Use of long acting injectable antiretroviral therapy in perinatally acquired HIV in England

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Background

Long acting injectable anti-retroviral therapy (LAI-ART) is now an option for people living with HIV (PLWHIV). LAI-ART offers an alternative to oral treatment and can address challenges faced by people with perinatally acquired HIV (PaHIV), who may have lower rates of viral suppression[a], complex cumulative resistance[b], and significant barriers to adherence[c]. While LAI-ART has been demonstrated to be highly acceptable amongst young adults[d], real-world data describing its use and outcomes in PaHIV remain limited. We aimed to describe the characteristics, indications and outcomes of LAI-ART in people with PaHIV

Method

A survey was distributed through the CHIVA Young Adult Special Interest Group to centres caring for individuals with PaHIV or prior paediatric HIV care who received LAI-ART (cabotegravir, rilpivirine, and/or lenacapavir). Data collected included demographics, HIV and ART history, comorbidities, use of LAI-ART and immunological outcomes.

Results

Demographics and HIV background

21 patients from 5 centres of care were reported to have received LAI-ART and included in the analysis, all located in England. Participants were highly treatment-experienced with low CD4 nadir. There was significant baseline comorbidity as detailed in Figure 1.

Figure 1. Baseline characteristics

	N=21
Demographics	
Median age in years	29 (IQR 25-30, range 24-39)
No. of female patients	15 (71%)
No. of Black African origin	19 (90%)
HIV Background	
Median years on ART	23 (IQR 19-27, range 8-29)
Median no. of previous regimes	7 (IQR 6-10, range 2-22)
Median nadir CD4 count, cells/mm^3	85 (IQR 3-240, range 0-490)
No. with previous AIDS defining diagnoses	12 (57%)
No. with pre-existing resistance mutations	15 (71%)
No. with previous adherence interventions	20 (95%)
Co-morbidities	
No. with mental health diagnosis	7 (25%)
No. taking other oral medications	13 (65%)
No. with history of other injectable medications - Contraceptive injection (Depo-Provera) - Psychiatric depot (olanzapine, aripiprazole)	6 (29%) 4 (19%) 2 (10%)

Previous ART

This cohort was highly treatment experienced with between 3 and 22 previous regimes (mean 8) and all but 1 had experience of four classes. 2 had not had an oral 2nd generation integrase (dolutegravir or bictegravir). 15 (71%) had preexisting drug resistance mutations (DRMs). Of the 10 described, 8 had NNRTI mutations and 4 patients had DRMs affecting rilpivirine (V108I, V179D, Y181C, A98G).

Starting LAI-ART

Patients started LAI-ART for a variety of reasons. 4 had difficulty with oral medications, 3 patient choice, and 7 had extensive resistance or adherence difficulties. 2 were described as having pill fatigue.

Patients started LAI-ART at a median CD4 of 300 (range 0-1274), with 10 patients below 200.

Figure 2. Choice of LAI-ART

	n=21
Cabotegravir + rilpivirine (CAB/RPV)	14
Cabotegravir + lenacapavir (CAB/LEN)	4
Cabotegravir + rilpivirine + lenacapavir (CAB/RPV/LEN)	3

7 patients did not have an oral lead in (OLI), for reasons including ongoing adherence concerns and having a suppressed viral load.

10 patients had oral ART during LAI-ART. 4 were given oral ART throughout LAI-ART use, all of whom had pre-existing DRMs. 2 had NRTI (Descovy) and 2 had NRTI and PI (Symtuza). 4 patients had oral ART during the OLI or later simplified – 1 had PI (darunavir/ritonavir), 1 had Symtuza, and 1 had integrase and PI (dolutegravir plus darunavir/ritonavir). 2 patients had Symtuza added during LAI-ART.

Of the 4 patients who had preexisting rilpivirine DRMs, all had additional ART: 2 had Symtuza (with CAB/RPV), one had CAB/LEN with Symtuza added later, and one had Descovy with CAB/RPV.

Results of LAI-ART

11 (52%) patients were viraemic at initiation (VL>200); of these, 7 achieved viral suppression (mean 10.7 weeks) and 2 experienced virological failure.

Median duration on LAI-ART was 13 months (range 1.25-86). At time of data collection, 17 remained on LAI-ART, and all but 1 were virologically suppressed. Of those who discontinued LAI-ART, 2 were due to virological failure and 2 due to patient choice (including wishing to conceive).

Since starting LAI-ART, 6 patients (29%) gained additional resistance mutations. 2 patients (10%) developed virological failure, and 2 (10%) developed non-significant mutations to NRTI and PI classes, possibly emerging as an unmasking phenomenon (they had Symtuza added and later suppressed. 2 patients (10%) developed resistance after discontinuing LAI-ART whilst on subsequent regimes

Figure 3. Nature of significant resistance developed on LAI-ART

		Mutations developed
NNRTI	2	K103N, Y181C, H221Y, M230L, E138G
Integrase	2	E138K, G140A, S147R, Q148R, E157Q
Capsid	0	

Both patients with virological failure did so with dual class resistance mutations after an initial period of suppression below 200. 1 had monthly CAB/RPV and 1 had 2 monthly CAB/RPV plus Symtuza.

At the time of data collection, 6 of 7 patients on lenacapavir were undetectable. 4/7 had oral ART (3 Symtuza, 1 Darunavir/ritonavir), but 2 discontinued after the OLI. The 7th patient had started 4 months prior to data collection and their viral load had improved from 900,000 to 500.

6 patients had improvement or resolution of HIV-related comorbidities. Injection-site pain (n=8) and nodules (n=6) were the most frequent adverse effects. 5 patients experienced clinically significant weight gain (BMI rise >2, range -2 to +15), although this was both a positive and negative phenomena (3 became newly obese) and complicated by other factors such as return to health and variable periods spent on LAI-ART. 1 patient developed lymphoma as a possible IRIS phenomena.

1 patient was pregnant twice during use of LAI-ART, with 1 intrauterine death and 1 live birth who was HIV negative. All had LAI-ART delivered in a hospital setting. Most patients (13) accessed LAI-ART by a compassionate access or trust-funded route, and 2 were from commissioned pathways

Discussion

Suppression was achieved in almost all patients in this dataset despite high viraemia at baseline in around half, advanced HIV, complex resistance and previously unsuccessful intensive adherence strategies. Both patients who later experienced virological failure did achieve a period of suppression. Owing to the length of diagnosis, patient mobility, and the complexity of medical record systems over time, there were data gaps regarding resistance, ART exposure and response.

Conclusion

In this highly treatment-experienced PaHIV cohort, LAI-ART was feasible, well tolerated and enabled viral suppression in individuals with prior deep-rooted adherence difficulties and resistance. These findings support LAI-ART as an important option for those with PaHIV, including access to lenacapavir alongside cabotegravir/rilpivirine, but caution is needed to prevent limitation of future options.

References

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