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Expanding the Menu of HIV Prevention Options: A Qualitative Study of Experiences with Long-Acting Injectable Cabotegravir as PrEP in the Context of a Phase II Trial in the United States

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Abstract

Adherence challenges with oral pre-exposure prophylaxis have stimulated interest in alternate modes of administration including long-acting injections. We conducted 30 in-depth interviews with 26 male trial participants and 4 clinical providers in a Phase IIa study (ÉCLAIR) evaluating the use of long-acting cabotegravir (CAB-LA) injections in New York and San Francisco. Interviews exploring attitudes and experiences with CAB-LA were audiotaped, transcribed, and analyzed using thematic content analysis. Despite a high frequency of some level of side effects, almost all participants reported being interested in continuing with CAB-LA, versus a daily oral, due to its convenience and the perceived advantage of not worrying about adhering to pills. Providers reinforced the importance of CAB-LA as a prevention option and the need for guidelines to assist patient decision-making. Further research is needed on the acceptability of CAB-LA among men and women at higher risk for HIV in different settings.

Keywords

PrEP; Long-acting injectable; HIV; Risk behavior; Qualitative; Men; Providers

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Compliance with Ethical Standards

Conflict of interest Deanna Kerrigan received support via a GSK contract. Andrea Mantsios received support via a GSK contract. Robert Grant was an investigator on trials supported in part by ViiV/GSK. Martin Markowitz was an investigator on trials supported in part by ViiV/GSK. Patricia Defechereux was staff on trials supported in part by ViiV/GSK. Melissa La Mar was staff on trials supported in part by ViiV/GSK. S. Wilson Beckham received support via a GSK contract. Paige Hammond received support via a GSK contract. David Margolis is an employee of ViiV Healthcare. Miranda Murray is an employee of ViiV Healthcare.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Introduction

Since the beginning of the epidemic, HIV has been responsible for an estimated 35 million deaths and has infected approximately 70 million people worldwide [1]. The disease continues to spread with approximately 2.1 million new infections in 2015 [2]. In the United States (U.S.), there are an estimated 1.2 million people living with HIV (PLHIV) [3]. Although there has been a 19% decline in overall HIV diagnoses between 2005 and 2014, the rate among men who have sex with men (MSM) rose 6% over this period, largely due to the increase in diagnoses in MSM of color, who bear a disproportionate burden of HIV [4, 5]. The U.S. Centers for Disease Control and Prevention (CDC) estimates that if the current incidence rates continue to increase, 1 in 2 Black MSM and 1 in 4 Latino MSM will be diagnosed with HIV in their lifetime [5].

Tenofovir-based pre-exposure prophylaxis (PrEP), a daily oral antiretroviral that reduces the risk of HIV acquisition, is one component of comprehensive prevention efforts. Successful trials of PrEP agents have shown reductions in HIV incidence ranging from 44 to 75% in diverse populations including MSM (iPrEX trial), heterosexual men and women (TDF2 trial), serodiscordant heterosexual couples (Partners PrEP), and injection drug users (Bangkok Tenofovir Study) [6–9]. Further reductions have been observed when adherence is accounted for. In the iPrEX trial, a 92% reduction in HIV acquisition was found when comparing those with and without detectable blood levels of the study drug [6]. Despite these successes, two trials conducted among women, the FEM-PrEP and VOICE trials, notably failed to find efficacy [10, 11]. Researchers have attributed differences in efficacy in daily oral PrEP to lack of adherence, with less than 24% of uninfected women in the FEM-PrEP study having target levels of the drug tenofovir [10, 12]. When examining the various PrEP clinical trials, there appears to be a dose–response relationship between adherence and risk reduction, highlighting the importance of optimal adherence [13].

Research among potential PrEP users has revealed varying but frequently high levels of willingness to use PrEP [14–22]. One multi-country study of potential users suggested that 61% were willing to use PrEP while other studies among Thai, American, Peruvian, Chinese, and Scottish MSM and transgender women found similar moderate-to-high willingness to use PrEP, even in the presence of low awareness [14–18, 23]. However, relatively low willingness has been noted in specific populations, including Canadian injection drug users (35.4%) and Australian MSM (28.2%) [19, 20]. Among MSM in the U.S., a key population for HIV prevention, studies have found moderate-to-high willingness to use PrEP. Two recent studies found that 55% of individuals in a sample of 184 MSM and transgender women in New York City were willing to use PrEP while 60% of Black MSM at a community event in the southeastern U.S. were willing to use PrEP [24, 25]. The generally high willingness to use PrEP, combined with the efficacy observed in clinical trials, has generated optimism in utilizing PrEP as one component of comprehensive HIV prevention programs.

Nevertheless, numerous barriers to successful PrEP implementation exist including slow uptake, poor adherence, potential risk compensation behaviors and costs associated with

a complex rollout program [14]. Despite studies that report a willingness to use PrEP among populations at higher risk of HIV and an estimated 1.2 million Americans who have behavioral indications for use per current CDC guidelines [26], uptake has remained limited [27]. Between July 2012 (the time of FDA approval) and March 2013, only 1774 people in the US were prescribed PrEP [28]. Over the past couple years, the initiation rate appears to have increased [27]. Data from the IMS National Prescription Database indicates that 8,512 individuals have been prescribed PrEP since 2012, with increasing numbers of male users [29]. Given that only 39% of prescriptions are represented in this sample, we can extrapolate and estimate a total of 22,000 individuals have been prescribed PrEP in the United States between 2012 and 2015 [30]. PrEP initiation remains low among African Americans, Hispanics, women, and persons under 25 years of age [31].

Barriers to use may include perceived cost, concerns about long- and short-term health effects, self-perceived risk of acquiring HIV, and social stigma [32, 33]. These barriers are likely unequally distributed across subgroups of MSM. For instance, medical distrust and concern about health effects of PrEP have been noted as particularly significant barriers for Black MSM [24, 25, 34]. Provider-initiated barriers to PrEP use have also been noted, including limited awareness [33, 35–37]. For instance, although primary care provider (PCP) awareness of PrEP has increased with time, in 2015, 34% of surveyed PCPs were not aware of PrEP [35].

In addition to slow uptake, sub-optimal adherence hinders the potential benefits of PrEP [6, 10–12]. Thus far, limited research has been completed on real-world adherence to oral PrEP [38–40] but suboptimal adherence is expected to be an issue, particularly given current experiences with antiretroviral therapy for treatment of HIV and post-exposure prophylaxis for those at risk for contracting HIV [36]. Qualitative research among providers indicates a concern that adherence may be an even bigger issue outside clinical trial settings and that adherence may be particularly difficult to achieve in populations at higher risk for whom PrEP is best suited [36].

Alternative delivery mechanisms, including long-acting injectable (LAI) PrEP may address some of these limitations. Similar to injectable contraception, LAI PrEP would be administered through periodic injections in a clinical setting [41]. Cabotegravir (CAB), an integrase inhibitor, is currently being evaluated for use as a LAI PrEP agent [41–43]. A phase IIa trial (ÉCLAIR) was conducted between March 2014 and March 2016 to evaluate the safety and tolerability of long-acting cabotegravir (CAB-LA) in male subjects. The trial indicated that CAB-LA was well-tolerated and preferred by participants to oral dosing [44, 45].

The limited research on PrEP delivery mechanisms indicates that LAI PrEP is of interest to patients [14, 15, 46–49]. A study among MSM of color in New York City evaluating preference for a daily pill or an injection every 3 months to protect against HIV found that 79% preferred a periodic injection compared to daily pills [46]. A qualitative study of American women at risk for HIV also documented substantial interest in LAI PrEP [47]. Conversely, among Thai MSM, pills were preferred, although injectables were also acceptable [15]. Importantly, a study among MSM in China found that among the

respondents who were not willing to consider oral PrEP, over half of them would consider injectable PrEP indicating that including an injectable option could yield increased uptake of PrEP [50].

LAI PrEP may address certain barriers to uptake and adherence, particularly those related to social stigma and convenience. Concerns about judgment from friends and family have been cited as a barrier to both uptake and adherence to PrEP by those at higher risk for HIV [32, 33]. As compared to daily pills, LAI PrEP provides a more discrete option that individuals can access periodically in the privacy of a clinic. In addition, LAI PrEP may be a more convenient option than taking a daily pill, given challenges with remembering to take pills in the context of other competing demands in daily life. To date, limited research has been conducted among those who have used LAI PrEP, to inform future rollout beyond the clinical trial setting. Here, we qualitatively explored the views and experiences of patients and providers from the phase II ÉCLAIR trial of long-acting injectable cabotegravir.

Methods

Study Design

We employed a cross-sectional qualitative study of participants from the ÉCLAIR trial. The ÉCLAIR trial was a double-blinded, randomized trial evaluating the safety, tolerability, and acceptability of intramuscular injections of CAB-LA for HIV PrEP [44, 45]. The trial included 126 participants between March 2014 and March 2016. Participants in the ÉCLAIR trial were adult, HIV-uninfected men who were sexually active and at risk of HIV (e.g. one or more casual partner in the past 24 months), but not at high risk (e.g. three or more partners in the past 3 months, report of unprotected receptive anal intercourse, STI diagnosis in past 6 months). Participants were randomized to 4 weeks of oral cabotegravir pills or placebo followed by three injections of CAB-LA or placebo every 12 weeks. Participants from the CAB-LA arms of the ÉCLAIR trial were contacted for possible participation in the qualitative study at least 52 weeks after enrollment in ÉCLAIR. ÉCLAIR study staff at each site drew upon demographic data from the parent study in order to assist the qualitative research team with purposive sampling based on the characteristics delineated for the qualitative sample. ÉCLAIR study staff provided the qualitative research team with participants' age, race, ethnicity, and sexual orientation to ensure the participants enrolling in the qualitative sub-study met the sampling frame.

Data Collection Procedures

Thirty participants (twenty-six trial patients and four clinical care providers) were recruited from the New York (NY) and San Francisco (SF) ÉCLAIR sites. The sites had similar numbers of participants enrolled in the study (NY had 27, SF had 17) but the demographic make-up of the ÉCLAIR study sample at each site differed with the NY site having 56% MSM, 41% African American, 22% Hispanic, 44% Caucasian, 15% Asian and the SF site having 94% MSM, 0% African American, 12% Hispanic, 65% Caucasian, 12% Asian, and 24% other. Data collection occurred between June and August 2015. Participants were contacted by the ÉCLAIR trial staff who provided initial information on the study and its objectives. Those who expressed interest were referred to the qualitative study team for

verbal informed consent. The ÉCLAIR staff recruited a diverse sample in terms of sexual orientation, race/ethnicity, and CAB-LA experiences to the extent the parent study sample allowed.

Patient interviews were held at the local ÉCLAIR clinic sites in private rooms. All interviews were anonymous and conducted by study staff trained in qualitative methods. The interviews were audiotaped for purposes of later transcription. The semi-structured interviews were facilitated by a flexible guide of open-ended questions to elicit participant views, experiences, and stories. Topics of discussion included: injection experiences, perceived advantages/ disadvantages of daily oral and LAI PrEP, impact on relationships and sexual risk behaviors, appropriate candidates for LAI PrEP, willingness to pay for LAI PrEP, and service delivery preferences. Provider interviews explored perceptions around prescribing LAI PrEP. Patient participants were compensated $50 for the interview. The study was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

Data Management and Analysis

Patient contact information was managed by ÉCLAIR staff who conducted the recruitment. The qualitative study team used unique identifiers to label interview forms and audiotapes. No identifiers were included in the transcriptions of the anonymous in-depth interviews. The data was analyzed using iterative thematic content analysis [51]. After transcription, interviews were read multiple times in their entirety. A codebook was developed from an initial coding structure of a priori question-based codes from the original field guide and study objectives. Themes emerging from the data were discussed by the two independent coders and added to the codebook during the process of refining the thematic coding structure. All textual data was then coded in Atlas.ti© [52] for both a priori and emergent domains of interest [53]. Code output was synthesized across these key domains and salient themes were then extracted and developed from that output. Diversity in perceptions, experiences, and views related to LAI PrEP were explored across sampling categories (e.g. provider vs. patient), study sites, and population sub-groups (such as sexual orientation). Based on our interest in understanding and comparing and contrasting experiences of trial participants, the findings reported here include both deductive, question-based themes and themes that emerged from the data.

Sample Characteristics

As seen in Table 1, the sample included 15 trial participants from NY and 11 from San Francisco. Per the ÉCLAIR study eligibility criteria, all participants were male. The mean age in years was similar across sites, with most participants in their 30s (32 in NY; 39.5 in San Francisco). Approximately half of participants (8/15) in NY were MSM, while almost all (10/11) were MSM in San Francisco. The sample was more racially/ethnically diverse in NY (4/15 Caucasian) versus San Francisco (7/11 Caucasian) reflecting the demographics of the participants of the larger trial. Three participants had prior experience with PrEP in San Francisco compared to none in New York. Four were interested in using PrEP after their participation in the trial in San Francisco compared to 2 in NY. Four key informants (2 per

site) were also interviewed including two study investigators (both physicians) and trial staff (1 nurse and 1 study coordinator) from the ÉCLAIR sites.

Results

Experiences with CAB-LA: High Satisfaction and Interest, Despite Side Effects

Almost all participants (23/26) described some level of side effects associated with receiving CAB-LA injections. Side effects ranged from very minor (e.g. irritation or soreness at the injections site) to severe (e.g. fever and impaired mobility). Half (13/26) of all participants experienced moderate pain and soreness at the injection site for a couple of days post injection, with many using ibuprofen to manage the pain. A minority (5/26) stated that receiving the injection was similar to a "needle stick", meaning a brief prick that did not connote significant pain, and experienced just a "few hours of minor irritation." An additional small number (5/26) of participants experienced more pronounced reactions to the injections such as fever, chills, nausea and impaired mobility and difficulty sitting, which in some cases required medications (e.g. Tylenol with Codeine). While a few considered it, none of the participants withdrew from the trial due to these side effects.

Instead, there was significant consensus that while the injections were "not always pleasant," the side effects were worth the pain if long-acting PrEP was found to be effective. The majority of participants rated their satisfaction "very high" and almost all indicated their interest in potentially using CAB-LA. Only one participant stated that if he were to have sustained severe side effects such as the impaired mobility that he experienced during the trial, he may not continue. The idea of significant side effects being perhaps the only potential downside of CAB-LA was relayed by a participant from NY as follows:

> Yeah, so people might enjoy having the control of taking the pill every day or choosing when to and when not to. If they feel the need to stop or if they're having an adverse side effect it's a lot easier to stop the pill daily than have to wait for the injection to wear off after a while. So I think if someone was getting side effects (from CAB-LA), the pill would probably be a better option for them, but outside of that I think the shot is a little bit easier. –MSM, NY

The main drawback of the injections described by participants were the injection site reactions but other disadvantages were described as the large size of the needle being problematic for anyone afraid of needles and the "embarrassment" of exposing one's buttocks to receive the injection. Overall, acceptability of injectable PrEP was high among this sample. However, due to the sampling of lower risk participants in this Phase II trial, most participants did not perceive themselves to be at high enough risk to warrant PrEP use in the future. Participants noted that a change in their sexual behaviors or having an HIV positive partner in the future would make them want to be on PrEP and the injectable option would be their preference.

Preference for Injectable Versus Oral PrEP: Long-Acting PrEP as "Peace of Mind"

Participants described the convenience of receiving injections every 3 months and the perceived advantage over not having to worry about adhering to a daily oral regimen. Most

reported long-acting PrEP as being preferable to oral PrEP. The convenience and simplicity was relayed by many who suggested that with CAB-LA, "you don't have to think about it anymore" or at least not "all the time." The sentiment that a daily pill can be "burdensome" to some people was common, with some participants remarking even "highly educated," or "organized people," or those "with a lot of time" forget to take pills once in a while. This convenience was described by many participants as an easy alternative that they would recommend to those already on oral PrEP.

> Oh totally, especially if they're already on PrEP, on Truvada, I would definitely recommend this as an alternative. And the fact that they don't have to remember to take it every day, I think would make a big difference and people probably don't need to be convinced very hard, or very much, to make the switch. –MSM, SF

Given the possibility for non-adherence, many participants described CAB-LA as conveying a certain "peace of mind" as they would not need to remember to take a daily oral regimen. With CAB-LA, many found that they could be less worried about adherence for themselves, as well as their sexual partners. The idea of being able to "play safely" and "be spontaneous" assumes that these individuals can potentially prepare for the HIV risk that might arise unexpectedly. This perception was particularly common among the MSM participants and in particular among MSM participants from San Francisco. The quote below relays the highly dynamic nature of HIV-related risk that many participants conveyed and how CAB-LA fits more easily into their lives and desire to "play smart."

> I'm thinking why not do injectable PrEP because there could be that one night where you're not even planning for that, you're like, oh wait, I have to take pills for a week before I even consider doing this. Because for men who have sex with men, being spontaneous is there. The hookup culture is so prevalent, where I think it's just smarter to take injectable PrEP. –MSM, SF

Several participants noted the desire not to become HIV-infected due to what was termed "one stupid mistake," whether it is not using a condom in a given act or forgetting daily oral PrEP. CAB-LA allowed for greater assurances against this possibility and was perceived as offering ongoing protection. Interest in using CAB-LA to avoid this type of unexpected risk was more pronounced among MSM participants, who more commonly reported engaging in multiple sexual partnerships than did the heterosexual participants. This was particularly prominent among MSM from San Francisco, where oral PrEP was reported as becoming common and described as almost normative among MSM. Other participants also remarked on the fact that CAB-LA afforded more confidentiality and privacy than daily oral pills, since there was less chance someone would be seen taking PrEP via an injection. This privacy and lack of stigma that could be associated with being on PrEP was seen as an additional advantage of CAB-LA.

Being a "Responsible" Sexual Partner in the Era of PrEP

Despite earlier stigma and condemnation towards those taking oral PrEP when it was first approved for use, MSM participants, and particularly MSM in San Francisco, described a prevailing culture whereby men were now expected to be on PrEP to be seen as safe sex partners.

The notion of the "Truvada Whore" [54] assigned to those taking PrEP in its early days has begun to decrease, according to many participants. Instead, participants suggested that there was actually increasing stigma linked to not being on PrEP as this was seen as being "irresponsible" towards the gay community. Several participants indicated that MSM-oriented dating sites and apps include information regarding whether the person is on PrEP, and one can select potential sex partners based on this criterion. As such, some participants indicated that there was a replacing of the concept of the "Truvada Whore" [54] with that of the "PrEP Hero" [55], connoting the idea that those who are taking PrEP are pioneers and "responsible citizens" helping to curb the epidemic and "End AIDS" [56].

Some participants suggested that while the desire to prevent HIV was a positive trend, it also had some unexpected consequences. For example, some participants reported the ability to have daily oral PrEP reimbursed through their insurance company, while others found it more difficult to be on PrEP as they could not afford it. Therefore, the ability to access and pay for PrEP can be a divisive issue and mark distinctions of socio-economic status among individuals within the gay community, especially in San Francisco. There was fear among a few participants that they would be seen as "a bad gay man" if they were not taking PrEP, and not seen as attractive sexual partners. On the issue of cost, most participants stated that they would be willing to pay around $100 per month for CAB-LA ($106 mean; range $10–$300), with the idea that it would most likely be covered by insurance through a co-pay.

Many participants felt that PrEP including CAB-LA had the potential to increase sexual risk behavior (e.g. condomless sex), due to lowered HIV risk perception and the idea that PrEP makes people feel "invincible." There was a sense that this type of increased sexual risk-taking was occurring in the gay community in San Francisco. However, only a few participants actually reported increased risk taking due to being in the trial and their perception that they were receiving the drug (LA cabotegravir) as opposed to the placebo. In New York, several participants specifically noted they felt that they engaged in less risk while being on LA cabotegravir and in the trial due to periodic reminders to "stay safe," risk-reduction counseling, and receiving free condoms from study staff.

Beyond the Trial Setting: Who, Where and How to Best Deliver CAB-LA

When asked who are the "right people" for CAB-LA versus oral PrEP, participants including providers, commonly suggested that people with adherence challenges were the right people for CAB-LA. This involved those with "unstable lives," "lack of routine," or an "erratic schedule" such as migrant/mobile populations, homeless, substance users, or young people. Additionally, populations at "high risk" (serodiscordant couples, sex workers, MSM, IDU, etc.) were commonly thought of as "good candidates." In the case of MSM, particularly in San Francisco, many participants said this should include all MSM because risk behaviors change quickly and are dynamic. Similarly, a heterosexual man in NY suggested that risk was prevalent in his inner-city community, and that CAB-LA could really benefit "everyone." Young women, and/or people in general, in Sub-Saharan Africa were discussed as a critical group, particularly given prevailing inequitable gender norms and the idea that women can get an injection without partner knowledge, allowing them more autonomy

over their sexual health. Overall, participants indicated that CAB-LA is for people and communities who are "comfortable with needles."

Participants felt that clinics, similar to the ones they attended during the trial, or their doctor's office would be appropriate places to receive CAB-LA. Some, particularly gay men in San Francisco, suggested the role of community health centers as potential sites, while providers in New York discussed the importance of mobile outreach to specific population groups or geographic communities who may be less likely to access care. There was also some mention of having CAB-LA available in pharmacies. However, participants noted the need for someone who is "skilled" and well "trained" to administer injections given the fact that CAB-LA is administered as an intramuscular injection, hence the need for large needles and the potential side effects from the injection. For many this was specifically a clinician such as a doctor or a nurse. Very few participants could imagine giving themselves this type of injection as indicated below.

> To me that means that you need to be in a safe environment and with a trained person– to me the drug that's being administered is not something that you can just do on your own… it needs to be done by a professional. It's not like if you're drawing blood, like if you have diabetes or you're just taking an insulin shot or an EpiPen shot. –Heterosexual male, NY

Providers' Views and the Need for Clinical Care Guidance and Tools

Providers interviewed suggested that CAB-LA was an important potential option, to be included in a menu of HIV prevention options. They were quick to note that CAB-LA may not be right for everyone, but that it would be a critical tool and should be made widely accessible. Those interviewed indicated that some providers may be more cautious to prescribe LA versus oral PrEP as it is harder to clinically manage and more difficult to discontinue quickly because the drug remains in the body for a longer period of time than daily oral PrEP.

Providers demonstrated few concerns about increased sexual risk behavior in the context of the trial or once it is commercially available in relation to taking PrEP (oral or injectable) as conveyed in the quote below:

> This is a lot like contraception…when the pill first came out, there was a huge hue and cry about the 'whores' that were going to take the birth control pill and how it was going to promote sexuality amongst unmarried women and da-da-da-da-da, and it's nonsense, right? Same about Truvada as PrEP, 'It's going to cause this, and people are going to be disinhibited.' There are going to be some people who are disinhibited, but it's also going to… prevent a lot of infections because people don't have unsafe sex all the time. They make mistakes, so it's a way of helping people prevent the – one thing we've learned from contraception is that the more options people have, the more effective it is. And to me this is a good example of another option if it works. –Provider, NY

However, some providers did raise the concern that CAB-LA may not encourage "mindfulness." That is, oral PrEP may be more effective in promoting reflection about

sexual decision-making, relationships, and planning for HIV prevention because one has the daily reminder of taking a pill. All providers emphasized the importance of trusting, open relationships and ongoing communication between individuals and providers about HIV/STI risk assessment and reduction, whether in the context of injectable or oral PrEP. Providers also acknowledged the dilemma that people who are less likely to adhere to daily oral PrEP may theoretically be those better served by injectable PrEP but adherence challenges are not eliminated by this modality since people still need to show up for appointments. One provider commented:

> [Injectable PrEP] is going to possibly circumvent adherence issues if proven to be effective, which is a good thing, if it's really difficult for people to take a pill every day—but for some folks, it's harder to have to go to the clinic and have an injection every 3 months. –Provider, SF

Additionally, providers expressed the need for guidelines and screening and assessment tools to help when choosing to start, stop and/or transition between oral PrEP and CAB-LA. They also emphasized the idea that potential candidates need information and a menu of options, not judgment, reflecting on prior judgmental attitudes in the media and broader community towards oral PrEP use, as one provider noted: "*We should celebrate people who act to protect themselves."* –Provider, San Francisco

Discussion

Given the convenience, ease of use and peace of mind associated with CAB-LA, as well as adherence challenges associated with oral PrEP, CAB-LA was seen by those who participated in this qualitative study as an important additional HIV prevention option, which may also be appealing to many who are interested in PrEP. The ability of CAB-LA to allow people to have more spontaneity and control around and over sexual health was seen as a key positive feature by many participants, given the often dynamic and unanticipated nature of HIV risk.

Study participants, particularly those from San Francisco, described an emerging "play safe" culture, where PrEP was seen as allowing people to engage in sexual relationships with lower levels of HIV risk. Given the known challenges with daily oral PrEP adherence, many felt that CAB-LA was the "safer" of the two PrEP options. In such a "play safe" culture, there appeared to be decreasing levels of stigma associated with PrEP use overall. This was discussed as a means to reduce HIV risk and be a "responsible" sex partner, casting a positive light on a kind of prevention activism that could potentially have a positive impact on sustained risk reduction [57]. Several NY study participants reported reduced sexual risk taking during the study, echoing recent findings from a PrEP demonstration project indicating that the majority of patients used other HIV/STI risk reduction strategies in conjunction with PrEP use [58], perhaps adopting what has been called a "preventionist identity" [59]. However, participants also remarked on the need to balance "rights" and "responsibilities" linked to HIV prevention and risk reduction strategies, including the need to respect and not stigmatize those who may not choose or be able (e.g. due to financial constraints or lack of insurance) to use PrEP.

Providers were also positive about the potential contribution of CAB-LA as part of a "menu" of HIV prevention options. However, they noted the need for clinical and practical caution and mindfulness around sexual health, and highlighted the need for guidance and tools to determine when and how to employ its use. Additionally, CAB-LA requires that providers actively manage their patients as there is some complexity related to switching patients to CAB-LA from daily oral regimens and vice versa. Given both the potential for changing levels of an individual's risk and the fact that PrEP (whether oral or injectable) does not offer protection from other sexually transmitted infections (STI), open and trusting patient-provider communication about sexual behaviors was seen as critical for both oral or injectable PrEP [27]. While participants in this study reported a high level of engagement and comfort with providers at the participating sites, consideration must be given to how to create enabling environments for potential PrEP users to engage in dialogue with their clinicians. This includes communication around whether CAB-LA or oral PrEP is right for them in a given moment, particularly given the potential for medical mistrust to impede access and uptake [25, 60].

Our findings indicate that future quantitative work in the area of CAB-LA should continue to assess the role of side effects on interest in use, and possible changes in sexual risk behaviors. This includes both reduced risk behavior as well as the possibility for increased risk behavior through "PrEP optimism," such as decreases in condom use and, in turn, increases in other STI [61]. Despite participants saying that attending injection appointments every 3 months was feasible for them, they also felt that the fewer the visits, the more appealing the injectable option would be. Further qualitative research is needed to understand changes in interest and acceptability if CAB-LA injections are to be administered every 2 instead of every 3 months. Additional qualitative research that is longitudinal in nature and can follow participants' trajectories and experiences with CAB-LA over time would further strengthen and enhance findings from this study, as would work with other populations including women and higher risk groups, and in lower-income countries and generalized epidemics.

This study has several limitations including its crosssectional nature and its focus on solely men participating in a clinical trial. An important area for future research will be to explore how feasible it is for individuals outside of a trial setting to attend regular medical appointments. Our ability to interview patients from varied ethnicities and socio-economic backgrounds was limited by the parent trial study population in the given clinics. The participants appeared highly motivated to contribute to science and HIV prevention. By design, the sample of key informants was limited to investigators and staff involved in the ÉCLAIR study and the providers involved were highly skilled and dedicated to the advancement of PrEP, as opposed to a more "real world" clinical care setting. Future research should include exploring the perspective of staff outside of a study setting who would eventually be responsible for provision of injectable PrEP.

Findings from this work have several implications for future research and implementation. Overall, among our study participants, CAB-LA was found to be highly acceptable and feasible. Injection side effects, while common, were not characterized as a significant deterrent to use. Most were interested in CAB-LA if they were to use PrEP in the future.

This study involved a lower risk population involved in a clinical trial. It is necessary to expand these inquiries to explore feasibility and acceptability of injectable PrEP beyond the trial setting and with higher risk groups. CAB-LA may be a key prevention option for individuals who have difficulty adhering to an oral regimen or who prefer this modality.

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Table 1

Select demographic and behavioral characteristics of male trial participant sample (n = 26)

Variables	New York (n = 15)	San Francisco (n = 11)
Mean age in years (range)	32 (22–58)	39.5 (25–59)
Sexual orientation	8/15 MSM	10/11 MSM
	7/15 non-MSM	1/11 non-MSM
Race/ethnicity	4/15 Caucasian	7/11 Caucasian
	5/15 African American	2/11 Asian
	3/15 Hispanic	1/11 hispanic
	3/15 Asian	1/11 Native Hawaiian
PrEP use prior to trial	0/15	3/11
Post-trial PrEP plans	2/15	4/11