⁷

²⁴ Implementation of the Rights of Government for Sofosbuvir Tablet to Increase Access for Hepatitis C Treatment in Malaysia, Press Statement Minister of Health, September 2017. <https://kpkesihatan.com/2017/09/20/press-statement-minister-of-health-20th-september-2017-implementation-of-the-rights-of-government-for-sofosbuvir-tablet-to-increase-access-for-hepatitis-c-treatment-in-malaysia/>

²⁵ Pharmaniaga, Pharco and DNDi sign agreement to provide affordable hepatitis C treatment in Malaysia, November 2017. <https://www.dndi.org/2017/media-centre/press-releases/pharmaniaga-pharco-dndi-agreement-affordable-hep-c-treatment-malaysia/>

²⁶ <https://www.thestar.com.my/news/nation/2018/03/02/hope-for-hepatitis-c-patients-18-state-hospitals-offering-treatment-through-affordable-medicine/>

²⁷ FIND & DNDi (2018). FIND and DNDi team up to support Malaysian MOH efforts to simplify and decentralize hepatitis C screening and treatment. Press release. 23 July 2018. Available at: <https://www.dndi.org/2018/media-centre/press-releases/find-dndimalaysianmoh-efforts-hepatitisC-screening-treatment>

Conclusions and next steps

The initial results from the STORM-C-1 trial show that the RDV/SOF combination has the potential to be a pan-genotypic and simple treatment, and a promising, additional therapeutic option, of particular interest to countries unable to access affordable DAAs. DNDi and its industrial partners are committed to making RDV/SOF available to patients on an affordable basis in our licence territories, where there are no barriers to entry of generic SOF.

Much of DNDi's work in the coming months will focus on demonstrating this potential. This includes further establishing the pan-genotypic profile of RDV by including genotypes currently under-represented in the first trials; confirming its safety and effectiveness in vulnerable populations, such as active injecting drug users and HIV/HCV co-infected patients; working with MSF to gather data from special populations and larger cohorts; and working with FIND and the Malaysian Ministry of Health, to develop a "test-and-cure" model with simpler diagnostic and treatment monitoring algorithms.

Seizing the public health potential of DAAs will require the development of new approaches and new models to deliver and develop pan-genotypic, simple, and affordable treatment tools. It is important to look beyond our trials, however, and view RDV as one tool within a broader access framework whose ultimate goal is to enable a public health approach to treating HCV, so that people currently excluded from the DAA therapeutic revolution can benefit.

Only a collaborative effort bridging science and policy and uniting multiple public health stakeholders will succeed in ensuring no patients are left behind.

The challenges to reaching HCV elimination are many, and will need to be addressed. Treatment providers will need to develop a public health model of care for HCV, for example by reducing the costs and complexity of diagnosis

and monitoring, and leveraging the most innovative ways to facilitate HCV care, while ensuring the needs of more vulnerable populations such as injecting drug users and people co-infected with HCV and HIV, are addressed.

Strong leadership from Ministries of Health and governments will be needed to achieve affordable access to pan-genotypic DAAs, through price/volumes negotiation, price control, pooled procurement, or access to generics thanks to voluntary licences or use of TRIPS flexibilities to remove patent barriers. Governments will also need to show the political will necessary to launch ambitious screening and test-and-treat programmes, and donors will need to provide multilateral funding support, similar to the Global Fund model or through innovative financing mechanisms, to support countries' efforts for hepatitis C treatment scale-up.

Only a collaborative effort bridging science and policy and uniting multiple public health stakeholders will succeed in ensuring no patients are left behind.

DNDi would like to acknowledge the immense contribution to the HIV and HCV fight in Malaysia of our dear friend Roslan (at far left) who passed away from HCV complications. She will be dearly missed. May she rest in peace. Photo: Mazlim Husin.



DNDi's HCV programme is funded by Médecins Sans Frontières; the Ministry of Health, Malaysia; the Ministry of Public Health, Thailand; the Department for International Development of the UK government; the Starr International Foundation; Fondation ARPE; and the Foundation for Innovative New Diagnostics (financed by Unitaid).



Drugs for Neglected Diseases *initiative*

15 Chemin Louis-Dunant
1202 Geneva, Switzerland
Tel: +41 22 906 9230
Fax: +41 22 906 9231
Email: dndi@dndi.org

www.dndi.org

-  facebook.com/dndi.org
-  linkedin.com/company/dndi
-  twitter.com/dndi
-  youtube.com/dndiconnect
-  instagram.com/drugsforneglecteddiseases
-  [Subscribe to DNDi's newsletter: www.dndi.org/newsletter](http://www.dndi.org/newsletter)

DNDi AFRICA

Tetezi Towers, 3rd Floor, George Padmore Road, Kilimani, P. O. Box 21936-00505 Nairobi, Kenya | Tel: +254 20 3995 000

DNDi DRC

Avenue Milambo, no.4, Quartier Socimat, Commune de la Gombe, Kinshasa, Democratic Republic of the Congo
Tel: +243 81 011 81 31

DNDi INDIA

PHD House, 3rd Floor, 4/2 Siri Institutional Area, New Delhi 110016, India
Tel: +91 11 4550 1795

DNDi JAPAN

3F Parkwest Bldg, 6-12-1 Nishi-Shinjuku, Shinjuku-ku, Tokyo 160-0023, Japan
Tel: +81 (0)3 4550 1199

DNDi LATIN AMERICA

Rua São Jose, 70 – Sala 601 20010-020 Centro, Rio de Janeiro, Brazil
Tel: +55 21 2529 0400

DNDi SOUTH-EAST ASIA

L10-7, Menara Sentral Vista, 150, Jln Sultan Abdul Samad, Brickfields 50470, Kuala Lumpur, Malaysia | Tel: +60 3 2716 4159

DNDi NORTH AMERICA

40 Rector Street, 16th Floor, New York, NY 10006, USA | Tel: +1 646 215 7076

DNDi SOUTH AFRICA

South African Medical Research Council
Francie van Zijl Drive, Parow Valley
Cape Town, 7501, South Africa

A not-for-profit research and development organization, DNDi works to deliver new treatments for neglected diseases, notably leishmaniasis, human African trypanosomiasis, Chagas disease, specific filarial infections, and mycetoma, and for neglected patients, particularly those living with paediatric HIV and hepatitis C. Since its inception in 2003, DNDi has delivered seven treatments: two fixed-dose antimalarials (ASAQ and ASMQ), nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness, sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa, a set of combination therapies for visceral leishmaniasis in Asia, paediatric dosage forms of benznidazole for Chagas disease, and a 'super-booster' therapy for children co-infected with HIV and TB.

DNDi's ambition is to enable access to HCV treatment, through the development and registration of affordable, safe and efficacious pan-genotypic DAAs, and by supporting policy change and political will to remove barriers to DAA access globally.

Cover image: Dr. Hj. Rosaida binti Hj Md Said, Senior Consultant Gastroenterologist and Head of Medical Department, Hospital Ampang, Malaysia. Photo: Bobby Tan/DNDi. Drugs for Neglected Diseases *initiative*, 2018. All rights are reserved by DNDi. The document may be freely reviewed and abstracted, with acknowledgement of source. This document is not for sale and may not be used for commercial purposes. Requests for permission to reproduce or translate this document, in part or in full, should be addressed to the Communications and Advocacy Department of DNDi.