**UCSD Human Research Protections Program**
**New Biomedical Application**
**RESEARCH PLAN**

## 1. PROJECT TITLE

InstaCare: A Prospective Study of Clinical Outcomes Following Rapid ART Initiation Among Persons with HIV and Out of Care

## 2. PRINCIPAL INVESTIGATOR

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## 3. FACILITIES

The study will be conducted at:

1)The UCSD AVRC-Antiviral Research Center, 220 Dickinson Suite A, San Diego, CA 92103 and

2) The UCSD Owen Clinic, 3rd Floor Medical Offices South, 4168 Front St, San Diego, CA 92103.

## 4. ESTIMATED DURATION OF THE STUDY

3 years

## 5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

The human immunodeficiency virus (HIV) continues to cause significant illness and death in the USA despite availability of effective treatment. People who are aware of their HIV status, but who are out of care and not on medications, are therefore at risk of developing HIV related health problems. In addition, people with HIV who are out of care are at greater risk of transmitting HIV compared to people on HIV treatment with suppressed levels of virus in plasma. To date, there are no interventions that have been shown to successfully link this "out of care" population back into care and successfully maintain viral suppression.

This study will test a strategy of providing immediate HIV therapy drugs, linkage to care, and a randomized intervention (60-minutes for health or diet and nutrition session). The goal of the study is to demonstrate that the 60-Minutes-for-Health intervention improves the rate of viral suppression at 24 weeks.

The use of rapid antiretroviral therapy (rapid ART), defined as the initiation of ART within 7 days of HIV diagnosis, has been associated with improved rates of linkage to care, retention in care and virological suppression after 1 year among persons newly diagnoses with HIV. In addition, the behavioral intervention, "60-Minutes-for-Health", was shown in a pilot study to improve retention in care among PWH-OOC. We aim to undertake a study to evaluate the feasibility of providing rapid-ART to people who are aware of their HIV status, but have been out of care at the time they re-engage in care. In addition, study participants will be randomized to either the "60-Minutes-for-Health" intervention or a 60 minute diet and nutrition control session.

## 6. SPECIFIC AIMS

**AIM 1.** To compare the proportion of persons with HIV and out of care (PWH-OOC) undergoing rapid-ART initiation that are on ART with VL ≤50 copies/mL at week 24 between those randomized to 60-Minutes-for Health vs. a time-and-attention control session at baseline.

**AIM 2.** To compare the proportion of participants in care at week 24 between those randomized to 60-Minutes-for Health vs. a time-and-attention control session at baseline.

**AIM 3.** To compare the role of genotypic susceptibility scores (GSS) derived from HIV Genosure archive resistance testing as a predictor of achieving virologic suppression on rapid ART among PWH-OOC.

**AIM 4.** To determine the acceptability of rapid ART among PWH-OOC using quantitative surveys and focus groups on patient-reported outcomes and perspectives at week 4.

## 7. BACKGROUND AND SIGNIFICANCE

HIV continues to cause substantial morbidity and mortality in the USA with over 38,000 new diagnoses in 2017[1]. Historically, the majority of HIV transmissions in the USA were thought to arise from persons who were HIV infected but unaware, or who had acute HIV infection[2,3]. However, more recent data suggests the dynamics of HIV transmission in parts of the US are changing. Fewer than 60% of PWH are retained in care and achieve viral suppression[4]. As a consequence, over 40% of HIV transmissions in the US are now estimated to arise from PWH and aware of their diagnosis but out-of-care (PWH-OOC)[5]. Local data from San Diego County support a similar shift in regional transmission dynamics[6]. Using National HIV Behavioral Surveillance data applied to local prevalence, San Diego County estimates that 90% of PWH are aware of their diagnosis and that the number of new diagnoses have declined by 21% (data through 2017)[6]. However, despite these encouraging data, the HIV Care Continuum in San Diego also demonstrates that among those diagnosed with HIV infection, only 75% have been linked to care, and of these only 60% have achieved viral suppression[7]. Together, these data suggest that strategies to engage and treat PWH-OOC may play a vital role in preventing transmission of HIV[5].

Delays between re-linkage to care and initiation of ART may represent a missed opportunity for immediate engagement resulting in some loss to follow up. Rapid ART initiation, generally defined as ART initiation <7 days from diagnosis[8], has been shown to improve linkage, retention and viral suppression rates compared to standard of care ART in persons newly diagnosed with HIV in low and middle income countries [9-12]. In the U.S., rapid ART initiation has been associated with shorter time to virologic suppression than historically treated persons[13]. To date, no studies have investigated rapid ART among PWH-OOC[14], many of whom have been previously engaged in the healthcare system, but were unable to sustain engagement[15]. Our group has successfully implemented rapid ART among persons newly diagnosed with HIV[16]. We propose to leverage this expertise to evaluate rapid ART among PWH-OOC.

Multiple brief, single-session, POC interventions have successfully changed complex HIV-related behaviors in other areas[17-27]. Most of these interventions range from 15-60 minutes long and are delivered in clinic settings by a variety of people (e.g. lay health educators, outreach workers, nurses). Significant changes in behavioral outcomes include reductions in condomless sex[17,18], decreased incidence of sexually transmitted infections[19,20,24], increased odds of HIV testing[21], returning for HIV test results[22], and improvements in ART adherence[23]. Most follow-up periods were 6 months or less, though one study observed significant changes over 12 months[19]. All but one[23] intervention integrated evidence-based motivational interviewing (MI)[28] and/or social cognitive theories (e.g. Information Motivation Behavioral Skills model[29]) to inform the interventions' delivery and content. MI promotes behavior change by eliciting the individual's own motivation for change and solutions to overcome their perceived barriers to change[28]. Social cognitive theory targets the conversation around behavioral determinants most proximal to change (i.e. correct misinformation driving decisions to avoid HIV care, build motivation by improving ART attitudes, or increase behavioral skills to navigate structural barriers like transportation[29]).

***Preliminary Data***

Rapid ART. The UCSD NIH-funded Primary Infection Resource Consortium (PIRC) is the largest, most intensively studied and well-characterized cohort of people identified with acute and early HIV infection in the U.S.. Since December 2014, the PIRC has implemented a rapid ART program[16,30] in an effort to improve uptake of ART and time to virologic suppression[10,12,13]. Since this program began, 66 of the 69 (95.7%) participants diagnosed with acute and early HIV infection have initiated rapid ART with an integrase-based treatment regimen, with a median time from HIV diagnosis to ART start of 1 day (IQR 0-6 days). The proportion with VL suppression at 12 and 24 weeks was 80% and 98%, respectively.

"60-Minutes-for Health": To date, there are no interventions with a strong evidence base to effectively re-engage PWH-OOC[31]. "60-Minutes-for Health" is a brief, low resource, single session, theory-based behavioral

intervention for PWH-OOC[29,32]. In a pilot randomized controlled trial (by Co-I Smith), "60-Minutes-for Health", was found to be acceptable and feasible and was associated with improved retention in HIV care at both 12- and 24-month follow-up among participants randomized to the intervention (87.5% and 62.5% respectively) compared to a time-and-attention control (62.5% and 25.0% respectively)[32].

## 8. PROGRESS REPORT

N/A

## 9. RESEARCH DESIGN AND METHODS

The overall strategy is to perform a feasibility study of rapid ART initiation among PWH-OOC who are randomized (1:1) to an unblinded behavioral intervention "60-Minutes-for Health", compared to a 60 minute time-and-attention control session focused on diet and nutrition.

Individuals eligible for participation will be enrolled and followed for 48 weeks. They will be offered a same day (or within 1 week) appointment to enable the initiation of ART within 7 days of contact. Eligible individuals, after completing informed consent, will start ART for HIV with Bictegravir/Emtricitabine/tenofovir alafenamide (B/F/TAF) or appropriate alternative therapy if B/F/TAF is not thought to be an optimal regimen. Individuals will undergo computer-generated randomization (1:1) to onsite 60-Minutes-for Health intervention vs an onsite theory-based time-and-attention control session focused on diet and nutrition. After completion of the intervention participants will receive standard-of-care case management services between day 0 and week 4. A 60-day supply of B/F/TAF or alternative will be provided for participants of both study arms. The timeline of visits and study interventions is summarized in **Table 1**.

**Table 1. Schedule of Evaluations**

| Study Assessment | Baseline (Day 0) | Wk 1 | Wk 2 | Wk 4 | Wk 4-8 | Wk 12 | Wk 24 | Wk 36 | Wk 48 |
|---|---|---|---|---|---|---|---|---|---|
| **Assessments** | | | | | | | | | |
| Eligibility checklist | X | | | | | | | | |
| Informed Consent/HIPAA | X | | | | | | | | |
| Randomization | X | | | | | | | | |
| Release of information[4] | X | | | X | | | X | | X |
| Limited history[5] | X | | | | | | | | |
| Concomitant medications | X | | | | | | | | |
| Baseline Risk Assessments | X | | | | | | | | |
| Follow-up Risk Assessments | | | | X | | | X | | X |
| Linkage to Care Assessment | X | | | X | | X[6] | X | X[6] | X |
| STI Treatment/Referral Tracking[7] | X | | | | | | | | |
| Targeted physical examination | X | | | | | | | | |
| Historical ART assessment | X | | | | | | | | |
| ART Adherence Monitoring | | X | X | X | | | X | | X |
| Adverse Event Monitoring | X | X | X | X | | | X | | X |
| Ensure Provision of ART | X[8] | X | X | X[8] | | | | | |
| ART acceptability survey | | | | X | | | | | |
| **Behavioral Services** | | | | | | | | | |
| 60 Min Intervention vs. Control | X | | | | | | | | |
| Case Management | X | X[6] | X[6] | X | | | | | |
| Telephone follow-up | | X | X | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Focus Group (optional) | | | | | X | | | | |
| **Laboratories** | | | | | | | | | |
| INSTI HIV Rapid Test[9] | X | | | | | | | | |
| HIV Ultra RNA PCR | X | | | | | | X | | X |
| CD4/CD8 Panel | X | | | | | | | | |
| GC/CT NAT (x3 sites) | X | | | | | | | | |
| Syphilis EIA | X | | | | | | | | |
| w/reflex to titer and TP-PA | X | | | | | | | | |
| Comprehensive Metabolic Panel | X | | | | | | | | |
| CBC w/diff | X | | | | | | | | |
| HepBsAg | X | | | | | | | | |
| HIV Genosure archive resistance test (w/Integrase) | X[3] | | | | | | | | |
| Urine Pregnancy test[1] | X | | | | | | | | |
| **Specimen Collection** | | | | | | | | | |
| Plasma Bank | X | | | | | | | | |
| PBMC for cell pellet | X | | | | | | | | |
| **Stipends** | | | | | | | | | |
| Study stipend[2] | X | | | X | X | | X | | X |

[1] In women any time pregnancy is suspected
[2]Compensation rates: Day 0 [$20]; Survey Wk 4 [$20]; Focus Group [$50]; Wk 24 [$50]; Wk 48 [$75].
[3]Sample is banked for future analysis
[4]Baseline and at any time a new care provider is identified
[5]Medical history, STI, HIV and Hepatitis
[6]Phone call, email, text message, WhatsApp message, Facebook Messenger, and other participant-approved methods will be used to contact participant
[7]Complete for participants who test positive for Syphilis, Gonorrhea and/or Chlamydia at their Day 0 visit
[8]Study-provided ART will be dispensed at week 0 and 4
[9]For participants without documentation of HIV positive test results

**Antiretroviral Therapy (ART) drugs:** Drugs proposed for use in the study are currently standard of care for PWH and are all FDA approved. For participants without a clinical history or documented evidence of integrase inhibitor resistance, a regimen of bictegravir, emtricitabine & tenofovir alafenamide (B/F/TAF) will be offered. For individuals with evidence of integrase inhibitor resistance, an alternative ART regimen will be determined, based on prior treatment regimens – in collaboration with the participants primary care physician.

**Clinical assessments:** All subjects will undergo history and physical examination at baseline (Day 0) for the purposes of documenting features consistent with HIV infection, subject demographics, income, insurance status and employment status. Adverse event monitoring and reporting will start at baseline and continue at each study visit. Serious adverse events, grade 2 rashes, and all grade 3 or 4 adverse events will be reported in line with the International Conference on Harmonization (ICH) guidelines.

**Laboratory Assessments**
***HIV Monitoring Laboratories*** **–** All subjects will have an HIV rapid test performed on Day 0 on confirm HIV status if documentation of HIV status is not available to determine study eligibility. HIV related laboratories including: viral load (6 ml) and CD4 cell counts (3 ml). A 6 ml blood sample will be banked for future HIV drug resistance testing to assess ART resistance mutations (HIV GenoSure Archive). HIV viral load testing will be repeated at weeks 24 and 48.

***Hepatitis Laboratories:*** Blood (6 ml) will be collected to test for hepatitis B virus surface Ag. If subjects are identified as HBV, they will be referred for case management to provide linkage to care and treatment.

***STI screening*** will occur at Baseline (Day 0) as defined in Table 1. Urine, throat and rectal swab specimens will be sent for GC/CT NAT and blood will be sent for RPR (syphilis). Testing for syphilis will involve collection of 6 ml of blood. All patients will be informed of their STI test results. If any STIs are identified, notification will occur by phone or in person, and referral will be made to subject's primary medical doctor or to a public health clinic for treatment. Negative STI results will be provided via participants preferred method of communication (text, e-mail, or phone). STI reporting will be completed according to state requirements.

***Safety Laboratories:*** A urine pregnancy test will be performed at any time during study participation that pregnancy is suspected.

**Biological Specimens**
***Plasma and peripheral blood mononuclear cells (PBMC)*** – whole blood will be collected for blood plasma and PBMC (20 mL) for cryopreservation.

The total blood drawn for the screening and first four (4) study visits (12 weeks) is approximately 50 ml.

**Additional study assessments:** Linkage and retention in care – the number of HIV care visits ≥90 days apart between enrolment and 24 weeks (visit window 24 weeks + 12 weeks); the number of HIV care visits ≥90 days apart between enrolment and 48 weeks (visit window 48 weeks + 12 weeks). The time between enrolment and first HIV primary care visit.

**Baseline, follow-up and focus group assessments:** Participants will take structured surveys. Answers will be recorded into Redcap. We will use validated survey instruments of known determinants predicting engagement in HIV care: (a) unmet need addressing current and past 6-month structural barriers (i.e., housing and food stability, transportation), (b) substance use assessed by the Drug Abuse Screening Test (DAST) and AUDIT-C, (c) mental health symptoms related to depression (CESD-10) and anxiety (GAD-7), (d) antiretroviral (ART) medication regimen and overall ART adherence, (e) HIV care beliefs scale, (f) internalized HIV stigma, (g) resilience, (f) HIV affect skills, (g) sexual risk behavior and (h) the Engagement in HIV care index. Participants in the focus group will be reminded to not state anything in the focus group visit that they would not want to be heard outside of the group.

**Experimental study aspects:** Experimental aspects of the study are listed here:

- Rapid initiation of ART among PWH-OOC: Rapid ART among PWH with newly diagnosed infection is widely used though the use among PWH-OOC, while used in some physicians' clinical practice, is not currently established standard of care and would be considered experimental
- 60-Minutes-for Health: this is a psychological intervention which seeks to correct factors underlying decisions to delay or avoid HIV care and strengthen abilities to overcome HIV care utilization barriers. This is achieved through assistance identifying and reducing misinformation guiding HIV care attendance decisions; enhancing motivation to maintain HIV care via personal health goals; building skills for coping with negative feelings related to living with HIV; and increasing self-efficacy for navigating structural barriers and maintaining HIV care amidst competing priorities. The session will be provided by staff HIV testers (trained by Dr Smith, Co-I)

**Pregnancy**: Participants that are pregnant at time of enrolment to the study will be eligible to participate. US HIV guidelines indicate all individuals without contraindication should start ART immediately and so rapid-ART for pregnant participants falls within established guidelines. B/F/TAF is not standard of care for pregnant individuals and so ART regimens will be selected after discussion between investigators and according to national guidelines.

Pregnant individuals will be assisted in establishing care with HIV providers with experience in treating HIV in pregnancy and will assist with establishment in care with obstetrics providers with HIV expertise if not done prior to enrolment. The schedule of evaluations will remain the same for pregnant participants.

**Data collection**: data collection will be performed at each visit according to the schedule of evaluations and entered into the Research Electronic Data Capture (REDCap) data management system. Participants will be requested to provide release of information (ROI) to allow capture of HIV primary care visit data, primary care visit details (clinical notes) and HIV viral load for the duration of the study (48 weeks).

Primary outcomes are:

- the proportion of individuals with HIV VL ≤50 copies/ml at week 24; and
- the number of clinical care visits ≥90 days apart between study enrollment and week 24 (window +12 weeks).

Secondary outcomes are:

- the self-reported initiation of ART;
- the proportion of participants with HIV VL ≤50 at week 48;
- the proportion of participants with ≥2 clinical care visits >90 days apart between enrollment and week 48;
- to compare discrete genotypic susceptibility score (derived from banked archive genotype at enrolment) between individuals with and without virologic suppression at week 24 and 48; and
- to assess the acceptability of rapid ART through quantitative surveys at week 4 and among four focus groups help between week 4-8.

**Statistical considerations:** Based on preliminary data from the 60-Minutes-for-Health pilot study, we expect a difference of 30% in the proportion of participants with suppressed viral load at week 24 between study groups. Assuming a loss to follow-up of 20% and a 70% rate of viral suppression in the intervention arm, we will need to enroll 124 individuals to detect a significant difference ($p<0.05$) in suppression (≥30%) between the two groups. The proportion of participants with the primary and secondary outcomes will be compared using Fisher's exact test between intervention groups. 95% confidence intervals for the overall proportion of PWH-OOC that are on ART with HIV VL≤50 copies/ml and the overall proportion that are in care at week 24 will be compared to the analogous proportions among acute and early HIV (AEH) participants undergoing rapid ART initiation. Comparison with this historical cohort will be performed using Fisher's exact test.

**Collaboration with other Academic Research Groups studying Rapid ART**: Coded data, that have been stripped of identifiers, from HIV infected participants may be shared with research investigators in the U.S. and abroad, to better understand the acceptability and durability of Rapid ART and to gain a better understanding of this treatment strategy in all populations. InstaCare investigators will maintain the codebook in order to access identifiers to link data sets outside of the InstaCare research study.

Collaborations with other rapid ART investigators and collaborators are anticipated that will utilize InstaCare data and will involve the statistical, modeling, and inference needs of specific projects. The needs of these studies are expected to range from traditional biostatistical design and analyses needs (e.g., formulation of testable hypotheses, power calculations, and multivariate regressions), to novel analytical techniques (next generation sequence analysis, phylogenetics, and molecular epidemiology), which are increasingly crucial for interdisciplinary biomedical research. Summary data only will be shared with Gilead - consistent with materials prepared for publication. No individual-level data will be shared.

## 10. HUMAN SUBJECTS

We will enroll 124 participants in this study. Prospective participants will be identified through a number of means to ensure an equitable representation of PWH-OOC:

1. Potential subjects from UCSD Owen Clinic that fulfill the entry criteria will be contacted and offered an appointment for study recruitment
2. Subjects identified in the UCSD emergency department HIV screening program will be contacted and offered an appointment for study recruitment
3. San Diego Public Health Department (SDPHD) has implemented routine evaluations of their local HIV surveillance data in conjunction with other data to identify PWH who may be OOC[33]. This Data to Care program results in the evaluation of ~ 250 new cases per year in San Diego (~20-21 PWH-OOC a month), many of whom are found to be viremic and out-of-care. Once located, SDPHD will offer immediate transportation vouchers (Lyft) to and from the AVRC to expedite study enrollment and rapid ART start.
4. If after 12 weeks enrollment falls below ~7/month we will initiate an additional social media campaign (Facebook and Instagram). We will use the existing UCSD AVRC platform to promote study participation and work within our existing partnerships with local gay bars to increase our social media reach.

**Inclusion Criteria:**

- 18 years of age or older;
- documented HIV infection status (or rapid HIV will be repeated);
- out-of-care defined as not seen in HIV provider clinic for ≥6 months AND not receiving ART for ≥1 month (by self-report);
  - available for follow-up according to schedule of evaluations.

**Exclusion Criteria:**

- Co-morbid condition(s) that in the opinion of the investigator could limit the participant's ability to comply with the visit schedule or safely initiate rapid ART (e.g. psychiatric comorbidities or suspected central nervous system opportunistic infection);
- Prior ART regimens that in the opinion of the investigator precludes selection of a treatment option likely to result in virologic suppression (e.g. documented treatment failure on INSTI based regimen and multiple prior NRTI, NNRTI and PI regimens or documented resistance mutations likely to result in treatment failure)
- Participants that are unable to speak sufficient English or Spanish to consent to the study will be excluded

## 11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

Candidates for participation will be recruited through avenues listed in item 10. In situations where clinical data for a subject already exists on UCSD health electronic records, reasonable pre-screening will be undertaken to assess eligibility. A recruitment/educational flyer (Appendix X) is included and will be posted in area clinics, shelters, foodbanks, etc to outreach to potential participants. The text and imagery from the same flyer may also be used as part of a social media outreach effort if we are not reaching our enrollment goals with our initial print media outreach efforts.

For the purposes of pre-screening ONLY: A request for partial waiver of consent is requested.

The investigator believes the pre-screening to be used for recruitment meets the following requirements for this request per 46 CFR 46.116:

1. The (pre-screening) research involves no more than minimal risk to the participants;

2. The waiver or alteration will not adversely affect the rights and welfare of the participants;
3. The (pre-screening) research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the participants will be provided with additional pertinent information after participation.

Recruitment procedures will also involve the review of participant records by designated study personnel (e.g., investigators and/or study coordinators) in order to identify potentially eligible participants.

Since Protected Health Information (PHI) will be accessed via the study team's record database prior to contacting the potential participant about the research study, we are requesting a partial waiver of HIPAA authorization for access to PHI for purposes of pre-screening only.

Standard HIPAA authorization to collect research data from the participant's medical record will be obtained at the time of informed consent.

A brief subset of preliminary eligibility criteria such as age, diagnosis, co-morbid conditions and prior treatment, will be reviewed by study personnel to determine participants' preliminary eligibility for the research study. No written record of this information will be created. The study coordinator will then approach the participant to further discuss the research study with the participant and ask whether they would like to participate in the study. Eligibility may be formally determined at the time of counseling, but any research-specific screening procedures will only be performed after informed consent is obtained.

For the partial waiver of individual authorization for pre-screening recruitment purposes ONLY of individual HIPPA/Protected Health Information. The following conditions apply:

1. The (pre-screening) research involves no more than minimal risk, since we will not perform any procedure and the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life.
2. Granting of waiver for recruitment purposes only will not adversely affect privacy rights and welfare of the individuals whose records will be used. as no written record of the potential participants' information will be created.
3. The pre-screening could not practicably be conducted without a waiver. Obtaining consent from all participants prior to determining eligibility would lead to a high screen fail rate, and as a result, place an increased burden on participants
4. The pre-screening could not practicably be conducted without use of PHI.
5. The privacy risks are reasonable relative to the anticipated benefits of research.
6. An adequate plan to protect identifiers from improper use and disclosure is included in Item 16.
7. Participant identifiers/sensitive information shall be removed/destroyed as soon as they are no longer needed and in accordance with AVRC policy. The investigators have procedures in place to periodically review collected participant identifiers/sensitive information to ensure it is still required to satisfy a particular purpose or carry out a function.
8. The participants' PHI will not be re-used or disclosed for other purposes.

Recruitment to the study will occur through two routes: the first is through identification of UCSD Owen Clinic subjects eligible for recruitment and the second is through referral of participants from the emergency department, SDPHD or through social media campaign to the AVRC. Recruitment to the study will be performed by a named

member of the study team.

**UCSD Owen Clinic:**

- Participants will be prospectively identified by Owen Clinic and an appointment made at Owen Clinic for re-establishment of care
- At this visit, a study team member will attend UCSD Owen Clinic, assess the subject for eligibility and if eligible perform consent for the study, HIPAA consent and ROI.

**AVRC:**

- Participants identified through the UCSD emergency department, SDPHD or media campaign will be contacted by the study coordinator and offered an appointment at the AVRC within 7 days. Free Lyft transport will be provided by the study coordinator
- At the AVRC, the project manager will assess the subject for eligibility and if eligible perform consent for the study, HIPAA consent and ROI.

After completion of consent, HIPAA and ROI, the study coordinator will request relevant data from the subject's primary care provider. For subjects under the care of a UCSD provider, one of the study investigators will access the subject's clinical record to abstract relevant information (comorbidities, ART treatment history, HIV resistance assays (genotypes, phenotypes), substance use history, social documentation, baseline laboratory values including HIV VL)

## 12. INFORMED CONSENT

This protocol, the informed consent document and any subsequent modifications will be reviewed and approved by the UCSD Institutional Review Board responsible for oversight of the study. Written informed consent will be obtained from the participant by a member of the study staff. At the time potential participants contact us regarding the study, any questions they may have will be answered by a member of the study staff. If the potential participant is still interested in participating, the day 0 study visit will continue or be scheduled within 7 days. The participant will be informed of the time that needs to be allotted for their first visit in which the informed consent will be administered.

Individuals unable to speak English will not be excluded from participating in a study. The approved informed consent and any subsequent versions will be translated into Spanish and on a case-by-case situation any other language that is deemed necessary. The translated informed consents will be submitted to the IRB for approval. The consent process will include a qualified translator in the participant's native tongue. If a qualified UCSD translator is not available the Cyrom Language Line will be utilized as they have certified medical interpreters. The interpreter will sign and date at the end of the approved informed consent unless the Cyrom interpreter is utilized. In this situation, the study staff member involved in the consent process will document translator's name, ID#, and date of the translation at the end of the approved informed consent.

The informed consent process will describe the purpose of the study, the procedures to be followed, and the risks, and benefits of participation. This information will be explained to the study participant in a face-to-face setting by the individual consent the participant. Participants will be encouraged to ask questions throughout the consent process and encouraged to discuss their participation with trusted advisors, such as family members, close friends, etc. Participants will be allotted sufficient time to consider whether or not to participate in the research study. After allowing the potential participant time to read the informed consent the study staff and/or investigator will answer and address any questions or concerns the participant may have. Once all questions and concerns have been addressed and the participant wishes to participate, they will be asked to sign the informed consent.

Also, during the consent process, the informed consent process will be documented in the study CRF. A copy of

the consent form will be given to the participant.

## 13. ALTERNATIVES TO STUDY PARTICIPATION

Participants may choose not to join this study. Persons who are HIV infected and out of care will be referred to an HIV care provider treatment and support services.

## 14. POTENTIAL RISKS

Potential risks to participants in the study are listed below:

**Personal Questions Risks:** Participants will be asked about personal issues during this study. These types of personal questions could make them uncomfortable.

**Risks of Blood Draws:** The subject may experience temporary discomfort from the blood draws. The needle sticks may cause local pain, bleeding, bruising and swelling, as well as lightheadedness, dizziness and rarely, blockage of the vein, fainting and/or a local infection.

**Waiting for Test Results:** Subject may experience anxiety while waiting for test results.

**Stored Samples Containing DNA:** blood and cells containing genetic materials will be stored. The blood and cells will be identified only be an identification number. However, there is an inherent risk of inadvertent disclosure of identity because DNA can be used to identify an individual.

**Unknown Risks**: There may be unknown risks that are unforeseen, or at this time cannot be predicted. Subjects will be informed of any new risks that arise during the study.

**Reporting Requirements:** Per California law, we will report information about known or reasonably suspected incidents of abuse or neglect of a child, dependent adult or elder including physical, sexual, emotional, and financial abuse or neglect. If any investigator has or is given such information, he or she is required to report such information to the appropriate authorities.

**Loss of Confidentiality:** Study participation involves use of personal health information (PHI) including HIV status. As with all studies there is a risk of loss of confidentiality. Loss of confidentiality could lead to difficulty with employment, including situations where blood borne viruses preclude employment. The ability to obtain health insurance or life insurance may be compromised in situations where loss of confidentiality occurs. The likelihood of loss of confidentiality, while potentially serious, is believed unlikely.

UC San Diego Health System participates in a health information exchange (HIE) associated with the implementation of the federal Affordable Care Act (ACA). The HIE shares portions of participants medical records in a "view only" format with other doctors outside UCSD to help improve the participants' overall medical care. Clinical research tests that are performed at UCSD, including records from this research study, will be shared on the HIE. This means that through the participant's participation in this study, some doctors outside UCSD who might be participating in their overall medical care will see some portions of the participants' medical records, including but not limited to lab results. If participants do not agree to allow the study staff to share their research records for this study on the HIE, they may not participate in this study.

## 15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

Procedures taken to minimize risks to subjects are listed below:

- Loss of confidentiality: see section 16.
- Initiation of an ineffective HIV treatment regimen: The risk of using ineffective regimens will be minimized through obtaining as clear a history of prior ART regimens from the participant as possible, including using drug identification charts as standard. The proposed primary regimen (B/F/TAF) has a high barrier to resistance and resistance to this regimen in San Diego country is thought to be rare. The proposed study

follow-up timetable would be expected to rapidly identify cases of resistance allowing for regimen alteration in a timely manner.

- Phlebotomy will be undertaken by experienced practitioners to minimize discomfort.

***Quality Assurance Monitoring and Record Availability****:* The AVRC quality assurance team will perform an on-site review of individual participant records, including: consent forms, CRFs, and laboratory specimen records. Monitoring will ensure protection of study participants, compliance with the protocol, and accuracy and completeness of records. The quality assurance team will also inspect regulatory files to ensure requirements are being met. Quality assurance monitoring will occur when 10 participants are enrolled and then at 6-month intervals during the remainder of study conduct. Participants will be monitored clinically and will be given the 24-hour number to call for emergencies. Participant will be informed to call at any time for adverse experience during study participation. This will be recorded in the research notes.

All deviations from protocol or unanticipated problems involving risk (UPR) to subjects, as defined by the UCSD UPR fact sheet, will be reported to the UCSD IRB within 10 days. Problems or events that do not fulfill the definition of a UPR will be summarized in a table and submitted to the IRB in a timely manner.

At year 1 and year 2 of full recruitment, the study team (PI, Co-Is) will review the data acquired and progress of the study. Details of virological failure will be reviewed for inadvertent initiation of an ineffective HIV treatment regimens.

## 16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

***Privacy:*** Recruitment to the study will take place in a private room either at Owen Clinic or via a direct telephone call to the individual. Discussion of the study and informed consent will take place in a private clinic room either in UCSD Owen Clinic or at the AVRC to ensure participants can ask questions about the study. The initial visit will include a physical exam which will be undertaken in the same private room by an experienced practitioner.

***Confidentiality:*** Case report forms will be stored in locked secure cabinets at the AVRC. Only authorized persons will have access to the case report forms (PI, Co-Is, study coordinators). Information gathered as part of this study will be recorded on REDCap data management system supported by the UCSD Clinical and Translational Research Institute (CTRI) and the San Diego Supercomputer Center (SDSC) for IT and HIPAA compliant data and server support. Data entry will use coded numbers where possible. Access to the records on REDCap will be restricted to essential study staff. For analysis of data, only records with all PHI removed will be downloaded from REDCap. Electronic data will be stored on REDCap indefinitely. Laboratory samples taken as part of this study will be labeled with coded identifier thereby reducing the chance of loss of confidentiality from blood draws.

All members of the study team have undergone the CITI Biomedical Human Research and Good Clinical Practice training along with UCSD HIPAA training.

It is reasonably foreseeable that study participants may report information that ethically could require action. The most likely of these is suicidal ideation or thoughts of harming others. In instances where a clinician deems there to be a real and imminent threat, this will be reported to the subject's primary care provider and/or will escort the subject for assessment at UCSD emergency department. In cases where a threat is deemed real and imminent but the subject refuses emergency department assessment, then the study team will alert the police for assistance.

## 17. POTENTIAL BENEFITS

There is no guarantee that participants will directly benefit from being in this study or upon completion of the study. However, what is learned from this study may help other people who are infected with HIV.

## 18. RISK/BENEFIT RATIO

Overall the risks of participation in the study are thought to be low as discussed above. The therapy offered for rapid ART is already established standard of care for individuals with a new diagnosis of HIV and have shown benefit in this population. The behavioral intervention was not associated with adverse events in a pilot study performed at UCSD and so it is reasonable to assume that the risk associated with this is low.

Given the low risk of the study and the possibility of improved re-engagement in care of PWH-OOC, it is reasonable to expect the risk/benefit ratio of the study is favorable.

## 19. EXPENSE TO PARTICIPANT

No additional expenses to the participant are expected through their participation in the study. Every effort will be made through our case-management team to facilitate insurance coverage and linkage with care. Travel expenses will be available to all participants who are unable to cover their own travel expenses.

## 20. COMPENSATION FOR PARTICIPATION

Participants will receive compensation for attending the following visits:

1. Screening visit - $20
2. Completing the week 4 quantitative survey - $20
3. Participating in a focus group - $50
4. Attendance at week 24 study visit - $50
5. Attendance at week 48 study visit - $75

The most a participant can receive for study participation is $215.

Subjects will be able to park free while visiting our clinic in the parking slots allocated for our patients. Should a subject express a need for a meal, ride share, taxi or bus fare, we will provide transportation and/or meal vouchers to the subject by way of our patient discretionary funds.

## 21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Drs. Susan Little (PI), David Smith, and Thomas Martin currently have privileges at UCSD Medical Center in the Department of Medicine; Division of Infectious Disease and are licensed and certified by the State of California to perform all the medical procedures discussed in the protocol at UCSD. In addition to having privileges with UCSD Medical Center, Dr. Susan Little has privileges at the VA Medical Center.

Dr. Little will serve as the main PI and accept responsibility for all aspects of the protocol and the overall conduct of the study. The co-investigators will serve as after-hours/research study doctor(s) on-call, in Dr. Little's absence.

Dr Laramie Smith PhD is an assistant professor at UCSD. Dr Smith will have access to subject data, which includes identifiers, as part of her role in providing the intervention 60-Minutes-for-Health.

Helene Le and Joseph Lencioni, MABMH will serve as the regulatory affairs administrators for this study.

The AVRC nurses (NP: Aurora Verduzco-Gonzalez; RNs: Alina Burgi, Stephanie Solso and Steven Hendrickx) will be involved with the consent process and study visits. The study nurses are all licensed by the State of California.

DeeDee Pacheco, DeLys Brooks, Christopher Houston, Rebecca Gonzalez, and Jessica Lloyd will perform all lab duties for this study.

Liliana Harkness, Audrey Sanchez and Kelly Walsh will serve as staff research associates and assist the study nurse in performing study procedures.

Leticia Muttera PharmD and Niamh Higgins, PharmD are our site pharmacists and will assist with the immediate ART procedures.

Tara Tenenbaum and Audrey Sanchez will be responsible for QA/QC of study related data.

Support of the statistical portion of this study will come from Christy Anderson, MS Department of Medicine. These data will include PHI information.

Miriam Zuazo and George Lara are case managers and will assist with the linkage to care procedures.

Marvin Hanashiro and David Vance are the outreach coordinators for this study. They will help with recruitment of new subjects.

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**23. FUNDING SUPPORT FOR THIS STUDY**

This is an investigator sponsored research (ISR) project supported by Gilead Sciences, Inc.

**24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT**

None.

**25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER**

None.

**26. IMPACT ON STAFF**

The AntiViral Research Center (AVRC) is an HIV/AIDS research facility. The nurses and other study personnel assigned to this study are funded by the grant.

**27. CONFLICT OF INTEREST**

Gilead Sciences, Inc. paid a one-time consulting fee and travel reimbursement in the $500 - $9,999 range to Susan Little, M.D. (PI). She provided consulting to Gilead in the form of a single lecture given on 12/6/19 at the Gilead HIV Advisory Program - "Rapid Start: Implementation Insights", which took place on December 5-6, 2019 In Foster City, CA. A 700-U and Addendum Form has been submitted to the CTO and COI office. Dr. Little stated that she intends to keep her interest and obligations separate from those of the sponsor by: “I am willing to provide infrequent educational updates, sponsored by Gilead, to other researchers (as with the lecture given on 12/6/19) related to my own research interests. I will not embark on any greater level of financial relationship with this study sponsor (i.e., speaker’s bureau) while engaged in studies sponsored by the same entity.”

Dr. Thomas Martin has no conflict of interest with the study sponsor funding this study. In addition, no other study staff member or study investigator has a conflict of interest with the study sponsor funding this study.

**28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES**

None.

**29. OTHER APPROVALS/REGULATED MATERIALS**

None.

**30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT**

Not applicable – The participants enrolling/participating in this study will have the ability to:

- Understand, i.e., the ability to comprehend the disclosed information about the nature and purpose of the study, the procedures involved, as well as the risks and benefits of participating versus not participating;
- Appreciate, i.e., the ability to appreciate the significance of the disclosed information and the potential risks and benefits for their own situation and condition;
- Reason, i.e., the ability to engage in a reasoning process about the risks and benefits of participating versus alternative, and

- The ability to express a choice about whether or not to participate.