Factors Contributing to HCV Treatment Failure and Successful Retreatment in People Who Use Drugs

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Background

- HCV treatment with DAAs leads to high sustained viral response (SVR) rates in people who use drugs (PWUD). However, a minority of patients do not achieve SVR.
- We leveraged a multidisciplinary expert team to investigate potential reasons for why PWUD failed DAA treatment and discuss optimal retreatment strategies.

Methods

- The Montefiore Wellness Centers are opioid treatment programs (OTPs) in the Bronx which serve approximately 3,200 patients annually. Within the HCV Program, 320 patients initiated treatment between 10/28//2014 and 5/21/2018. 11 patients were lost to follow-up.
- HCV case conferences, as part of general primary care, were conducted weekly at each of the three OTP clinics.
- We conducted retrospective chart reviews for PWUD (n=13) with a chronic HCV infection who failed to achieve SVR with combination DAA regimens.
- In April 2019, a multidisciplinary expert team consisting of primary care providers, counselors, health educators, and specialists in addiction medicine, infectious diseases, and hepatology, reviewed each case using a structured instrument outlining potential reasons for failure, as well as retreatment strategies and outcomes.
- Formal case reports were developed.

Results

- 9 of 13 treatment failure patients were retreated – sofosbuvir/velpatasvir/voxilaprevir (n = 1) and glecaprevir/pibrentasvir (n=1). Reasons for not being retreated included: throat cancer and inability to swallow medication (n = 1); not offered retreatment due to unstable diabetes and recent below the knee amputation (n = 1), lost to follow up (n = 2).
- 6 of the 9 retreated patients who were retreated achieved an end of treatment (ETR) response including 5 with a SVR. One retreated patient who achieved ETR died from diabetes-related complications prior to SVR determination.
- 1 of the 9 retreated patients was lost to follow-up after receiving his full course of medication (ETR/SVR not documented).
- 2 of the 9 retreated patients discontinued treatment due to major depression and suicidality (n = 1) and newly diagnosed hepatocellular carcinoma (n = 1).
- Please see attached table for more patient characteristics.

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Case Studies: Barriers & Factors for Treatment Success

Patient 1	**History:** Patient 1 was a 38 year old HCV-monoinfected, unstably housed Puerto Rican man at the time of his first treatment with sofosbuvir/ledipasvir for 12 weeks with genotype 1a and stage F1/2 disease. Patient injected opiates and cocaine prior to HCV treatment and continued to inject opiates during antiviral treatment. Patient was maintained on methadone. He was treated in a weekly group treatment between 4/19/16 and 7/12/16 where medication was dispensed weekly. He was undetectable at week 4, but did not achieve ETR or SVR. Follow up mutations (NS5A): H58D. Patient was successfully retreated with sofosbuvir/velpatasvir/voxilaprevir using a DOT model.
	Barriers: Patient 1 had poor adherence to group due to employment and had poor adherence to HCV treatment (34.2%). Patient reported severe headaches due to medication, but patient had chronic headaches due to traumatic brain injury (TBI) secondary to gun shot, and chronic seizures. Patient had not been evaluated by psychiatrist but exhibited labile emotions, anger, paranoia, mistrust, and polysubstance use. Treatment was complicated because patient changed primary care provider (PCP) right before treatment, and we were no longer able to conduct laboratory testing.
	Interventions: DOT via OTP nursing station improved adherence which allowed close monitoring by the multidisciplinary team (counselor, educator, nurse, peer educator and physician). We worked with his offsite PCP to laboratory tests included HCV viral load. Weekly sessions with HCV Health Educator and onsite HCV treater allowed patient to express dissatisfaction/fears, which promoted continued adherence when patient attempted to discontinue treatment three separate times (ex. throwing medication at the dispensing nurse, yelling at counselor and health educator). Despite referrals to psychiatric care, patient did not follow up. Post treatment, patient 1 reported he took none of his weekend doses.

Results Continued

- Successful patient-centered shared decision-making retreatment strategies included not requiring DOT despite documented prior poor adherence (n = 2); collaboration with outside primary care provider who conducted laboratory ,monitoring (n = 1); and modified DOT (n = 2).
- Potential retreatment strategies include continuing to engage precontemplative patients around issues that are of primary concern to the patient; peer educator escorts to offsite appointments; case management around comorbidities and psychosocial barriers; communication with offsite primary care and mental health providers, weekly dispensing of medications when DOT is not feasible; frequent virtual care coordination through phone calls and texts; comprehensive expert multidisciplinary team meetings focused on patients who have failed treatment and those with advanced fibrosis; onsite psychiatric care; and offering DOT with smart-phone based applications for patients who are not able to come to their OTP clinic daily.

Case Studies: Continued

Patient 2	**History:** Patient 2 was a 45 year old, HCV-monoinfected, stably housed African American woman at the time of her initial treatment with sofosbuvir/ledipasvir (8 weeks) with genotype 1a and stage F1/2 disease. She received individual treatment between 08/14/15 and 10/09/15, and was maintained on methadone. HCV medications were dispensed every 2 weeks. She achieved ETR but not SVR . Follow up mutations (NS5A): Q80K. Urine toxicology prior to treatment indicated opiate and cocaine use. Patient did not use illicit drugs during treatment. Patient had anxiety but demonstrated poor adherence to offsite psychiatry and anxiolytic medications. Patient was successfully retreated with sofosbuvir/velpatasvir/voxilaprevir individually with HCV medications dispensed weekly. At week 5, patient received one month supply due to planned vacation.
	Barriers: Patient failed due to poor adherence (adherence of 31.4%) as well as likely inadequate duration of treatment. After patient completed treatment, AASLD guidelines were changed recommending 12 weeks instead of 8 weeks of sofosbuvir/ledipasvir for African American patients even with low stage disease. Patient 2 reported headaches which contributed to nonadherence. Patient was unable to be given DOT as she came one day of the week.
	Interventions: Directly observed treatment (DOT) was not required for this patient despite demonstrated poor adherence during initial treatment. New patient-center strategies included weekly dispensing of medication, daily check-ins by Hepatitis Educator via phone calls and texts, and weekly visits with physician. Counselor had frequent meetings with offsite psychiatrist.

Discussion and Clinical Implications

- PWUDs who fail DAA treatment can be successfully retreated leveraging patient-centered models of care.
- Potential clinical reasons for treatment failure were initially identified though weekly case conferences based on patient feedback and expanded upon through this panel of experts.
- Directly observed therapy should be considered but not required when retreating patients.
- Although the majority (93%) of PWUD achieved SVR, these 13 failures were correlated to gaps in care, which may be prevented using individualized strategies to overcome barriers to HCV care.