Single Center Experience Evaluating and Initiating People with HIV on Long-Acting Cabotegravir/Rilpivirine

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Background

- Long-acting injectable (LAI) cabotegravir and rilpivirine (CAB/RPV) was approved in the United States in January 2021, with the option for every 2-month dosing approved in February 2022
- LAI CAB/RPV has shown equivalent efficacy to oral antiretroviral therapy (ART) with a well tolerated safety profile, however the use of in-clinic administered LAI ART presents unique logistical challenges as compared to using oral ART[1,2]
- At the UC San Diego Owen clinic, an HIV primary care clinic, individuals are referred to our clinical pharmacy team by their providers for clinical assessment for appropriateness of treatment with LAI CAB/RPV, additional clinical work-up, insurance coverage assessment, and education and initiation of LAI CAB/RPV
- We describe our experience evaluating individuals that expressed interest in LAI CAB/RPV

Methods

- Retrospective single center study conducted at an HIV primary care clinic in San Diego, California.
- Our protocol for ART resistance evaluation for CAB/RPV is to consider an archive genotype if no baseline or prior resistance test is available to evaluate for transmitted or acquired drug resistance or polymorphisms that can impact activity of CAB or RPV.

Inclusion Criteria

- All individuals who expressed interest and were referred for evaluation for LAI CAB/RPV from 4/2021 to 6/2022
- Having a definitive decision made on starting vs. not starting LAI CAB/RPV

Primary Outcome

- Comparison of characteristics between those started on CAB/RPV vs those who did not to evaluate factors associated with successful initiation of LAI CAB/RPV

Secondary Outcomes

- Evaluate reasons for not initiating LAI CAB/RPV
- Describe pre-existing or newly identified drug resistance that prevented the use of LAI CAB/PRV

- Electronic medical record was reviewed for all individuals to obtain demographics, ART regimen history, insurance, resistance testing history, BMI, active substance use, hepatitis B status, PPI use, reasons for not starting treatment, or if initiating on CAB/RPV, baseline HIV viral load and CD4 count

Results

Table 1: Comparison of those that did and did not start LAI CAB/RPV

	Total (n=383)	Initiated CAB/RPV (n=201)	Did not start CAB/RPV (n=182)	p-value
Median age (IQR)	44 (35-54)	42 (34-53)	45 (37-56)	0.02
Race (%)				
White	194 (50.7)	96 (47.8)	98 (53.8)	
Black	67 (17.5)	35 (17.4)	32 (17.6)	0.56
Asian	11 (2.9)	5 (2.5)	6 (3.3)	
AI/AN	6 (1.6)	4 (2.0)	2 (1.1)	
Other/mixed race	95 (24.8)	56 (27.9)	39 (21.4)	
Unknown	10 (2.6)	5 (2.5)	5 (2.7)	
Ethnicity (%)				
Hispanic	142 (37.1)	82 (40.8)	60 (33.0)	0.11
Non-Hispanic	235 (61.4)	116 (57.7)	119 (65.4)	
Unknown	6 (1.6)	3 (1.5)	3 (1.6)	
Sex assigned at birth				0.93
Female (%)	49 (12.8)	26 (12.9)	23 (12.6)	
Gender Identity				
Male	327 (85.4)	173 (86.1)	154 (84.6)	0.69
Female	48 (12.5)	25 (12.4)	23 (12.6)	
Trans/Non-binary	8 (2.1)	3 (1.5)	5 (2.7)	
Body mass index (IQR)	26.8 (24.4-30.2)	27.0 (24.4-30.2)	26.7 (24.4-30.5)	0.87
Active substance use (%)	53 (13.8)	25 (12.4)	28 (15.4)	0.40
Baseline ARV regimen (%)				
2nd Gen INSTI+2 NRTI	240 (62.7)	119 (59.2)	121 (66.5)	
1st Gen INSTI+2 NRTI	31 (8.1)	21 (10.4)	10 (5.5)	
NNRTI+2 NRTI	26 (6.8)	16 (8.0)	10 (5.5)	0.0003
PI+2 NRTI	17 (4.4)	3 (1.5)	14 (7.7)	
2 drug regimen	41 (10.7)	31 (15.4)	10 (5.5)	
Multi-class	28 (7.3)	11 (5.5)	17 (9.3)	
Primary Insurance				
Medicaid	163 (42.6)	94 (46.8)	69 (37.9)	
Medicare/Medicaid	46 (12.0)	23 (11.4)	23 (12.6)	0.40
Medicare only	11 (2.9)	4 (2.0)	7 (3.8)	
Ryan White/ADAP	22 (5.7)	12 (6.0)	10 (5.5)	
Commercial	141 (36.8)	68 (33.8)	73 (40.1)	
HBV status				
Negative	275 (71.8)	151 (75.1)	124 (68.1)	
CoreAb+, SAg-, SAb+	90 (23.4)	42 (20.9)	48 (26.4)	0.09
CoreAb+, SAg-, SAb-	14 (3.7)	8 (4.0)	6 (3.3)	
SAg+	4 (1.0)	0 (0.0)	4 (2.2)	
On PPI at baseline	53 (13.8)	24 (11.9)	29 (15.9)	0.26

Table 2: Reasons for not starting LAI CAB/RPV (n=182)

Reason for not starting	Number (%)
Inconsistent clinic attendance/not easily reached	36 (19.8)
Patient decision not to start	34 (18.7)
Previously known NNRTI resistance	28 (15.4)
NNRTI resistance found on archive genotype	22 (12.1)
HIV viral load not suppressed	15 (8.2)
Failed to complete resistance work up	15 (8.2)
Insurance coverage issues	8 (4.4)
Concerns about out of pocket costs	5 (2.7)
Known INSTI resistance	5 (2.7)
INSTI resistance found on archive genotype	3 (1.6)
Active hepatitis B	4 (2.2)
Other	7 (3.8)

- Among the entire cohort a baseline HIV-1 genotype was available for 159 (41.5%) individuals and a prior HIV genotype, phenotype, or archive genotype other than baseline in 92 (24%) of individuals

Results (cont'd)

- An archive genotype was performed in 135 (35.2%) individuals as part of the work-up for LAI CAB/RPV
- Of those that had an archive genotype, 25 (18.5%) had a resistance mutation identified that may impact effectiveness of CAB/RPV

Table 3: summary of resistance mutations found on archive genotype

Resistance mutation	# patients	Resistance
Y181C	4	RPV
E138G	3	RPV
E138A	4	RPV
E138K	3	RPV
G190S	1	RPV
H221Y	2	RPV
K238T	1	RPV
K101E	2	RPV
L100I	1	RPV
Y143H	1	CAB
Q148H	2	CAB
T97A+K103N	1	Concern for additional NNRTI resistance

- Of those that started LAI CAB/RPV 180 (89.5%) had a HIV viral load < 50 copies/mL, and of those with a viral load >50 copies/mL the median viral load was 108 copies/mL (range 52-12800 copies/mL)
- The median CD4 count in those that started LAI CAB/RPV was 744 cells/mm^3 (range 92-1733 cells/mm^3)

Discussion

- There was an association with starting LAI CAB/RPV and the current oral ARV regimen, with those starting LAI CAB/RPV more likely to be on a 2- drug regimen and less likely to be on a protease inhibitor or multi-class regimen, which likely reflects the presence of known or suspected pre-existing ART resistance
- Despite logistical challenges using LAI ART, it is encouraging that few patients did not start treatment due to insurance related issues.
- In those that did not have prior resistance testing, performing an archive genotype identified resistance mutations that precluded the use of LAI CAB/RPV in 18.5%, highlighting the importance of thoroughly ruling out preexisting resistance.

References

1. Rizzardini G, Overton E, Orkin C. et al. Long-acting cabotegravir+rilpivirine for HIV maintenance therapy: week 48 pooled analysis of phase 3 ATLAS and FLAIR trials. *J Acquir Immune Defic Synd.* 2020;85:498-506
2. Overton E, Richmond G, Rizzardini G. et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomized, multicentre, open-label, phase 3b, non-inferiority study. *Lancet.* 2020;396:1994-2005.