Abstract # 881

Understanding pain and anxiety experienced around long-acting injectable PrEP

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BACKGROUND

- Clinical trials and demonstration projects have shown that oral PrEP with a tenofovir-based regimen is very effective in preventing HIV among men who have sex with men (MSM) who adhere to the daily dosing schedule (1-4). In addition, IPERGAY has shown evidence of high efficacy with peri-coital dosing, or dosing of at least four pills a week. (5)
- Almost all individuals who have seroconverted while enrolled in a PrEP program have been found to have suboptimal adherence, either by self-report or by drug level in plasma. (2,5) We anticipate that as PrEP is scaled up beyond early adopters there may be more individuals for whom adherence to daily oral PrEP is a challenge.
- Long-acting injectable PrEP may improve adherence and acceptability compared to daily oral dosing, particularly for individuals who have difficulty adhering to a daily dosing schedule.
- However acceptability may be limited by anxiety about injections and concerns about injection site reactions, especially pain.
- We interviewed a subset of participants of the ECLAIR Study, a Phase 2 safety and acceptability trial of cabotegravir long-acting (CAB LA), to assess their experience with injections.

METHODS

- ECLAIR is a double-blind, randomized, multi-center study in 127 HIV-negative men at low risk of HIV infection during which IM injections of 800mg CAB LA or PBO (saline) q12 weeks X 3 cycles were given.
- This substudy approached 48 participants of ECLAIR who self-reported as MSM or male-to-female transgender women at 4 out of 10 sites (Columbia University, New York Blood Center, Rockefeller University, University of Pennsylvania) and offered the first 31 individuals who responded the opportunity to be interviewed. One individual who later reported no history of same-sex sexual activity and two men who received placebo are excluded from results presented here.
- Interviews were conducted a mean of 35 days after the final injection (range: same day to 84 days post-injection).
- Measures collected included pain assessments using a validated verbal pain scale from no pain to intense pain, a numerical pain scale (0-6), and a degree of "bothersomeness" scale (1-5); Likert-like agreement scales to statements around pain and anxiety around injections generally and CAB-LA in particular; intention to use CAB-LA if found efficacious and preference between daily oral pills and quarterly injections.
- Descriptive statistics were generated for demographics, sexual behaviors, adverse events, anxiety around injections, and interest in daily oral PrEP and long-acting injectable PrEP. We calculated chi-square and when appropriate, fisher's exact test, to test associations between interest in LAI-PrEP and demographic and behavioral predictors.

RESULTS

Injection experience

- 23/28 (82.1%) reported pain in the buttocks associated with the injections. Of those 23 subjects, 13 (56.5%) reported that pain lasted more than three days. For those who reported pain, mean duration ranged from 3 to 4 for the 3 injections (range 0.5 days to 9 days). Details on pain experienced are shown in Table 2.
- 21/28 (75%) stated the first injection hurt less than expected.
- Adverse events are shown in Table 3. Out of 17 participants queried about OTC medication to manage pain, 8 (47.1%) reported taking OTC for 1 to 4 days post-injection.
- One participant withdrew because of injection intolerance after the second injection.
- There was no correlation between any demographic factors and pain. There were no differences in pain report across trial sites.

TABLE 1. Summary of Sample Characteristics (N=28)

Characteristics		N	(%)
Age	<30	18	(64.3)
	30+	10	(35.7)
Race/ ethnicity	Black non-Latino	9	(32.1)
	Hispanic/Latino	4	(14.3)
	Multiracial	2	(7.1)
	White non-Latino	11	(39.3)
Identity	Other	2	(7.1)
	Bi	4	(14.3)
	Gay	19	(67.9)
	Queer	4	(14.3)
	Other	1	(3.6)
Education	High school or less	5	(17.9)
	Any college	17	(60.7)
	Graduate degree	6	(21.4)
Employment	Full time	12	(42.9)
	Part time	11	(39.3)
	Part time (student)	3	(10.7)
	Unemployed (student)	2	(7.1)
Income	<$20,000	8	(28.6)
	$20-$29,999	9	(32.1)
	$30-$49,999	5	(17.9)
	$50-$74,999	4	(14.3)
	>=$75,000	2	(7.1)
Housing	Live alone	6	(21.4)
	Live with parents / family	6	(21.4)
	Live with friends	11	(39.3)
	Live with domestic partner	4	(14.3)
	Live in a shelter	1	(3.6)
Partnership status	Partner/lover	5	(17.9)
	Boyfriend	9	(32.1)
	Casually dating	3	(10.7)
	Single	11	(39.3)
Partner HIV status among those with partners (n=14)	Knows partner is HIV-positive	2	(14.3)
	Thinks partner is HIV-positive	1	(7.1)
	Thinks partner is HIV-negative	3	(21.4)
	Knows partner is HIV-negative	8	(57.1)
History of STI in last 6 months (n=15)	No	14	(93.3)
	Yes	1	(6.7)
Condom use (n=13)	100%	8	(61.5)
	Less than 100%	5	(38.5)
Position (n=13)	More often top	6	(46.2)
	More often bottom	6	(46.2)
	Top and bottom equally	1	(7.7)

Table 2: Summary of (A) verbal and (B) numerical pain ((0-6) rating across 50 injections experienced by 17 participants

(A) Verbal Pain Rating	N during injections (%)	N after injections (%)
No pain	17/50 (34.0)	13/50 (26.0)
Mild pain	19/50 (38.0)	7/50 (14.0)
Minor pain	8/50 (16.0)	11/50 (22.0)
Moderate pain	6/50 (12.0)	11/50 (22.0)
Severe pain	0/50 (0.0)	5/50 (10.0)
Intense pain	0/50 (0.0)	3/50 (6.0)

(B) Injection	Mean pain Score (during injection)	Mean pain score (after injection)
First injection	1.06	2.19
Second injection	1.00	1.79
Third injection	1.13	1.78

Effect on daily life

- 3/17 (17.6%) respondents noted that they did not go to the gym or exercise for a few days after the injection.
- One participant who reported "flu-like symptoms" felt unable to go to work for a few days.
- 2/17 (11.8%) respondents noted that they delayed the timing of sex post-injection due to discomfort associated with the injection.

Anxiety

- Anxiety before the first injection was felt by 20/28 (64.3%), however this decreased to just 8/28 (28.6%) by second and third injections. There was no correlation between anxiety and pain.

Interest in the CAB-LA

- Despite discomfort and anxiety cited by a significant proportion, interest in the product remained high: out of the subset of participants queried, 15/16 (93.8%) reported that if proven effective, they would definitely or very likely use CAB-LA.
- In addition, 10/16 (62.5%) reported that they would prefer to receive injections of CAB-LA every twelve weeks over daily oral PrEP.

TABLE 2. Adverse Events (N=28)

Events	N experienced (%)	Mean "bothersomeness" score
Pain in the buttocks	24 (85.7)	3.2
Difficulty moving / walking	17 (60.7)	2.8
Pain changing positions at night	12 (42.9)	3.1
Swelling	6 (21.4)	2.7
Pain / difficulty falling asleep	5 (17.9)	3.7
Itching	4 (14.3)	2.0
Headaches	4 (14.3)	3.3
Redness	2 (7.1)	2.0
Hardening	2 (7.1)	3.5
Fever	2 (7.1)	3.0
Whole body aches	2 (7.1)	5.0
Unintentional weight loss	2 (7.1)	1.0

DISCUSSION

- CAB-LA injections are acceptable in the subset of ECLAIR participants included in this study. The pain profile is less focused on the injection itself and more on the post-injection period. While there was significant anxiety around injections, this decreased as participants gained experience with injections.
- Injections appear to impact the daily life of a small number of participants, however interest in CAB-LA remains quite high, even among those who suffered side effects.
- These findings suggest that patient education about CAB-LA should focus on informing patients about the true nature of pain associated with injections, and managing both expectations and anxiety. More research is required to develop accurate descriptions of the experience of the injections and to validate these findings on a broader scale.
- Given the results of the ECLAIR study which suggest that the dosing schedule for CAB-LA will be changed from Q12w to Q8w injections (6), additional research should be conducted to assess how the shorter dosing interval will impact interest in CAB-LA.

LIMITATIONS

- The small sample size means that the findings should be taken as very preliminary and as a foundation on which additional research can be designed and expanded.
- This study was conducted among men who reported behavior that put them at low risk for acquiring HIV and therefore may be considered of low relevance to the true target population for CAB-LA PrEP intervention. However our interviews reveal that while respondents are low-risk in this period, they report fluctuations of risk over their lifetime and can envision a period in the future when their behavior would make them good candidates for PrEP.

REFERENCES

(1) R.M. Grant *et al*, NEJM 363(27), 2587-99(2010).
(2) R.M. Grant *et al*. The Lancet Infectious Diseases, 14(9), 820-9 (2014).
(3) S. McCormack *et al*, Lancet 387(10013), 53-60 (2015).
(4) A.Y. Liu *et al*, JAMA Internal Medicine 176(1), 75-84 (2016).
(5) J.M. Molina *et al*. NEJM 373(23), 2237-46 (2015).
(6) M. Markowitz *et al*, 23rd Conference on Retroviruses and Opportunistic Infections, Boston, MA, Feb. 22-25 2016.

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