ID: IN-US-342-5516

The No One Waits Study: acceptability and feasibility of community-based point-of-diagnosis HCV treatment

Document date: September 17, 2023

Study design
The NOW study is a nonrandomized, single-arm, open-label, phase 4 study evaluating the feasibility, acceptability, and safety of a point-of-diagnosis HCV treatment model at a non-medical community site in San Francisco (NCT03987503).

From July 2020 to October 2021, the study team screened participants for HCV infection using the OraQuick® HCV Rapid Antibody (Ab) test and for HIV infection using the Alere Determine™ HIV-1/2 Ag/Ab Combo with a fingerstick blood sample. Those who tested HIV positive without a prior diagnosis were referred to clinical care. For participants with a reactive HCV Ab result, on-site venipuncture was performed for HCV RNA quantification and reflex genotype testing as well as hepatitis B surface antigen (HBsAg) testing. Participants returned in one week for in-person HCV RNA results and were offered same-day initiation of HCV treatment if their HCV RNA was detectable and they met eligibility criteria. Participants self-selected, rather than randomized, to receiving the intervention (starting HCV treatment at the HCV diagnosis visit). The study team provided medication through an investigator-initiated grant from Gilead Sciences and dispensed it to participants. Consented participants were given a 14-day starter pack of sofosbuvir 400 mg and velpatasvir 100 mg (SOF/VEL) and took their first dose on day of enrollment. (Figure 1).

Participants
Participants were identified through: (1) flyers and study cards posted in neighborhoods and venues frequented by PWID; (2) referrals from service organizations; (3) street-outreach to PWID and people experiencing homelessness; and (4) lists of participants in the investigators' previous research studies who gave contact permission for future research.

Eligibility was assessed and consent obtained at two time-points: (1) HCV screening and (2) HCV treatment (Figure 2). For HCV screening, eligible participants were 18 years or older and reported either injecting drugs in their lifetime or having a blood transfusion in or before 1992. Second, participants with confirmed HCV viremia were assessed for eligibility at their HCV RNA results disclosure. Clinical exclusion criteria included: positive HBsAg, untreated HIV, history of hepatic decompensation, prior treatment with an NS5A-inclusive DAA regimen for more than 2 weeks (unless there was evidence of prior SVR12 with HCV reinfection), pregnancy or breastfeeding, current medication use incompatible with SOF/VEL or sofosbuvir-velpatasvir-voxilaprevir (SOF/VEL/VOX), or a life expectancy of < 12 months as assessed by the study clinician.

Late study exclusion criteria were considered based on pre-treatment labs (drawn at study entry): albumin <3.0 g/dL, hemoglobin <8.0 g/dL (women) or <9.0g/dL (men), platelets <50,000, creatinine clearance (estimated by Cockcroft-Gault) <30 ml/min, aspartate aminotransferase or alanine aminotransferase > 10 x upper limit of normal (ULN), total bilirubin >1.5 times ULN, or INR >1.5 times ULN. For participants with genotype 3 and suspected cirrhosis based on FIB-4 >3.25, NS5A resistance associated substitution testing was performed using a pre-treatment sample to assess for the presence of the Y93H mutation; if detected, patients were switched to SOF/VEL/VOX.

Persons not meeting eligibility criteria or who declined enrollment received harm reduction counseling and referrals to community-based medical clinics for HCV and medical care needs.

Study enrollment and follow-up procedures. After written informed consent, participants completed a research questionnaire, a blood draw for pre-treatment labs (complete blood count [CBC], comprehensive metabolic panel [CMP] and prothrombin time; hepatitis B surface antibody and hepatitis B core antibody if no prior clinical documentation), received clinical assessment via staff-assisted telemedicine, received a 14-day SOF/VEL starter pack, and were observed taking the first SOF/VEL dose by the staff. The study pharmacy team submitted documentation to authorize participants' transition to insurance provided SOF/VEL treatment. If insurance-provided medication was delayed or not authorized, participants received study-issued SOF/VEL until insurance provided SOF/VEL was attained or for the duration of treatment.

The study team scheduled follow-up visits every two weeks during the 12 weeks of treatment and at 4- and 12-weeks post-treatment. At each follow-up study visit, participants picked up medication and completed research questionnaires. For patients who missed follow-up study visits, medication pickup or delivery was arranged. Clinical assessments conducted via staff-assisted telemedicine at the end of treatment. Additionally, participants were offered clinical consults with a clinician at treatment weeks four and eight and 12-weeks post treatment. For all telemedicine visits, staff set up the telemedicine technology on a computer provided by the study and introduced the clinician. The telemedicine visit was led by a physician or clinical nurse practitioner.

Enrollment and follow-up questionnaires collected demographics, physical and emotional health, current living context, healthcare access, sexual and drug use behaviors, and medication adherence. Study blood draws were obtained at treatment mid-point and completion and at ≥least 12-weeks post-treatment. We approach research participation as a form of specialized work and consulted our community advisory board to determine suitable compensation[1,2]. Participants received reimbursement ranging from $20 to $60 per visit, with a total potential compensation of up to $325 USD over the course of the 10 study visits.

Research site

The study was conducted at: (1) a fixed community space located in a neighborhood close to public transit and social service organizations, in an area where PWID were known to congregate; and (2) a mobile medical van parked in the neighborhood with the highest percentage of African American and Black people in San Francisco and few city-supported social or medical service organizations. In 2018 and 2019, Black/African-American San Franciscans made up approximately a quarter of HCV cases reported despite being only about 5% of the overall population.[3] Study procedures at the mobile site were discontinued in January 2021 due to COVID-19 and participants were rolled over to the fixed site. Both sites had private spaces for interviews and clinical research activities. Wrap-around services, including food, harm reduction supplies, COVID information and vaccination, were also available. Site staff were trained in HIV and HCV testing and disclosure counseling, harm reduction, ethical human research practices and de-escalation methods.

Study materials were refined in partnership with local advocacy organizations and members of the target population. The study protocol was approved by the University of California, San Francisco Institutional Review Board (protocol number 19-27751).

Endpoint measures

Acceptability, feasibility, and safety of HCV treatment were assessed for all participants who received the intervention, starting HCV treatment (defined as receiving at least one dose of study drug) at the HCV status disclosure visit. The primary treatment feasibility outcome measure was treatment response defined as undetectable HCV RNA at least 12 weeks post-treatment (SVR12). SVR12 was calculated by intention-to-treat (ITT group), defined as those who initiated treatment, and per-protocol (PP group) defined as those who completed a 12-week course of DAA therapy. Participants with undetected HCV RNA after treatment completion who subsequently developed HCV viremia with an HCV genotype different from their pre-treatment genotype within 12 weeks of DAA completion were considered to have post-treatment reinfection within 12 weeks and were classified as not achieving SVR12. Secondary treatment feasibility endpoints were undetectable HCV RNA at treatment completion. Primary acceptability endpoints included treatment initiation at time of HCV RNA result disclosure and treatment completion. Safety endpoints were treatment discontinuation because of late exclusion criterion or adverse event.

Statistical analyses

All acceptability and safety results and secondary outcomes were summarized with descriptive statistics. Treatment initiation was evaluated among all participants with current HCV infection meeting eligibility who returned for their HCV RNA results disclosure visit. Treatment response was evaluated among those who initiated treatment (ITT group, N=87) and those who completed DAA therapy (PP group, N=69. Point estimates and two-sided 95% confidence intervals were also calculated for primary endpoints. Significance assessments were conducted using appropriate statistical tests, with p-values calculated using either the Wilcoxon rank-sum test for continuous or ordinal data, or chi-squared tests and Fisher's exact test for categorical data, based on the nature of the variables and data distribution. All analyses were performed using STATA software version 15.[4]

References

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