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ORIGINAL ARTICLE

Lenacapavir: Patient and healthcare provider perceptions and the potential role for a twice-yearly injectable HIV treatment

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Abstract

Background: The twice-yearly, long-acting lenacapavir (LA LEN) antiretroviral therapy (ART), when combined with an optimised background regimen, provides a subcutaneous injectable treatment option for people with HIV. This study aimed to understand the preferences, barriers and facilitators for uptake and implementation of LA LEN, with a view to informing clinical implementation.

Methods: In-depth qualitative interviews and focus groups with purposively sampled people with HIV and healthcare workers (HCWs) from UK HIV services were conducted. Transcripts were analysed using summative and conventional content analysis.

Results: Thirty-four people with HIV with varied ART experience were recruited from two HIV services. Participants included 22 (65%) identifying as cisgender men and 12 (35%) identifying as cisgender women; median age was 55 years (range 26–76 years). Fourteen HIV HCWs took part in three focus groups. Four key themes and 12 subthemes were identified: LA LEN as a treatment option; LA LEN versus oral ART; switching considerations; and administration of LA LEN. The majority (88%) of people with HIV were interested in switching to LA LEN if offered. Preference was markedly reduced if an oral ART pairing was required. Convenience of the dosing schedule, reduced pill burden and issues around stigma were reasons for interest in LA LEN, but concerns regarding efficacy, dosing interval windows, monitoring and side effects were described. HCWs felt the benefit of LA LEN was as a treatment option for those with adherence issues, drug resistance and a high pill burden. Broader use of LA LEN raised concerns over drug resistance, delivery capacity and storage.

Conclusions: LA LEN was viewed as a preferable treatment choice for many people with HIV, provided an all-injectable regimen was available. Feasibility assessments for provision of injectable ART and research on its potential for self-administration are needed.

KEYWORDS

community perceptions, HIV, long-acting injectable ART, long-acting lenacapavir, qualitative research

INTRODUCTION

Since the introduction of antiretroviral therapy (ART), HIV incidence and prevalence has fallen in most countries worldwide, though the total number of people with HIV increases year on year [1]. In the UK over 100 000 people are currently accessing HIV care [2] and ART has led to markedly improved medical outcomes including high rates of viral suppression, improved immune functioning, reduced HIV-related morbidity and mortality, near-normal life expectancy and a better quality of life [1, 3, 4]. As such, HIV is now a manageable long-term condition provided people with HIV maintain a lifetime adherence to ART [1, 5]. Adherence can be defined as the way a person's health behaviour corresponds with the recommendations of a healthcare provider [6], which, for those with HIV, means taking ART, usually daily, as prescribed.

Despite the benefits of oral ART, some people struggle to adhere to the stringent daily dosing regimen resulting in treatment failure, viral resistance and onwards transmission of the virus [7]. Factors influencing non-adherence stem from individual factors (e.g., pill burden, pill fatigue, denial, substance use, mental health issues, side effects), societal factors (e.g., stigma, discrimination, lack of social support) and healthcare system factors (e.g., trust or satisfaction with a healthcare provider, ineffective counselling service); these factors can be intertwined and non-adherence is often multifactorial [8]. Alternative approaches to treatment, for example, injectable ART, may be helpful in addressing adherence challenges, particularly where an individual is experiencing pill burden, pill fatigue, privacy or disclosure concerns or treatment stigma.

A long-acting (LA) ART formulation of cabotegravir (CAB) and rilpivirine (RPV) administered via intramuscular injections every 2 months is already available in the UK and several other high-income countries [9]. However, specific eligibility criteria must be met, [10, 11] limiting its uptake in the UK. Arguably those who would be most likely to benefit as regards improving treatment adherence are considered ineligible [12, 13]. Thus, additional injectable antiretroviral drugs are needed to expand LA treatment options.

A novel LA injectable option is lenacapavir (LEN), a first-in-class HIV-1 capsid inhibitor hindering viral replication at both early and late phases of the viral lifecycle [14–16]. LA LEN, administered either via twice-yearly subcutaneous injections or as a weekly tablet [17], has demonstrated impressive rates of viral suppression in both highly treatment-experienced (HTE) people with HIV [18] when paired with a background optimised background regimen. LA LEN has the capability to be an important treatment option in HTE individuals, particularly those with limited treatment options [19]. LEN is further being developed for future therapies focused on synchronous long-acting oral and injectable formulations providing a diverse range of options to make sustained virologic suppression accessible to the majority of people with HIV while addressing individual needs and preferences and reducing barriers to care.

In order to optimise LA LEN, an understanding of the personal preferences, and the potential barriers and facilitators for uptake and implementation in clinical practice is necessary. We conducted a qualitative study with a diverse range of people with HIV and HIV healthcare workers (HCWs) to the explore preferences and views of LA LEN in HIV clinical practice.

METHODS

Study design

Semi-structured qualitative interviews and focus groups were conducted with people with HIV and HCWs, respectively, who were recruited from two UK HIV services. Findings are reported in line with the Consolidated Framework for Reporting Qualitative Research guidance [20].

Ethical and local governance approvals were obtained prior to commencing this research (Research Ethics Committee Ref. No. 17/YH/0328).

Participants

People with HIV accessing HIV services and aged 16 years or over were purposively sampled to enable maximum variation, by age, gender, ethnicity, sexual orientation, situation and HIV treatment status (triple class resistance, tolerability issues with limited treatment options, toxicity issues with limited treatment options, polypharmacy and pill burden concerns, and adherence challenged).

Procedures

People with HIV participants were recruited from HIV services in University Hospitals Sussex NHS Foundation Trust (UHS) and University Hospitals Oxford NHS Foundation Trust (UHO) between October 2022 and July 2023. Clinicians checked eligibility and approached individuals during clinic visits. If eligible and interested, they were given a participant information sheet and asked permission to pass their contact details to the study research team (KA/SS). Thereafter, a member of the study team contacted the individual to discuss the project and answer any questions. If they were happy to participate, an interview was scheduled at a mutually convenient time. Participants were offered their preferred method and location for the interview, that is, face-to-face, via telephone, at home or at their HIV service.

HCWs were invited via email to participate and offered the option of participating in a face-to-face or online (MS Teams) focus group. Prior to participating, all participants were required to provide consent; this was received either electronically (using Qualtrics [21]) or using a paper consent form.

Interviews and focus groups followed a semi-structured topic guide, developed from relevant literature and through consultation with a patient and public involvement representative. Participants were briefly introduced to the concept of LA injectable ART and the characteristics of LA LEN. The topic guide explored feelings towards LA LEN, perceived positives and negatives of LA LEN compared to oral ART, how it may impact quality of life, concerns regarding LA LEN and injectable ART, acceptability preferences of differing regimen schedules (e.g., LA LEN plus oral regimen vs. all-injectable regimen) and administration preferences (e.g., location). Additionally, HCW were asked about which specific group of people with HIV they felt may benefit from LA LEN specifically and LA injectable ART broadly, along with concerns regarding the implementation of LA injectable ART within their HIV service. Table 1 details the key questions and probes.

Interviews and focus groups were conducted by experienced qualitative researchers (KA and/or SS). Recruitment continued until data saturation was indicated (i.e., no new codes or themes relevant to the study objectives emerged). This was determined by constant comparison of new data with existing findings [22], and study team discussions following preliminary analysis of interview transcripts. We anticipated this would occur after recruitment of 30–35 people with HIV and 15–20 HCWs.

TABLE 1 Topic guide: key questions.

1. How would you feel about switching to an injectable treatment?
2. How would you feel about taking your HIV medicine this way rather than pills?
3. How do you think taking an injectable HIV treatment would affect you and your quality of life?
4. Do you feel having a 6-monthly injectable HIV treatment, like lenacapavir, might be better or worse than taking daily pill? If so, why? In what ways?
5. Would injectable antiretroviral medication be something you would want to switch to?
6. Would you still be interested if it needed to be paired with an oral pill? At what frequency would be acceptable for an accompanying oral pill? Would you have a preference for an all-injectable regimen? Why?
7. What would be your preferred administration? Would you be comfortable self-administrating at home or prefer to see a HCW? Why?
8. If it was to be conducted by a HCW, where would you like to see that person (e.g., at home, community pharmacy, GP, HIV clinic)?
9. If you were thinking of switching to an injectable ART what would be your concerns? Why? How could these be addressed?
HCWs were asked a modified version of the above that included the following questions:
10. How do you feel about delivering 6-monthly subcutaneous injections to your patients? What factors make/would make this easier? Or harder?
11. Which group of patients in your care do you think would benefit most from injectable ART and why? Are there groups for whom injectable treatment is inappropriate?

Abbreviations: ART, antiretroviral therapy; GP, general practice; HCW, healthcare worker.

Data analysis

Interviews were audio-recorded and transcribed verbatim, with care taken to anonymise patient- or staff-identifiable references. A combination of conventional and summative content analysis was conducted supported by NVivo software [23]. Initial conventional content analysis was inductive and commenced with immersion in the data. Codes were derived from transcripts to capture key thoughts and concepts. Codes were then refined and sorted into categories or meaningful clusters. Coding was supported by the qualitative lead for the project (KB), who conducted line-by-line coding on a sample of transcripts, and any discrepancies were discussed and resolved with the

TABLE 2 Participant characteristics.

Characteristic n (%) or median (IQR) People with HIV participants($n = 34$)	
Age (years)[a]	**55 (26–76)**
Gender	
Male	22 (64.7)
Female	12 (35.3)
Ethnicity	
White–British	14 (41.2)
Black–African	9 (26.5)
White–European	5 (14.7)
South Asian	2 (5.9)
Sexuality	
Gay MSM	17 (50.0)
Heterosexual	17 (50.0)
Years with HIV[a]	16 (3–32)
On cART	33 (97.1)
Triple class resistance	4
Tolerability or toxicity issues (with limited treatment options)	11
Polypharmacy and pill burden issues	9
Adherence challenged	4
Number of non-HIV medication	
0	13 (38.2)
1–2	11 (32.4)
≥3	9 (26.5)
Healthcare providers participants ($n = 14$)	
Gender	
Male	4 (28.6)
Female	10 (71.4)
Job role	
Staff Nurse	6 (42.9)
Consultant in HIV and Sexual Health	7 (50.0)
HIV Clinical Nurse Specialist	1 (7.1)

Abbreviations: cART, combination antiretroviral therapy; IQR, interquartile range; MSM, men who have sex with men.
[a]Median (interquartile range).

TABLE 3 Themes and subthemes.

Themes/subthemes
1. LA LEN as a treatment option
i. Representing an advancement in HIV care
ii. Perceived benefits of LA LEN
iii. Acceptability of other LA injectable ART
iv. Concerns about LA injectable ART
2. LA LEN versus oral ART
i. Advantages of LA injectable ART over oral ART
ii. Preferences for an all-injectable regimen
3. Switching considerations
i. Requirements for considering a switch to LA LEN
ii. Balancing risk
iii. Types of patient groups who are offered LA injectable ART
4. Administering LA LEN
i. Administration environment preferences
ii. Self-administration potential and preferences
iii. Practicalities of implementation

Abbreviations: ART, antiretroviral therapy; LA LEN, long-acting lenacapavir.

wider research team as required. Findings were discussed with the broader research team on the development of the initial coding frame, following refinement and on completion of the analysis. A summative approach was employed to describe patterns in views, specifically responses to questions around acceptability and preferences for LA LEN. An iterative and concurrent process of recruitment and analysis was used in the development and refinement of categories [23].

RESULTS

Thirty-four people with HIV completed interviews and 14 HCWs took part in three focus groups. Interviews lasted between 29 and 66 min and focus groups between 62 and 87 min. Twenty-eight people with HIV took part from UHS and 6 from UHO. Twenty-two were cisgender male (64.7%) and 12 were cisgender women, median age was 55 years (range 26–76 years), 14 (41.2%) were White British, 9 (26.5%) were Black African, 5 (14.7%) were White European and 2 (5.9%) were South Asian (Table 2).

Participants' views on LA LEN use and implementation have been grouped into four main themes with 12 subthemes (Table 3): (1) LA LEN as a treatment option; (2) LA LEN versus oral ART; (3) switching considerations; and (4) administering LA LEN. Table 4 details associated quotes.

LA LEN as a treatment option

The majority of participating people with HIV stated that they would be interested in switching to a twice-yearly injectable regimen (30/34, 88%). They viewed it as a significant advancement in HIV treatment, describing it as "amazing" and a "step forward", a sentiment echoed by HCWs (Subtheme: Representing an advancement in HIV care). They described the relief of not having to remember to take ART daily and how this would remove the worry around adherence. They spoke of the freedom a twice-yearly regimen would give and described how

TABLE 4 Themes identified and supporting quotes.

LA LEN as a treatment option
"It would stop me worrying for 6 months, I'd know I've got the injection, I've had it, so I just don't need to worry anymore...I can get on with everything and just forget". (P27) (Subtheme: Representing an advancement in HIV care)
"I'm very positive about injectables, particularly injectables that are more than 3 months, so 6 months is real progress". (HCW Group 1) (Subtheme: Representing an advancement in HIV care)
"At the moment I'd be quite hesitant...I've only just got myself comfortable with like the undetectable untransmissible and it's taken a lot of research to get my mind feeling better about it...[so] I wouldn't say I'd be 100% keen". (P24) (Subtheme: Concerns about LA injectable ART)
"There's a high risk...if they're not adherent to the medication, because lenacapavir if you're not partnering it with other active drugs you're going to get drug resistance very rapidly...it will fail and then you're much worse off". (HCW Group 2) (Subtheme: Concerns about LA injectable ART)
LA LEN versus oral ART
"When I started the antiretrovirals [it was] *because I was dying...so you know it is a constant reminder that something's wrong, really wrong...every day"*. (P13) (Subtheme: Advantages of LA injectable ART over oral ART)
"Imagine if it's an injection every 6 months?! It means you will forget even about the stigma...and it's hard work because when a friend is coming, I have to hide them...when you take them you hide them, you don't want anybody to ask you or see you are taking this tablet...". (P31) (Subtheme: Advantages of LA injectable ART over oral ART)
"Well there's no point [laughs]*...I may as well carry on with Eviplera...almost sounds as if the injectable part would be PrEP and then you are taking a top up pill...so then no, I'd just stick to the Eviplera*". (P28) (Subtheme: Preferences for all injectable regimen)
"You'd just have to sort of balance it up, in what is the least hassle...if you are having some sort of injectable and you are taking fewer pill, or pills not so often, then it would still be of interest to me". (P32) (Subtheme: Preferences for all injectable regimen)
Switching considerations
"Not having to take three pills every day would be nice, but it's not the major factor. The major factor is effectiveness, number 1, side effects, sustainability and security [of supply], *number 2"*. (P01) (Subtheme: Requirements for considering a switch to LA LEN)
"[What] *I am worried about is the long-term effects...with an injection I don't know, I might get some serious ones or are they going to be long-term?...If it's one big dose, is that really strong? How will that make me react?"*. (P19) (Subtheme: Balancing risk)
"In the past when I switched medication I was always told I couldn't go back to the previous one, because it wouldn't work. So, in a way it's a bit of a risk to switch off a working medication for convenience's sake". (P02) (Subtheme: Balancing risk)
"It's very different to what we initially thought...we thought it would be perfect for really chaotic people...who don't take tablets, hard to engage, and its completely the opposite...[it's being given to] *people who are good at coming to appointments and taking their tablets"*. (HCW Group 2) (Subtheme: Types of patient groups who are offered LA injectable ART)
Administering LA LEN
"I'd rather let people who know what they are doing actually do it...I have Tourette's and [I have] *involuntary spasms, so there would be a risk for me...I'd be more comfortable with a professional doing* [it]". (P17) (Subtheme: Administration environment preferences)
"I quite like the staff at the HIV clinic...I'd rather visit them than anyone else, I don't mind going...it keeps everything nice and neat. So bloods then injection". (P28) (Subtheme: Administration environment preferences)
"I don't think I would feel confident enough...if I don't take my pill properly I know...but I'd be worried that if I didn't administer it [the injection] *right, and you wouldn't know if you had or not"*. (P24) (Subtheme: Self-administration potential and preferences)
*"We're not especially well set up to deliver injectables at the moment...we are all learning iteratively about how to deliver care in this way...we need to work more on how services realign to deliver this kind of treatment". (*HCW Group 3) (Subtheme: Practicalities of implementation)

Abbreviations: ART, antiretroviral therapy; HCW, healthcare worker; LA LEN, long-acting lenacapavir; P, participant; PrEP, pre-exposure prophylaxis.

much more convenient and simpler it would be for their lifestyle. Individuals likened it to routine vaccinations and believed it would help to normalise living with HIV. One individual expressed regret that this option was not available when they were first diagnosed, indicating they would have been more inclined to start treatment earlier (Subtheme: Perceived benefits of LA LEN). HCWs described acceptability among patients currently on injectable ART (i.e., CAB/RPV) (Subtheme: Acceptability of other LA injectable ART) and the increased benefits of having a robust, twice-yearly LA injectable ART, particularly considering convenience concerns associated with the currently available LA CAB/RPV option (Subtheme: Perceived benefits of LA LEN).

Participating people with HIV did, however, have concerns about the efficacy of LA ART and questioned the rationale for changing a regimen they were comfortable with and believed to be effective. Additionally, concerns were raised about potential side effects, and participants wanted assurance that they could easily revert to an oral regimen if necessary. Three individuals expressed aversion to needles, while others described feelings of HIV/treatment fatigue and reluctance to undergo treatment changes. HCWs expressed similar worries about potential side effects

and the complexities involved in reverting back to previous treatments if such side effects arise. Furthermore, they highlighted concerns about the absence of partner agent drugs for LA LEN, the risk of developing drug resistance, and apprehensions about patient adherence to appointments, especially considering the longer 6-month intervals which might result in missed opportunities to address emergent issues quickly. Additionally, HCWs voiced concerns about the availability of injectable ART and emphasized the importance of ensuring equal and equitable access to this treatment option for all individuals in need (Subtheme: Concerns about LA injectable ART).

LA LEN compared to oral ART

People with HIV interviewed broadly considered the concept of LA injectable ART to be superior to oral ART. Similar to the aforementioned comments, individuals felt a key advantage of LA ART over oral regimens was the removal of needing to remember to take pills and the reduction in stress and guilt associated with poor adherence. They believed LA ART would be safer, especially for those with memory or adherence issues. Practical benefits, such as increased spontaneity, alleviation of travel concerns and restrictions, and feelings of safety at not needing to carry oral ART, were also expressed by participants. Indeed, individuals liked the discretion afforded by an injectable regimen, contrasting it with the embarrassment associated with taking pills in public. They discussed the emotional toll of daily pill-taking, which serves as a constant reminder of their HIV status and the negative experiences associated with this. HCWs widely echoed these benefits, highlighting the potential to enhance adherence, remove pill burden and emphasizing the significant advantage of future possibilities for self-administration (Subtheme: Advantages of LA injectable ART over oral ART).

Concerning drugs to accompany LA LEN in a treatment regimen, both groups felt that pairing it with an oral drug would negate the benefits of switching to an injectable ART. Indeed, only one in four (9/34, 26.5%) people with HIV were interested in using LA LEN if a daily oral pill was required (Subtheme: Preferences for all injectable regimen).

Switching considerations

Participating people with HIV identified several concerns regarding the potential switch to LEN. First, there were concerns about the strictness of the dosing window, with participants expressing the need for flexibility in scheduling appointments to accommodate their plans or unforeseen circumstances. Additionally, they raised concerns about the security of the LEN supply and the organization of appointments, emphasizing the importance of numerous reminders to prevent missed appointments. The efficacy of LA LEN was deemed the most critical consideration for many participants. They emphasized the need for LA LEN to be as effective as their current regimen in maintaining viral suppression and sustaining their undetectable status. A number of participants expressed a desire to do their own reading into the evidence base on LA LEN's efficacy and safety and stressed the importance of discussing any switch with a partner due to potential safety implications. Increased monitoring upon switching to LA LEN was deemed important by people with HIV, although excessive monitoring could negate the benefits of switching by increasing clinic visits and burden (Subtheme: requirements for considering a switch to LA LEN).

Concerns about potential side effects of LA LEN were considerable and prevalent among participants; many expressed anxiety about the lack of research on long-term side effects and the possibility of experiencing unwanted or unusual reactions. Participants emphasized the importance of detailed information on side effects before switching and the need for swift discussions with clinicians if side effects arise (Subtheme: Balancing risk).

Participants indicated that they would be willing to remain on LA LEN if side effects were comparable to their previous regimen. However, they emphasized the importance of having the option to revert to a prior regimen if intolerable side effects or viral rebound occur (Subtheme: Requirements for considering a switch to LA LEN). Four participants expressed concerns that unnecessary switches could limit their ART options if drug resistance were to develop, with two participants suggesting that this option should be offered when necessary, rather than as a broad treatment choice (Subtheme: Balancing risk).

HCWs were asked about the potential beneficiaries of LA LEN among people with HIV. They outlined a paradox between the theoretical beneficiaries and those who are, in reality, switched to LA injectable ART Specifically, HCWs discussed how individuals facing challenges such as adherence issues, stigma or disclosure concerns, chaotic lifestyles, polypharmacy, and high resistance could greatly benefit from LA LEN. However, in practice, only individuals deemed likely to adhere to appointment schedules and with histories of maintaining undetectable viral loads are offered LA injectable ART by healthcare services currently (Subtheme: Patient subgroups offered LA injectable ART).

Administering LA LEN

We explored preferences for LA LEN administration among participants and found that approximately three-quarters of people with HIV preferred LA LEN to be administered by a trained HCW. Individuals believed this would be easier, safer and more comfortable for them. Most had no specific preference regarding location of administration and considered locations such as their general practitioner's surgery, HIV service or a local pharmacy suitable. However, six participants stated they would prefer to receive their injection at their HIV service, as they felt it could conveniently coincide with other appointments such as blood tests, and they valued the positive relationships they had with staff at their HIV clinic (Subtheme: Administration environment preferences). HCWs highlighted an advantage of LA LEN being its potential for administration by various health services beyond traditional HIV clinic settings. However, there was a consensus that such an implementation would be intricate and necessitate thorough planning and research efforts (Subtheme: Practicalities of LA LEN administration).

Nine people with HIV expressed interest in self-administration due to the convenience it could offer. This view was particularly prevalent in those with prior experience with injecting medications like insulin or interferon. They did, however, emphasize the need for initial in-person training to ensure proper administration and expressed concerns or queries regarding storage, disposal, potential pain or discomfort, and ensuring correct administration (Subtheme: Self-administration preferences and considerations).

HCWs expressed satisfaction with LA LEN's subcutaneous route of administration, seeing it as a step towards facilitating potential self-administration for interested individuals in the future. However, HCWs raised concerns about the cost of LA LEN and its delivery and implementation in general. Specifically, HCWs voiced worries about the increased workload on services, which would include additional appointments, training sessions, and the need to follow up with individuals who miss appointments. They felt that rolling out injectable ART on a broader scale presented significant complexities which some admitted feeling ill-equipped to handle, highlighting a need for better understanding of optimal 'real-world' implementation (Subtheme: Practicalities of implementation).

TABLE 5 Summary of key findings.

Summary of key findings
• A twice-yearly LA LEN regimen would be a preferable treatment choice for many people with HIV. • Pairing LA LEN with a partner drug which aligns with the twice-yearly dosing interval was important and preference is markedly reduced if a regular oral ART pairing is required. • Convenience of dosing schedule, reduced pill burden and improving disclosure or experiences of stigma were considered key benefits. • Treatment efficacy and side effects were the primary considerations for people with HIV when considering switching to a twice-yearly LA LEN regimen. • Most participants said they would prefer a LA injectable ART treatment to be administered in a health setting, ideally their HIV service. Those interested in self-administration would require training to ensure competency and confidence. • HCWs raised concerns around service capacity and viral resistance if large numbers of patients were using LA LEN. • HCWs expressed concerns around equity of access to LA injectable ART broadly, with many who may benefit from it unlikely to be offered these treatment types due to stringent eligibility criteria.

Abbreviations: ART, antiretroviral therapy; HCW, healthcare worker; LA LEN, long-acting lenacapavir.

DISCUSSION

This qualitative study explored the perceptions and preferences of the community – both a diverse group of people with HIV and HIV HCWs in the UK – regarding the twice-yearly LA injectable LEN. LEN is a promising agent in the management of HIV provided it is equitably and effectively implemented. It is vital to understand the needs and perceptions of the community before implementing any new intervention, therefore this research is timely in informing policies, local practice and future development of the drug in combination regimens (Table 5).

Through the in-depth interviews and focus groups four key themes were identified: LEN as a treatment option; LEN versus oral ART; considerations around switching; and administration of LEN. Almost all the people with HIV we interviewed were interested in switching to LEN if offered; this aligns with other studies and highlights the prevailing desire to move beyond pill-based HIV treatments [24, 25]. This did, however, hinge on an all-injectable regimen being available, with considerably reduced interest if oral ART pairing was required. In line with other qualitative research on individuals who are already on LA CAB/RPV, our participants cited similar, albeit perceived, benefits which included convenience, freedom from pill burden, not needed to remember to take pills regularly, reduced stigma by not being reminded of HIV status, and reduced concerns of accidental disclosure as reasons for interest in LA LEN [26–29]. However, other studies have described participants on LA CAB/RPV struggling with clinic attendance and administration via injection [30]. This was not described by participants specifically in the current study;

however, they did state a preference for infrequent clinic visits. Given that the present study asked participants to consider LA LEN hypothetically, understanding 'real-world' experiences of those who are on this treatment is important to fully understand the impact and issues of LA LEN.

The extended dosing interval offered by LA LEN was considered particularly attractive, with participants in this study reporting its potential to alleviate treatment burden compared to the currently available 2-monthly LA CAB/RPV regimen. This is consistent with existing research indicating a preference for ART regimens with longer dosing intervals [26].

The uncertainty surrounding the choice of partner drugs to accompany LA LEN emerged as a concern among a number of those interviewed in our study. Pairing with partner drugs with a dosing interval that aligns with the twice-yearly injection schedule of LA LEN was considered important. Individuals perceived pairing with daily oral ART to significantly diminish the benefits of injectable ART and a mixed injectable/oral regimen was unacceptable to the majority. Current approved indications of LEN for HTE people with HIV is in combination with an optimised background regimen; due to extensive drug resistance and a lack of LA options currently with a similar dosing interval, this, at present, remains an unavoidable unmet need. Ongoing development is aiming to address this with several late-stage programmes currently underway. One such solution is the potential pairing of LEN with injectable CAB (two injectables, albeit with CAB requiring a 2-monthly dosing) for those with non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance [31]. These findings underscore the importance of tailoring treatment options to individual preferences and highlights the limited role for LA LEN pending availability of an efficacious all-injectable regimen. Other concerns, which align with reports elsewhere [32], include efficacy, dosing window intervals, monitoring and side effects, and emphasize the need for appropriate counselling prior to switching.

It is important to note that for many participants, despite no significant treatment challenges being reported, interest in LA LEN was motivated by the stigma related to their HIV status and the daily visual reminder in the form of their oral ART. These experiences echo factors documented in the literature as predictors of ART adherence [33]. The introduction of LA ART, particularly regimens with longer dosing intervals, holds great promise in addressing stigma-related barriers, including disclosure concerns. It is essential to recognize that stigma remains a prevalent issue in the lives of many people with HIV, impacting treatment outcomes [34, 35]. While LA ART may serve as a biomedical tool and contribute to reducing HIV-related stigma, it is imperative to comprehensively address structural factors that perpetuate stigma.

HIV healthcare providers echoed similar sentiments regarding the possible benefits of LEN, and LA ART in general, highlighting their potential to enhance patient adherence and reduce treatment burden. In line with other research [36], however, the HIV HCWs viewed the role of LEN currently as a targeted treatment option for those with adherence issues, multiclass resistance and those experiencing high pill burdens. LEN is not currently perceived as a first-line treatment option pending a suitable partner drug, availability of more data and competitive pricing. Additionally, HCWs felt the development of LA injectables broadly represented considerable promise but had similar concerns to those reported in other studies including concerns regarding clinical capacity to accommodate a change in treatment delivery in the face of stretched clinical services [37–39], management of missed injections, resistance development of LEN specifically, and equity in access [40].

The potential for self-administration of LA LEN emerged as an important difference given that current LA treatment (e.g., LA CAB/RPV) requires intramuscular injection by a trained HCW. Subcutaneous administration was noted by HCWs to be an extremely promising development. However, if self-administration were available, any change in delivery method raised multiple considerations around implementation among HCWs, including adequate training and counselling to ensure patient competency with injections and significant planning/management by clinics. Perhaps surprisingly, self-administration of LA LEN was not considered preferable by many people with HIV we interviewed who felt that HCWs would be better placed to ensure correct and comfortable administration. However, this may change with experience of injectable ART and training initiatives to assure competency.

HCWs further suggested that the stringent eligibility criteria for LA ART in the UK may inadvertently exclude individuals who could benefit most from this treatment modality and advocated for greater flexibility in eligibility criteria. This, it was felt, would improve issues of equitable access for patients, thereby maximizing the potential impact of LA injectable ART on improving HIV care outcomes. HCWs emphasized the importance of adopting a nuanced approach to patient accessibility. Addressing these concerns will be crucial in ensuring successful integration of this innovative treatment approach into routine clinical practice and maximizing its potential to improve outcomes for people with HIV.

Our study is limited by the inclusion of two UK regions, which is unlikely to be representative of people with HIV in other geographical locations or cultural settings. Second,

we interviewed only those who were engaged in HIV care and willing to participate in research, and so we were unable to represent the views of individuals whose engagement with care and research is poorer. Furthermore, we relied on self-reported hypothetical preferences instead of actual observed behaviour. References to attributes of a potentially available product were made rather than a specifically available treatment to the individual. This may have influenced the positive view of this treatment type. Despite these limitations, our findings may be useful in guiding the future development of LA LEN and ensure it matches patients' and HCWs' preferences, ultimately enhancing successful implementation.

Further research is required to explore the 'real-life' experiences pertaining to LA LEN in people receiving this treatment and HCWs delivering this treatment when it becomes more widely used. Additionally, future implementation research exploring different methods of administering LEN is important. In conclusion, our study adds to the growing body of evidence supporting the preference for LA ART as a paradigm-changing treatment tool, provided regimens are all-injectable and with long dosing intervals. The twice-yearly dosing interval of LA LEN goes further than existing LA regimens in addressing both practical and emotional barriers to treatment adherence and has the potential to significantly improve the lives of people with HIV if effectively implemented.

AUTHOR CONTRIBUTIONS

KA and SS contributed to the data collection, analysis, interpretation of data and drafting of the manuscript. KB contributed to the analysis, interpretation of data and critical revision of the manuscript. PC contributed to data collection and critical revision of the manuscript. FC and JHV contributed to the study concept, design, interpretation of the data, drafting of the manuscript and critical revision of the manuscript. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

KA has been an investigator on studies and received funding from ViiV Healthcare and Gilead Sciences Ltd. SS and PC declare no conflicts of interest. KB has been an investigator in studies, and received honoraria for training content development, from Gilead Sciences. JHV has received honoraria and research grants and been a consultant or investigator in trials sponsored by Merck, Janssen Cilag, Piramal and Gilead Sciences. He has received sponsorship to attend scientific conferences from Janssen Cilag, Gilead Sciences and AbbVie. FC reports grant funding from Janssen, ViiV and Gilead, and fellowship funding from Wellcome (300 088/Z/23/Z) and the National Institute for Health and Care Research (NIHR) UK (CL-2020-27-001).

DATA AVAILABILITY STATEMENT

Anonymised transcripts are available on request.

ETHICS APPROVAL STATEMENT

This study was approved by the UK Health Research Authority (HRA) and Yorkshire & The Humber—Bradford Leeds Research Ethics Committee (REC).

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