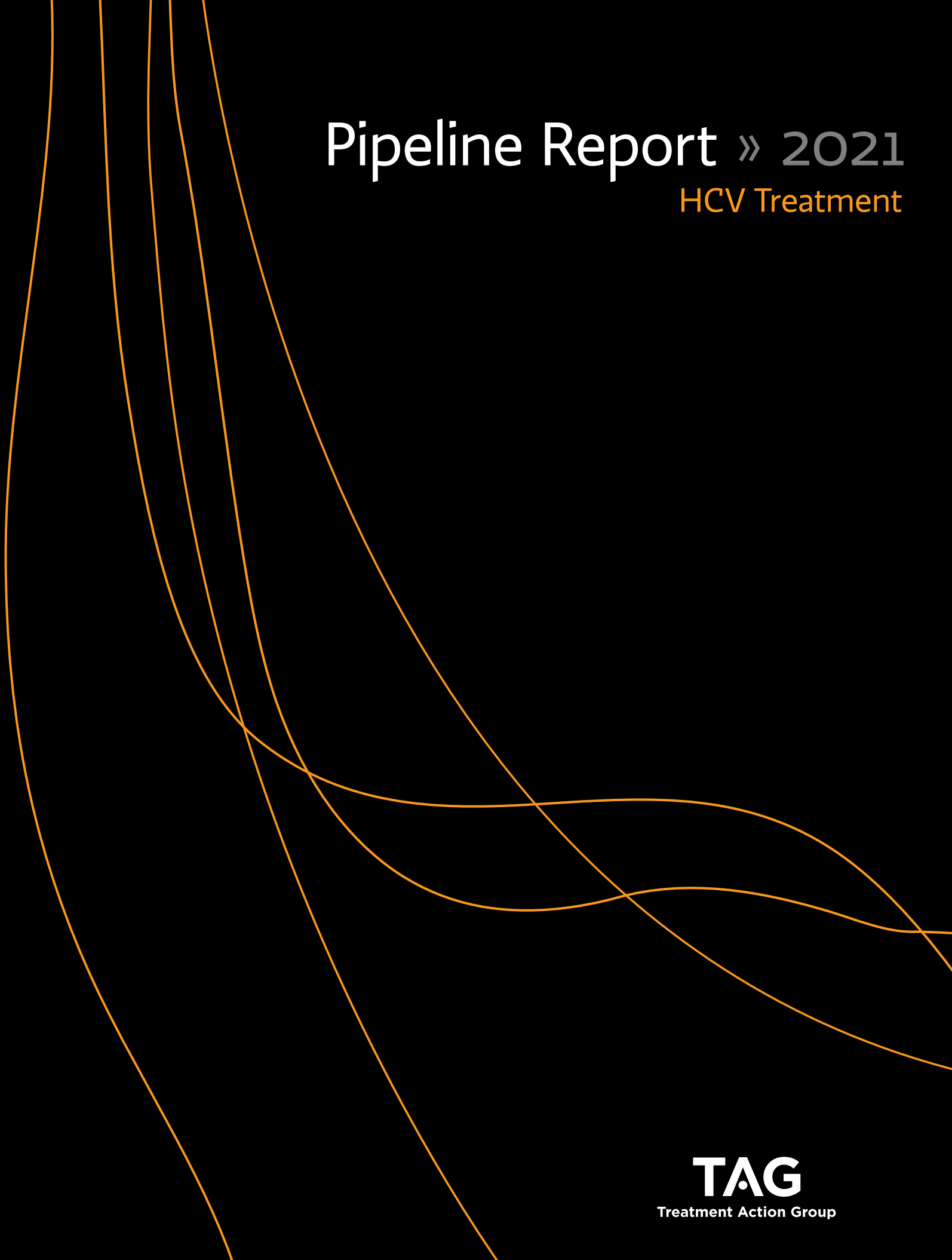
Pipeline Report » 2021

HCV Treatment



TAG
Treatment Action Group

HCV Treatment Pipeline 2021

By Bryn Gay

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Updates on the State of Hep C Treatment

COVID-19 halted nearly everything this past year. Unfathomable loss, human suffering, and millions of deaths were all preventable with the worldwide adoption of public health policies based on science and universal equitable access to treatments, diagnostics, vaccines, and solidarity. Health systems in high-burden countries continue to be overwhelmed, and staff and resources have been redirected to respond to this pandemic. Despite progress in global (and US) direct-acting antiviral (DAA) uptake, systemic inequities and injustices and enormous implementation challenges—combined with COVID-19's disruptions to health systems—could thwart the gains we've made. Viral hepatitis programs, including in countries on track to meeting global 2030 elimination targets, were largely sidelined. Several public health–oriented initiatives, such as early release of at-risk incarcerated people to avoid exposure, compassionate and isolated sheltering of unstably housed people who were exposed to or recovering from COVID-19, and take-home or extended prescriptions of DAAs and opioid substitution therapy could be made permanent after the pandemic, with the appropriate political will and leadership.

One study in Iran, a placebo-controlled, double-blind trial with 55 participants, suggested that the hepatitis C medications sofosbuvir and daclatasvir might reduce COVID-19 mortality and improve recovery time. However, a larger trial, conducted between July and December 2020, with 1083 participants taking sofosbuvir/daclatasvir or a placebo did not show significant clinical benefits.

Box 1. COVID-19 Vaccines for People with Viral Hepatitis and Chronic Liver Disease

People living with viral hepatitis, chronic liver diseases (including cirrhosis), chronic kidney disease, people waiting for liver transplants, and immunosuppressed liver transplant recipients face an increased risk of acquiring infections, including SARS-CoV-2 infection. COVID-19 vaccine responses may be lower in these groups, yet meta-analysis of efficacy of other vaccines among people with chronic liver conditions show that vaccination benefits outweigh the risks. The European Association for the Study of the Liver (EASL) recommends that COVID-19 vaccination should be completed during earlier stages of chronic liver disease, before liver transplant surgery, or 3–6 months after the transplant. COVID-19 vaccine trials did include the overall safety and tolerability of the vaccines specifically for liver transplant patients, and while this is not yet confirmed, real-world data, including among the large numbers of adults with mild and moderate liver disease, indicate the vaccines

are safe and effective. EASL and the American Association for the Study of Liver Disease (AASLD), following U.S. Food and Drug Administration (FDA) emergency use approvals for COVID-19 vaccines, recommend people age 18 and older with advanced cirrhosis, decompensated liver disease, hepatobiliary cancer, people with chronic kidney disease and risk factors for severe COVID-19, household members, and health care workers caring for these patients should be prioritized for COVID-19 vaccines during cases of limited supply. All patients with chronic liver disease should be vaccinated whenever possible.

People taking hepatitis B virus (HBV) and/or HCV treatment, or people with hepatocellular carcinoma undergoing treatment should continue their treatment while receiving the COVID-19 vaccines. However, anyone with recent infections, fever, or respiratory or other symptoms should not receive the vaccine until they have recovered and are medically stable. Research on COVID-19 vaccine immunological responses in solid organ transplant recipients and people with cirrhosis, chronic liver disease, and other chronic conditions is ongoing, with the need to recruit racially and ethnically diverse participants.

For a closer look at the research and development (R&D) and policy implications from the pandemic on HCV, read more here.

As of 2019, World Health Organization (WHO) global progress and access reports reported a reduction in HCV-related mortality from 400,000 to 290,000 deaths and a cumulative uptake of 9.4 million people receiving DAAs, including 4.4 million people treated in Egypt alone, since 2015. However, only 22 percent of people living with HCV worldwide have been diagnosed. Accelerating access to testing and treatment, particularly pangenotypic generics, rolling out pediatric and adolescent treatment regimens, and preventing parent-to-child transmission are essential for achieving elimination goals. Interim guidance to assess and validate countries' achievement of viral hepatitis elimination goals was developed and is being piloted in 2021.

Much of the HCV-related research on vaccines, safety, and efficacy in pregnancy and children, and implementation, including disbursement of government grants and recruitment in studies, was paused or delayed in 2020. The HCV treatment pipeline has been coming to an end, with a few additional oral treatments showing some results this year. Interim results on ravidasvir/sofosbuvir demonstrate its safety and efficacy as a multi-genotypic combination, which could provide alternative, cost-saving options for high-burden, resource-limited countries. Researchers are also exploring novel combinations for exclusive in-country use in China (SH229 + daclatasvir) and Russia (narlaprevir/ritonavir + sofosbuvir) for HCV genotype 1.

Long-acting technologies for HCV are under investigation in the pre-clinical stage. If proven safe and effective, a long-acting formulation for HCV using glecaprevir/pibrentasvir could provide an additional choice for patients, particularly those needing re-treatment, improve treatment adherence for some people, provide additional privacy and discretion, require just one or two health visits to achieve cure, and facilitate test-and-treat approaches. To learn about this work, check out TAG's Long-Acting Technologies Trials Tracker.

We don't expect a new class of HCV treatments, but we've amassed additional evidence on DAA safety and efficacy in real-world settings and additional understanding for fine-tuning regimens for understudied HCV subtypes, children, and pregnant and breastfeeding individuals.

Guidance for HCV Subtypes

Additional clinical trial and real-world data and guidelines for treating difficult-to-treat HCV subtypes have been published. In 2020, EASL recommends using pangenotypic regimens, including sofosbuvir/velpatasvir and glecaprevir/pibrentasvir, without requiring genotype testing or knowledge of subtype, which can achieve high sustained virologic response (SVR) rates. Where genotype and subtype sequencing are available, and in geographic areas where HCV subtypes are resistant to NS5A inhibitors (e.g., GT 1l, 4r, 3b, 6u, 6v, among others), patients can benefit from knowing the subtype and tailoring the treatment regimen and duration. AASLD guidance should be updated to ensure optimal pangenotypic treatment options are available to people with these subtypes in the US context.

Updates on HCV Treatment in Children

There are an estimated 13.2 million children aged 1–15 living with HCV. Several DAA treatment options have been approved for children and adolescents since 2019. Dosing and duration of pediatric formulations of sofosbuvir and sofosbuvir/daclatasvir with/without ribavirin are under study. The WHO is expected to update its consolidated guidelines, including HCV treatment in children, by the end of 2021/early 2022.

Table 1. Summary of WHO Pediatric Treatment Guidelines and Other Regimens Under Investigation

Sofosbuvir (SOF)	Sofosbuvir and Daclatasvir (SOF + DAC) or (SOF/DAC)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Glecaprevir/ Pibrentasvir (G/P)	Sofosbuvir/ Ledipasvir (SOF/LED)	Ribavirin (RBV)
Under investigation SOF + RBV in ages 3–17; GT 2, 3	Under investigation	All genotypes for 12 or 24 weeks Age ≥6, weighing >17 kg (37 lbs) + RBV for severe cirrhosis All liver disease severity	All genotypes for 8 weeks; seen as a re-treatment or salvage treatment Dosage: 250 mg GLE and 100 mg PIB Age 12 to <18; weighing 30–45 kg (66–99 lbs) All liver disease severity	GT 1, 4, 5, 6 for 12 weeks Age >3; weight 35 kg (77 lbs) All liver disease severity	Age >3 years Not for adolescents or people of reproductive age

HCV Treatment During Pregnancy and Breastfeeding

A pregnant person who is monoinfected with HCV carries around a five percent risk of transmission to the baby. The risk of perinatal transmission of HCV is higher—an estimated 11 percent—if the pregnant person is also HIV-positive and not on antiretroviral therapy (ART). HCV infection among people of reproductive age and pregnant people in the US has risen due to increased unsterile injection drug use related to the opioid epidemic: an increase of 400 percent from 0.8 to 4.1 per 1,000 birth deliveries.

There are currently no DAAs approved to take during pregnancy or breastfeeding, or for children younger than three years old. However, one small (n=9) Phase 1 study of pregnant individuals with genotype 1 showed preliminary safety and efficacy of sofosbuvir/ledipasvir, taken for 12 weeks, starting at 23 weeks of gestation. All nine pregnant participants achieved SVR; none of the nine infants acquired HCV, and no other maternal or neonatal issues were reported or observed. Larger studies with pangenotypic regimens are urgently needed.

Due to routine exclusion of pregnant individuals from clinical research, data and global guidance for these patients is lacking. Ethical and responsible inclusion of pregnant participants in HCV research should follow accepted practices: basic clinical safety and efficacy data is available and established in the general population; there is sufficient

preclinical and initial data on the risks and benefits of HCV treatment during pregnancy that indicate the potential benefit for the pregnant person and/or baby; and risks can be reduced. Given that DAAs are well tolerated in the general population, with minimal drug-drug interactions, it's possible to bridge the research gap and investigate treatment options for pregnant and breastfeeding people.

France, Italy, Pakistan, Poland, and Taiwan recommend universal screening during each pregnancy. The U.S. Preventive Services Task Force (USPSTF) and Centers for Disease Control and Prevention (CDC) recommend universal screening of people of reproductive age and during each pregnancy, except in areas where HCV prevalence is <0.1 percent, followed by linkage to treatment after birth and when not breastfeeding. Infant and pediatric infection is mostly asymptomatic with slow progression, with five percent of children spontaneously clearing the virus. However, HCV diagnosis in young children remains challenging. The potential presence of maternal antibodies requires waiting until the child is older than 18 months for antibody testing. As previously noted, there are no FDA approved treatments for children under 3 years of age. This contributes to significant patient loss to follow-up.

Several studies are under investigation to understand the pharmacokinetics, dosing, safety, efficacy, and tolerability of different DAAs during pregnancy and breastfeeding.

Table 2. Ongoing Studies on HCV Treatment During Pregnancy and Breastfeeding

Study Name	Status	Regimen	Population(s)	Funder(s)/ Sponsor(s)
Pharmacokinetics of sofosbuvir/daclatasvir in HCV-infected lactating women NCT04852614	Recruiting; results expected end-2021	400 mg sofosbuvir + 60 mg daclatasvir with food for 12 weeks	People living with HCV who are lactating and weaning, or people with HCV who decided not to breastfeed to initiate HCV treatment GT 1, 4, 5, or 6	Ain Shams University
Treatment of chronic hepatitis C during pregnancy with sofosbuvir/velpatasvir NCT04382404	Recruiting; results expected 2023	sofosbuvir + velpatasvir for 12 weeks	Pregnant individuals during 2nd trimester	Gilead Sciences, National Institute of Child Health and Human Development (NICHD)
Sofosbuvir/velpatasvir in postpartum women with opioid use disorder and chronic hepatitis C infection NCT03057847	Recruiting; results expected end-Aug 2021	400 mg sofosbuvir + 100 mg velpatasvir for 12 weeks, starting 2 weeks postpartum	Postpartum individuals in opioid substitution therapy	Dr Elizabeth Krans, University of Pittsburgh

Is a Preventive HCV Vaccine Still Necessary?

DAAs are powerful, lifesaving medicines to control and cure HCV. Yet, with an estimated two million new infections each year and low diagnosis rates, many people remain asymptomatic and go untreated for years, then progress to cirrhosis and liver cancer. A preventive vaccine could complement existing treatment strategies, help curb transmission, and ramp up efforts to meet HCV elimination goals by 2030.

Thanks to targeted advocacy by Treatment Action Group and partners, in fiscal year 2020, US$8 million was awarded to the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and Veterans Affairs. In fiscal year 2021, there has been increased funding of US$14 million for vaccine-related research, which has been granted to look at the role of broadly neutralizing antibodies and specific immunological responses to prevent transmission of HCV. Messenger (mRNA) and adenovirus-based technology used in the development of COVID-19 vaccines have also informed researchers about protective immunity, applicable for developing a preventive HCV vaccine. One University of Alberta team, led by Nobel-laureate Sir Michael Houghton, is investigating an adjuvanted recombinant vaccine, which may stimulate antibody production and prevent infection. Phase 1 is expected to begin in 2022 with the use of different adjuvants; human efficacy trials are anticipated from 2023–2026.

The following table summarizes the additional HCV vaccine-related funding for the 2021 fiscal year.

Table 3. HCV Vaccine-Related Grants

Project Title and Number	University/Sponsor	Principal Investigator	Fiscal Year	Funding Agency	Funding Total (USD)
Development of standardized immunoassays and virus panels 1R24AI158193-01	Johns Hopkins University	Bailey, Justin Richard	2021	NIAID	567,950
Molecular and structural characterization of broadly neutralizing anti-HCV antibodies 5R01AI127469-05	Johns Hopkins University	Bailey, Justin Richard	2021	NIAID	709,188
Development of a single-cell antibody cloning protocol for isolation of hepatitis C virus-specific broadly neutralizing antibodies 5R21AI151353-02	Johns Hopkins University	Bailey, Justin Richard	2021	NIAID	204,688

Project Title and Number	University/Sponsor	Principal Investigator	Fiscal Year	Funding Agency	Funding Total (USD)
Mechanisms of spontaneous and vaccine mediated hepatitis C virus control to direct rational development of a novel HCV vaccine 1U19AI159822-01	Johns Hopkins University	Cox, Andrea L.	2021	NIAID	2,632,704
Mechanisms of spontaneous and vaccine mediated hepatitis C virus control to direct rational development of a novel HCV vaccine 1U19AI159822-01	Johns Hopkins University	Cox, Andrea L.	2021	NIAID	477,419
Mechanisms of spontaneous and vaccine mediated hepatitis C virus control to direct rational development of a novel HCV vaccine 1U19AI159822-01	Johns Hopkins University	Cox, Andrea L.	2021	NIAID	140,102
Characterization of HCV vaccine induced-neutralizing antibody response in non-human primates 1U19AI159822-01	Johns Hopkins University	Bjorkman, Pamela J.	2021	NIAID	392,336
Mechanisms of antibody-mediated control of repeated hepatitis C virus infection in humans 1U19AI159822-01	Johns Hopkins University	Bailey, Justin Richard	2021	NIAID	516,331
Immunologic and metabolic profiles of T cells that control diverse HCV infections 1U19AI159822-01	Johns Hopkins University	Cox, Andrea L.	2021	NIAID	817,644
Immunization strategies to elicit broadly neutralizing antibodies against HCV 5K99AI153465-02	California Institute of Technology	Flyak, Andrew I.	2021	NIAID	129,465
Selection of vaccine antigens for protection from hepatitis C Virus infection 5R01DK122401-02	Saint Louis University	Ray, Ranjit	2021	NIDDK	340,875
Design of immunologically intact soluble HCV E1E2 complexes using transmembrane-mimic scaffolds 5R21AI154100-02	University of Maryland, College Park	Pierce, Brian G.	2021	NIAID	230,519
Structure-based vaccine design for hepatitis C virus 5R01AI132213-05	University of Maryland, College Park	Fuerst, Thomas R.	2021	NIAID	1120,994

Project Title and Number	University/Sponsor	Principal Investigator	Fiscal Year	Funding Agency	Funding Total (USD)
Hepacivirus control by vaccine-elicited T cells 5F30AI143060-03	Research Institute Nationwide Children's Hospital	Hartlage, Alex Stephen	2021	NIAID	51,036
Immune correlates of protection against hepacivirus persistence 1R01AI151175-01A1	Research Institute Nationwide Children's Hospital	Kapoor, Amit	2021	NIAID	642,072
Correlates of protective immunity to HCV and rational vaccine design: Project 3 1U19AI159819-01	Emory University	Amara, Rama Rao	2021	NIAID	692,666
Correlates of protective immunity to HCV and rational vaccine design 1U19AI159819-01	Emory University	Grakoui, Arash	2021	NIAID	2,018,828
Correlates of protective immunity to HCV and rational vaccine design: Clinical core 1U19AI159819-01	Emory University	Shoukry, Naglaa H.	2021	NIAID	240,597
Dynamics of antigen specific B and Tfh responses during acute and chronic HCV 5R01AI136533-04	Emory University	Grakoui, Arash	2021	NIAID	742,154
Transcriptional regulation of T cell immunity 1I01BX005106-01	VA San Diego Healthcare System	Chang, John T.	2021	VA	
5I01BX004281-03	James H. Quillen VA Medical Center	Yao, Zhi Q.	2021	VA	
Strategies to enhance vaccine-primed T cell immunity against HCV 1U19AI159840-01	Stanford University	Walker, Christopher M.	2021	NIAID	353,143
Structure-guided vaccine design of HCV E1E2 to induce broadly neutralizing antibodies (bNAbs) 1U19AI159840-01	Stanford University	Foung, Steven	2021	NIAID	703,062
Genetic viral and host adaptations to breach species barriers of HCV 5R01AI107301-09	Princeton University	Ploss, Alexander	2021	NIAID	474,798
Total					**14,198,571**

Advocacy Points:

For National Governments:

Access to Treatment

- Expand generic access to DAAs using TRIPS flexibilities and accelerate registration of pangenotypic regimens, such as through the Global Fund's Pooled Procurement Mechanisms and WHO Collaborative Registration Procedure;
- Waive any requirement for in-country clinical registration trials for proven DAA combinations from validated generic manufacturers;
- Ensure competition between generics manufacturers;
- For high-income countries, refrain from retaliatory trade practices in response to the use of TRIPS flexibilities for access to medicines;
- Lift all treatment restrictions and inform medical providers on the ability to treat patients with the appropriate DAAs, regardless of fibrosis stage, and on the lack of evidence for requiring abstinence before initiating DAA treatment.

Access to Screening and Testing

- Enact opt-out HCV screening of all people upon incarceration, with robust linkage to care during incarceration and upon release;
- Align public health system payment/reimbursement to expand HCV screening to all adults 18 years and older, and during each pregnancy;
- Simplify, decentralize, and scale up HCV test-and-treat programs.

Expand Harm Reduction Services

- Make the abovementioned harm reduction measures, such as take-home DAA and medications for opioid use disorder permanent, and scale up low-threshold harm reduction services, such as community-led naloxone, drug supply testing, and needle/syringe programs, to prevent overdose and HIV/viral hepatitis reinfections.

Fund Viral Hepatitis and Harm Reduction

- Sustain funding for R&D on a preventive HCV vaccine as an essential part of HCV elimination; and
- For high-income countries, increase investments in viral hepatitis and harm reduction programs, notably in low- and middle-income countries (LMICs).

For NIH and FDA:

- In coordination with the FDA, the National Institutes of Health (NIH) should include HCV study sites in an established network (e.g., International Maternal Pediatric Adolescent AIDS Clinical Trials Network) with a track record of performing clinical studies on maternal infectious diseases during pregnancy. The aim should be to find 100 pregnant individuals across these trials to receive each DAA regimen, and if safety and efficacy aligns with that seen in individuals who are not pregnant, the FDA could expand the DAA label for use during pregnancy.
- Create a mandatory pregnancy registry for post-approval treatment to assess the safety and efficacy in real-world settings. This should link data registry enrollment and reporting requirements, which would then require insurance payors to cover DAAs for pregnant individuals as for other patients.
- Ensure a safety monitoring committee to review all DAA outcomes during pregnancy, which could immediately notify health care providers of any adverse events.

For Companies:

- Include India and other high-burden countries in AbbVie's glecaprevir/pibrentasvir license.

For AASLD:

- Adopt EASL's 2020 updated treatment guidelines regarding difficult-to-treat HCV subtypes.

For Donors:

- Commit to multilateral and bilateral funding for universal access to generic DAA treatment and diagnostics in LMICs;
- Facilitate the integration of disease-specific programs by supporting treatment of HCV-monoinfected people who are at risk for HIV and other infectious diseases;
- Expand access to regional and central procurement platforms, such as the Global Fund's Pooled Procurement Mechanism, beyond HIV, TB, and malaria, at a minimum for DAA treatment for those with coinfections.

The HCV treatment updates were compiled between June 1, 2020 and August 31, 2021 and will be updated on an annual basis. Please send updates, corrections, or suggestions to Bryn Gay at bryn.gay@treatmentactiongroup.org.

Table 4: HCV Treatment Updates

Drug	Class/ Type	Company/Sponsor*	Regulatory Status	Price
Ravidasvir (+ sofosbuvir)	NS5A inhibitor	*Supporters and donors: Drugs for Neglected Diseases initiative; Ministry of Health Malaysia; Ministry of Public Health Thailand; National Science and Technology Development Agency, Thailand; Médecins Sans Frontières (MSF); MSF Transformational Investment Capacity; UK Aid; Médecins Sans Frontières (MSF); MSF Transformational Investment Capacity; Pharmaniaga; Starr International Foundation, Switzerland; Foundation for Art, Research, Partnership and Education; Swiss Agency for Development and ; Anonymous Individuals and Organizations	Pharco approved license in Medicines Patent Pool; Registered in Malaysia in June 2021; under WHO review	US$300 (expected to be lowered depending on volume and competitive market)

STORM-C-1 is a two-stage, open-label, phase II/III single arm clinical trial with nine sites in total in Malaysia and Thailand. Six sites are in stage 1 and seven sites in stage 2. Some sites are only involved in both stages, and some only in stage 1 or 2. Interim results are from a multicenter trial with six sites in Malaysia. The public health funded and developed multi-genotypic treatment regimen provides an additional, simple, public health option for limited resource settings, such as LMICs, to scale up generic treatments.

- N=301
- N=220 non-cirrhotic patients (12-week regimen); 170 (77%) men; 50 (23%) women (Malaysia); transgender patients not reported
- N=81 cirrhotic patients (24-week regimen); 61 (75%) men; 20 (25%) women (Thailand)
- Ravidasvir (200 mg) with sofosbuvir (400 mg) taken once daily (ribavirin-free)
- Achieved SVR12 for genotypes 1, 3, 4, 6
- SVR12 achieved in 291/301 patients (97%; 95% CI 94–99)
- Given the small number of patients with GT 2 and 6, there are no firm conclusions about ravidasvir efficacy until results from second stage of STORM-C-1 conclude
- No difference in SVR12 for patients with HIV/HCV coinfection or treatment experience (with PEG-INF)
- No patients lost to follow-up; 6/301 (6%) discontinued treatment

Patients with cirrhosis	78/81 (96%) at SVR12
153/158 (97%) patients with GT3	SVR12
51/53 (96%) patients with GT3 and with cirrhosis	SVR12
GT 1a	N=98/301 (33%); 96% SVR12
GT 1b	N=27/301 (9%); 100% SVR12
GT 2	N=2/301 (2%); 100% SVR12*
GT 3	N=158/301 (52%); 99% SVR24
GT 6	N=16/301 (5%); 81% SVR12
Compensated cirrhosis	81/301 (27%)
HIV/HCV coinfection	90/301 (30%)
Treatment experienced (with PEG-INF)	99/301 (33%)
Current drug use	1 (<1%)
Past injection drug use	133 (44%)
No reported drug use	120 (55%)

*Refers to limited number of patients with genotype 2 in the study.

No deaths or discontinuation of ravidasvir treatment due to adverse events. Mild adverse events: slight fever (12%), cough (9%), upper respiratory tract infection (8%), and headache (7%) reported. One adverse event in a patient with transient acute kidney injury caused discontinuation of treatment because it was possibly related to sofosbuvir.

Women of childbearing age with negative pregnancy test at screening and baseline; patients with controlled HIV coinfection; people who formerly injected drugs, people who currently use drugs but not currently injecting drugs; patients on medication for opioid use disorder (MOUD)/opioid substitution therapy (OST) were eligible for inclusion.

Patients with decompensated cirrhosis; hepatocellular carcinoma; HBsAg coinfection; serum creatine more than 1/5 times the upper limit of normal or end-stage renal disease (ESRD); or treatment experienced with previous NS5A inhibitor were ineligible for inclusion in the trial.

Drug	Class/ Type	Company/Sponsor*	Regulatory Status	Price
Glecaprevir/ pibrentasvir (G/P) + sofosbuvir	NS3/4A, NS5A inhibitor + NS5B inhibitor	Off-label studies	TK	TK
STRIVE-4 Phase IV study at Kirby Institute is investigating G/P (300 mg/120 mg), combined with sofosbuvir (400 mg), to evaluate the safety, efficacy, and feasibility of achieving SVR at week 4 and at week 12 post-treatment follow-up in treatment-naive patients with mild liver disease. ■ A Canadian off-label study investigated treatment with G/P + sofosbuvir for one patient with GT 3 and Y93H mutation as a possible re-treatment option, particularly for people with resistance-associated substitutions (RAS). The patient achieved undetectable viral load at week 4 and remained undetectable post-SVR12. Larger trials are needed to evaluate efficacy in broader clinical and real-world settings.				
SH229 + daclatasvir	NS5B inhibitor + NS5A inhibitor	TK China	TK	TK
Phase II, open-label study of multi-genotypic regimen of SH229 plus daclatasvir in Chinese patients with chronic HCV infection. ■ Daclatasvir (60 mg) taken with SH229 once daily in three different patient cohorts: A (400 mg); B (600 mg); C (800 mg) ■ Treated GT 1, 2, 3, 6 ■ N=124 enrolled; 122 at post-SVR12 follow-up; two patients lost to follow-up ■ No discontinuation due to adverse events ■ Seen as an effective and safe treatment candidate for Chinese patients with most genotypes; for domestic use.				
Narlaprevir/ ritonavir + sofosbuvir	NS3/CYP3A inhibitor + NS5B inhibitor	R-Pharm, Russia	TK	TK
Phase II, multi-center, open-label study to investigate the safety and efficacy of an all-oral combination of narlaprevir/ ritonavir combined with sofosbuvir in treatment-naive patients with GT1. ■ N=85 ■ Cohort A=narlaprevir (200 mg)/ritonavir (100 mg) + sofosbuvir (400 mg) taken once daily for 12 weeks ■ Cohort B=narlaprevir (200 mg)/ritonavir (100 mg) + sofosbuvir (400 mg) taken once daily for 8 weeks ■ INF- or RBV-experienced; pregnancy or breastfeeding; a male partner with a pregnant partner; people coinfected with HIV/HBV; substance use within 1 year of screening are part of the exclusion criteria.				

Patients with cirrhosis	8.9%
IL28B at baseline	88.7%
Treatment experienced (with PEG-INF)	6.5%
GT1	N=64/124 (51.6%); 62/62 (100%) SVR12
GT 2	N=31/124 (25.0%); 31/31 (100%) SVR12
GT 3	N=14/124 (11.3%); 10/14 (71.4%) SVR12
GT 6	N=15/124 (12.1%); 14/15 (93.3%) SVR12
Cohort A	37/40 (92.5%) at SVR12
Cohort B	40/42 (95.2%) at SVR12
Cohort C	40/40 (100%) at SVR12